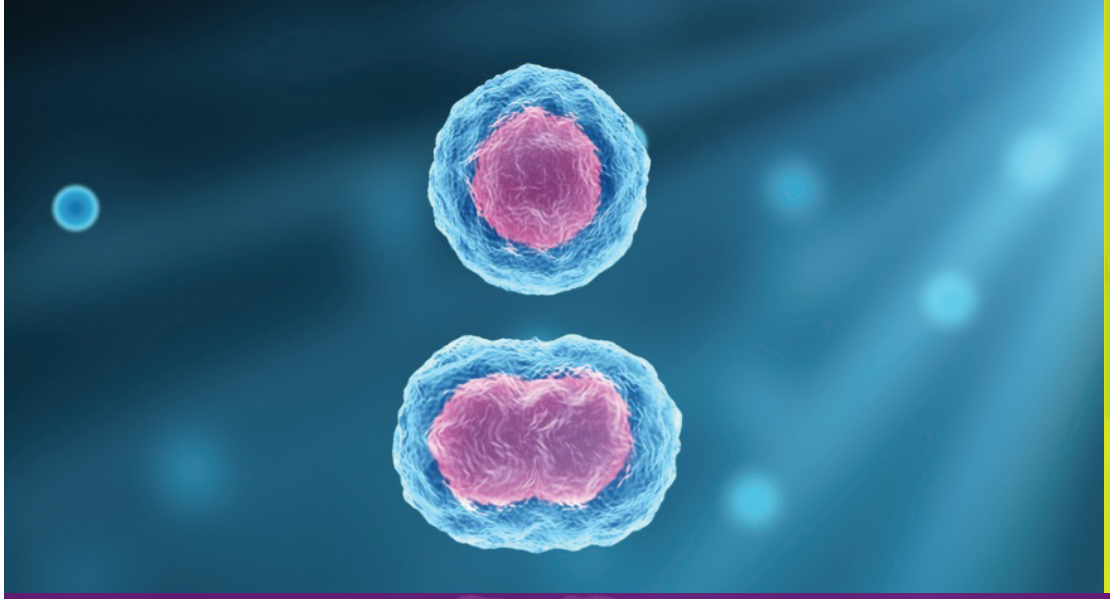
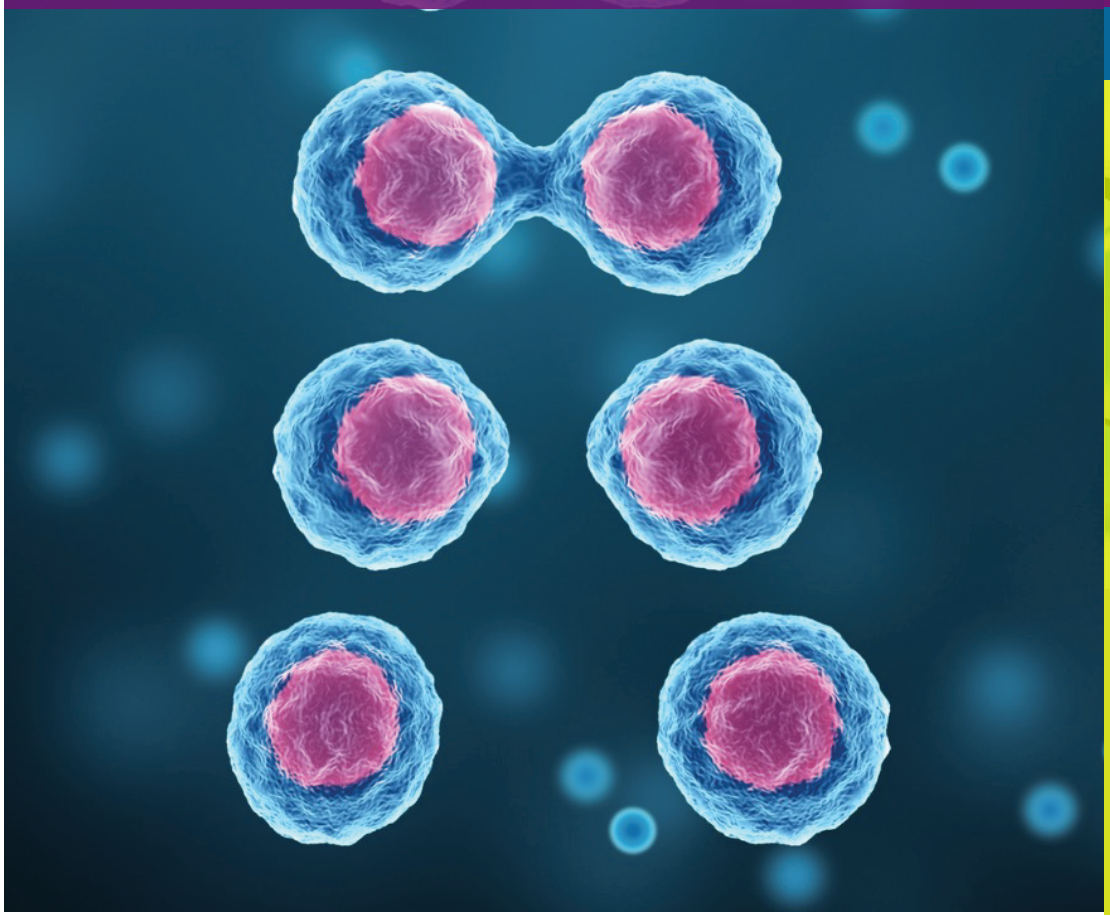


ISSN 2675-374X

DOI:10.46765/2675-374X.2021v2n3

JOURNAL OF BONE MARROW TRANSPLANTATION AND CELLULAR THERAPY

JBMTCT



IN THIS EDITION

Proceedings of XXV Annual Meeting of the Brazilian Society of Bone Marrow Transplantation and Cellular Therapy

6TH EDITION

SBTMO

SOCIEDADE BRASILEIRA DE TERAPIA CELULAR E TRANSPLANTE DE MEDULA ÓSSEA

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JBMTCT
v.2, n. 3
Jul-Sep, 2021

JBMTCT - Journal of Bone Marrow Transplantation and Cellular Therapy

EDITORS-IN-CHIEF
Fernando Barroso Duarte and Nelson Hamerschlak

MANAGING EDITOR
Romélia Pinheiro Gonçalves Lemes

E-MAIL
journalbmtct@sbtmo.org.br

WEBSITE
www.jbmtct.com.br

ADDRESS
Rua Haddock Lobo 72, sala 407
Estácio – Rio de Janeiro
Zip Code: 20260-132
Phone: +55 21 2273-8390

The JBMTCT, Journal of Bone Marrow Transplantation and Cellular, is an official publication of the Brazilian Society of Bone Marrow Transplantation and Cellular Therapy (SBTMO).

Journal of Bone Marrow Transplantation and Cellular Therapy – JBMTCT

Proceedings of XXV Annual Meeting of the Brazilian Society of Bone Marrow Transplantation and Cellular Therapy. Rio de Janeiro, Brazilian Society of Bone Marrow Transplantation, v. 2, n. 3, Jul./Sep., 2021.

317 p.: il. color.

ISSN: 2675-374X

1. Bone Marrow Transplantation. 2. Cellular Therapy. I. Title.

CDD: 610.73072

Dear transplant colleagues

In 2019 we celebrated the 40th anniversary of the first bone marrow transplant (BMT) in our country, with the pioneering spirit of Professor Ricardo Pasquini, Eurípides Ferreira and his team, a fact that was undoubtedly a milestone and the driving force for us to arrive where we are. Today, we are 84 BMT-enabled centers in Brazil and we have seen the great success of these teams, demonstrating a process of maturation of our transplant recipients.

Our company was founded in 1996 by a group of specialists and within this same premise. Today we are prominent in the worldwide transplanting community, having entered into several partnerships with international entities, such as ASCT, LABMT, CIBMTR, FACT, among others.

We have a research group at GEDECO (Grupo de Estudo Doença Enxerto Contra o hospedeiro e complicações tardias) ,coordinated by our dear Dr. Mary Flowers and Dr Afonso Celso Vigorito. This started small as a group of studies on graft disease and because of its quality and empathy, it has now become the gateway to cooperative studies on various topics in our society. SBTMO also maintains a Pediatrics Group, a flow cytometry group, a multidisciplinary group and one of data managers. Every two years, a consensus of indications and complications of transplants is performed, which serves as a guide for the guidance of specialists and public policies.

Faced with this scenario, in a natural way, arose the need to have a journal that could disseminate the work of this scientific community, doctors and multidisciplinary professionals, thus strengthening our interaction with transplantation professionals from various countries.

It is with this spirit of joy and hope that we launched this volume of JBMCT, Journal of Bone Marrow Transplantation and Cellular Therapy, which will certainly be a periodical to publicize the work of all those who believe that science , research and caring for patients, is the best way to improve our walking.

Fernando Barroso Duarte *Nelson Hamerschlak*

PROCEEDINGS OF XXV ANNUAL MEETING OF THE BRAZILIAN SOCIETY OF BONE MARROW TRANSPLANTATION AND CELLULAR THERAPY

Summary

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HSCT Pediatric

Quality and Data Management

Hemotherapy and Cell Therapy

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Allogeneic HSCT

Autologous HSCT

HSCT Pediatric

Infectious Complications

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MULTIDISCIPLINARY

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Social Service

SBTMO MEETING
BEST ABSRACTS

MARY FLOWERS AWARD
BEST ABSTRACT IN CLINICAL ASPECTS OF HSCT

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT FOR MYELOFIBROSIS IN BRAZIL: FACING OUR CHALLENGES

Vaneuza Araujo Moreira Funke[1], Alberto Cardoso Martins Lima[1], Nelson Hamerschlak[2], Vergilio Colturato[3], Mair Pedro de Souza,[3] Afonso Celso Vigorito[4], Gustavo Machado Teixeira[5], Vanderson Geraldo Rocha[6], Livia Mariano[6], Decio Lerner[7], George Maurício Navarro Barros[8], Ricardo Pasquini[9], Alessandra Paz[10], Heliz Regina A. Neves[1]Anderson Simione, Cinthya Correa Silva[2], Vinicius Martins Nascimento[4], Clara Leal Voltarelli[1], Bin Chang Tan[1], Mary E.D. Flowers, MD[11].

1BMT Center, Complexo Hospital de Clínicas, Federal University of Parana, Curitiba, Brazil; 2 Bone Marrow Transplantation, Hospital Israelita Albert Einstein, São Paulo, Brazil; 3 Hospital Amaral Carvalho, Jaú, SP; 4 Hematology and Transfusion Medicine Center, University of Campinas, Campinas, Brazil; 5 Bone Marrow Transplant, Clinical Hospital of Federal University of Minas Gerais, Belo Horizonte, Brazil; 6 BMT Center at University of São Paulo (USP), SP; 7 BMT Center at National Cancer Institute (CEMO), Rio de Janeiro, Brasil; 8 BMT Center Bone Marrow Transplant at Hospital de Amor, Barretos, SP; 9Instituto Pasquini, Hospital Nossa Senhora das Graças , Curitiba, PR; 10 BMT Center at Hospital de Clínicas of Porto Alegre,11 Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA

Background: Allogeneic hematopoietic stem cell transplantation (allo-SCT) is a well-established treatment modality for myelofibrosis (MF) and the only potentially curative treatment. However, adequate engraftment, relapse and transplant related mortality are big challenges in transplantation for this disease.

Objectives: Primary objective is to evaluate overall and disease-free survival of allogeneic HSCT for myelofibrosis in Brazil. Secondary objective is identifying risk factors for survival and relapse.

Patients and methods: We analyzed retrospectively from charts and database data from 141 patients with the diagnosis of MF who received allo-SCT at six centers in Brazil from 1997 to 2020. Patients and Transplant characteristics are disposed on Table 1. Statistical analysis was performed using EZR software. Bivariate analysis and estimation of OS and DFS were performed using Log Rank and Kaplan Meier method. A landmark analysis of survival was performed for acute (100 days) and chronic (180 days) GVHD. Cox Survival Model was used for multivariate analysis of survival and Multivariable Fine-Gray competing risks regression model was used or relapse/rejection at 2 years and non-relapse mortality at one year. Characteristics of patients are showed in table 1.

Results: Overall Survival (OS) for the whole cohort was 61% at one year, 56% at 2 years and 46% at 5 years. The transplant related mortality at 100 days and at one year was 14 and 26%, respectively. One- and two-year cumulative incidence of relapse or rejection was 10 % and 15% respectively. Cumulative incidence of non-relapse mortality (competitive risk) at one and two years was 33% and 37% respectively. At multivariate analysis by Cox Model, CD 34 > 5 x 106 HR 0.4405 (0.2396- 0.8101; p= 0.008) was associated to better survival, while KPS < 80% HR 2.3010 (1.01-5.19; p= 0.044) and DIPSS intermediate 2 or high-risk HR 5.7490 (2.33-14.18; p= 0.0001) were significantly associated with inferior survival.

At Multivariable Fine-Gray competing risks regression model for relapse/rejection, previous therapy with ruxolitinib was identified as a risk factor HR 3.245(1.427- 7.379; p= 0.005). At Multivariable Fine-Gray competing risks regression model for non-relapse mortality, KPS < 80% HR 3.2380(1.3030-8.046; p= 0.011) and DIPSS Intermediate 2-High risk were identified as independent risk factors -HR 8.8760 (1.9280 -40.870; p= 0.00510)

At landmark analysis development of acute GVHD stage 3-4 was a significant risk factor for survival (0.00194).

Conclusions: 1) DIPSS score was validated in this Brazilian cohort as a tool to estimate survival and non-relapse mortality after transplant, in agreement with international experience; 2) CD34 dose < 5 x 106 and Karnofsky score < 80% were significant risk factors for survival; 3) Karnofsky score < 80% and Intermediate-2 or High risk DIPSS were also significant risk factors for non-relapse mortality.

TABLE 1: Stem Cell Transplantation. Primary myelofibrosis. Risk factors.

Patients Charactheristics	*n=141 (%)*
Age, years	49 (4-74)
Sex	
Male	55 (39)
Female	86 (61)
Previous therapy	
Hidroxyurea/ support	53 (38)
IFN-a/ thalidomide	38 (27)
Jak 2 inhibitor	29 (20)
Radiation/splenectomy	13(9)
DIPSS	
High risk	29 (21)
Intermediate II	64 (45)
Intermediate I	23 (16)
Low Risk	21 (15)
Transfusions	
≥10	38 (27)
<10	54 (38)
KPS	
≥80	101 (71)
<80	11 (8)
Donor type	
Related	105 (75)
Non-related	29 (21)
Haplo	07 (5)
Source of the graft	
BM	57 (40)
PB	84 (60)
CD34 cells (× 10^6/kg)	4.39 (0.47 - 12.10)
Conditioning	
MAC	66 (47)
RIC	75 (53)

JÚLIO VOLTARELLI AWARD
BEST ABSTRACT IN CELL THERAPY AND BASIC RESEARCH

VIABILITY OF CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY IN LATIN AMERICA

Camila Dermínio Donadel[1], Lucas Oliveira[1], Patrícia Oliveira da Cunha Terra[1], Diego Villa Clé[1], Leonardo Carvalho Palma[1], Thalita Cristina de Mello Costa[1], Juliana Bernardes Elias Dias[1], Fabiano Pieroni[1], Ana Beatriz Pereira Lima Stracieri[1], Caio Raony Farina Silveira[2], Marcelo Lourencini Puga[3]; Amanda Mizukami Martins[2]; Sâmia Rigotto Caruso[2]; Lucas Eduardo Botelho de Souza[2]; Leticia Maria Defendi Barboza[3]; Maria Fernanda Lima Giuberti[3]; Gabriel de Carvalho Pereira[1]; Taisa Risque Fernandes[2]; Rosane Maria Falasco Bolzoni[2]; Mário Soares de Abreu Neto; Ana Carolina de Jesus Vieira[1]; Benedito de Pina Almeida Prado Júnior[2]; Fernando Chahud[4]; Patricia Vianna Bonini Palma[2]; Anibal Basile Filho[3], Eduardo Magalhães Rego[1/2]; Rodrigo T. Calado[1/2], Maristela Delgado Orellana[2], Gil Cunha De Santis[1/2], Dimas T. Covas[1/2], Renato Luiz Guerino-Cunha[1/2]

1 Department of Medical Images, Hematology and Clinical Oncology, Ribeirão Preto Medical School of University of São Paulo, Ribeirão Preto, SP, Brazil. 2 Center for Cell-Based Therapy of Ribeirão Preto, Ribeirão Preto Medical School of University of São Paulo, Ribeirão Preto, SP, Brazil. 3 Department of Surgery and Anatomy, Ribeirão Preto Medical School of University of São Paulo, Ribeirão Preto, SP, Brazil. 4 Department of Pathology, Ribeirão Preto Medical School of University of São Paulo, Ribeirão Preto, SP, Brazil.

Introduction: Treatment of relapsed/refractory (R/R) diffuse large B cell lymphoma (DLBCL) may be a challenge in low and middle-income countries, where strategies to reduce economic burden of oncological care are needed. In this scenario, immunotherapy with CD19-targeted chimeric antigen receptor (CAR) T-cell is a promising therapy. We report the development and clinical application of a Brazilian platform to manufacture genetically modified T-cells to treat patients with R/R leukemia and lymphomas, which can expand the access for this new therapy and offer new perspectives for these patients.

Methods: We developed and validated in vitro and in vivo anti-CD19 CAR T cell expression, expansion and cytotoxicity. In-house lentiviral good-manufacturing practice protocols were established for clinical purposes. Procedures to deliver anti-CD19 CAR T cells were established in order to guarantee the effectiveness and safety. Once these steps were implemented, we were able to treat three patients with anti-CD19 CAR-T cells referred to our center for compassionate use. The treatment was authorized by the hospital medical ethics committee. Patients were scheduled for lymphopheresis and, prior to infusion, were given lymphodepletion with cyclophosphamide and fludarabine. They were monitored for the occurrence of cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS), which were graduated according to the criteria of the American Society for Transplantation and Cellular Therapy.

Results: Patient characteristics and outcome after anti-CD19 CAR T cell therapy are provided in Table 1. Figure 1 shows in vivo CAR T-cell expansion and kinetics.

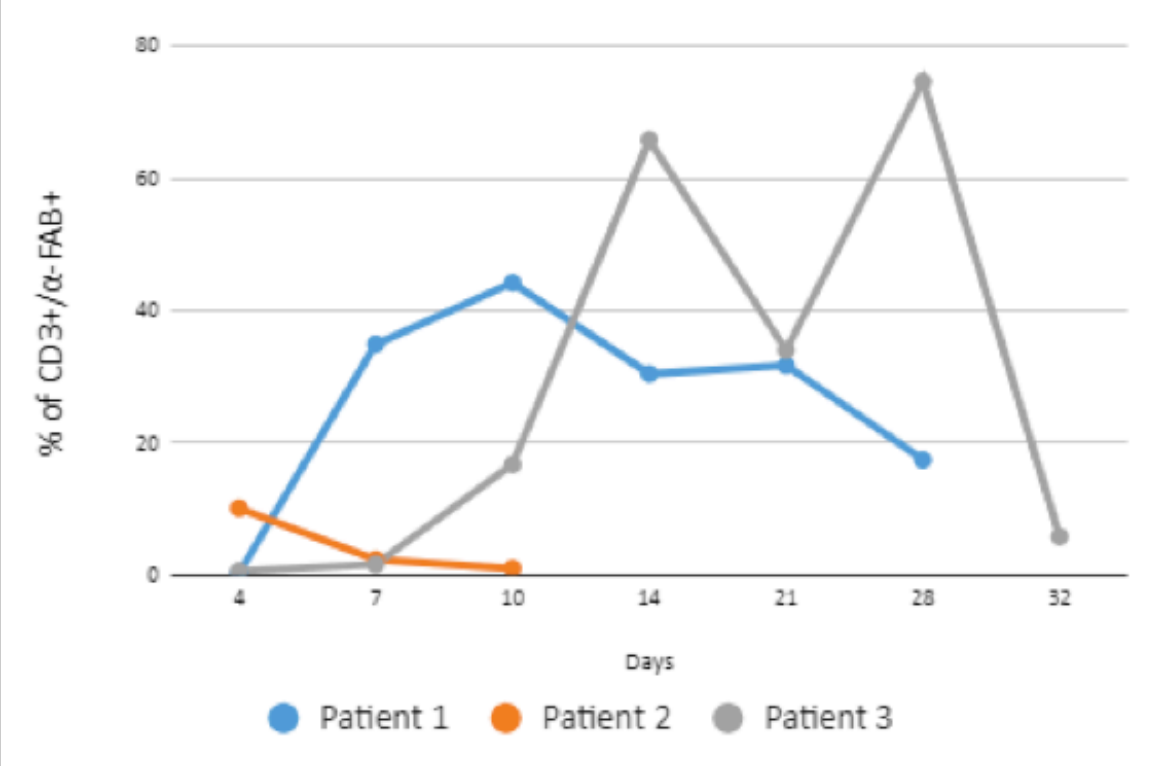
Discussion: Two of the reported patients presented improvement of their disease and the other one died before the expected response could have been evaluated. None of the patients died from complications related to manufacturing or infusion procedures, highlighting the safety profile of the platform. Although these are preliminary results, the CAR-T cell expansion, presence of systemic inflammatory response and lack of early disease progression suggest the treatment effectiveness.

Conclusion: These results demonstrate that therapy with CAR-T cells manufactured locally is feasible. Besides, implementation of advanced cellular therapy can also contribute to enhancing the quality of other cellular therapies.

TABLE 1. Patient characteristics and outcomes

CHARACTERISTICS	PATIENT 1	PATIENT 2	PATIENT 3
Age, years	64	40	36
Diagnosis	DLBCL	High grade B-cell lymphoma	DLBCL
CD19 expression	Weak	Yes	No
Nº of prior therapies	4	3	5
CAR T cell dose infused/kg	$2.1x10^6$	$7.4x10^6$	$1.67x10^6$
CRS	3	4	1
ICANS	1	0	0
Tocilizumab / Steroids	Yes	Yes	No
Response on D+30	Complete	N/A	Partial
Survival status	Dead	Dead	Alive
Cause of death	Domestic accident	Sepsis	N/A

FIGURE 1. In vivo CAR T-cell expansion kinetics.



FANI JOB AWARD
BEST MULTIDISCIPLINARY ABSTRACT

ORAL HEALTH CONDITION AS A RISK FACTOR FOR EARLY COMPLICATIONS IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

Fernanda Bortolotto[1]; Vanessa Tonetto Marques Galves[1]; Thiago De Carvalho Reis[1]; Tatiane Cristina Ferrari[1]; Lara Maria Alencar Ramos Innocentini[1]; Camila Campos Mesquita[1]; Ana Carolina De Jesus Vieira[1]; Thalita Costa[1]; Renato Luiz Guerrino Cunha[1]; Leandro Dorigan De Macedo[1].

1 Ribeirão Preto Clinical Hospital, University Of Medicine Of Ribeirão Preto, University Of São Paulo, Ribeirão Preto.

Introduction: Allogeneic Hematopoietic Stem Cell Transplantation (hsct) is a potentially curative treatment for hematological and autoimmune diseases. The most common oral and systemic complications during the early phase of hsct are mucositis, infection, fever and bacteremia.

Objective: The aim of this study was to evaluate pre-HSCT oral health condition as a risk factor for oral and systemic complications until neutrophilic engraftment and for the development of acute graft versus host disease (aGVHD) and death before d+100 in patients undergoing their first allogeneic hsct.

Methods: This prospective observational cross-sectional study included patients older than 12 years old. The oral health variables: oral hygiene; periodontal bone loss; oral infectious focus; and the index of decayed, missing and filled teeth (DMFT) pre-HSCT were treated as exposure. age, gender, type of disease, type of transplant, type of conditioning and use of total body irradiation (TBI) were treated as confounding variables. The outcomes were: incidence, degree, and duration of oral mucositis (OM), oral infection, febrile neutropenia (FN), and positive blood cultures in the pre-engraftment phase.

Results: in total, 81 patients were included (44 male/37 female), with a median age of 26 years old; 48.1% with benign disease; 82.7% undergoing allogeneic-HSCT and 17.3% haploidentical; 60.5% of transplants involved a reduced intensity or non-myeloablative conditioning regimen, 39.5% used myeloablative conditioning, and 24.7% of patients were submitted to tbi. in the oral health assessment, 44.4% of the patients had poor oral hygiene, 14.8% had periodontal bone loss and 30.9% had at least one infectious focus in the oral cavity. The incidence of om was 58% and 28.4% of patients developed oral infection during the pre-engraftment period. Overall, 71.6% of patients had FN; 34.6% had positive blood cultures, 22.2% developed agvhd and 14.8% had died at d+100. Oral condition was not a risk factor for OM; the presence of an infectious focus in the oral cavity before hsct increased the risk of oral infection 6.86-fold (ci: 2.30–20.47, p = 0.00). Poor oral hygiene increased the risk of FNtwo-fold (ci: 1.45–2.80, p = 0.00). Periodontal bone loss showed a strong risk trend (rr: 5.44; ci: 0.99–29.8; p = 0.05) for the development of agvhd. The simple risk model showed poor oral hygiene (RR: 13.13), periodontal bone loss (RR: 2.03) and higher dmft (RR: 1.05) as risk factors for oral infection. In addition, the presence of an infectious focus in the oral cavity (RR: 1.37) was a risk factor for FN. Oral health condition wasn't a risk factor for positive blood cultures and death.

Conclusion: the treatment of infectious and the optimization of oral hygiene have a potential role in reducing infection in the oral cavity and the occurrence of fn during the period between conditioning and neutrophilic graft. The relationship between periodontal disease activity and aGVHD should be investigated.

RICARDO PASQUINI AWARD – YOUNG SCIENTIST AWARD
BEST AUTHOR ABSTRACT

IMMUNOPHENOTYPIC MARKERS ASSOCIATED WITH MINIMAL RESIDUAL DISEASE STATUS AND OUTCOME IN PATIENTS WITH MULTIPLE MYELOMA UNDERWENT AUTOLOGOUS STEM CELL TRANSPLANTATION

Gabriela Missassi[1], Anderson João Simioni[2], Camila Marques Bortolucci[3], Joana Esprícigo Conte[3], Mair Pedro de Souza[2], Vergilio Antonio Rensi Colturato[2], Maura Rosane Valério Ikoma-Colturato[3,4]

1.Programa de Residência Multiprofissional, Hospital Amaral Carvalho, Jaú, São Paulo, Brasil. 2. Serviço de Transplante de Medula Óssea, Hospital Amaral Carvalho, Jaú, São Paulo, Brasil. 3.Laboratório de Citometria de Fluxo, Hospital Amaral Carvalho, Jaú, São Paulo, Brasil. 4.Sabin Medicina Diagnóstica, Brasilia, DF

Introduction: The expression of antigens on the plasma cell membrane in patients with multiple myeloma (MM) varies according to the stage of the disease. Due to the biological diversity of MM, more effective and individualized therapies are needed. Minimal residual disease (MRD) is a very important prognostic factor in MM patients. Recognition of immunophenotypic markers associated with MRD status can provide relevant information for disease monitoring and management.

Aim: to evaluate the impact of the immunophenotypic markers in association with MRD status before autologous stem cell transplantation (ASCT) on the survival of MM patients.

Material and Methods: this is a retrospective study including data from 154 MM patients, aged 29 to 73 years, underwent TCTH between June 2013 and September 2018. Mean follow-up was 14 months. During the cohort, pre-ASCT MRD was assessed by conventional flow cytometry (sensitivity 10-4) and by next-generation flow cytometry (10-5). The expression of each immunophenotypic marker CD27, CD28, CD45, CD56 and CD117 was related to survival. The impact of these markers on survival was assessed alone and in association with MRD status. Pearson's correlation was used to assess whether the number of prognostic markers had significance on overall survival (OS) and progression-free survival (PFS). The Kaplan-Meier method was used for survival analyses, with significance at $p < 0.05$.

Results: expressions of CD27 and CD45 on plasma cells from MM patients, alone and in association with undetectable MRD (MRD-), were associated with higher OS ($p = 0.00$) and PFS ($p = 0.00$) for both markers, compared to cases with absence of these markers (fig 1 and 2). On the other hand, expressions of CD28 and CD56 were associated with lower OS ($p = 0.023$ and $p = 0.009$, respectively) even in patients with MRD- (fig 1 and 2). CD117 expression was associated with higher OS ($p = 0.04$) only in patients with positive MRD (MRD+). Based on these results, a scoring system (ranging from 0 to 5) was developed, considering as markers of good prognosis (GPM) the expressions of CD27, CD45 and CD117, and the absence of CD28 and CD56. The expressions of CD28 and CD56 and the absence of CD27, CD45 and CD117 were considered as poor prognosis markers (PPM). The results showed that patients with lower levels of MRD had higher numbers of GPM ($p = 0.04$), and patients with increasing levels of MRD had progressively higher numbers of MPP ($p = 0.04$) (fig 3). However, the persistence of MRD+ before ASCT remained the most relevant poor prognostic marker (fig 4).

Conclusion: the recognition of immunophenotypic biomarkers in association with MRD results allowed the identification of subgroups of MM patients with different risks of disease progression. This additional information can be useful in establishing more appropriate intervals for assessments during the follow-up of MM patients and for clinical decisions to prevent relapse of the disease.

Keywords: Multiple Myeloma. Minimal residual disease (MRD). Prognostic immunophenotypic markers. Autologous hematopoietic stem cell transplantation.

FIGURE 1: Impact of immunophenotype markers on overall survival and progression free survival in MM patient before ASCT

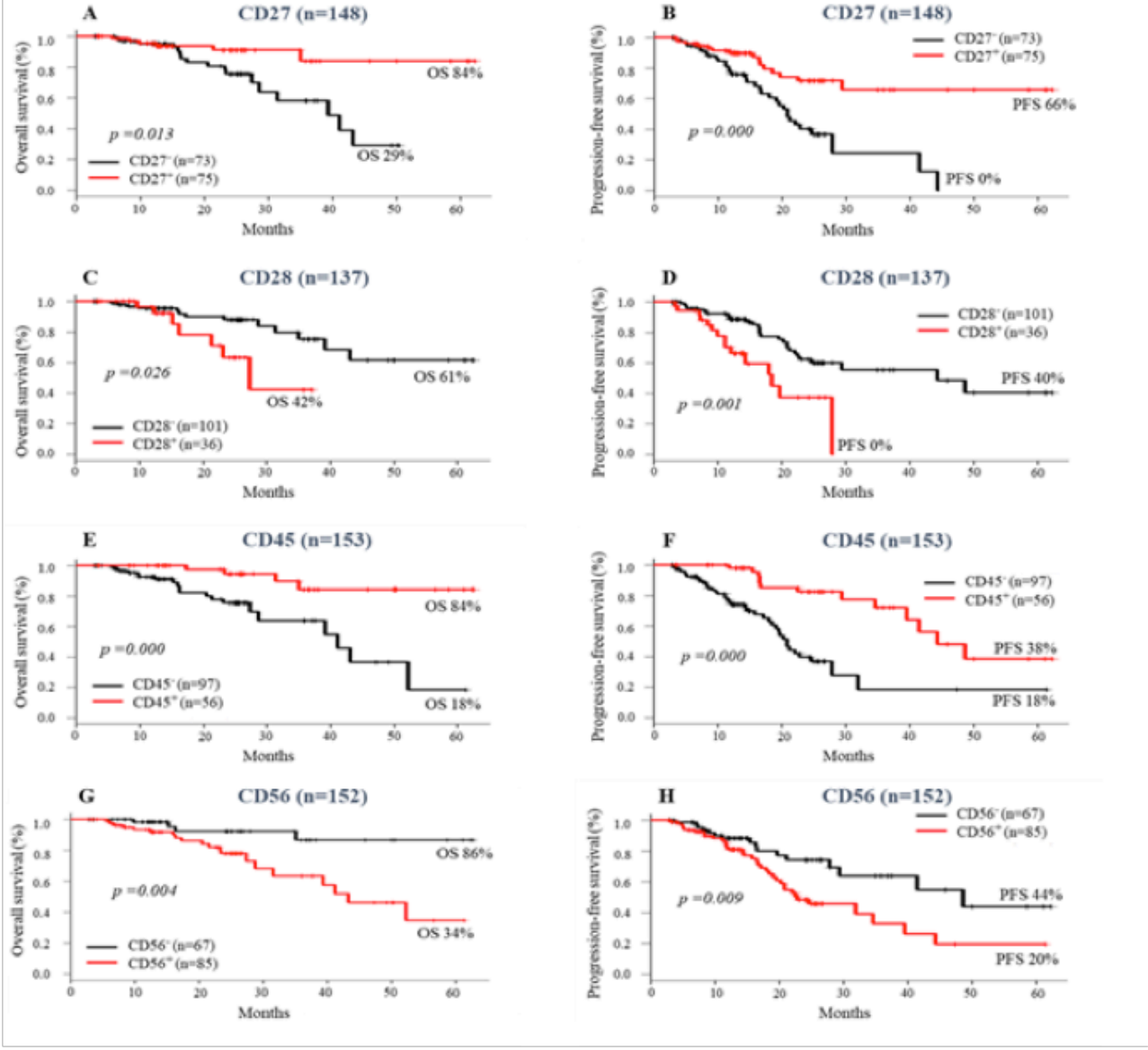


FIGURE 2: impact of the presence or absence of immunophenotypic makers associated with MRD <0.01% pre- ASCT on overall survival and progression-free survival in MM patients.

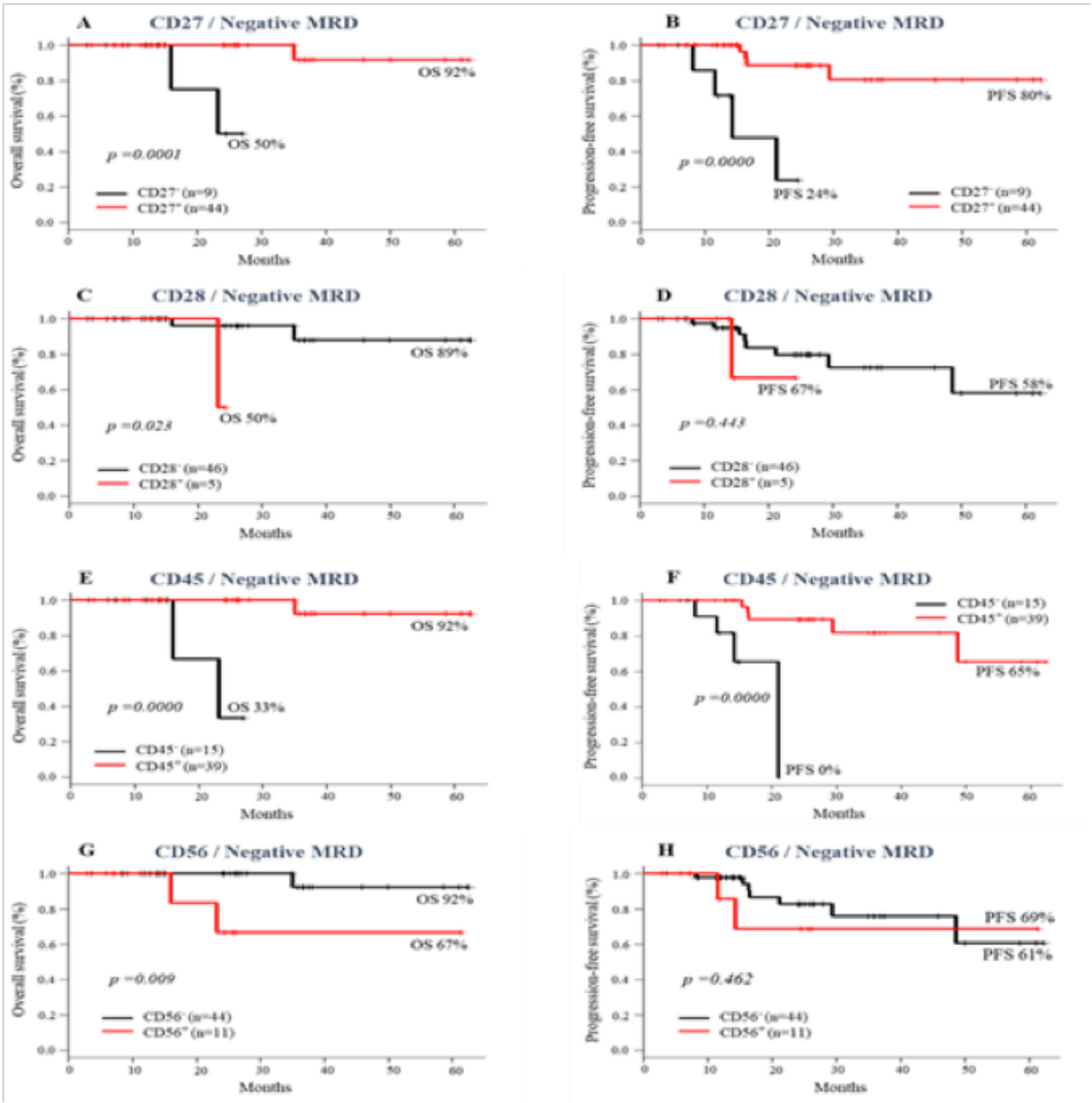


FIGURE 3: Inverse correlation between scores o f immunophenotypic makers and pre-ASCT MRD levels in Multiple Myeloma patients. (A) Good Prognostic Makers (GPM) and (B) Poor Prognostic Makers (PPM).

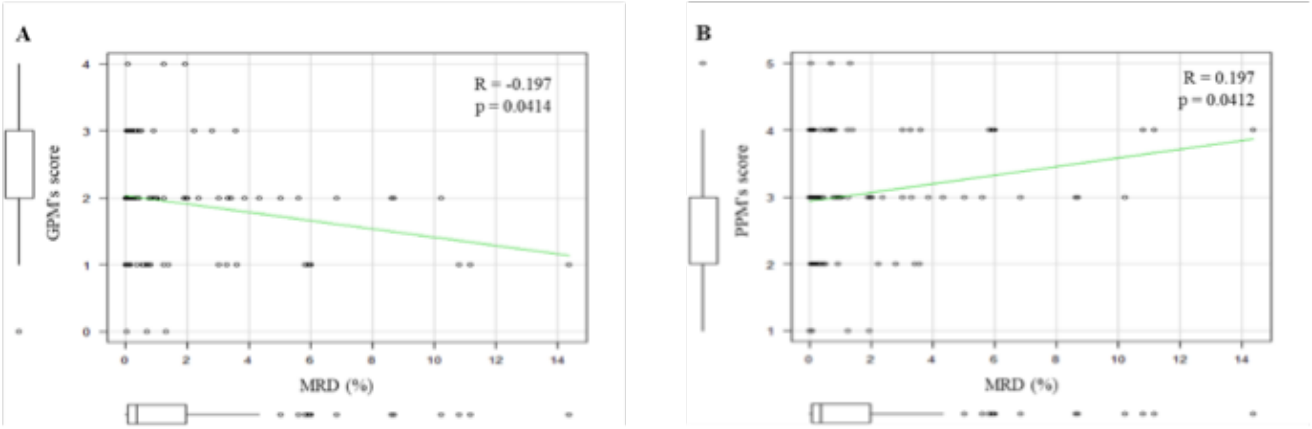
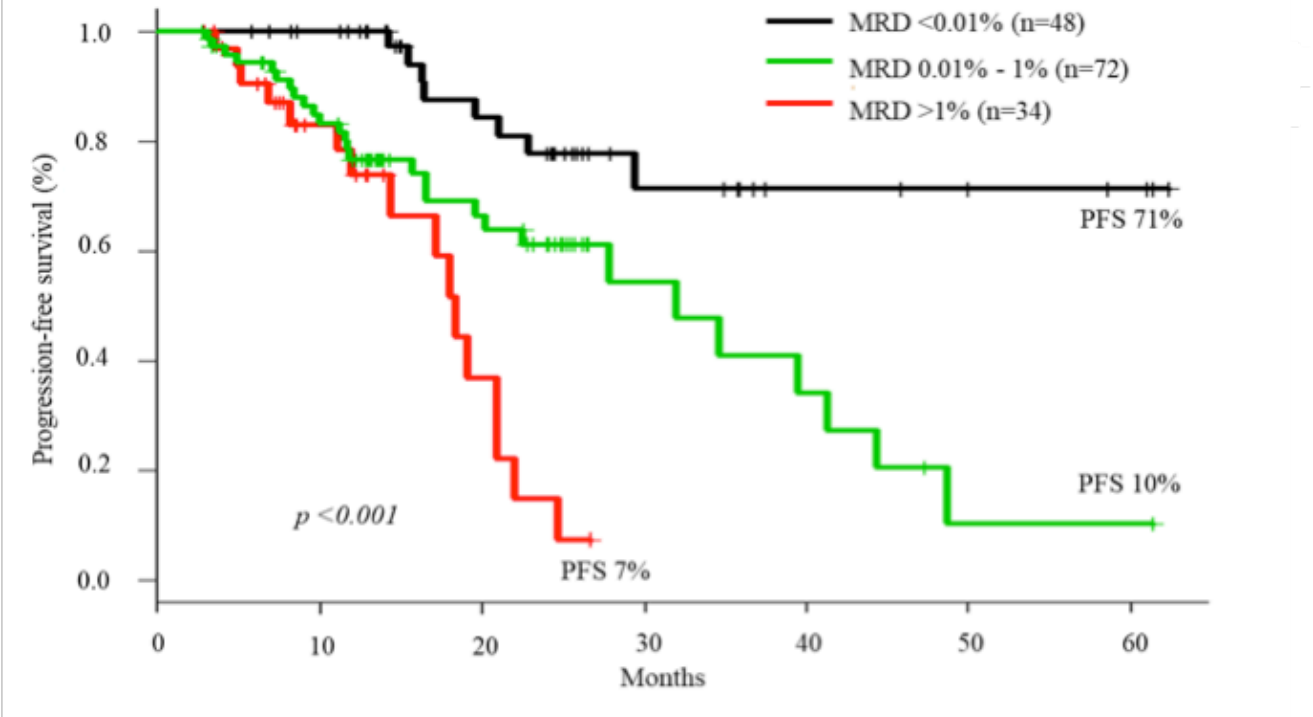


FIGURE 4: Progression- free survival of Multiple Myeloma patients according to pre ASCT MRD level.



CARMEM BONFIM AWARD
BEST ABSTRACT IN THE PEDIATRICS AREA

EXCELLENT OUTCOMES AFTER HEMATOPOIETIC CELL TRANSPLANTATION FOR PATIENTS WITH WISKOTT-ALDRICH SYNDROME

Barbara Fernanda Magalhães De Souza Conti[1], Samantha Nichele[1,3], Adriana Koliski[1]), Gisele Loth[1,2], Joanna Trennepohl[1,3], Lara Gouveia[3], Adriana Mello Rodrigues[1,2] , Carmen Laura Sejas Soliz[1], Lisandro Ribeiro[1], Rafaella Ribas Muratori[1], Rebeca Amélia Toassa Gomes[1,2], Cilmara Cristina Kuwahara Dumke[2], Fernanda Moreira de Lara Benini[2], Pollianny Roberta Dorini Pelegrina[2], Carolina Martins de Almeida Peixoto[2], Juliana Luiza de Mello Bach[2], Alberto Cardoso Martins Lima [4](LIMA, ACM), Ricardo Pasquini [1], Carmem Bonfim[1,2, 3]

1 Hospital de Clínicas de Curitiba- Universidade Federal do Paraná - 2 Hospital Pequeno Príncipe, Curitiba - 3 Hospital Nossa Senhora das Graças, Curitiba - 4 Immunogenetics Laboratory, Complexo Hospitalar de Curitiba, Federal University

Introduction: Wiskott–Aldrich syndrome (WAS) is a rare X-linked disease, characterized by microthrombocytopenia, immunodeficiency and eczema. Hematopoietic cell transplantation (HCT) is the only curative treatment.

Objective: Describe the outcomes of WAS patients (pts) who underwent HCT at 3 Brazilian centers between April 1992 and March 2021.

Material and methods: Retrospective, longitudinal, non-randomized, observational study of 92 transplants in 83 pts with WAS. Database and medical records were analyzed. Statistics were performed using the EZR program.

Results: The median age was 2 years (range 0,6 - 14) and 47% had a WAS clinical score of 4 or 5. Donors were unrelated (URD; n=53), matched related (MRD; 13) or haploidentical (HAPLO; 17). Bone marrow (BM) was the stem cell source in 59% and cord blood (CB) in 41% (HLA 6/6: 8pts; 5/6: 16pts; 4/6: 10pts). All but one patient received a myeloablative regimen (MAC) with busulfan, fludarabine with or without ATG and the majority received cyclosporine and metotrexate as GVHD prophylaxis. The median time for neutrophil and platelet engraftment was 22 and 33 days, respectively. The 1-year CI of rejection was 10%. Nine pts received a 2nd HCT for primary or secondary graft failure and 8 are alive and fully engrafted. At D-100, the CI of grade II-IV acute GVHD was 23 % and chronic GVHD was 6,2 % at 2-years. Viral reactivation occurred in 65 pts (78 %) and CMV reactivation was the most frequent complication. Hemorrhagic cystitis occurred in 7 patients. Haploidentical transplantation with post-transplantation cyclophosphamide (HAPLO-PTCY) was performed upfront in 17 pts, the majority (n=14) received a MAC regimen and 15 are alive and well, one after a 2nd HAPLO-PTCY transplant. The HAPLO-PTCY platform (with a reduced intensity regimen) was also used to rescue another 5 pts after primary or secondary GF and all are alive and engrafted. Eleven pts died between 20 days to 5 years after HCT (median 64 days) and most deaths were related to viral, bacterial or fungal infections. At a median follow-up of 8 years, 72 pts are alive with a 5 and 10-year OS of 88 % and 85 %. In univariate analyses, the only factor associated with a better survival was the use of BM grafts compared to CB (93% vs 79%, p= 0,0341). Donor chimerism was analyzed in all surviving pts and it was full donor in 57 and mixed in 15. Mixed donor chimerism was associated with thrombocytopenia post-HCT (11 pts with thrombocytopenia, median 64, range 16 to 253.000).

Conclusion: Overall, this study shows excellent outcomes after HCT for WAS independent of age or type of donor. We also report the largest data using the HAPLO-PTCY platform showing an excellent survival for pts without matched donors. Early diagnosis and reference to specialized centers is essential before establishment of comorbidities such severe infections, bleeding and autoimmunity that may impose additional risk for transplant.

Keywords: Wiskott-Aldrich syndrome. Hematopoietic cell transplantation. Microthrombocytopenia.

NELSON HAMERSCHLAK AND MARCELO PASQUINI AWARD

BEST AREA IN THE DATA MANAGEMENT AREA (NEW!)

EVALUATION OF THE APPLICATION OF NEW DATA MANAGEMENT ROUTINES AND THE IMPACT ON RESULTS IN THE CONTINUOUS PROCESS IMPROVEMENT (CPI) PROGRAM OF CIBMTR

Anderson João Simione[1], Bruna Fernanda Sona Mathias[1], Ana Claudia Ferrari dos Santo[s1], Iago Colturato[1], Jaine Cristina de Oliveira Silva[1], Tais Pinheiro[1], João Gabriel Silva Resende Lima[1], Fernanda Rodrigues Barbieri[1], Juliana Silva Santos[1], Erika Rodrigues Pontes Delattre[1], Anna Beatriz Coelho de Souza[1], Vergilio Antonio Rensi Colturato[1], Mair Pedro de Souza[1]

1 Hospital Amaral Carvalho – Jaú, SP, Brasil

Introduction: The Center for International Blood and Marrow Transplant Research (CIBMTR) aim to improve survival and quality of life for patients receiving hematopoietic stem cell transplant (HSCT) and other cellular therapies, using your large database. Each participating transplant center (TC) in the CIBMTR sends pre- and post-transplant information about procedures performed at their institution. Data management in HSCT involves balancing the requirements established by CIBMTR with the internal activities of the service. The center's productivity is evaluated by the CIBMTR by the continuous process improvement (CPI) program, which monitors the center's capacity to handle the volume of forms sent and the deadlines requested by the CIBMTR. The deadlines requested are defined by the initial date of completion of the form (Earlist) and the final date of completion (Due), the forms completed before the Due date are considered to be completed on time, CPI requirements are assessed 3 times per year, TC that complete 90% of the forms within the CPI deadline are considered "Good Standing".

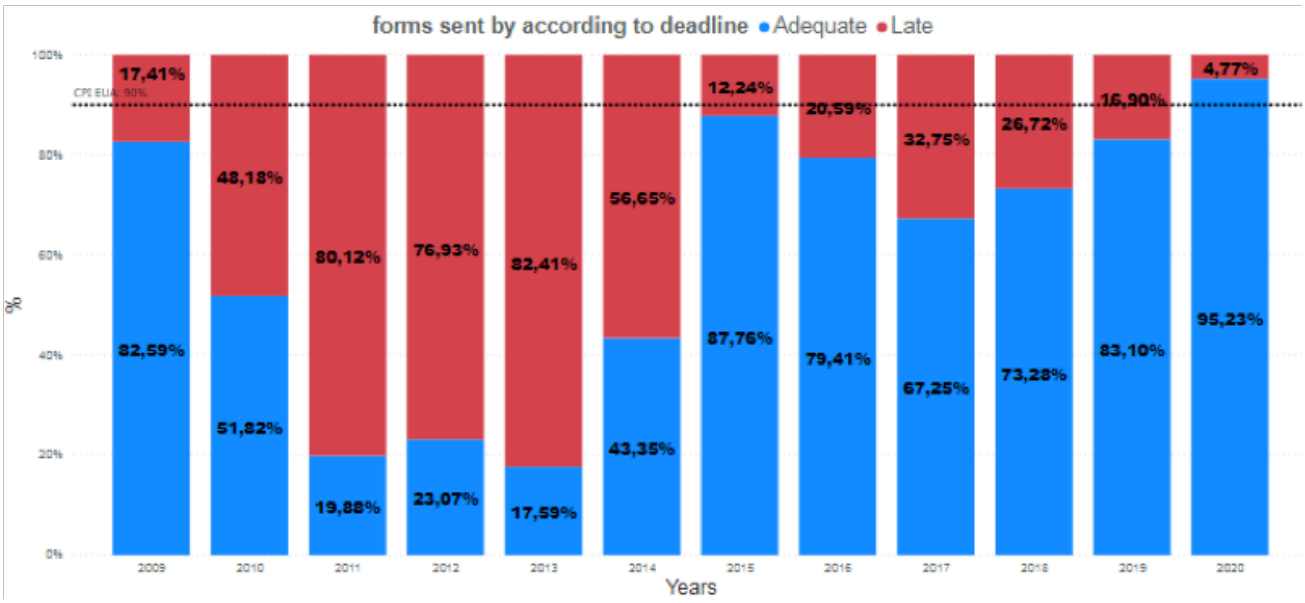
Objective: Evaluate changes in the routine of the hospital's data management service and the impact of this new routine on meeting deadlines for sending post-transplant follow-up forms and the CPI results.

Material and Methods: Data from the CPI reports, sent weekly from CIBMTR to the TC was used to analyze center performance during the year 2020. Between January/2009 and May/2019, the activity control of the forms that were sent to the CIBMTR was done by an excel spreadsheet with functions to control the request deadlines, where were extracted the forms with due date for the following month and through this control the data was included on the CIBMTR website. As of June 2019, the form control was changed, using the center forms due in the FormsNet3 as a basis to extract the list of forms to be filled out, using the Earlist date, at the beginning of the current month we extracted from the site all forms that can already be started, aiming optimize the time to complete the forms before the Due date.

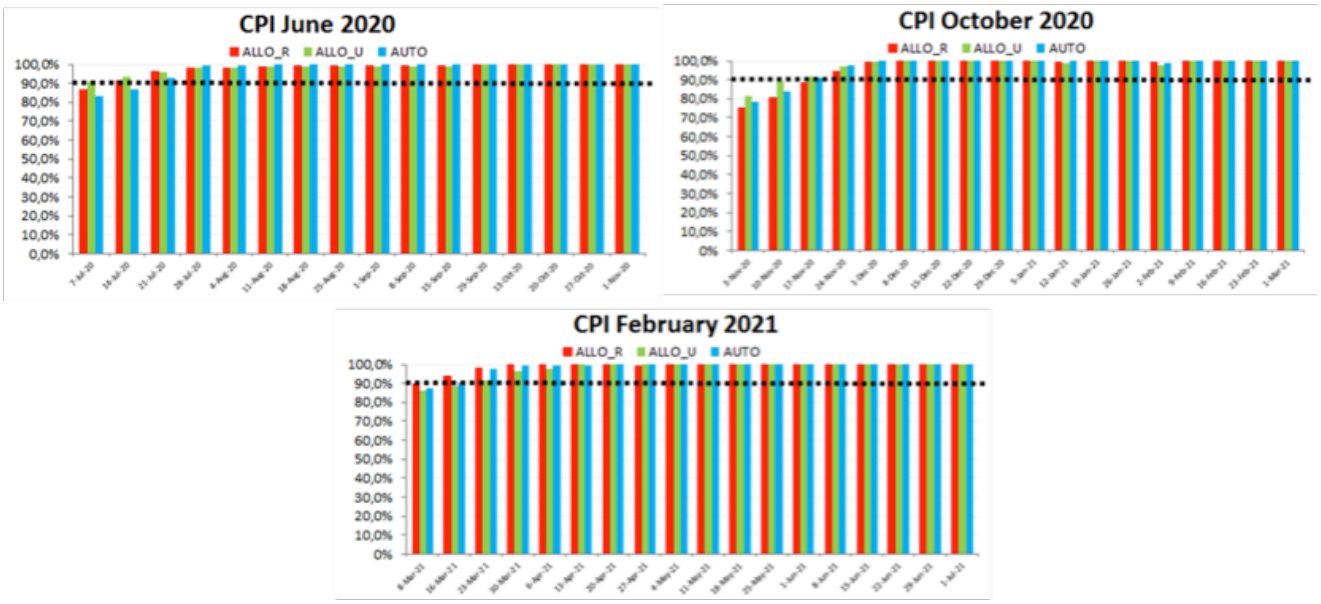
Results: Between 2009 and 2020, 2,498 transplants were performed, all registered in the CIBMTR, during this period 16,861 post-transplant follow-up forms were sent. When we evaluated the forms sent within the deadline requested by the CIBMTR, between 2009 and 2019, we sent the total 13,381 forms, being that 8,725 (65%) were sent before Due. From the change in the routine, in 2020, 3,480 forms were sent, of these 3,314 (95%) were within the appropriate deadline requested by the CIBMTR (Graph 1). With this work routine, it was possible to reach the necessary CPI levels for the US centers with more than 90% of the forms sent in the quarter prior to the requested period (Graph 2).

Conclusion: The new routine adopted proved to be efficient, allowing the TC to reach the CPI requirement level, in the standards used for the US centers, using only tools made available by the CIBMTR.

GRAPH 1. Forms sent annually by deadline for filling in CIBMTR



GRAPH 2. CPI reports for the June, October e February deadlines



ALIRIO PFIFFER AWARD

BEST WORK IN THE MEDULAR FAILURE AREA

NONPERMISSIVE HLA-DPB1 MISMATCHES ARE ASSOCIATED WITH POOR GVHD-FREE/REJECTION-FREE SURVIVAL AFTER PEDIATRIC UNRELATED DONOR TRANSPLANTATION FOR NONMALIGNANT DISORDERS

Alberto Cardoso Martins Lima[1], Margareth Kleina Feitosa[1], Geovana Borsato do Amaral[1], Luciane Rocha Ernlund Pangracio[1], Gisele Loth[2], Samantha Nichele[2], Samir Kanaan Nabhan[2], Ricardo Pasquini[2], Noemi Farah Pereira[1], Carmem Bonfim[2]

1Immunogenetics Laboratory, Complexo Hospital de Clínicas, Federal University of Parana, Curitiba, Brazil
2 Bone Marrow Transplantation Unit

Introduction: The composite endpoint GVHD-Free/Rejection-free survival (GRFS), defined as being alive without graft failure, grades II-IV acute GVHD, and any grade of chronic GVHD, has been proposed as an accurate parameter for assessing quality of life after unrelated donor hematopoietic cell transplantation (URD-HCT). Indeed, this endpoint is particularly relevant for patients with nonmalignant disorders (NMDs), which present higher risks of Host-versus-Graft (HvG) rejection and for whom the Graft-versus-Host (GvH) alloreactivity is only detrimental. Moreover, the impact of HLA-DPB1 permissiveness on GRFS following pediatric URD-HCT for NMDs has not yet been reported.

Objective: We sought to evaluate whether the DPB1 alloreactivity would adversely affect the GRFS after URD-HCT.

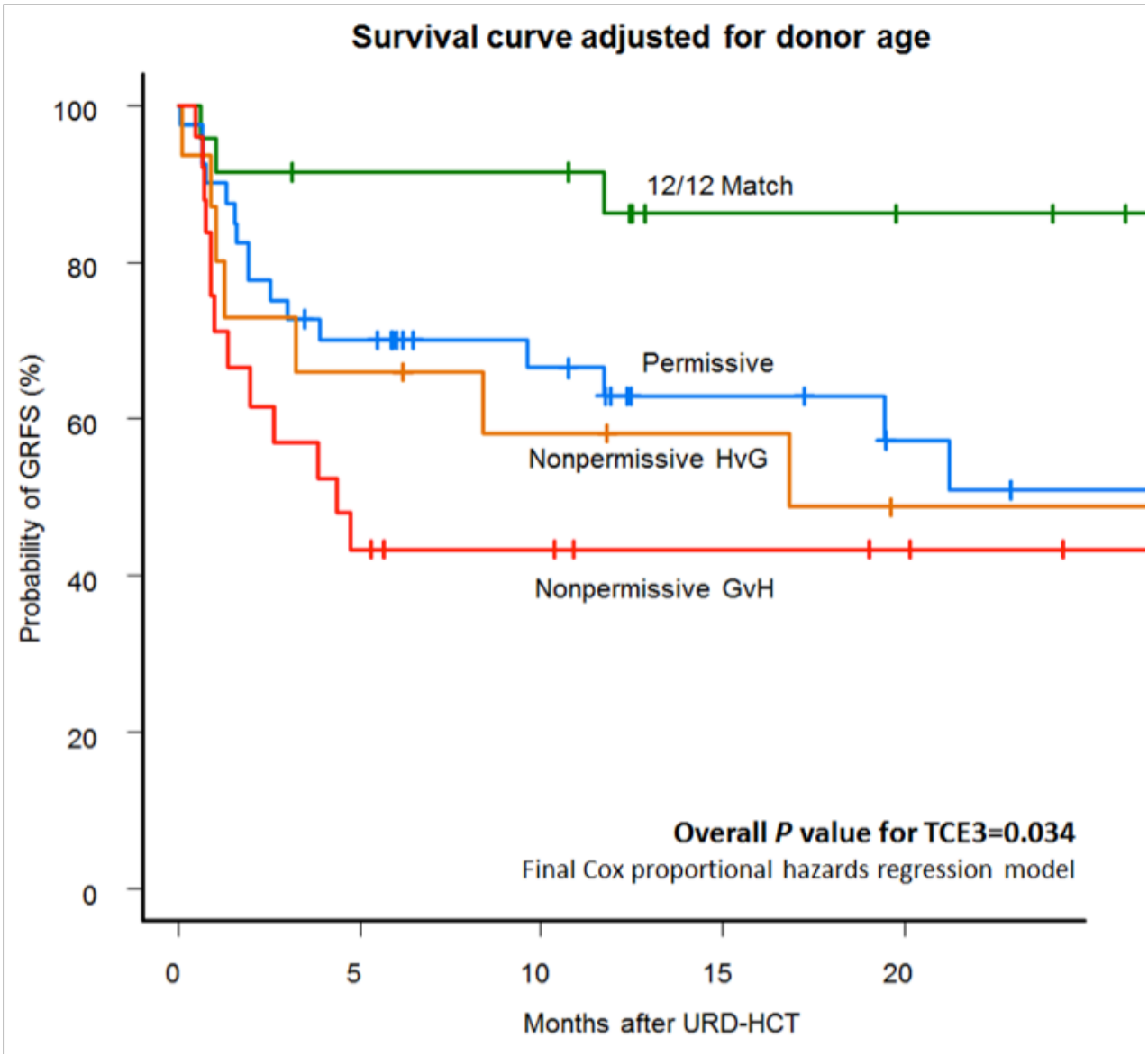
Methods: This single-center retrospective observational study included 94 pediatric patients (<21 years old) with NMDs who received their first URD-HCT from 2008 to 2017 at our center. All donor-patient pairs were 10/10 matched at high resolution. HLA-DPB1 permissiveness was assessed with TCE3 algorithm v2.0. Unadjusted 1-year GRFS rates were estimated according to the Kaplan–Meier method and compared among groups by the log-rank test. A Cox proportional hazards regression model was used to examine the independent predictors for GRFS. Only covariates that attained P-values≤0.05 were held in the final adjusted Cox model. Statistical analyses were performed using EZR software.

Results: The median age of patients was 9 years (IQR=5.25-11.75), and 62.8% were male. Most frequent NMDs were Fanconi anemia (n=33; 35.1%), acquired severe aplastic anemia (n=28; 29.8%), and dyskeratosis congenita (n=8; 8.5%). All patients received bone marrow as graft source, 89 (94.7%) had in vivo T-cell depletion with ATG, and 87 (92.5%) received cyclosporine+methotrexate as GVHD prophylaxis. Patients were divided into four groups: 12/12 match (n=19; 20.2%), permissive mismatch (n=38; 40.4%), nonpermissive HvG (n=14; 14.9%), and nonpermissive GvH (n=23; 24.5%). In the entire cohort, 1-year GRFS was 60.4% (95% CI: 49.4%-69.7%). Unadjusted 1-year GRFS rate was 83.1% in 12/12 group, 60.9% in permissive group, 56.2% in nonpermissive HvG, and 43.5% in nonpermissive GvH (P=0.09). In the multivariable Cox regression, the only significant independent predictors of inferior GRFS were nonpermissive GvH (HR=5.43; 95% CI=1.71-17.21; P=0.004), nonpermissive HvG (HR=3.69; 95% CI=1.07-12.74; P=0.039), and donors older than 30 years (HR=2.52; 95% CI=1.30-4.88; P=0.006). Interestingly, permissive DPB1 showed a trend (HR=2.95; 95%CI=0.98-8.91; P=0.055) of worse GRFS when compared to 12/12 matched group.

Conclusion: Our data highlight that considering HLA-DPB1 matching and TCE-permissiveness may optimize unrelated donor selection, thus improving the GRFS post-HCT for NMDs. Also, GvH and HvG nonpermissive mismatches should be avoided whenever possible. Further studies are warranted to validate these novel findings.

Keywords: HLA-DPB1, nonpermissive mismatches, nonmalignant disorders, unrelated donor, pediatrics, GVHD-Free/Rejection-free survival

FIGURE: Probability of GRFS by HLA-DPB1 TCE3 permissiveness, adjusted for donor age



ORAL ALOGENEIC HSCT

ENGRAFTMENT SYNDROME IN ALLOGENEIC STEM CELL TRANSPLANTATION: THINK ABOUT IT OR MISS IT

Júlia Plentz Portich[1], Aline Sinhorelo Ribeiro[1], Sheila Nogueira do Amaral[1], Marina de Almeida Furlanetto[1], Fernanda Fetter Scherer[1], Liane Esteves Daudt[1], Lúcia Mariano da Rocha Silla[1], Claudia Caceres Astigarraga[1], Alessandra Paz[1] & Lisandra Della Costa Rigoni[1]

1 Bone Marrow Transplantation and Hematology Department from Hospital de Clínicas de Porto Alegre, Brazil.

Introduction: Engraftment Syndrome (ES) is a constellation of characteristics that occurs during neutrophil recovery in patients undergoing hematopoietic stem cell transplantation (HSCT).Incidence of ES varies between 5 and 72%,as there are different criteria according to different authors.Diagnosis is based on criteria proposed by Spitzer and Maiolino.ES can resemble acute graft versus host disease (aGVHD),and there is data showing a strong association between them before day 28.Objective:Thus, the primary aim of this study was to investigate the incidence of ES according to Spitzer or Maiolino criteria in an allogenic population in a tertiary center of Brazil.The secondary aim was to analyse a possible relationship between ES and acute and chronic GVHD.

Methods: This was an observational retrospective cohort study with patients from any age who underwent allogenic HSCT (alloHSCT).Based on electronic chart review,all patients between January first,2015 and December 31,2016 were included.The study was approved by the ethics committee (2020-0062).Definition of ES was made according to Spizter or Maiolino.To compare dichotomous variables,Chi-square test was used. Kaplan-Meyer analysis was performed to examine mortality rate.P <0.05 was considered statistically significant.SPSS 21.0 (SPSS Inc., Chicago, IL, USA) was used for the analysis.

Results: A total of 79 patients underwent alloHSTC. The incidence of ES based on Spitzer criteria was 3.8% (3 patients) and,based on Maiolino,16.5% (13 patients).Incidence of ES among the adult population was 9.8%,compared with 28.6% on younger than 14 y/o,finding a correlation between ES diagnosis and age less than 14 years (P=0.03,Pearson Chi-Square PCS).The mean length of hospitalization was significantly higher between patients with ES (P=0.01,PCS). Use of broad spectra antibiotics for multiple drug resistance bacteria was seen in 24 (30.4%) patients. There was a positive correlation between ES and the use of these drugs (P=0.006, PCS).There was a correlation between ES and the use of amphotericin B (P=0.002,PCS).In 3 (3.8%) cases the team deliberated this diagnosis, and none patient received focused treatment for it.C reactive protein on engraftment day was significantly higher in patients with ES (Mean value of 84.5 versus 29.1; P=0.012; T-Student).Twenty-six (32.9%) had a diagnosed aGVHD, but there was no correlation between aGVHD and ES (P= 0.09, PCS).The prevalence of chronic GVHD was 39.2%. Forty-one (51.9%) patients died.Patients without ES had a mean survival of 39.96 months, compared with 24.9 of patients with ES diagnosis.There wasn't a significant difference in survival between those groups (P=0.19, log-rank [Mantel-Cox] test).

Conclusions: In our cohort, the general incidence of ES was comparable to previous literature.Remarkably, ES was associated with a prolonged length of hospitalization (14 days longer).Moreover, patients using antibiotics for multidrug resistant bacteria had a higher incidence of ES.

Keywords: allogeneic stem cell transplantation. Engraftment syndrome. Neutrophil engraftment.

IMPROVED SURVIVAL AFTER HAPLOIDENTICAL CELL TRANSPLANTATION WITH POST-TRANSPLANTATION CYCLOPHOSPHAMIDE IN PATIENTS WITH FANCONI ANEMIA

Bonfim C[1,2], Nichele S[2,3], Loth G[1,2], Trennepohl JP[2], Gouvêa LMM[3], Koliski A[2], Mosquer RATG[2], Ribeiro L[2], Dumke CCK[1], Benini FML[1], Pelegrina PRD[1], Rodrigues AM1,[2], Pilonetto DV[1] , Muratori RR[2], Fernandes JF[4,5], Arrais C[6], Lima ACM[2], Pasquini R[2,3].

1 Hospital Infantil Pequeno Príncipe, Curitiba, Brazil
2 Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, Brazil
3 Hospital Nossa Senhora das Graças, Curitiba, Brazil
4. Instituto do Tratamento do Câncer Infantil – Instituto da Criança – HCFMUSP, São Paulo, Brazil
5. Hospital Albert Einstein, São Paulo, Brazil
6. Hospital São Paulo – Escola Paulista de Medicina - São Paulo - Brazil

Introduction: Fanconi anemia (FA) is the most common inherited bone marrow failure in childhood. Hematopoietic cell transplantation (HCT) can cure the hematological complications related to the disease with better results when patients (pts) are transplanted at young age, in aplastic phase and with a matched related or unrelated donor. When a matched donor is not available, the use of haploidentical donor or unrelated cord blood grafts can be an alternative.

Objective: Evaluate the outcomes of FA pts receiving a haploidentical transplantation using post-transplantation cyclophosphamide and serotherapy (HAPLO-PTCY-serotherapy) compare with an historical cohort of pts who underwent unrelated cord blood transplantation (UCBT)

Method: Retrospective, longitudinal, non-randomized, observational study including 89 pts with FA transplanted in 3 HCT centers. Database and records were revised, and statistics performed using the EZR program. Sample: UCBT cohort: 42 pts with a median age of 8 years (3-19) transplanted between 2000 and 2011. Only 2 pts were older than 16 years. The majority had transfusion dependent aplastic anemia (n=41) and received a fludarabine based regimen (n=38). GVHD prophylaxis consisted of cyclosporine (CSA) + steroids in 57%. HLA compatibility: 6/6 (n=5); 5/6(n=16) and 4/6(n=21). Haplo-PTCY serotherapy cohort: 47 pts with a median age of 10 years (4-45) transplanted between 2013 and 2020. 83% had transfusion dependent aplastic anemia and 12 were older than 16 years. All received bone marrow from HAPLO donors and a modified reduced intensity protocol with Fludarabine+TBI200+ Serotherapy (ATG/Campath) and PTCY 50-60mg/kg+ Csa+MMF.

Results: When compared to the UCBT cohort, the Haplo-PTCY-serotherapy platform had a much lower D100 rejection rate (6% vs 31%, p=0.003). The cumulative incidence (CI) of D100 acute grade II-IV GVHD was similar (HAPLO:28% vs UCBT: 19%; p=0.13), but the 2-year CI of chronic GVHD was significantly higher (HAPLO:48% vs UCBT:19%; p=0.003). CMV reactivation and hemorrhagic cystitis at D100 were much higher after HAPLO-PTCY than UCBT (79% vs 38%; p=0.0001) and (55% vs 9%; p=0.0001) respectively. Transplant related mortality (TRM) at D180 was higher in the UCBT group (55% vs 6%; p=0.0001). Overall, 2-year survival was significantly improved after haplo-PTCY when compared to the historical UCBT group (82% vs 36%; p=0.0001), even though the HAPLO-PTCY cohort also included more adults and pts with advanced disease (eleven out of 12 older pts and 6 out of 8 pts with advanced disease are alive and engrafted).

Conclusions: Compared to historical UCBT cohort, the haplo-PTCY-serotherapy platform significantly increased the survival in FA pts by decreasing rejection rate and TRM. This excellent survival came with the high cost of viral reactivation and GVHD, suggesting new strategies are needed to prevent and treat these complications.

LATIN AMERICAN EXPERIENCE WITH HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN MDS

Fernando Barroso Duarte[1], Talyta Ellen de Jesus dos Santos Sousa[2], Vaneuza Araújo Moreira Funke[3], Virgílio Antônio Rensi Colturato[4] , Nelson Hamerschlak[5] , Neysimélia Costa Vilela[6] , Maria Cristina Martins de Almeida Macedo[7] , Afonso Celso Vigorito[8] , Rodolfo Daniel de Almeida Soares[9], Alessandra Paz[10] , Mariana Stevenazzi[11] , Abrahao Elias Hallack Neto12 , Gustavo Bettarello[13] , Breno Moreno de Gusmão[14] , Marco Aurélio Salvino[15] , Rodolfo Froes Calixto[16] , Maria Cláudia Rodrigues Moreira[17] , Gustavo Machado Teixeira[18] , Cinthya Corrêa da Silva[5] , Romélia Pinheiro GonçalvesLemes[2] , Yhasmine Oliveira Garcia[2] , Eduardo José de Alencar Paton[19] , Vanderson Rocha[20], Alicia Enrico[21] , Carmem Bonfim[22] , Ricardo Chiattone[23] , Anderson João Simioni[4] , Celso Arrais[24] , Erika Oliveira de Miranda Coelho[25] , Lilian Diaz[11]

1. Hospital Walter Cantídio, Hematology, Fortaleza, Brazil, 2. Hematology Research Laboratory - Federal Universityof Ceara, Hematology, Fortaleza, Brazil, 3. Federal University of Paraná, Bone Marrow Transplantation, Curitiba, Brazil, 4. Hospital do Câncer Amaral Carvalho - Fundação Amaral Carvalho, Bone Marrow Transplant, Jaú, Brazil, 5. Hospital Israelita Albert Einstein, Bone Marrow Transplant, São Paulo, Brazil, 6. Hospital de Câncer Infantojuvenil de Barretos, BoneMarrowTransplant, Barretos, Brazil, 7. Instituto Brasileiro de Controle do Cancer, Bone Marrow Transplant, São Paulo, Brazil, 8. Universidade Estadual de Campinas - UNICAMP / Hemocentro, Bone Marrow Transplant, Campinas, Brazil, 9. Natal Hospital Center, Bone Marrow Transplant, Natal, Brazil, 10. Hospital das clínicas de Porto Alegre, Bone Marrow Transplant, Porto Alegre, Brazil, 11. Centro TPH-SMI Serviço Médico Integral, Bone Marrow Transplant, Montevideo, Uruguay, 12. Hospital Universitário Universidade Federal de Juiz de Fora, Bone Marrow Transplantation, Juiz De Fora, Brazil, 13. Unidade de Transplante de Medula Óssea Pietro Albuquerque - ICDF, Bone Marrow Transplantation, Brasília, Brazil, 14. HOSPITAL SÃO JOSÉ, Bone Marrow Transplantation, São Paulo, Brazil, 15. Hospital Universitário Prof. Edgard Santos, Bone Marrow Transplantation, Salvador, Brazil, 16. Real Hospital Português de Beneficência em Pernambuco, Bone Marrow Transplantation, Recife, Brazil, 17. CEMO-INCA, Bone Marrow Transplantation, Rio De Janeiro, Brazil, 18. HC-UFMG, Bone Marrow Transplantation, Belo Horizonte, Brazil, 19. ONCOBIO Serviço de Saúde S.A., Bone Marrow Transplantation, Nova Lima, Brazil,20. Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Bone Marrow Transplantation, São Paulo, Brazil, 21. Hospital Italiano La Plata, Bone Marrow Transplantation, La Plata, Argentina, 22. Hospital Pequeno Principe, Bone Marrow Transplantation, Curitiba, Brazil, 23. Hospital Samaritano de São Paulo, Bone Marrow Transplantation, São Paulo, Brazil, 24. Hospital Sírio Libanês, Bone Marrow Transplantation, São Paulo, Brazil, 25. Hospital Santa Joana, Bone Marrow Transplantation, Recife, Brazil

Introduction: Hematopoietic stem cell transplantation (HSCT) is the only curative strategy for treating patients with myelodysplastic syndromes (MDS). However, several factors may interfere with the response to hematopoietic stem cell transplantation (HSCT) in Myelodysplastic Syndrome (MDS).

Objective: to evaluate the HSCT results in patients with MDS from 32 centers in Latin America. METHODS: it is multicenter study of Brazil, Uruguay and Argentina. Data of 331 patients (both sexes) from 1989 to 2021 were analysed. Patients were stratified according to the Revised International Prognostic Classification System (R-IPSS). Conditioning regimen, graft versus host disease (GVHD) prophylaxis and supportive treatment were performed according to the protocol of each institution. Statistical analysis by GraphPad Prism version 5.0 and SPSS software v.23.1 and v.24, considering significance of $p < 0.05$.

Results: the mean age was 46,29 years. Most patients were <51 years (n=162; 48,94%). There was a predominance of male patients (n=194; 59%) e Caucasian (n= 288; 87%). According to R-IPSS patients were Intermediate (24,17%), High risk (18,73%), very hig risk (5,14%) and low risk/very low risk (11,17%). No response was observed in 40,79% cases. The Conditioning regimen used was Myeloablative (244; 73,72%) and Reduced Intensity / Nonmyeloablative (87;26,28%). Most donor type was Related (229; 69,18%). Cell sources were: bone marrow (179; 54,08%), peripheral blood (146; 44,11%) and umbili-

cal cord (6; 1,81%). Treatment Prior to HSCT was performed in 217 (65,56%) cases with predominant use of Chemotherapy (134; 61,75%). Overall survival in 5 years was 28,4%. According to the cell source, OS was higher when used peripheral blood compared to bone marrow and umbilical cord (p< 0,001). When patients were stratified by age <60 and ≥60 or < 55 and ≥ 55 years there was no significant difference between groups for risk of death. There was no difference in overall survival according to treatment prior to HSCT, type of donor and conditioning regimen.

Conclusion: Data presented correspond to the results obtained through the cooperative work of several centers in Latin America, which have different approaches to patients, and reflect their reality and challenges. However, our data reinforce the concept that HSCT can be influenced by Treatment/No treatment prior to HSCT, type of conditioning and cell source adopted. The correlation of these results with those described in the literature is important to strengthen this discussion, which will certainly contribute to a better management of patients with MDS before and after transplantation.

MULTICENTRIC STUDY OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHRONIC MYELOMONOCYTIC LEUKEMIA IN LATIN AMERICA

Fernando Barroso Duarte[1], Talyta Ellen de Jesus dos Santos Sousa[2], Vaneuza Araújo Moreira Funke[3] , Virgílio Antônio Rensi Colturato[4] , Nelson Hamerschlak[5] , Neysimélia Costa Vilela[6] , Maria Cristina Martins de Almeida Macedo[7] , Afonso Celso Vigorito[8] , Rodolfo Daniel de Almeida Soares[9] , Alessandra Paz[10] , Mariana Stevenazzi[11] , Abrahao Elias Hallack Neto12 , Gustavo Bettarello[13] , Breno Moreno de Gusmão[14] , Marco Aurélio Salvino[15] , Rodolfo Froes Calixto[16] , Maria Cláudia Rodrigues Moreira[17] , Gustavo Machado Teixeira[18] , Cinthya Corrêa da Silva[5] , Romélia Pinheiro GonçalvesLemes[2] , Yhasmine Oliveira Garcia[2] , Eduardo José de Alencar Paton[19] , Vanderson Rocha[20], Alicia Enrico[21] , Carmem Bonfim[22] ,Ricardo Chiattone[23] , Anderson João Simioni[4] , Celso Arrais[24] , Erika Oliveira de Miranda Coelh[o25] , Lilian Diaz[11]

1. Hospital Walter Cantídio, Hematology, Fortaleza, Brazil, 2. Hematology Research Laboratory - Federal Universityof Ceara, Hematology, Fortaleza, Brazil, 3. Federal University of Paraná, Bone Marrow Transplantation, Curitiba, Brazil, 4. Hospital do Câncer Amaral Carvalho - Fundação Amaral Carvalho, Bone Marrow Transplant, Jaú, Brazil, 5. Hospital Israelita Albert Einstein, Bone Marrow Transplant, São Paulo, Brazil, 6. Hospital de Câncer Infantojuvenil de Barretos, BoneMarrowTransplant, Barretos, Brazil, 7. Instituto Brasileiro de Controle do Cancer, Bone Marrow Transplant, São Paulo, Brazil, 8. Universidade Estadual de Campinas - UNICAMP / Hemocentro, Bone Marrow Transplant, Campinas, Brazil, 9. Natal Hospital Center, Bone Marrow Transplant, Natal, Brazil, 10. Hospital das clínicas de Porto Alegre, Bone Marrow Transplant, Porto Alegre, Brazil, 11. Centro TPH-SMI Serviço Médico Integral, Bone Marrow Transplant, Montevideo, Uruguay, 12. Hospital Universitário Universidade Federal de Juiz de Fora, Bone Marrow Transplantation, Juiz De Fora, Brazil, 13. Unidade de Transplante de Medula Óssea Pietro Albuquerque - ICDF, Bone Marrow Transplantation, BrasÍlia, Brazil, 14. HOSPITAL SÃO JOSÉ, Bone Marrow Transplantation, São Paulo, Brazil, 15. Hospital Universitário Prof. Edgard Santos, Bone Marrow Transplantation, Salvador, Brazil, 16. Real Hospital Português de Beneficência em Pernambuco, Bone Marrow Transplantation, Recife, Brazil, 17. CEMO-INCA, Bone Marrow Transplantation, Rio De Janeiro, Brazil, 18. HC-UFMG, Bone Marrow Transplantation, Belo Horizonte, Brazil, 19. ONCOBIO Serviço de Saúde S.A., Bone Marrow Transplantation, Nova Lima, Brazil, 20. Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Bone Marrow Transplantation, São Paulo, Brazil, 21. Hospital Italiano La Plata, Bone Marrow Transplantation, La Plata, Argentina, 22. Hospital Pequeno Principe, Bone Marrow Transplantation, Curitiba, Brazil, 23. Hospital Samaritano de São Paulo, Bone Marrow Transplantation, São Paulo, Brazil, 24. Hospital Sírio Libanês, Bone Marrow Transplantation, São Paulo, Brazil, 25. Hospital Santa Joana, Bone Marrow Transplantation, Recife, Brazil

Introduction: Hematopoietic Stem Cell Transplantation (HSCT) in Chronic Myelomonocytic Leukemia (LMMC) has a very important role, for being the only curative procedure in high-risk patients. Despite this statement, there is a small number of transplants in this pathology in Latin America. It is believed that several aspects interfere, from diagnostic difficulty, access to molecular classification and patient age, and many patients arrive with advanced disease, with a performance status that does not allow for better management.

Purpose: to evaluate the HSCT scenario in Latin America.

METHODS: data from 30 patients with LMMC from 32 centers of the Latin American Registry of Transplantation in MDS, from April/1988 to December/2020, were analyzed. Statistical analysis was performed using the R program. Survival was analyzed using the Kaplan Meier curve and the prognostic factors, by Cox proportional risk .

Results: the mean age was 55.03 years, with a predominance of males (80%, n=24). A total of 60% of patients underwent treatment before BMT, in which 72.22% took Azacitidine, 27.78% used Decitabine and 5.56% Conventional Chemotherapy. The Myeloablative regimen was the most frequent (63.33%, n=19), followed by the Reduced Intensity (20%, n=6) and Non-myeloablative (16.67%, n=5) regimen. In 83.33% of cases, the donors were related, and of these, 13.33% were haploidentical; 16.67% not related. The main sources of cells used were peripheral blood (60%, n=18) and bone marrow (40%, n=12). Post-transplant complications were observed in 73.33% (n=22) of patients. The most frequent was

infection (59.09%), mainly by CMV (76.92%). Second, acute GVHD (40.91%), chronic GVHD (31.82%), veno-occlusive disease (9.09%) and rejection (4.55%) of the patients. Recurrence occurred in 30% of cases. The percentage of deaths was 33.33% (n=10). The survival probability of transplanted patients was 53.20% in 5 years. Survival was longer when the cell source was peripheral blood compared to bone marrow (p 0.048). Patients aged 63 years or less had longer survival than those aged 63 years (0.034). Using the Cox regression model, the risk of death was 6.67 times greater in those patients in whom bone marrow was used and 10.5 times greater for patients over 63 years of age. There was no association of cell source, treatment prior to BMT and age group with the incidence of recurrence. Cox's model was evaluated using the proportional hazards hypothesis. The Global and individual Schoenfeld test was performed and the adequacy of the model was demonstrated.

Conclusion: cell source and age were the factors that influenced the survival of patients with LMMC. There was no association between the analyzed prognostic factors and relapse.

Keywords: Hematopoietic Stem Cell Transplantation. Chronic Myelomonocytic Leukemia. MDS Latin American Registry

OUTCOMES AFTER ALLOGENEIC STEM-CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA IN ADULTS: A BRAZILIAN MULTICENTER COHORT

Dalila N Cysne[1], Wellington F Silva[1], Mariana N Kerbauy[2], Iago Colturato3, Ana Carolina Arrais Maia1, Luciana Tucunduva[4], George MN Barros[5], Vergílio AR Colturato[3], Nelson Hamerschlak[2], Vanderson Rocha[1].

1Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, SP, Brasil, Hospital Israelita Albert Einstein, São Paulo, SP, Brasil, 3Hospital Amaral Carvalho, Jaú, SP, Brasil, 4Hospital Sírio Libanês, São Paulo, SP, Brasil 5Barretos Cancer Hospital, Barretos, SP, Brasil

Introduction: Allogeneic stem-cell transplantation (HSCT) remains a potentially curative approach for acute lymphoblastic leukemia (ALL), especially for high-risk patients and those with relapsed/refractory disease, although its efficacy is offset by a not negligible toxicity. Adult patients with ALL fare worse in developing countries with low data about the HSCT in this context.

Objective: To describe outcomes and examine risk factors for overall survival (OS), disease-free survival (DFS), cumulative incidence of relapse (CIR), non-relapse mortality (NRM) and graft-versus-host disease (GVHD) after HSCT for ALL in Brazilian centers. Patients with ALL or ambiguous lineage leukemia above 16 years who underwent a first HSCT in 5 Brazilian centers between January 2007 and December 2017 were included.

Methods: Kaplan-Meier method and competing risk analysis were used. Multivariable analysis (MVA) was performed using Cox regression. Center effect was analyzed using frailty model introduced in MVA.

Results: 275 patients were included with a median age of 31y (range, 16-65). Baseline characteristics are summarized in Table 1. Matched sibling donor (MSD), matched unrelated donor (MUD), mismatched unrelated donor (MMUD), haploidentical donor and umbilical cord were reported in 53%, 19%, 9%, 19%, and 5%, respectively. Median time to HSCT in CR1 was 7.8 months. Graft failure rate was 1.5%. Median follow-up was 6.4y. Cumulative incidence of acute grade II-IV and chronic GVHD were 54.2% and 26.2%, respectively. In MVA, the use of MUD (HR=2.3) and increased donor age (HR=1.02) were associated with GVHD. Five-year CIR was 28.1% (95% CI 22.9-33.6) and 5-y NRM was 34.1% (95% CI 28.4-39.8). NRM incidence was 22.6% at D+100. CNS involvement at the diagnosis (HR=2.2), and disease status (HR 1.8 for CR2+, and HR 7.9 for refractory) increased relapse incidence, whereas, use of PB graft (HR=0.51) and haploidentical donor (HR=0.4) significantly decreased relapse incidence. In MVA, NRM incidence was increased by patient's age (HR=1.04), refractory status (HR=4.2), MUD (HR=3.8) and donor age (HR=1.02). Center effect was significantly associated with relapse and NRM. Five-year OS and DFS were 40.7% (95% CI 35.1-47.1) and 37.8% (95% CI-32.3-44.1), respectively (Figure 1). Patient's age, donor age and disease status were independently associated with OS and DFS (Table 2). When GVHD (as time-dependent variable) was introduced in the MVA for OS and DFS, it was associated with decreased OS (HR 4.2, $p<0.001$) but not with DFS. Pre-HSCT positivity for minimal residual disease was associated with worse DFS in univariate analysis (HR=1.47).

Conclusions: This is the largest series of ALL adults receiving HSCT from Brazil. While OS and DFS were similar to published data, NRM was higher. There was no impact of the donor type or graft source on survival, whereas haploidentical HSCT related to lower CIR. Use of MUD was associated with higher NRM and GVHD rates.

TABLE 1. Patients, disease, donor and transplant procedure characteristics.

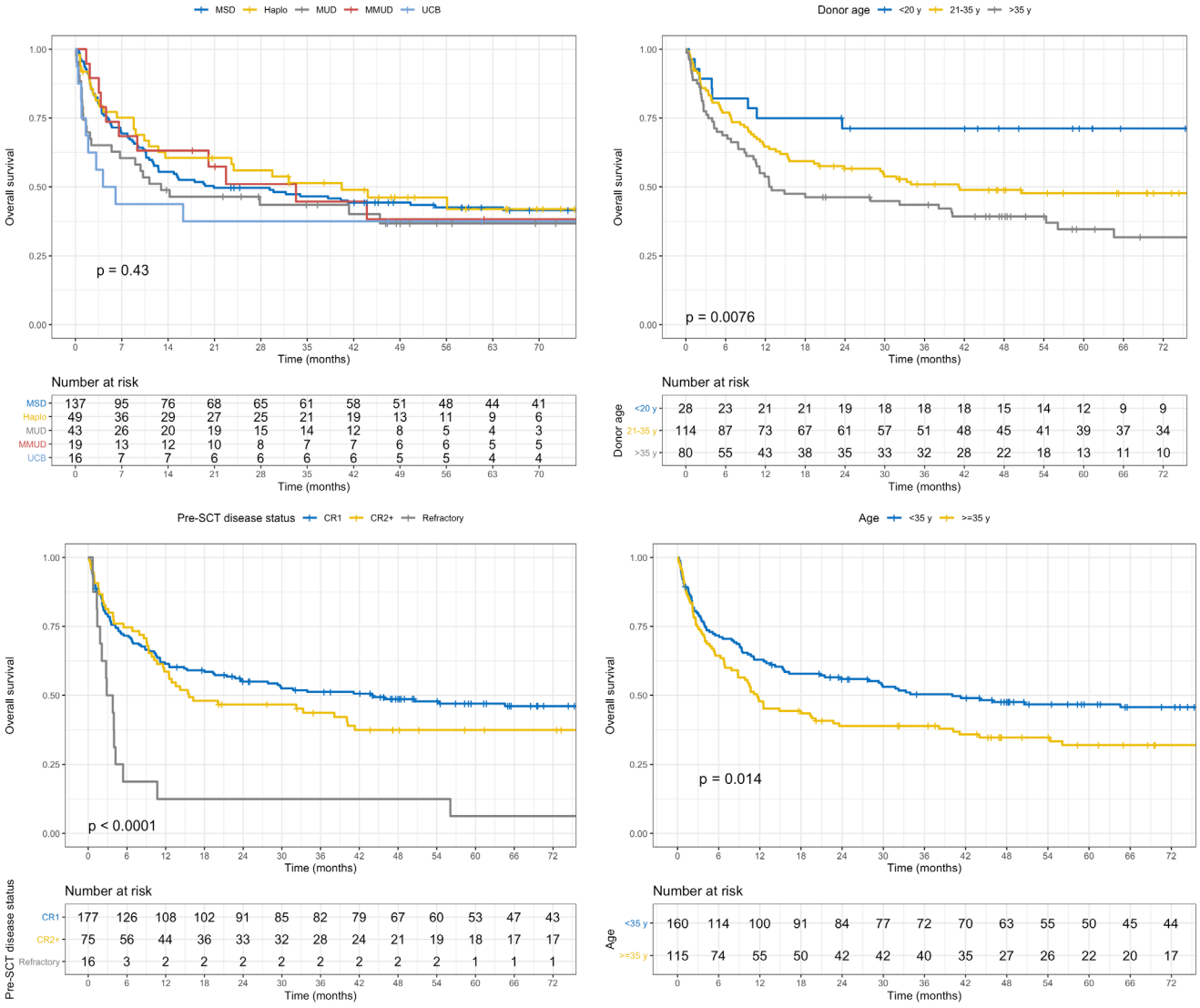
N = 275	
Age – median (range)	31 (16 - 65)
Sex – n (%)	Male: 161 (58.5)
Initial WBC (x109/L) – median (IQR)	9.4 (2.4 – 50.9)
Phenotype – n (%)	B-lineage: 216 (80.3) T: 41(15.2) Ambiguous lineage: 10 (3.7)
Ph-positive ALL - n (%)	84 (35)
BCRABL1 Transcript type – n (%)	p190: 41(60.3) p210: 27(39.7)
Genetic finding – n (%) Missing = 192 (69.8%)	KMT2A rearrangement – 3 (3.5) Normal karyotype – 44 (52.4) Abnormal karyotype – 34 (40.5) Hyperdiploidy – 2 (2.4)
CNS disease at diagnosis – n (%)	35 (14.2)
Disease status – n (%)	CR1: 177 (66) CR2+: 75 (28) Refractory: 16 (6)
BMI (kg/m2) – median (IQR)	24.4 (21.3 – 27.3)
Obesity - % (n)	29 (13)
Donor age (years) – median (range)	31 (4 - 64)
Donor gender – male – n (%)	136 (54.4)
Female donor to male recipient - n (%)	69 (27.6)
Donor type – n (%)	Related: 142 (51.6) Unrelated: 82 (29.8) Haploidentical: 50 (18.2) Syngeneic: 1 (0.4)
ABO incompatibility - n (%)	Isogroup: 164 (63.6) Minor: 38 (14.7) Major: 48 (18.6) Bidirectional: 8 (3.1)
Rh incompatibility – n (%)	30 (11.6)
CMV serologic status [donor/patient] – n (%)	Positive/positive: 161 (75.3) Negative/positive: 12.6 (27) Positive/negative: 16 (7.5) Negative/negative: 10 (4.6)
Graft source – n (%)	Peripheral blood stem cells: 134 (50.2) Bone marrow: 117 (43.8) Umbilical cord: 16 (6)
Conditioning intensity – n (%)	Myeloablative: 223 (83.2) Reduced intensity: 31 (11.6) Non-myeloablative: 14 (5.2)
MAC regimen – n (%)	TBI-based: 150 (67.4) Bu-based: 73 (32.6)
RIC regimen – n (%)	TBI-based: 38 (79) Bu-based: 7 (14.6) Mel-based: 3 (6.4)
No. of infused CD34+ cells (x106/kg) – mean (range)	5.9 (0.15-36)
Intrathecal chemotherapy during conditioning – n (%)	60 (26)

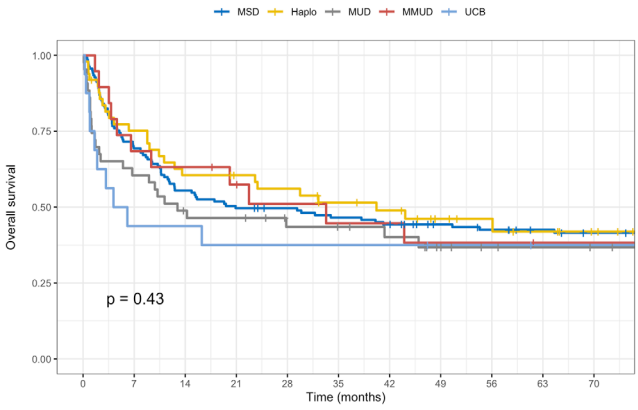
TABLE 2. Final multivariable model for OS, DFS, CIR and NRM.

Outcome	Covariate	HR (95% CI)	p-value
Overall survival (OS)	Age: < 35 years ³ 35 years	 reference 1.64 (1.11-2.43)	 0.013
	Disease status: CR1 CR2+ Refractory	 reference 1.32 (0.89-1.96) 4.18 (2.21-7.92)	 0.169 < 0.001
	Donor age: < 20 years 21-35 years > 35 years	 reference 2.07 (0.984-4.36) 2.54 (1.17-5.45)	 0.055 0.017
Disease-free survival (DFS)	Age: < 35 years ³ 35 years	 reference 1.71 (1.17-2.5)	 0.005
	Disease status: CR1 CR2+ Refractory	 reference 1.27 (0.85-1.89) 4.46 (2.35-8.48)	 0.237 < 0.001
	Donor age: < 20 years 21-35 years > 35 years	 reference 1.91 (0.97-3.73) 2.02 (1.01-4.05)	 0.059 0.048
Non-relapse mortality (NMR)	Age	1.04 (1.01-1.06)	0.001
	Disease status: CR1 CR2+ Refractory	 reference 1.02 (0.54-1.94) 4.24 (1.54-11.7)	 0.95 0.005
	Donor type: MSD Haplo MUD MMUD UCB	 reference 1.11 (0.52-2.36) 3.78 (1.97-7.26) 0.69 (0.16-3.02) 1.88 (0.2-17.2)	 0.79 < 0.001 0.626 0.578
	Donor age	1.02 (0.99-1.05)	0.069
Cumulative incidence of relapse (CIR)	CNS disease	2.19 (1.08-4.45)	0.03
	Donor type: MSD Haplo MUD MMUD	 reference 0.43 (0.2-0.88) 0.51 (0.21-1.26) 0.47 (0.16-1.35)	 0.022 0.148 0.161

	HSC source: BM PBSC	reference 0.51 (0.3-0.85)	 0.011
	Disease status: CR1 CR2+ Refractory	 Reference 1.76 (1.02-3.05) 7.92 (3.25-19.3)	 0.044 <0.001
GVHD incidence (A II-IV + C)	Donor type: MSD Haplo MUD MMUD UCB	 reference 1.46 (0.93-2.29) 2.35 (1.45-3.81) 0.6 (0.26-1.39) 1.78 (0.52-6.09)	 0.103 <0.001 0.234 0.358
	Donor age	1.02 (1.003-1.033)	0.018

Values in bold are statistically significant.




MSD Haplo MUD MMUD UCB
Overall survival
p = 0.43
Time (months)
Number at risk
MSD 137 95 76 68 65 61 58 51 48 44 41
Haplo 49 36 29 27 25 21 19 13 11 9 6
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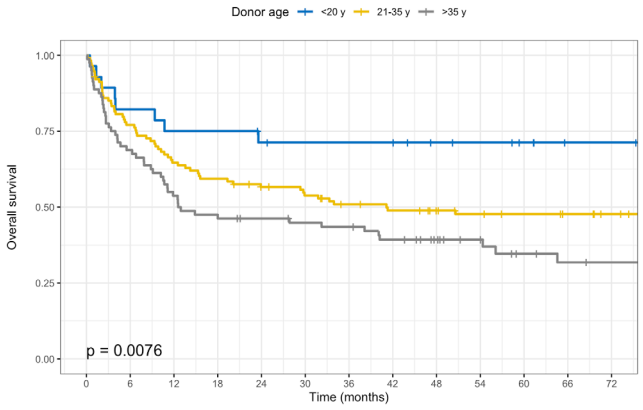
MMUD 19 13 12 10 8 7 7 6 6 5 5
UCB 16 7 7 6 6 6 6 5 5 4 4
Time (months)


Donor age <20 y 21-35 y >35 y
Overall survival
p = 0.0076
Time (months)
Number at risk
Donor age
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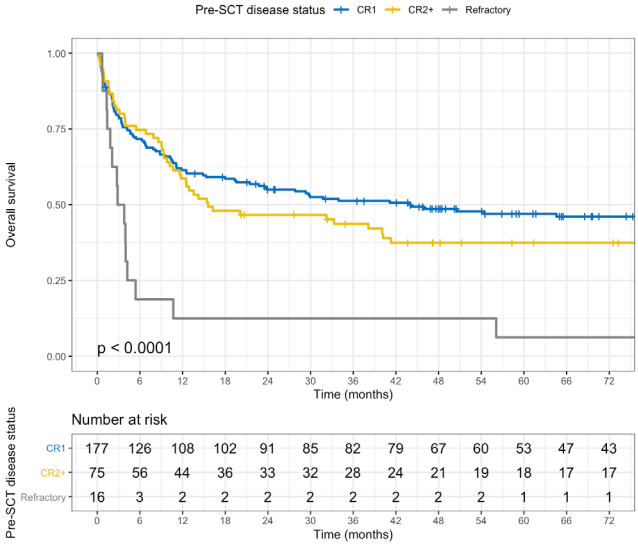
Time (months)


Pre-SCT disease status CR1 CR2+ Refractory
Overall survival
p < 0.0001
Time (months)
Number at risk
Pre-SCT disease status
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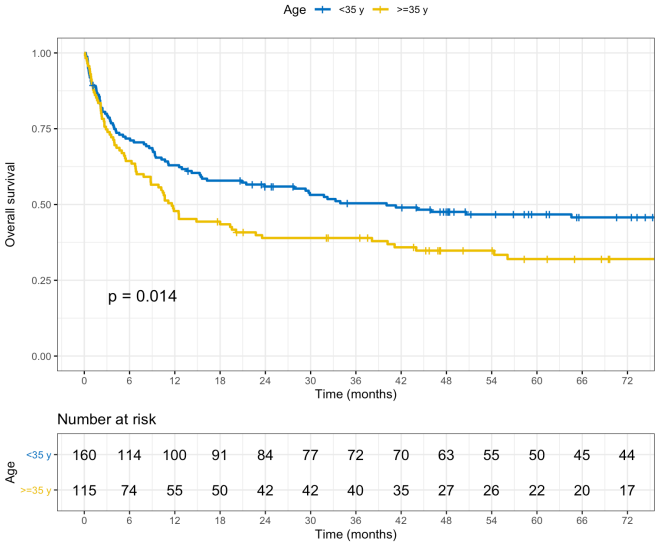
CR2+ 75 56 44 36 33 32 28 24 21 19 18 17 17
Refractory 16 3 2 2 2 2 2 2 2 2 1 1 1
Time (months)


Age <35 y >=35 y
Overall survival
p = 0.014
Time (months)
Number at risk
Age
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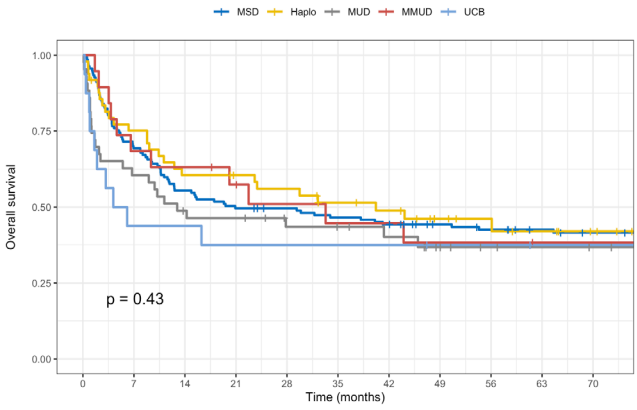
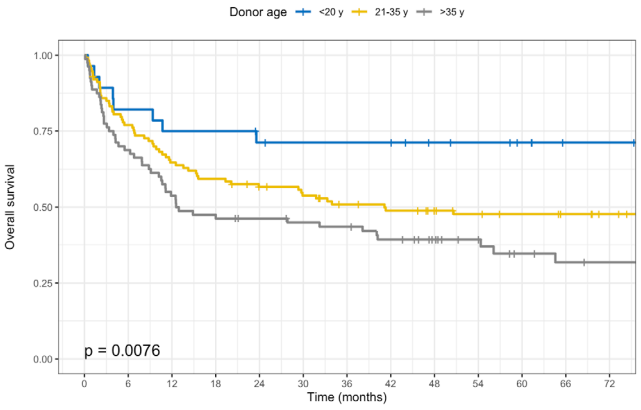
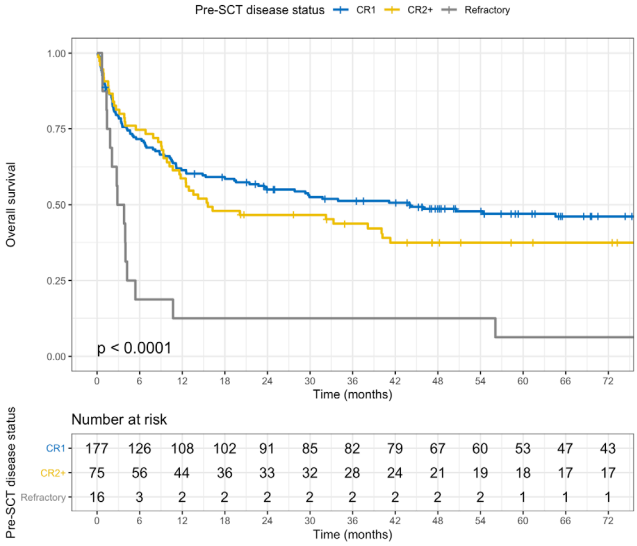
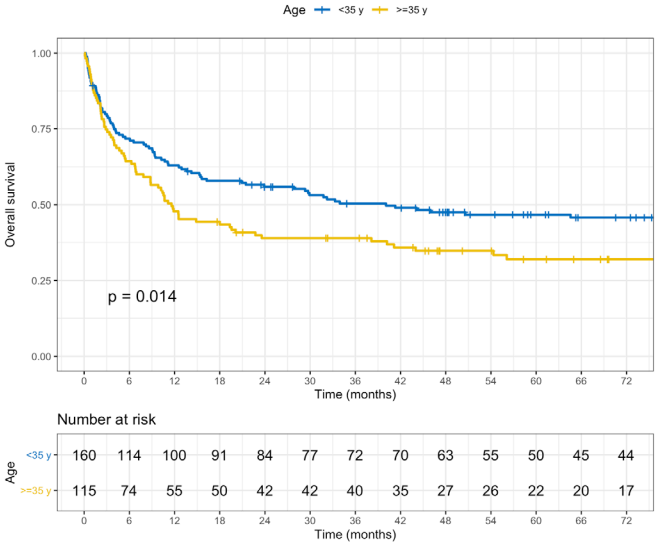
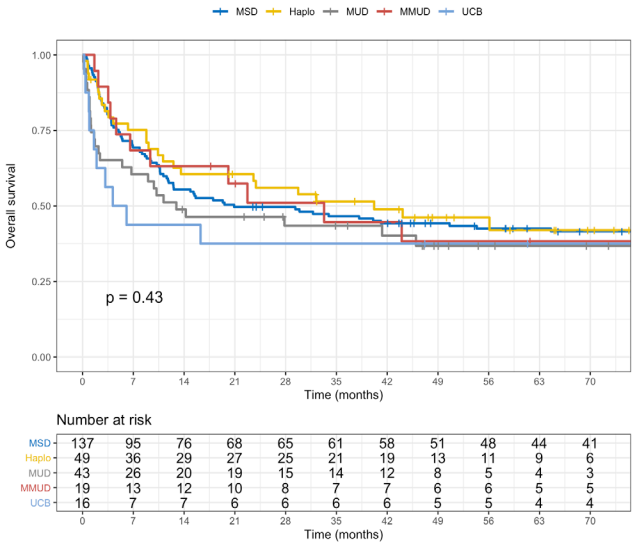
>=35 y 115 74 55 50 42 42 40 35 27 26 22 20 17
Time (months)


MSD Haplo MUD MMUD UCB
Overall survival
p = 0.43
Time (months)
Number at risk
MSD 137 95 76 68 65 61 58 51 48 44 41
Haplo 49 36 29 27 25 21 19 13 11 9 6
MUD 43 26 20 19 15 14 12 8 5 4 3
MMUD 19 13 12 10 8 7 7 6 6 5 5
UCB 16 7 7 6 6 6 6 5 5 4 4
Time (months)


Donor age <20 y 21-35 y >35 y
Overall survival
p = 0.0076
Time (months)
Number at risk
Donor age
<20 y 28 23 21 21 19 18 18 18 15 14 12 9 9
21-35 y 114 87 73 67 61 57 51 48 45 41 39 37 34
>35 y 80 55 43 38 35 33 32 28 22 18 13 11 10
Time (months)


Pre-SCT disease status CR1 CR2+ Refractory
Overall survival
p < 0.0001
Time (months)
Number at risk
Pre-SCT disease status
CR1 177 126 108 102 91 85 82 79 67 60 53 47 43
CR2+ 75 56 44 36 33 32 28 24 21 19 18 17 17
Refractory 16 3 2 2 2 2 2 2 2 2 1 1 1
Time (months)


Age <35 y >=35 y
Overall survival
p = 0.014
Time (months)
Number at risk
Age
<35 y 160 114 100 91 84 77 72 70 63 55 50 45 44
>=35 y 115 74 55 50 42 42 40 35 27 26 22 20 17
Time (months)


MSD Haplo MUD MMUD UCB
Overall survival
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Time (months)
Number at risk
MSD 137 95 76 68 65 61 58 51 48 44 41
Haplo 49 36 29 27 25 21 19 13 11 9 6
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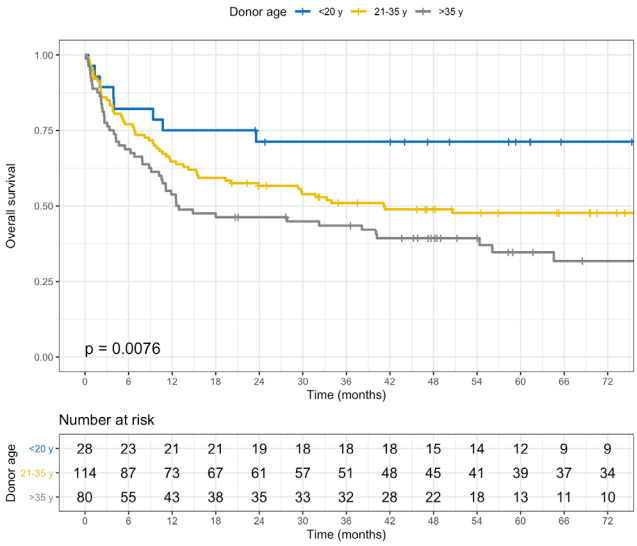
UCB 16 7 7 6 6 6 6 5 5 4 4
Time (months)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Overall survival
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Number at risk
Donor age
<20 y 28 23 21 21 19 18 18 18 15 14 12 9 9
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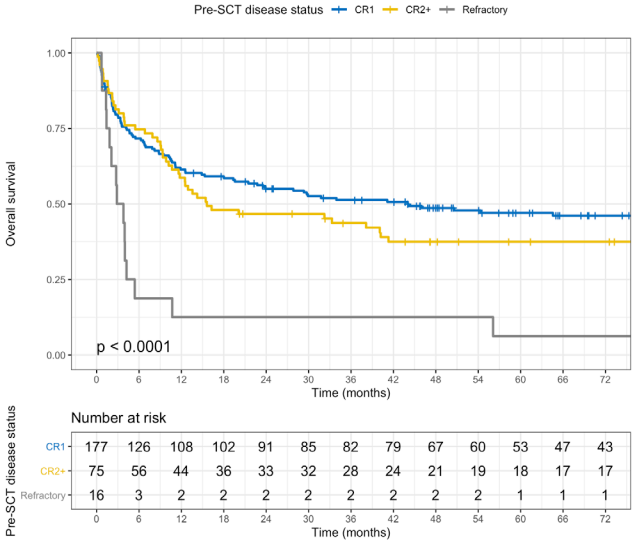
>35 y 80 55 43 38 35 33 32 28 22 18 13 11 10
Time (months)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Overall survival
p < 0.0001
Time (months)
Number at risk
Pre-SCT disease status
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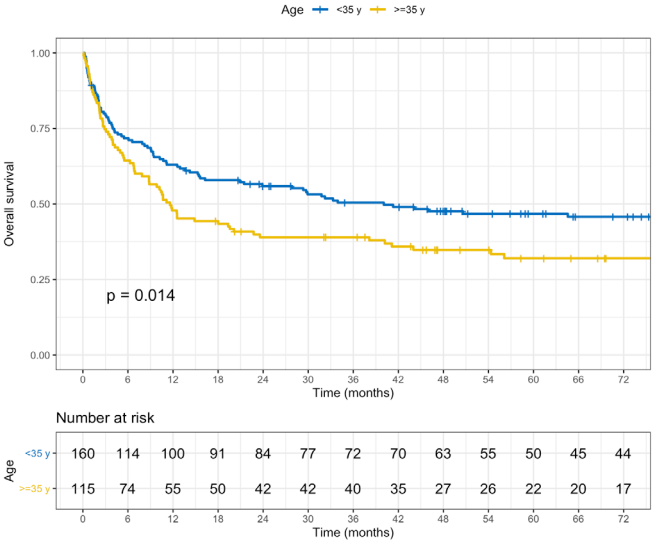
CR2+ 75 56 44 36 33 32 28 24 21 19 18 17 17
Refractory 16 3 2 2 2 2 2 2 2 2 1 1 1
Time (months)


Age <35 y >=35 y
Overall survival
p = 0.014
Time (months)
Number at risk
Age
<35 y 160 114 100 91 84 77 72 70 63 55 50 45 44
>=35 y 115 74 55 50 42 42 40 35 27 26 22 20 17
Time (months)

PATIENTS' AND HEALTHCARE PROVIDERS PERCEPTIONS FOR USING TELEHEALTH IN HEMATOPOIETIC CELL TRANSPLANTATION IN A PUBLIC HEALTH SYSTEM

Ana Cordeiro[1,2], Giancarlo Fatobene[1,3], Livia Mariano[1,4], Vanderson Rocha[1,3]

1 Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brasil
2 Hospital AC Camargo
3 Hospital Vila Nova Star – Rede Dor, São Paulo, Brasil
4 Centro Paulista de Oncologia, São Paulo, Brasil

Background: In March 2020, due to COVID-19 pandemic, we started performing telehealth using a institutional platform or telephone calls at HCT (Hematopoietic Cell Transplant) Outpatient Clinic.

Aim: Evaluate patients' and healthcare providers perspectives of telehealth as a permanent tool.

Methods: We sent three surveys: (1) main patient survey, to 401 post autologous or allogeneic transplant patients seen over the last 12 months; (2) healthcare provider survey, to 20 healthcare providers that work in HCT clinic; (3) complementary survey regarding socioeconomic profile of patients. All surveys were anonymous, made in Google Forms and sent to registered Whatsapp numbers. Of note, all patients have previously declared they could be reached through Whatsapp of their own or close contacts. We obtained 232 responses for the main survey, 17 responses from healthcare providers survey and 130 responses for the complementary survey. The first two surveys were open from August and October 2020; the complementary survey was sent in April 2021. Results: Patient's characteristics: median age 47 years; 53% were white; 15% lived in the city of São Paulo, 25% from another municipality in São Paulo State, and 65% from other states; 42% had elementary school or less, 42% had a monthly income per capita less than <US$ 220; 32% had some difficulty using a cell phone; 38% reported some degree of mobility disability. Regarding a typical clinic visit, about 30% of patients complained of long waiting times for in-person appointments. Commuting time (round trip) was <60 min for 30%, 60-120 for 38% and >120 min for 33%; with a total cost (for patient and eventual caregiver) of >US$ 10 for 42%; transportation was a private vehicle for 46%, government sponsored transportation for 17% or public transportation for 34%. Approximately half of the patients had at least one telehealth interaction, of whom 91% considered it a good experience. 83% of patients would like to receive telehealth care, 11% expressed some interest and 6% declared no interest. Considerable experience with telehealth was reported from 41% of healthcare providers that responded (9 physicians, 5 nurses, 1 pharmacist, 1 social assistant, 1 dentist). 53% think that telehealth would facilitate patient care in their areas and 6% would not like to provide telehealth. 82% said they will definitely or probably use a telehealth platform at our service but 18% have concerns.

Conclusions: Among patients and healthcare providers who had an incipient experience with telehealth at our service, the impression was overall positive. Limitations of this study are selection bias, lack of a formal assessment of costs, time saving and adherence. Although not always fit for all clinical scenarios, our findings suggest telehealth may be efficient and complementary to in-person interactions with HCT patients.

Keywords: Stem cell transplantation, telehealth, long term follow up

FIGURE 1: What is your commuting time (round trip from house to hospital)?

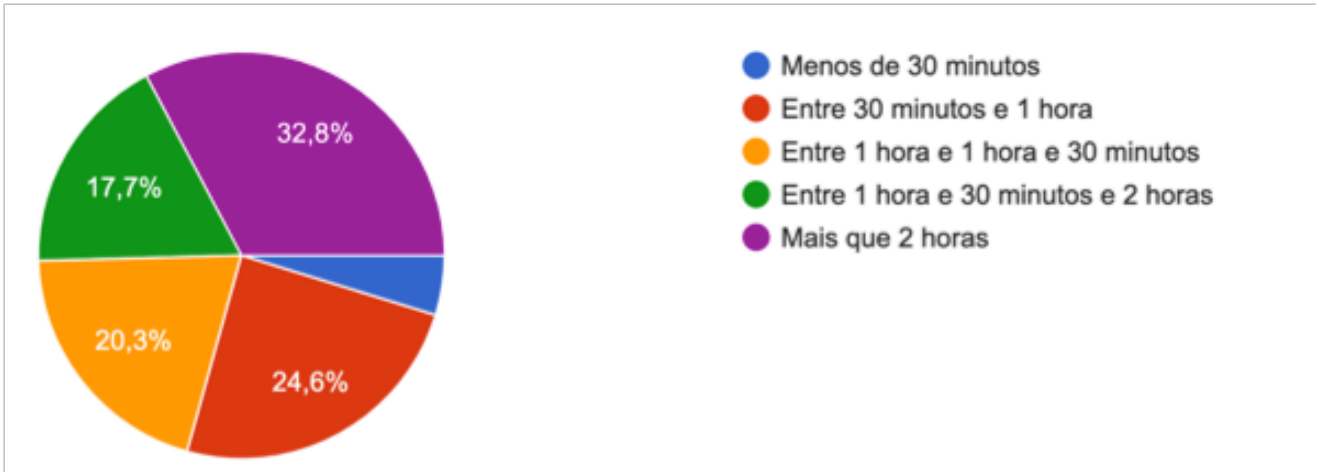
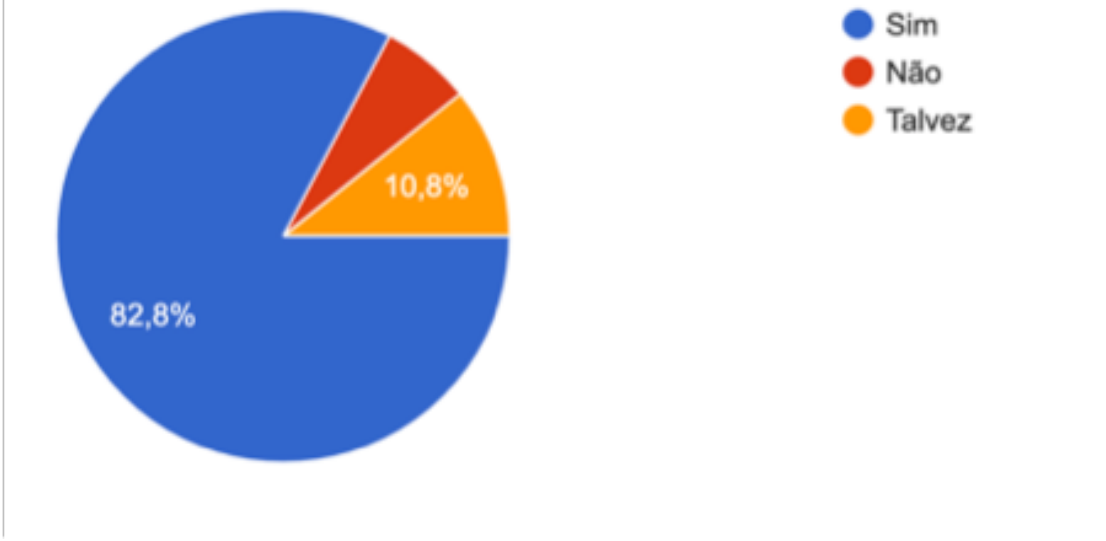


FIGURE 2: Would you like to receive telehealth care if possible?



POST-TRANSPLANT CYCLOPHOSPHAMIDE (PTCY) FOR GVHD PROPHYLAXIS IN MATCHED UNRELATED DONOR TRANSPLANTATION: COMPARING WITH UNRELATED TRANSPLANTATION WITH ATG PROPHYLAXIS AND WITH HAPLOIDENTICAL TRANSPLANTATION WITH PTCY

Andreza Alice Feitosa Ribeiro[1], Leonardo Javier Arcuri[1], Mariana Nassif Kerbauy[1], Lucila Nassif Kerbauy[1], Cinthya Corrêa Da Silva[1], Morgani Rodrigues[1], Nelson Hamerschlak[1]

1 Department of Hematology and Stem Cell Transplantation, Hospital Israelita Albert Einstein, São Paulo, Brazil

Introduction: Post-transplantation cyclophosphamide (PTCy) -based graft-versus-host disease (GVHD) prophylaxis in haploidentical transplantation (HAPLO) has greatly expanded the pool of donors. This is a cheap, easily reproducible and effective technique for preventing GVHD. Transplantation with an unrelated donor (URD HCT), on the other hand, is still an important and growing modality, with more than 30 years of experience worldwide. GVHD, however remains a major complication and is responsible for more than 15% of the post-transplant deaths. Alternative forms of immunosuppression, besides antithymocyte globulin (ATG), have been studied to decrease unrelated allogeneic post-transplant morbidity and costs, and one of them is PTCy.

Objective: Compare URD HCT with PTCy with URD HCT with ATG and HAPLO with PTCy.

Methods: This is a retrospective single-center study that included patients > 17 years old with hematologic malignancy who underwent HAPLO with PTCy and URD HCT (HLA 10x10 or 9x10) with PTCy or ATG from 2011 to 2021. In the PTCy group, Cy was given at a dose of 50mg/kg on days D+3 and D+4 followed by a calcineurin inhibitor (CNI) and mycophenolate (MM) starting on D+5. In the ATG protocol, patients received 5mg/kg of ATG from D-4 to D-1 associated with methotrexate and CNI. Cumulative incidence and Kaplan-Meier curves were built and compared with the logrank and Gray tests, respectively.

Results: We included 58 HAPLO, 71 URD-ATG and 17 URD-PTCy. Median follow-up was 2.6 years for the whole cohort and 1.4 for the URD-PTCy. Median age was 52 y/o and 52% were male. PBSC as graft (58% vs 33%, p=0.004) and MAC regimens (53% vs 24%, p>0.001) were more frequent with URD and URD were somewhat younger (median: 32 vs 39 y/o, p=0.01) compared to HAPLO. In the URD HCT, 87% of URD-ATG and 76% of URD-PTCy were 10/10 HLA -matched. One year OS was 62%, 63% and 79% for HAPLO, URD-ATG and URD-PTCY, respectively (p=0.70). Grades II-IV aGVHD were 32%, 45% and 32% for HAPLO, URD-ATG and URD-PTCY, respectively (p=0.16) and grades III-IV aGVHD were 8.8%, 26 and 6.3% (p=0.01). In multivariable analysis, the only factor associated with lower II-IV and III-IV aGVHD was PTCy-based prophylaxis. One year cGVHD rate were 11%, 12% and 29% for HAPLO, URD-ATG and URD-PTCy (p=0.12). One year relapse rate was 16%, 14% and 14% for HAPLO, URD-ATG and URD-PTCy.

Conclusions: There were no differences in overall survival and relapse between donor types or GVHD prophylaxis. The use of PTCy in URD combined with CNI and MMF is a safe and effective GVHD prophylaxis and might result in better prevention of severe acute GVHD than ATG-based prophylaxis.

Keywords: Post-transplantation cyclophosphamide; allogeneic transplant; DECH

RISK FACTORS FOR ADVERSE OUTCOMES FOLLOWING HAPLOIDENTICAL TRANSPLANTATION WITH POSTTRANSPLANT CYCLOPHOSPHAMIDE: A TWO-CENTER ANALYSIS

Viviane de Jesus Torres Lima[1]- Anderson Felipe da Silva (SILVA[1], Lucila Nassif Kerbauy[1] -Mariana Nassif Kerbauy[1] - Andreza Alice Feitosa Ribeiro[1] - Decio Lerner[2] - Marta Colares[2] - Cinthya Correa da Silva[1] - Leonardo Javier Arcuri[1,2] - Nelson Hamerschlak[1] - **Contributed equally*

1 Hospital Israelita Albert Einstein, Bone Marrow Transplantation Department, São Paulo, Brazil
2 Instituto Nacional de Cancer, Bone Marrow Transplantation Department, Rio de Janeiro, Brazil

Introduction: Allogeneic hematopoietic cell transplantation (HCT) is a potentially curative therapy for several malignant hematologic diseases. As only 30% of patients will have a matched related donor, alternative donors play a significant role in HCT [1]. Luznik et al [2] pioneered the use of posttransplant cyclophosphamide (PTCy) based GVHD prophylaxis in haploidentical transplantation (haplo-HCT), which greatly expanded the pool of donors and nearly revolutionized the field. Despite the increasing use of haplo-HCT with PTCy, some questions remain, namely the selection of the best donor, graft source and conditioning regimen, and risk factors for adverse outcomes [3-6]. The objective of the present study is to investigate risk factors for adverse outcomes after haplo-HCT with PTCy.

Methods: This is a retrospective study conducted at two Brazilian centers. All patients with hematologic malignancies who underwent first haplo-HCT with PTCy between 2010 and 2021, were included. In both institutions, PTCy was given on D+3 and D+4 with a calcineurin inhibitor (cyclosporine or tacrolimus) and mycophenolate mofetil (30 mg/kg or 45 mg/kg/day until D+35), starting on D+5. Outcomes were overall survival (OS) and progression-free survival (PFS), relapse, non-relapse mortality (NRM), and acute and chronic GVHD.

Results: A total of 103 patients were included (Table 1). Median follow-up was 2.6 years. OS at 2 years was 51.7% (Figure 1). Risk factors for death were age at transplant (HR=1.03 for each year; p=0.002), high/very high disease risk index (DRI [7]; HR=2.73; p=0.0008) and mother as the donor compared with other donors (HR=3.50; p=0.006). PFS at 2 years was 45.8%. In multivariate analysis (Table 2), PFS was significantly poorer for older patients (HR=1.02; p=0.009), high/very high DRI (HR=2.29; p=0.004), and mother as the donor compared with other donors (HR=3.15; p=0.007 / Figure 2). Two-year relapse rate was 22.2%. Risk factors for relapse were high/very high DRI (HR=3.55; p=0.006), and mother as the donor compared with other donors (HR=2.85; p=0.007). Two-year NRM was 32.0%. The only risk factor we found was age at transplant (HR=1.03 for each year; p=0.02). Rates of grades II-IV and III-IV aGVHD and 2y-cGVHD were 30.4%, 5.9% and 19.8%, respectively. The only risk factor identified for grades II-IV aGVHD was tacrolimus (HR=0.21; p=0.009) compared with cyclosporine. In multivariable analysis, peripheral blood (PBSC) was a risk factor for cGVHD (HR=3.33; p=0.01 / Figure 3), while tacrolimus was protective (HR=0.28; p=0.006).

Conclusion: Our results show that mother as the donor was an important risk factor for poorer OS, PFS and relapse, and mothers might not the best choice of donor. Tacrolimus was protective for both grades II-IV aGVHD and for cGVHD, suggesting that tacrolimus may be more effective than cyclosporine in preventing GVHD. PBSC was a risk factor for cGVHD without any impact on relapse, and this result does not support the systematic use of PBSC in detriment of BM. As expected, age at transplant negatively impacted OS, PFS and NRM as well as high/very high DRI led to poorer OS, PFS and relapse.

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Keywords: Haploidentical hematopoietic cell transplantation. Graft versus host disease. Non-relapse mortality. Posttransplant cyclosphosphamide.

TABLE 1. Baseline profile

	HIAE	INCA	Total
Total	66	37	103
Age, mean (SD)	46.9 (17.6)	26 (16.5)	39.4 (19.9)
Gender			
Female	33 (50%)	10 (27%)	43 (41.7%)
Male	33 (50%)	27 (73%)	60 (58.3%)
Diagnosis			
Acute leukemia, ambiguous lineage	1 (1.5%)	0 (0%)	1 (1%)
Acute lymphoblastic leukemia	6 (9.1%)	17 (45.9%)	23 (22.3%)
Acute myeloid leukemia	26 (39.4%)	13 (35.1%)	39 (37.9%)
Chronic myelomonocytic leukemia	2 (3%)	0 (0%)	2 (1.9%)
Chronic myeloid leukemia	0 (0%)	2 (5.4%)	2 (1.9%)
Hodgkin lymphoma	9 (13.6%)	1 (2.7%)	10 (9.7%)
Myelofibrosis	4 (6.1%)	0 (0%)	4 (3.9%)
Multiple myeloma	1 (1.5%)	0 (0%)	1 (1%)
Myelodysplastic syndrome	9 (13.6%)	3 (8.1%)	12 (11.7%)
Non-Hodgkin lymphoma	8 (12.1%)	1 (2.7%)	9 (8.7%)
Disease risk index			
Low/Int	48 (72.7%)	23 (62.2%)	71 (68.9%)
High/very high	15 (22.7%)	14 (37.8%)	29 (28.2%)
Missing	3 (4.5%)	0	3 (2.9%)
Graft			
Peripheral blood	23 (34.8%)	6 (16.2%)	29 (28.2%)

Bone Marrow	43 (65.2%)	31 (83.8%)	74 (71.8%)
Donor age, mean (SD)	37.9 (14.9)	36.9 (11.3)	37.6 (13.7)
Missing	2 (3.0%)	0	2 (1.9%)
Donor gender			
Female	25 (37.9%)	13 (35.1%)	38 (36.9%)
Male	41 (62.1%)	24 (64.9%)	65 (63.1%)
Female donor to male recipient	8 (12.1%)	9 (24.3%)	17 (16.5%)
Mother as donor	7 (10.6%)	10 (27.0%)	17 (16.5%)
Donor			
Parent	13 (19.7%)	18 (48.6%)	31 (30.1%)
Sibling	24 (36.4%)	16 (43.2%)	40 (38.8%)
Offspring	28 (42.4%)	3 (8.1%)	31 (30.1%)
Cousin	1 (1.5%)	0 (0%)	1 (1%)
Conditioning regimen			
Myeloablative	8 (12.1%)	27 (73%)	35 (34%)
Bu-based	8 (12.1%)	6 (16.2%)	14 (13.6%)
TBI-based	0	21 (56.8%)	21 (20.4%)
Reduced-intensity	36 (54.5%)	8 (21.6%)	44 (42.7%)
Non-myeloablative	22 (33.3%)	2 (5.4%)	24 (23.3%)
Mycophenolate mofetil			
30 mg/kg D+5 to D+35	0	31 (83.8%)	31 (30.1%)
45 mg/kg D+5 to D+35	66 (100%)	6 (16.2%)	72 (69.9%)
Calcineurin inhibitor			
Cyclosporine, starting D+5	3 (4.5%)	25 (67.6%)	28 (27.2%)
Tacrolimus, starting D+5	63 (95.5%)	12 (32.4%)	75 (72.8%)

HIAE, Hospital Israelita Albert Einstein; INCA, Instituto Nacional de Cancer; SD, standard deviation. Due to rounding, percentages may not sum up 100%

TABLE 2. Multivariate analyses

Outcome (number of events; N = 103)	HR	95%CI	p
Overall survival (50)			
Age (each year)	1.03	1.01-1.05	0.002*
High/v.high vs low/int. DRI	2.73	1.52-4.90	0.0008*
Mother as donor	3.50	1.44-8.47	0.006*
Progression-free survival (54)			
Age (each year)	1.02	1.01-1.04	0.009*
High/v.high vs low/int. DRI	2.29	1.30-4.04	0.004*
Mother as donor	3.15	1.37-7.22	0.007*
Relapse (22)			
High/v.high vs low/int. DRI	3.55	1.44-8.74	0.006*
Mother as donor	2.85	1.12-7.25	0.03*
Non-relapse mortality (32)			
Age (each year)	1.03	1.01-1.05	0.02*

Mother as donor	2.51	0.80-7.92	0.12
Grades II-IV acute GVHD (33)			
Conditioning regimen			
Myeloablative	1.00		
Reduced-intensity	0.81	0.34-1.93	0.63
Non-myeloablative	0.42	0.14-1.24	0.12
Tacrolimus versus cyclosporine	0.21	0.06-0.67	0.009*
Chronic GVHD (19)			
Peripheral blood vs bone marrow	3.33	1.34-8.26	0.01*
Tacrolimus versus cyclosporine	0.28	0.11-0.69	0.006*

*Statistically significant results.
Due to the low number of events for grades III-IV acute GVHD (7), we have not carried out multivariate analysis.
DRI, disease risk index; GVHD, graft-versus-host disease.

FIGURE 1. Overall survival

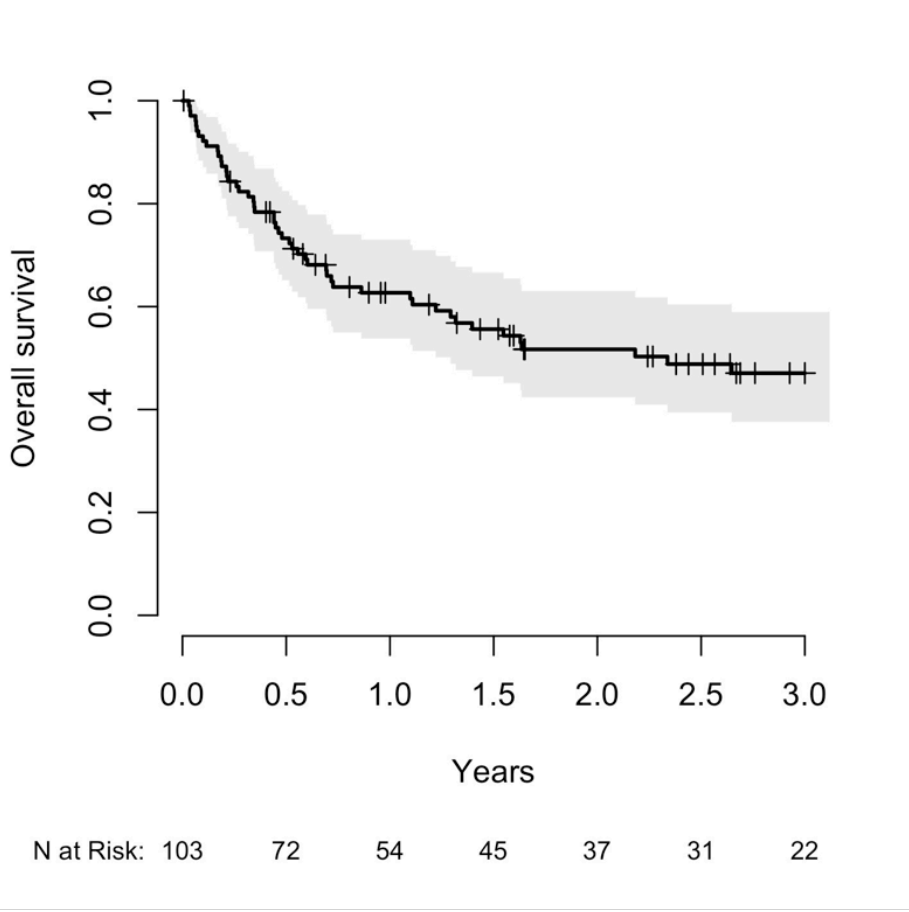


FIGURE 2. Progression-free survival, by gender match

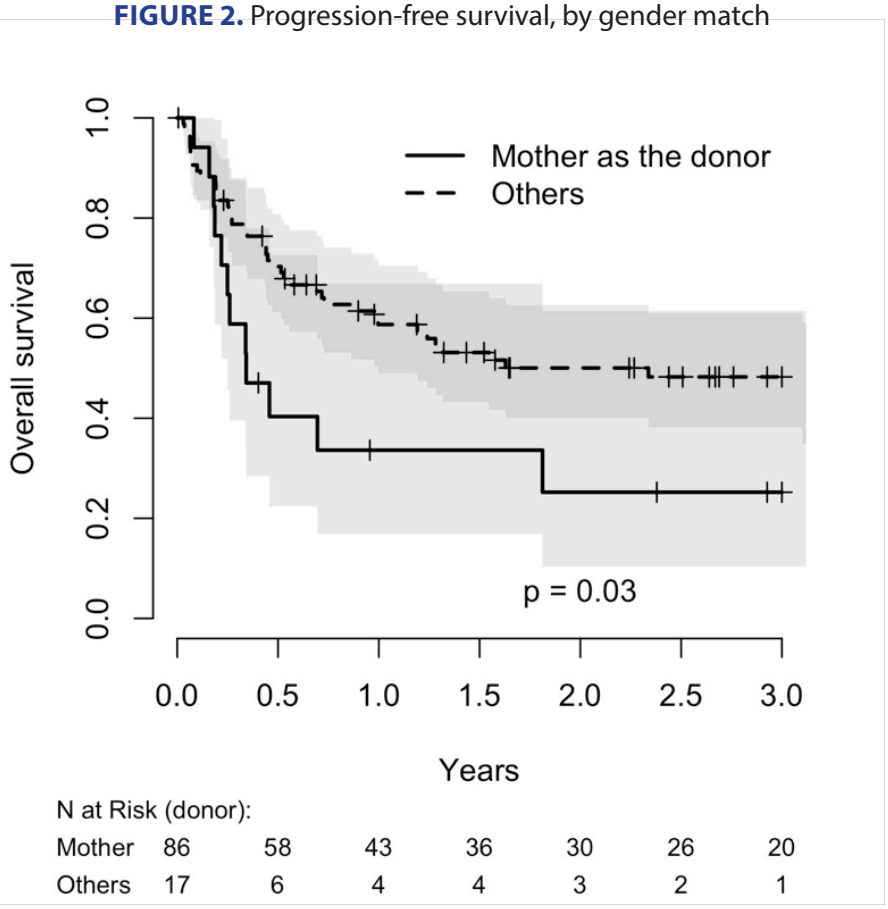
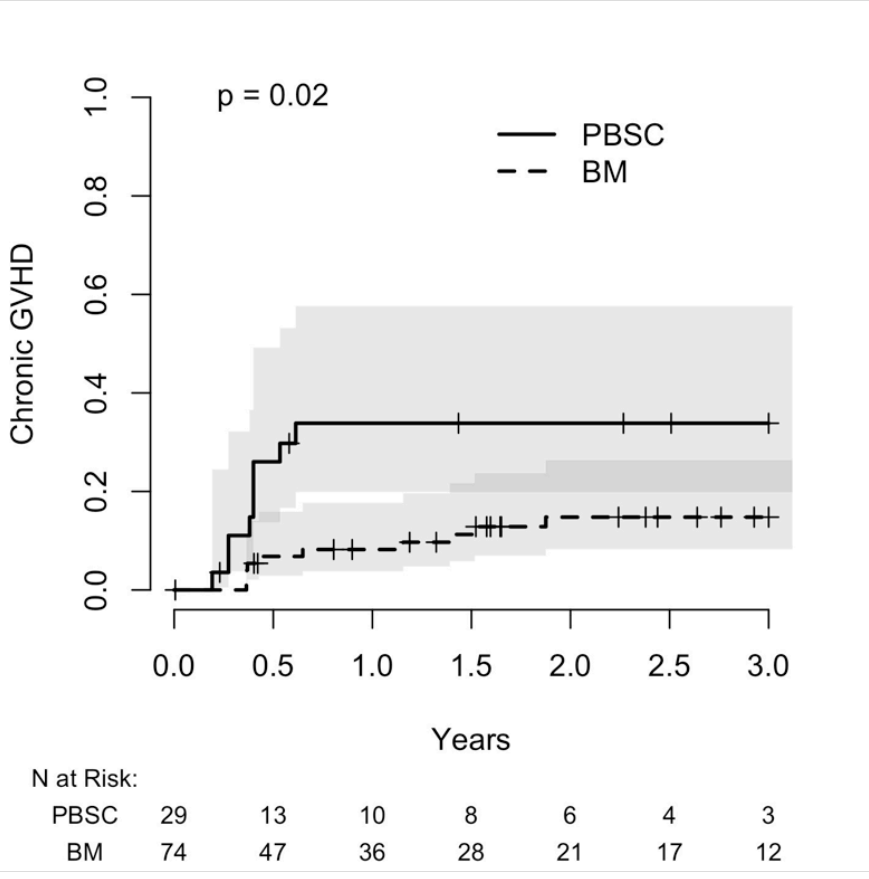


FIGURE 3. Chronic GVHD, by graft type



VIRAL INFECTION PROFILE IN PATIENTS SUBMITTED TO ALLOGENEIC HEMATOPOETIC STEM CELLS TRANSPLANTATION IN A REFERENCE HOSPITAL IN CEARÁ

Sarah Emanuelle Viana Campos[1]; Fernando Duarte Barroso[1]; Yara Ceres e Silva Ferreira Lima[1]

1 Hospital Universitário Walter Cantídio – HUWC/UFC

Introduction. Hematopoietic Stem Cell Transplantation (HSCT) is a well-established therapy for numerous hematological disorders, however, it is associated with several complications. Due to the need for immunosuppression for Graft Versus Host Disease (GVHD) prophylaxis, Allogeneic Transplantation is especially related to viral reactivation, impacting morbidity and mortality. The most epidemiologically relevant viruses today are: CMV, EBV, BKV and HV6, and their screening after transplantation is essential. Objectives. To evaluate the profile of viral infection in patients undergoing Allogeneic Hematopoietic Stem Cell Transplantation in the last 5 years in a reference hospital in Ceará.

Methods. This is a retrospective, descriptive, analytical and quantitative study with analysis of exam results and medical records. Allogeneic transplants performed in the last 5 years, in patients aged 16 years or older, were analyzed.

Casuistry. Between 06/03/2016 and 06/03/2021, 341 TCTH were carried out. Of these, 123 were allogeneic. Eleven patients were excluded from the sample by the absence of viral screening in the files and medical records. 112 patients remained in the study, of which 51.22% were women and 48.78% were men, with a mean age of 37.9 years (ranging from 16 to 70 years).

Results. As for the baseline diagnosis, most patients had AML (30.08%), followed by ALL (27.64%), aplastic anemia (13.82%), CML (8.94%) and MDS (8, 13%). The viral reactivation research was carried out based on PCR and cutoff points of 1,000 copies for CMV and EBV and detectable or undetectable for BKV and HV6 were used. 92 patients (82.14%) had detection of some virus (in any title) during post-BMT. Comparing the types of transplant, there was a prevalence of viral reactivation in haploidentical and unrelated transplants, with 85% and 87.5% of detection. CMV reactivation was the most frequent. Among the 112 patients in the sample, 71 (63.4%) had detectable values for CMV; 19 (17%) had <1,000 copies and 52 (46.4%) had >1,000 copies. 41 (36.6%) patients remained undetectable. Next, are the EBV numbers, with 63% detectable (20.4% with <1,000 copies and 42.6% with >1,000 copies) and 37% undetectable. Among all detectables, 49 patients (53.26%) had more than one virus and 6.52% had detection of 4. As for the reactivation time, HV6 was the virus with the earliest detection (mean of 73 days counting date of CTH infusion), followed by CMV (mean 116 days) and BKV (125 days). The latest reactivation virus was EBV (mean 214 days).

Conclusion. Viral reactivation is frequent in allogeneic HSCT, especially with the use of alternative donors. The frequency of CMV stands out and the early detection of HV6 is noteworthy. Knowledge of the viral reactivation profile of each service is essential to guide screening and preemptive treatment strategies.

Keywords. Hematopoietic Stem Cell Transplantation. Allogeneic Transplantation. Viral Reactivation.

COMPARATIVE ANALYSIS OF DATA ON THE INFLUENCE OF THE SARS-COV-2 PANDEMIC ON BONE MARROW TRANSPLANTATION AND THE PROTOCOLS ADOPTED IN BRAZIL BETWEEN MAY 2020 AND APRIL 2021

Fernando Barroso Duarte[1] , Talyta Ellen de Jesus dos Santos Sousa[2] , Abrahão Elias Hallack Neto[3] , Adriana Seber[4] , Afonso Celso Vigorito[5] , André Luís Gervatoski Lourenço[6] , Andresa Lima Melo[7] , Beatrice Araújo Duarte[8] , Beatriz Stela Gomes de Souza Pitombeira Araújo[9] , Carmem Bonfim[10], Celso Arrais[11], César Barian[12], Cilmara Kuwahar[13], Decio Lerner[14],Eduardo José de Alencar Paton[15], Garles Miller Matias Vieira[16], George Maurício Navarro Barros[17], Gisele Loth[18], Gustavo Machado Teixeira[19], Jayr Schmidt Filho[16], João Victor Piccolo Feliciano[20], Laura Maria Fogliatto[21], Leandro Celso Grilo[22], Leticia Navarro Gordan Ferreira Martins[23], Liane Esteves Daudt[24], Luís Fernando da Silva Bouzas[25], Marcio Soares Monção[26], Marco Aurelio Salvino[27], Maria Claudia Moreira[28], Maria Cristina M Almeida Macedo[29], Marina Assirati Coutinho[30], Nelson Hamerschlak[31], Ricardo Chiattone5, Roberto Luiz da Silva29, Rodolfo Soares32, Rony Schaffel33, Roselene Mesquita Augusto Passos[34], Thaisa Marjore Menezes Viana[1] , Tatiana Dias Marconi Monteiro[35], Vanderson Rocha[36], Vaneuza Araújo Moreira Funke[37], Vergílio Antônio Rensi Colturato[38], Victor Gottardello Zecchin[39], Wellington Morais de Azevedo[40], Yana Augusta S. Novis[12], Leandro de Pádua Silva[41], Antonella Zanette[42], Renato Luiz Guerino Cunha[36], Evandro Maranhão Fagundes[43], Angelo Atalia[44], Romélia Pinheiro Gonçalves Lemes[3] , Juliana Folloni Fernandes[45], Rodrigo Santucci[26], Marcelo Aduan[46], Milton Ruiz[47], Milton Aranha[48], Meide Daniele Urnau[49]

1 Hospital Universitário Walter Cantídio, Department of Surgery and Bone Marrow Transplantation – Fortaleza, Ceará, Brazil 2 Universidade Federal do Ceará - Research Laboratory in Hemoglobinopathies and Genetics of Hematologic Diseases, Fortaleza, Brazil, 3 Hospital Universitário da Universidade Federal de Juiz de Fora - Department of bone marrow transplantation, Juiz de Fora, Minas Gerais, Brazil, 4 Hospital Samaritano - Department of bone marrow transplantation in pediatrics, São Paulo, Brazil, 5 Hospital das clínicas da Universidade Estadual de Campinas - Department of bone marrow transplantation, São Paulo, Brazil, 6 Hospital dos Fornecedores de Cana de Piracicaba - Department of bone marrow transplantation, Piracicaba, São Paulo, Brazil, 7 Grupo Acreditar – Oncologia DO'r - Department of bone marrow transplantation, Brasília, Distrito Federal, Brazil, 8 Centro Universitário Christus (UNICHRISTUS) – Medicine, Fortaleza, Ceará, Brazil, 9 Hospital Unimed - Department of Bone Marrow Transplantation, Fortaleza, Ceará Brazil, 10 Hospital Nossa Senhora das Graças – Department of bone marrow transplantation in pediatrics, Curitiba, Paraná, Brazil, 11 Universidade Federal de São Paulo - Department of Medicine, São Paulo, Brazil, 12 ACCG - Hospital Araújo Jorge - Department of Bone Marrow Transplantation, Goiânia, Goiás, Brazil, 13 Hospital Pequeno Príncipe - Department of Bone Marrow Transplantation, Curitiba, Paraná, Brazil, 14 Instituto Nacional do Câncer (INCA) - Department of Bone Marrow Transplantation, Rio de Janeiro, Brazil, 15 Oncobio Serviços de Saúde - Department of Bone Marrow Transplantation, Nova Lima, Minas Gerais, Brazil, 16 Hospital A.C.Camargo Câncer Center - Department of Bone Marrow Transplantation, São Paulo, Brazil, 17 Hospital de Câncer de Barretos- Department of Bone Marrow Transplantation, Barretos, São Paulo, Brazil, 18 Hospital de Clínicas da Universidade Federal do Paraná, Department of bone marrow transplantation in pediatrics – Curitiba, Paraná, Brazil, 19 Hospital das Clínicas da Universidade Federal de Minas Gerais - Department of Bone Marrow Transplantation, Belo Horizonte, Brazil, 20 Hospital de Base de São Jose do Rio Preto - Department of Bone Marrow Transplantation, São José do Rio Preto, São Paulo, Brazil, 21 Santa Casa de Misericórdia de Porto Alegre - Department of Bone Marrow Transplantation, Porto Alegre, Rio Grande do Sul, Brazil, 22 Centro Médico de Campinas - Department of Bone Marrow Transplantation, Campinas, São Paulo, Brazil, 23 Hospital Universitário Regional do Norte do Paraná - Department of Bone Marrow Transplantation, Londrina, Paraná, Brazil, 24 Hospital de Clínicas de Porto Alegre - Department of Bone Marrow Transplantation, Porto Alegre, Rio Grande do Sul, Brazil, 25 Hospital Unimed Volta Redonda - Department of Bone Marrow Transplantation, Volta Redonda, Rio de Janeiro, Brazil, 26 Hospital Leforte Liberdade SA - Department of Bone Marrow Transplantation, São Paulo, Brazil, 27 Hospital Português da Bahia - Department of Bone Marrow Transplantation, Salvador, Bahia, Brazil, 28 Complexo Hospitalar de Niterói - Department of Bone Marrow Transplantation, Niterói, Rio de Janeiro, Brazil, 29 Instituto Brasileiro de Controle do Cancer (IBCC) - Department of Bone Marrow Transplantation, São Paulo, Brazil, 30 Hospital São Lucas - Department of Bone Marrow Transplantation, Rio de Janeiro, Brazil, 31 Hospital Israelita Albert Einstein, Department of Bone Marrow Transplantation, São Paulo,Brazil, 32 Hospital das Clínicas da Universidade Federal do Rio Grande, Petrópoles, Rio Grande, Brazil, 33 Universidade Federal do Rio de Janeiro - Department of Bone Marrow Transplantation, Rio de Janeiro, Brazil, 34 Instituto de Medicina Aeroespacial Brigadeiro Médico Roberto Teixeira - Department of Bone Marrow Transplantation, Rio de Janeiro, Brazil, 35 CEPON – Centro de Pesquisas Oncológicas - Department of Bone Marrow Transplantation, Florianópolis, Santa Catarina, Brazil, 36 Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Department of Bone Marrow Transplantation, São Paulo, Brazil, 37 Hospital das Clínicas da Universidade Federal do Paraná, Department of Bone Marrow Transplantation – Curitiba, Brazil, 38 Hospital Amaral Carvalho, Department of Bone Marrow Transplantation - Jaú, SãoPaulo, Brazil, 39 Instituto de Oncologia

Pediátrica (UNIFESP) - Department of Bone Marrow Transplantation, São Paulo, Brazil, 40 Santa Casa de Misericórdia de Belo Horizonte - Department of Bone Marrow Transplantation, Belo Horizonte, Minas Gerais, Brazil, 41 Hospital Santa Cruz - Department of Bone Marrow Transplantation, São Paulo, Brazil, 42 Hospital Erasto Gaerther, Curitiba, Paraná, Brazil, 43 Hospital Luxemburgo, Belo Horizonte, Minas Gerais, Brazil, 44 Hospital Monte Sinai, Juiz de Fora, Minas Gerais, Brazil, 45 Instituto da Criança - HCFMUSP. 46 Hospital Santa Rita de Cássia-Vitória ES, 47 Associação Portuguesa de Beneficência São José d Rio Preto, 48 Hospital São Camilo, 49 Hospital do Câncer de Cascavel

Introduction: a study of how HSCT centers faced COVID-19 pandemic in May/June 2020 was carried out. In April 2021, the analysis was remade, with a greater number of centers.

Objective: to assess the impact of the SARS-CoV-2 pandemic on HSCT and protocols adopted in Brazil.

Methods: a questionnaire of 14 questions was applied in April 2021. It was approved by the Research Committee of the Walter Cantídio University Hospital (HUWC) in Fortaleza, Brazil. Data were collected using Google Forms application.

Results: From 86 qualified centers, 51 centers (59.3%) responded to the questionnaire in May (85% of all adult and pediatric transplants performed in Brazil). In June, 52 centers (60.4%) responded to the questionnaire. In April 2021, 54 centers responded to the questionnaire (62.7%). In May, 4% of the centers discontinued the HSCT program and 12.2% maintained their operation without reduction. There was a decrease in the number of HSCT, ranging from 50% to 75% of the typical number in 59.2% of all centers. In June, this variation was 79.2%. In April 2021, 1.9% of centers responded that they discontinued the service and 40.7% of centers are 100% operational. The most recommendation cited was SBTMO in May (98%), in June (90.4%), and in April 2021 (98.1%). In April 2021, 100% of the centers indicated that they have availability to perform the PCR test, but in May (88.2%) and in June (88.5%) the collection of the RT-PCR exam was reported as the greatest difficulty. in April 2021, the time to receive the result was reported as the main difficulty (35.1%). The main symptoms were fever, cough, anosmia and headache. The most used drugs for treatment were azithromycin (75%), hydroxychloroquine (55%), corticosteroids and ivermectin (both 15%). In April 2021, the most used drugs were only symptomatic (50%) and corticosteroids (56.3%). Of those who used immunosuppressants, these were maintained in 38.1%, decreased in 19% and discontinued in 14.3%. In April 2021, 53.2% of the centers maintained immunosuppression, 2.1% discontinued it and 19.1% decreased it. About 58% of health workers were infected and removed in May. In June, this contamination was 73.1%. In April 2021, it reached 96.3% of health professionals in the centers. In May, 88.9% of these professionals underwent laboratory tests to confirm SARS-CoV-2 infection, in June 95% and in April 2021, 100%. Only 26% of centers tested asymptomatic health professionals directly involved with HSCT in May, 44.2% in June and 42.6% in April 2021.

Conclusion: the number of fully functioning centers increased considerably. The collection of the exam is no longer the main adversity to the diagnosis. Furthermore, with the new scientific discoveries related to the management of COVID-19, the use of some therapies was abandoned. The current profile of HSCT centers in Brazil, related to the recommendations for fighting the COVID-19 infection, will help in making public policy decisions in a country as Brazil.

Keywords: SARS-COV-2 pandemic. bone marrow transplantation. protocols.

AUTOLOGOUS HSCT

AUTOLOGOUS STEM-CELL TRANSPLANTATION FOR MULTIPLE MYELOMA: EXPERIENCE OF A PUBLIC CENTER IN BRAZIL

Lucas Oliveira[1], Mayara D'Auria Jacomassi[1], Leonardo Jun Otuyama[1], Bruna Del Guerra de Carvalho Moraes[1], Gracia Aparecida Martinez[1], Livia Mariano[1], Vanderson Rocha[1].

1 Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (USP), São Paulo, SP, Brazil.

Introduction: Several novel therapies have been developed in recent years improving multiple myeloma (MM) treatment, although autologous hematopoietic stem cell transplantation (HSCT) remains a fundamental strategy in eligible patients. HSCT is even more important where access to drugs such as bortezomib is not available in the Brazilian public health system.

Objective: To evaluate the outcomes after auto-HSCT in patients with MM treated at a public center in Brazil, identifying possible targets to improve assistance.

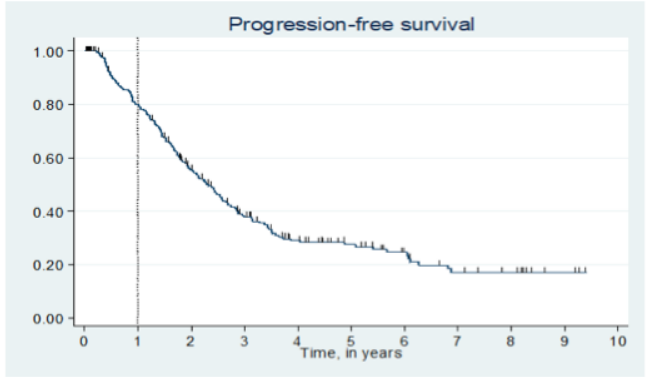
Methods: Between Jan-2010 and Oct-2018, 233 patients who underwent the first HSCT for MM were included. This was an observational, retrospective, and single-center study with data collected through medical records after approval by the local research ethics committee. The primary outcome was Progression-Free Survival (PFS) – defined as time between HSCT and death, date of last follow-up or disease progression according to current International Myeloma Working Group (IMWG) criteria. Secondary outcomes were: Overall Survival (OS), Transplant-Related Early Mortality (TRM) and HSCT toxicities (according to the Common Terminology Criteria for Adverse Events). Univariate analysis was performed followed by multiple Cox regression with regression elimination selection method, considering the following predictive variables: ISS, ECOG, Charlson index, number of treatments and pre-HSCT response, lactic dehydrogenase at diagnosis, age and time between diagnosis and TCTH.

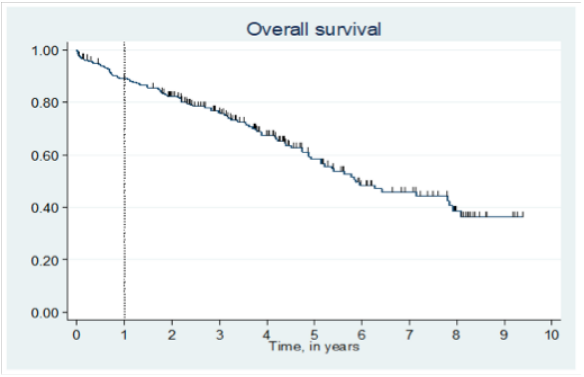
Results: At the time of HSCT, the median patient's age was 57 years (27-70) and 30% of them were over 60. There was a predominance of advanced stages by Durie-Salmon (87% stage IIIA/IIIB), ISS II/III (58%) and ECOG ≤2 (74%). Charlson's comorbidity index was ≥4 in 50.6% of the sample. Most patients had undergone only one previous treatment line (80%) and 23% had a complete response (CR) prior to HSCT. With a median follow-up after HSCT of 47.8 months, the 2-year PFS was calculated to be 52% (95%CI 45-58% - figure 1). Multivariate analysis showed significant risk of reduced PFS for Charlson index ≥4 (HR 1.52 95%CI 1.10-2.09) and pre-HSCT depth of response (partial response [HR 1.52 95%CI 1.10- 2.09] and very good partial response [HR 1.52 95%CI 1.10-2.09], compared to CR). The 2-year OS was 82% (95%CI 77-87% - figure 2). TRM was 4.3% and 41.8% of the patients had at least one toxicity classified as grade ≥3, the main ones being: oral mucositis, nausea and diarrhea.

Conclusions: With a median follow-up of 4 years, this study presents results of a Brazilian public center with similar rates of PFS and OS to those reported in the international literature prior to the advent of novel therapies for MM. HSCT proved to be safe and effective, with better outcomes in patients with fewer comorbidities and with deeper pre-HSCT responses, emphasizing the importance of incorporating new drugs to achieve even better results.

Keywords: Multiple myeloma. Autologous transplantation. Survival.

FIGURES 1 and 2: Progression-free survival and overall survival after auto-HSCT for multiple myeloma (N = 233).





CLINICAL AND PHARMACOECONOMIC COMPARISON OF HEMATOPOIETIC STEM CELL MOBILIZATION STRATEGY WITH PLERIXAFOR AND CONVENTIONAL PROTOCOLS

Rafael da Nóbrega de Alencar[1]; Lívia Mariano[1,2]; Frederico Rafael Moreira[1]; Leonardo Jun Otuyama1; Vanderson Rocha[1,3]

1 Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brasil
2 Centro Paulista de Oncologia, São Paulo, Brasil
3 Hospital Vila Nova Star – Rede Dor, São Paulo, Brasil

Introduction: Failure rate of hematopoietic stem cell mobilization (HSC) with traditional protocols described in literature ranges between 10-25%. Current evidence suggests a beneficial use of plerixafor in selected cases, with a reduction in failure rate of mobilization to 3%. However, its high cost is the major limiting factor for routine use in a public health system, with a scarcity of studies in Latin America evaluating the cost-benefit of this drug. Thus, the need to assess cost-effectiveness of using this drug in public health services in an emerging country such as in Brazil is meaningful.

Objective: To assess clinical and pharmacoeconomic effectiveness of HSC mobilization protocols adopted over 03 different periods: pre-Plerixafor protocol (Period 1), use of Plerixafor in mobilization failure (Period 2) and preemptive use of Plerixafor (Period 3).

Sample: Patients over 18 years of age who underwent hematopoietic stem cell mobilization between January 2014 and December 2020.

Method: Retrospective observational study. HSC mobilization failure was defined as collection of less than 2.0 x 106 CD34+ cells/kg after a mobilization protocol. The cost values used were based on SIGTAP (Brazilian public health cost chart) and on hospital cost of the drugs used.

Results: Of the 623 patients evaluated, 51.7% (n=322) were diagnosed with Monoclonal Gammopathies and 42.5% (n=265) with Lymphomas. 49.9% (n=311) of this cohort underwent mobilization with G-CSF while 50.1% (n=312) received G-CSF and chemotherapy. HSC mobilization failure rate was 13.43%. 96.5% (n=517) of patients who successfully mobilized needed only 1 apheresis session to collect HSC. Success rate of HSC mobilization with only 1 collection was of 89% in Period 1 (n=264), 82.7% in Period 2 (n=255) and 85.5% in Period 3 (n=106). Main factors associated with failure rate of HSC mobilization was age older than 32 years (p=0.013), pre-mobilization white blood count less than 5,800/mm3 (p=0.007) and previous use of Fludarabine, Lenalidomide or alkylating agents (p=0.017). Such factors did not show statistical significance after analysis by multivariate logistic regression. Cost per patient was of R$1,556.83 in Period 1; R$3,820.77 in Period 2; R$4,278.09 in Period 3. Incremental cost-effectiveness ratio for a 10% benefit with the use of Plerixafor was of R$24,160.63.

Conclusion: The impact of the use of plerixafor on clinical use and costs of should be better analyzed prospectively since its incorporation in a Brazilian public health service did not reduce the rate of HSC mobilization failure, although it significantly increased the cost per patient. Importantly, expenses of plerixafor are not included in the reimbursement of autologous HSCT in the public health system but included in the budget of the hospital. Evaluation of variables related to time until transplantation and associated morbidity can contribute to define the best use of new drugs.

Keywords: Stem cell mobilization, autologous stem cell transplantation, cost effectiveness

EVALUATION OF DISEASE PROGRESSION/RELAPSE IN PATIENTS WITH MULTIPLE MYELOMA WAITING FOR AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANT FROM A RESOURCE-CONSTRAINED COUNTRY

Giancarlo Fatobene[1,2], Frederico Moreira[1], Mayara Jacomassi[1], Bruna Carvalho[1], Leonardo Otuyama[1], Livia Mariano[1,3], Ana Cordeiro[1,4], Gracia Martinez1, Vanderson Rocha[1,2]

1. Laboratorio de Investigação Médica (LIM) 31, Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil;
2. Hospital Vila Nova Star–Rede D'Or, São Paulo, Brazil;
3. Centro Paulista de Oncologia – Oncoclinicas, São Paulo, Brazil;
4. AC Camargo Cancer Center, São Paulo, Brazil.

Introduction: Autologous hematopoietic cell transplant (auto-HCT) is considered standard of care in multiple myeloma (MM) and should be performed within 4-6 months after the start of induction therapy in eligible patients. Unfortunately, in resource-constrained countries, the waiting time for auto-HCT is longer due to the small number of HCT beds and difficulties in completing the pre-HCT process. Our objective was to evaluate the incidence, risk factors and impact of progression/relapse (P/R) in transplant waiting list among patients with MM.

Methods: Patients with MM referred to auto-HCT at our public institution between 2010 to 2018 were included. The primary outcome was cumulative incidence (CI) of P/R in transplant waiting list, defined as P/R requiring or not treatment after four months from the start of the most recent line of systemic treatment. Secondary outcomes were time in waiting list, CI of disease-free survival (DFS) after auto-HCT, proportion of referred patients actually proceeding to auto-HCT, and overall survival.

Results: 304 patients deemed eligible for auto-HCT were included in the analysis. Of these, 70 patients progressed or relapsed while waiting for transplant. Baseline characteristics were similar between patients with P/R or not in waiting list, except that the former were more likely to have non-IgG MM (Table 1). The CIs of P/R in transplant waiting list at 3, 6 and 12 months were 5, 11 and 17%, respectively. In a univariate analysis, ECOG 2-4, non-IgG MM, serum monoclonal protein ≥1.7g/dL, having high school (vs. elementary school) and no prior use of immunomodulator were significantly associated with higher risk of P/R in waiting list. In a multivariate analysis, non-IgG MM was the only independent risk factor for P/R in waiting list (Hazard ratio 1.74 [1.08-2.82], p=.02). Median waiting time was 231 days (IQR 131-429) for patients with P/R in waiting list compared to 149 days (IQR 95-213) for their counterparts (p < 0.001). Only 10% of patients were autografted within six months after the start of systemic therapy. Of the 70 patients with P/R in waiting list, 20 patients (29%) subsequently proceeded to auto-HCT compared to 214/234 (92%) of patients without P/F (p<.001). Post-transplant DFS of the 20 patients receiving auto-HCT after P/R in waiting list did not significantly differ from those proceeding directly to auto-HCT (p=.10). Overall survival was significantly inferior for those not receiving auto-HCT compared to those who did (Figure 1).

Conclusion: Patients with P/R in waiting list waited longer for auto-HCT than their counterparts and were less likely to be autografted after P/R. This finding suggests that waiting longer may increase the risk of P/R, making these patients lose performance status to undergo auto-HCT subsequently. Prioritizing patients with non-IgG MM and expanding outpatient transplantation may be strategies to avoid P/R in waiting list. These data may also help stakeholders address hindrances in the pre-HCT process and increase the number of HCT beds in the public setting.

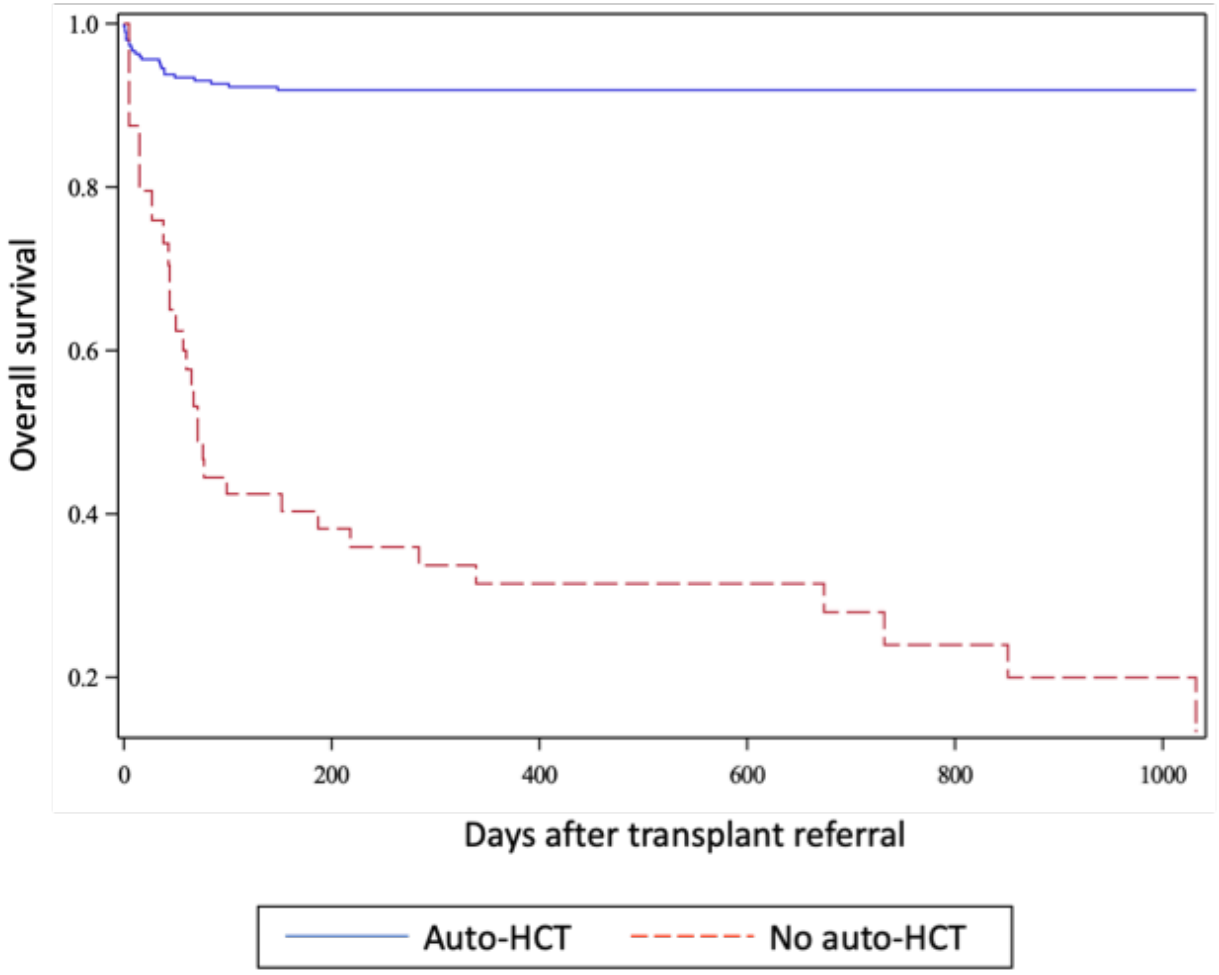
TABLE 1 – Patient and disease characteristics by progression/relapse in waiting list

Variable*	No progression/relapse in waiting list (N=234)	Progression/relapse in waiting list (N=70)	P-VALUE
Age at transplant referral, years			
<53 years	79 (34%)	23 (33%)	0.87
53 to 61	79 (34%)	22 (31%)	
≥ 61	76 (32%)	25 (36%)	
Gender			
Male	141 (60%)	42 (60%)	0.97
Charlson index at diagnosis			
2	47 (20%)	17 (24%)	0.72
3	60 (26%)	16 (23%)	
≥4	127 (54%)	37 (53%)	
ECOG at diagnosis			
0-1	111 (54%)	25 (40%)	0.058
2-4	94 (46%)	37 (60%)	
Missing	29	8	
Durie-Salmon at diagnosis			
IA-IIB	23 (11%)	7 (11%)	0.96
IIIA-IIIB	192 (89%)	57 (89%)	
Missing	19	6	
Dialysis at diagnosis			
No	231 (99%)	69 (99%)	0.93
ISS at diagnosis			
0	59 (30%)	16 (27%)	0.26
1	78 (40%)	19 (32%)	
2	60 (30%)	25 (42%)	
Missing	37	0	
Heavy chain type			
IgG	128 (58%)	30 (45%)	0.049
Non-IgG	91 (42%)	37 (55%)	
Missing	15	3	
Light chain type			
Kappa	151 (71%)	38 (62%)	0.088
Lambda	61 (29%)	22 (36%)	
Both	0 (0%)	1 (2%)	
Missing	22	9	
Number of prior treatment lines before referral to transplant			
1	203 (87%)	62 (89%)	0.69
≥2	31 (13%)	8 (11%)	
Prior use of immunomodulator			
Yes	206 (88%)	56 (80%)	0.09
Prior use of proteosome inhibitor			
Yes	12 (5%)	4 (6%)	0.85
Lactic acid dehydrogenase at diagnosis, U/L			
<192	75 (35%)	18 (27%)	0.29

192 to <309	67 (30%)	27 (41%)	
≥ 309	75 (35%)	21 (32%)	
Missing	17	4	
Beta-2 microglobulin at diagnosis, mcg/L			
<250	66 (31%)	22 (34%)	0.44
250 to <510	78 (37%)	18 (28%)	
≥510	68 (32%)	24 (38%)	
Missing	22	6	
Albumin at diagnosis, g/dL			
<3.3	75 (33%)	22 (31%)	0.37
3.3 to <4	69 (30%)	27 (39%)	
≥ 4	85 (37%)	21 (30%)	
Missing	5	0	
% bone marrow plasma cells at diagnosis			
<15	75 (33%)	22 (33%)	0.49
15 to <44	79 (35%)	19 (28%)	
≥44	72 (32%)	26 (39%)	
Missing	8	3	
Serum paraprotein at diagnosis, g/dL			
<2.1	25 (26%)	15 (48%)	0.06
2.1 to <4.4	37 (39%)	7 (23%)	
≥4.4	33 (35%)	9 (29%)	
Missing	95	31	
Education level			
Elementary School	124 (67%)	29 (56%)	0.072
High School	39 (21%)	19 (36%)	
Graduate/Post-graduate	21 (11%)	4 (8%)	
Missing	50	18	

* Continuous variables were grouped into terciles.

FIGURE 1 – Simon-Makuch curve of overall survival by autologous HCT group after transplant referral



The Simon-Makuch method takes into account the change in covariate status over time and properly represents the effect of a time-dependent covariate on survival. Auto-HCT: autologous hematopoietic cell transplantation

INCIDENCE OF EARLY TOXICITY AND MORTALITY AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR LYMPHOMA: A RETROSPECTIVE COMPARISON OF FOUR CONDITIONING REGIMENS

Jhonny Manuel Carranza Jara, Ana Costa Cordeiro, Giancarlo Fatobene, Leonardo Jun Otuyama, Aliana Meneses Ferreira, Livia Netto Chaer, Isabella Gonçalves Ramos, Livia Mariano, Vanderson Rocha.

Institution: Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo - HCFMUSP

Background: High dose chemotherapy followed by autologous stem cell transplantation (ASCT) is the standard treatment for relapsed or refractory lymphoma. Until recently, carmustine, etoposide, cytarabine and melphalan (BEAM) was the most used conditioning regimen. Despite the well-recognized success of BEAM, carmustine has been associated with several toxicities and market shortage, prompting research of alternative regimens.

Aims: To compare toxicities of BEAM, CBV (Carmustine, Etoposide, Cyclophosphamide), BendaEAM (Bendamustine, Etoposide, Cytarabine, Melphalan) and BuMel (Busulfan, Melphalan) conditioning regimens used for ASCT in patients with relapsed/refractory non-Hodgkin (NHL) and Hodgkin lymphoma (HL).

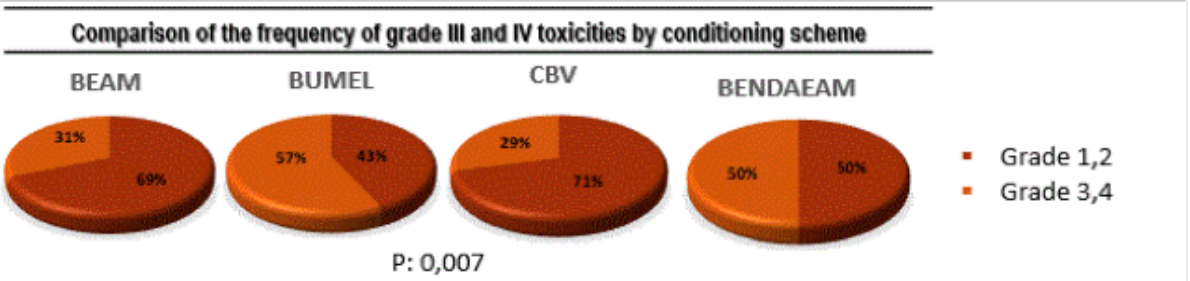
Methods: Patients diagnosed with NHL or HL, 18 years of age or older, who underwent ASCT from January 2014 to December 2020 at a University Hospital were included. The incidence of severe toxicity among conditioning regimens was compared using Fisher's exact test. For the toxicity analysis, a dimensional logistic regression model was performed, and the effect size was presented as the odds ratio. Overall survival curves for 100 days and 1 year were determined by the Kaplan-Meier method. Assessment of risk factors for mortality was performed using the Cox multivariate regression.

Results: We included 213 patients (CBV 65, BuMel 42, BEAM 68, BendaEAM 38), of which 56% were men, with a median age of 43 years (min-max 19-74), 91% had a ECOG ≤ 1. Regarding toxicities grade III and IV: oral mucositis was more frequent in the BuMel regimen (51%) and BendaEAM (26%), compared to CBV (10%) and BEAM (20%). Diarrhea was present in 30% in the BendaEAM group, 22% in the CBV and less frequently in the other groups (BEAM 16% and BuMel 10%); renal toxicity was only observed in the BendaEAM (44%). In the univariate logistic regression, there was an association of grade III-IV toxicities with type of conditioning regimen (p0.007). In fact, BuMel (OR 2.98; p0.007) and BendaEAM (OR 2.24; p0.054) were associated with a greater probability of developing grade III-IV toxicity. Estimated overall survival (OS) was 95% at 100 days and 85% at one year. We did not observe a statical survival difference among the four groups at day 100 and at 1 year. At 1 year, 20 patients (9.7%) had disease relapse.

Conclusion/Summary: BuMel and BendaEAM were associated with higher rate of grade III-IV toxicity compared to CBV and BEAM. Carmustine based conditioning regimens appear to be less toxic and safer, however CBV seems to be another good option when BEAM is not available. We did not found a significant association between conditioning protocol and risk of mortality.

Keywords: Autologous bone marrow transplant, Lymphoma, Stem cell transplant, Toxicity

FIGURE 1. Grade III-IV toxicities by conditioning regimen.

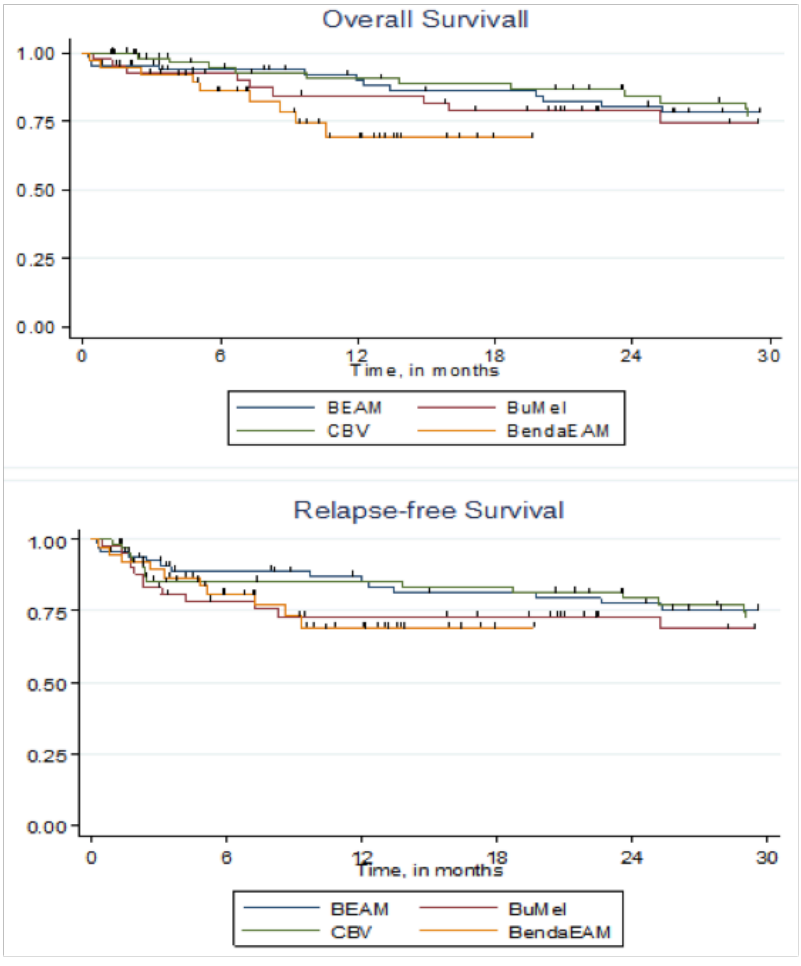


Univariate logistic regression due to any grade 3 and 4 toxicity (Oral Mucositis, nausea, vomiting, diarrhea, liver and kidney toxicity)

	OR	p-value	IC 95%	Sig
BEAM	1	.		
BuMel	**2.984**	**0.007**	**1.342-6.634**	***
CBV	0.924	0.836	0.44-1.941	
BendaEAM	**2.238**	**0.054**	**0.988-5.071**	*

*** p<.01, ** p<.05, * p<.1

FIGURE 2: Overall survival and relapse free survival up to 1 year



STUDY OF THE IMPACT OF THE TOXICITY OF HIGH DOSE CHEMOTHERAPY IN CONDITIONING REGIME FOR AUTOLOGOUS HEMATOPOIETIC STEM CELLS TRANSPLANTATION IN OVERWEIGHT AND OBESE PATIENTS WITH LYMPHOMA

Gabriela Santos de Souza[1], Bruna Del Guerra Carvalho Moraes[2], Leonardo Jun Otuyama[2], Luiz Henrique dos Santos de Assis[3], Lívia Mariano[2], Vanderson Rocha[2]

1 Hospital Cruz Azul, São Paulo, SP
2 Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, SP
3 Hospital São Rafael, Salvador, BA

Introduction: In autologous hematopoietic stem cell transplantation (auto-HSCT), the main mechanism used to control malignancy is the use of high doses of the Conditioning Regimen (CR). The calculation of the CR dose takes into account the patient's weight and body surface. To date, there is no consensus on the best dose adjustment for obese individuals, balancing toxicity and antitumor effect.

Objective: To compare the effects of chemotherapeutic dose adjustment on auto-HSCT CR based on actual or adjusted weight in patients with lymphoma. Casuistic: Patients aged 18 years or over who underwent first auto-HSCT as consolidation therapy for Hodgkin's or Non-Hodgkin's lymphoma in a public institution in the city of São Paulo between January 2014 and July 2019 were included.

Methods: Information related to the patient, the disease and the auto-HSCT of electronic medical records of outpatients and inpatients and also in the electronic examination system were collected. Data were collected with REDCap (Research Electronic Data Capture). The comparison of categorical outcomes between groups was performed using the chi-square or Fisher's exact test, depending on the number of observations in each group. Survival curves were determined using the Kaplan Meier method and compared between groups using the log-rank test. Cox multivariate regression was used to quantify the association of variables, using the hazard ratio with a 95% confidence interval. Results with p value under 5% were considered statistically significant.

Results: 192 patients participated in the study. Based on the Body Mass Index (BMI), 80 (42%) were eutrophic, 68 (35%) were overweight and 44 (23%) were obese. 41 patients received dose-adjusted CR to compare the effects of chemotherapeutic dose adjustment on CR auto-HSCT based on actual or weight-adjusted weight in obese and overweight patients. No statistically significant differences were found in toxicities (oral mucositis, nausea and vomiting), relapse or mortality between the groups, except in diarrhea, which was higher in the dose-adjusted group (p=0.03). The use of melphalan in CR increased the chance of toxicities by 2.29 times (p=0.02). When stratified by BMI, there is a trend towards greater relapse or disease progression up to D+100 in eutrophic patients (p=0.051), but without statistical differences in the analyses. The median follow-up time was 19 months with a survival rate of 80.53%. There was no statistically significant difference in survival between groups (p=0.1189). Conclusion: Dose adjustment did not increase relapse, disease progression or death rates in the population within one year. There was a higher risk of diarrhea in patients with an adjusted dose, however this outcome must have been influenced by factors that were not considered in this study. A prospective randomized trial is needed to establish the advantages or disadvantages of dose adjustment in overweight or obese patients.

TABLE 1. Description of population and disease

Characteristic	n	%
Sex		
Female	79	41,1
Male	113	58,1
Mean age (+/- SD)	43,3	15,2
Baseline disease		
Hodgkin Lymphoma	81	42,2
Non-Hodgkin Lymphoma	111	57,8
Type of lymphoma		
DGCB	36	32,4
Mantle	30	27
Follicular	4	3,6
T-Anaplasic	12	10,8
Angioimmunoblastic	2	1,8
Transformed	10	9
Other	17	15,3
Ann Arbor		
Staging		
I	3	1,6
II	41	21,4
III	42	21,9
IV	104	54,2
Presence of symptoms B	138	71,9
Location		
X	69	41,8
S	31	18,8
E	27	16,4
Other	60	36,4
Mean Pre-treatment lines (+/- SD)	2,2	1,1
Disease status		
Complete remission	125	65,1
Partial remission	52	38,6
Refractory	13	6,8

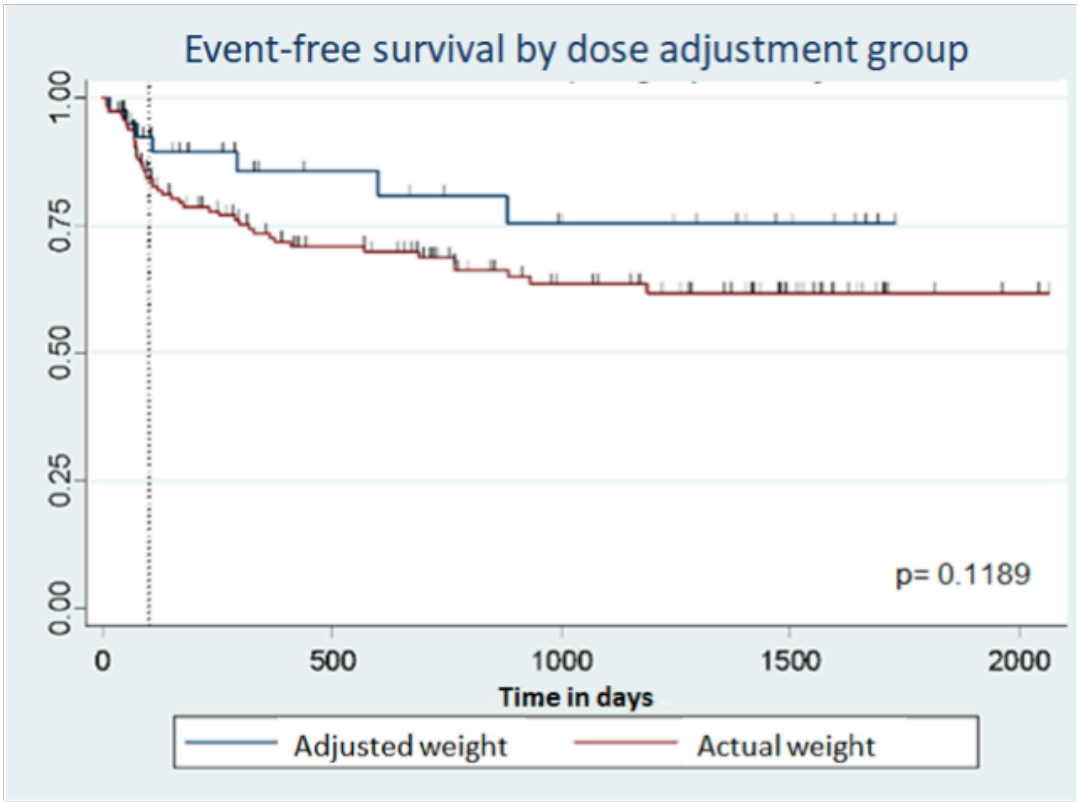
TABLE 2. Toxicity, and relapse, and disease progression and death in groups with actual weight and adjusted weight

	Adjusted weight	Real weight	Total	P
Mucositis	29 (70,7%)	109 (72,2%)	138 (71,9%)	0,8540
Nausea	32 (78,0%)	116 (76,8%)	148 (77,0%)	0,8680
Vomiting	21 (51,2%)	72 (47,7%)	93 (48,4%)	0,8160
Diarrhea	35 (85,4%)	103 (68,2%)	138 (71,9%)	0,0300
Return/disease progression D+100	2 (5,3%)	18 (12,4%)	20 (10,9%)	0,3280
Return/disease progression in 1 year	2 (4,9%)	9 (6,1%)	11 (5,8%)	0,7710
Death in 1 year	4 (9,8%)	33 (22,1%)	37 (19,5%)	0,1170

TABLE 3. Toxicity, and relapse, and disease progression and death by Body Mass Index (BMI)

	BMI < 25,00	BMI 25,00 - 29,99	BMI ≥ 30,00	Total	P
Mucositis	57 (71,2%)	50 (73,5%)	31 (70,4%)	138 (71,9%)	0,9270
Nausea	63 (78,7%)	52 (76,5%)	33 (75,0%)	148 (77,1%)	0,7660
Vomiting	39 (48,7%)	32 (47,0%)	22 (50,0%)	93 (48,4%)	0,8220
Diarrhea	55 (68,7%)	48 (70,6%)	35 (78,5%)	138 (71,9%)	0,4230
Return/disease progression D+100	12 (15,8%)	4 (6,2%)	4 (9,3%)	20 (10,9%)	0,0510
Return/disease progression in 1 year	4 (5,3%)	3 (4,4%)	4 (8,9%)	11 (5,8%)	0,5880
Death in 1 year	16 (20,5%)	15 (22,0%)	6 (13,3%)	37 (19,47%)	0,5220

FIGURE 1. Outcomes of lymphoma patients after autologous hematopoietic cell transplantation using actual weight (unadjusted) and weight adjusted to calculate chemotherapy doses. p value is shown on the panel.



HSCT PEDIATRIC

BLINATUMOMAB AND DONOR LEUKOCYTE INFUSION (DLI) AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) WITH ALTERNATIVE DONORS IN THE TREATMENT OF B-LINEAGE ACUTE LYMPHOID LEUKEMIA (ALL-B)

Gustavo Zamperlini[1,2]; Roseane Vasconcelos Gouveia[1,2,] Valéria Cortez Ginani[1,2,] Carla Maria da Costa Zanchetta Oliveira[1,2], Maria Gabriela Matos Alves Dias[1,2] , Carla Nolasco Monteiro Breviglieri[1,2,] Luciana dos Santos Domingues[1,2] , Marcia Vieira Pupim[1,2], Paola Azenha Milani Soriano[1,2], Juliana Francielli Marques[2], Claudinéia Farias Andrade[2], Francisca Vanóide Brito[2], Priscila Mendes Paiva[2], Adriana Seber[1,2]

1- Equipe Onco-TMO em Pediatria;
2- Hospital Samaritano – SP/Brazil;

Introduction: Patients with B-ALL and multiple relapses, high-risk karyotype, or presence of measurable residual disease (MRD) prior to conditioning therapy have a high risk of disease recurrence after transplantation and death. Blinatumomab, a bispecific antibody that binds healthy CD3 T lymphocytes to CD19-positive blasts, can be used to treat relapsed disease after HSCT, but the response is usually transient, and most children have a new relapse if not treated with CAR-T cell immunotherapy or if a second HSCT is not performed, despite the high-morbidity and mortality. In the first months after HSCT, when most relapses occur, patients still have an important deficit in the number and function of T lymphocytes. Thus, although the use of donor leukocyteinfusion (DLI) is not conventionally used in lymphoid diseases, it is a strategy that provides the administration of mature effector cells of the donor, capable of being activated by the blinatumomab to exert the anti-leukemic effect.

Objective: To evaluate the toxicity and response to blinatumomab and DLI administered after HSCT for treatment and prophylaxis of B-ALL recurrence after HSCT with alternative donors.

Method: Patients with hematological relapse or considered at very high risk for recurrence after transplantation (2 or more relapses pre-HSCT, positive MRD immediately prior to HSCT, mixed chimerism after HSCT) were started on blinatumomab infusions after engraftment at doses recommended to treat positive MRD (15mcg/m2/day for 28 days) at 15-day intervals. Upon resolution of blinatumomab related toxicities, at least a couple of days after the infusion was started, patients with no history of GVHD also received DLI with a starting dose of 1x10(6) CD3/kg and scaled up to 5x10(6) CD3/kg in subsequent cycles if the patient remained in remission, with no GVHD and no other toxicities. When treating hematological relapses, monthly DLI doses were increased up to 1 x 10(8) CD3/kg.

Results: Seven children received blinatumomab and serial DLIs after allogeneic HSCT to treat relapsed B-ALL after HSCT (4) or prophylactically, in the setting of very high risk of recurrence (3) Ages ranged from 1.7 to 16 years, median of 11 years. Four patients received haploidentical grafts and 3 had unrelated donor transplants (Table 1)

The number of blinatumomab cycles ranged from one to four. Patients had expected side effects, similar to pre-HSCT use: neurotoxicity (2 patients with seizures) and cytokine release syndrome (4 patients, none requiring intensive support). The number of DLI infusions ranged from zero (patient received double-cord as graft) to 5 infusions, and doses from 1x106 to 4.7x108 CD3/kg. Two patients had concomitant tyrosine kinase inhibitors due to the presence of Ph+ disease. None of the patients had acute GVHD and four had mild to moderate chronic GVHD. Two children died of negative CD19 disease and anti-CD22 treatment was not available at that time; one of them also had severe thrombotic microangiopathy. With a median follow-up of 5.2 months, 5 of the 7 children are alive in remission, 1 of the 3 who underwent unrelated HSCT and all 4 who had an haploidentical HSCT.

Conclusions: Blinatumomab associated with DLI is a strategy with a powerful graft versus leukemia effect and safe, if the team has expertise in the outpatient infusion of blinatumomab and in the management of its adverse effects. Two of the 7 children had cd19-negative disease escape, but none died from treatment toxicity.

TABLE 1. Patient Characteristics

	Age (Years)	Type of HSCT	Number of Blina Cycles	Indication	Toxicity	DLI – Number and cell dose (CD3/kg)	GVHD	Other therapies	Cause of death	Follow-up (months)
5	8	MUD	1	Hematological relapse	Cytokine release syndrome	none	No	None	TRM	1.7
1	10	Haplo	3	>2 remission; Mixed chimerism	None	1 dose - 1x106	No	None	-	4.4+
2	3	MUD	1	Hematological relapse	Seizure	1 dose - 5x106	No	None	CD19 negative relapse	4.8
3	12	Haplo	2	Mixed chimerism	Seizure, Cytokine release syndrome	2 doses - 1x106 - 5x106	Yes	None	-	5.2 +
4	1	Haplo	4	Pre-HSCT positive MRD	None	1 dose - 2x106	Yes	None	-	5.7 +
6	11	MUD	4	Hematological relapse	Cytokine release syndrome	3 doses - 1x108 - 4,.x108 - 4x108	Yes	TKI	-	70 +
7	15	Haplo	4	Hematological relapse	Cytokine release syndrome	5 doses - 1 x 104 - 1x105 - 1X106 - 3x107 - 1x108	Yes	TKI	-	84 +

+alive

HAPLOIDENTICAL STEM CELL TRANSPLANTATION WITH POST-TRANSPLANTATION CYCLOPHOSPHAMIDE IN PATIENTS WITH SEVERE COMBINED IMMUNODEFICIENCY (SCID)

Muratori RR[1], Nichele S[1,3], Loth G[1,2], Rodrigues AM[1,2], Koliski A[1], Trennepohl JP[1,3], Mosquer RATG[1], Ribeiro L[1], Peixoto CMA[2], Dumke CCK[2], Benini FML[2], Pelegrina PRD[2], Bach JLM[2], Gouvêa LMM[3], Lima ACM[1], Pasquini R[1,3], Bonfim C[1,2].

1 Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, Brazil
2 Hospital Infantil Pequeno Príncipe, Curitiba, Brazil
3 Hospital Nossa Senhora das Graças, Curitiba, Brazil

Introduction: Severe combined immunodeficiencies (SCID) may lead to early death from overwhelming infection, typically in the first year of life. Without a newborn screening program, most patients (pts) will have a delayed diagnosis and present with severe comorbidities and infections at the time of transplant. Haploidentical Cell Transplantation using post-transplantation cyclophosphamide (HAPLO-PTCY) allows immediate donor availability in these time-sensitive transplants, where any delays may result in catastrophic results.

Objective: Evaluate the outcomes of SCID pts undergoing HAPLO-PTCY at 3 pediatric HCT centers.

Method: Retrospective, longitudinal, non-randomized, observational study including all pts with SCID receiving a HAPLO-PTCY transplant. Databases and records were analyzed, and statistics performed using the EZR program.

Results: During the past 23 years, 67 pts with SCID were transplanted at our 3 HCT units and 31 (46%) received a HAPLO-PTCY between 01/2015 and 03/2021. The median age was 9,8 months (range, 1,9 to 109 months), 16% had Omenn syndrome and the most frequent phenotype was B-NK+. The majority were male (66%), malnourished (median weight 7,1 - range 2,2-20 kg), 71% had active infection at the time of transplant and only 5 had not been vaccinated with BCG. Bone marrow was the stem cell source in 95% and the father was the donor in 81%. Most regimen consisted in Busulfan+Fludarabine+ATG, and only 4pts received low-dose TBI-based conditioning. Since many were infected or had severe comorbidities at the time of the transplant, ICU transfer, need of mechanical ventilation and dialysis were frequent during the course of HCT (in 39%, 29% and 16% respectively), prolonged length of inpatient stay was also frequent, with a median of 58 days (range 21-245). Sinusoidal obstruction syndrome (SOS) was seen in 22% of cases. The cumulative incidence (CI) of neutrophil and platelet recovery were 93 and 92% respectively. At 100 days, the CI of acute GVHD grade II-IV was 26% and, at 2 years, the CI of chronic GVHD was 14%. CMV reactivation at Day-100 was 32% and only 2 pts had hemorrhagic cystitis. BCG reactivation occurred in 50% of the vaccinated pts and led to prolonged admissions. Eight pts died at a median of 19 days after HCT (range 8-308), with 5 very-early deaths (median survival of 11 days), four due to bacterial infection and one due to SOS. With a median follow-up of 25 months, 2-year survival was 73%.

Conclusions: This is one of the largest series of SCID pts receiving a HAPLO-PTCY. Although most of our pts are referred with severe infections and multiple comorbidities, the use of haploidentical donors allow immediate treatment for pts without matched donors. For better outcomes, SCID pts should be referred to specialized centers as these transplants require collaboration with the ICU group. Newborn screening programs may allow these children to be diagnosed at better clinical conditions and have superior outcomes.

HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR THE TREATMENT OF ACUTE MYELOID LEUKEMIA (AML) - EXPERIENCE WITH CONDITIONING REGIMENS ADOPTED BY THE CHILDREN'S AML STUDY GROUP (GELMAI)

Carla Nolasco Monteiro Breviglieri[1], Roseane Vasconcelos Gouveia[1], Valeria Cortez Ginani[1], Carla Maria da Costa Zanchetta Oliveira[1], Luciana dos Santos Domingues[1], Gustavo Zamperlini[1], Maria Gabriela Matos Alves[1], Paola Azenha Milani Soriano[1], Márcia Vieira Pupim[1], Juliana Francielle Marques[1], Adriana Seber[1]

1 Equipe Onco-TMO em Pediatria; Hospital Samaritano - SP

Introduction: The survival of children with AML undergoing HSCT in Brazil between 2008 and 2012 was 47% (de Melo Rodrigues, 2020). GELMAI is initiating a prospective protocol with the induction with low doses of chemotherapy to reduce early mortality. HSCT will be indicated according to cytogenetic/molecular characteristics and disease response to the first two induction cycles.

Objective: To describe the experience of our group with the HSCT strategies adopted by the GELMAI protocol.

Method: Conditioning regimens and graft-versus-host disease (GVHD) prophylaxis are described in Table 1. Survival was calculated using the Kaplan-Meier method.

Results: Between 2016 and 2021, 11 children with AML were transplanted with the GELMAI recommended conditioning regimens, 4 girls, median age of 3 years. The median time from diagnosis of AML to HSCT was 162 days, and the time between indication to actual HSCT was 60 days. The characteristics of the patients and transplants are described in Tables 2 and 3. At HSCT, 5 had refractory disease, 4 were in 2nd remission and 2 in 1st remission. Most HSCT were haploidentical (82%). Five were conditioned with FLAMSA (45%) and 5 with busulfan, fludarabine and melphalan (45%) and one with busulfan, cyclophosphamide and melphalan (9%). Six patients received bone marrow grafts (54%). All received GVHD prophylaxis as dictated by the protocol. They all engrafted. Five children (46%) received prophylactic donor lymphocyte infusion (DLI) and all had GVHD. Two of the six children without prophylactic DLI had acute GVHD. The median follow-up is 194 days. Three of the 11 children died (27%): one due to disease progression, one due to infection and one due to severe venocclusive disease; only one child relapsed (on D+102). The overall survival (OS) of the entire cohort was 70% (Figure 1). The OS of children conditioned with FLAMSA due to active disease at HSCT was 67%.

Conclusion: HSCT performed according to GELMAI protocol were well tolerated, with low transplant-related mortality and overall survival of 70%. Only one transplanted child with active disease had disease relapse. As acute GVHD, venocclusive disease and viral reactivations are expected complications, teams should be very alert to early and aggressive treatment of complications.

Keywords: AML. HSCT. Pediatric

TABLE 1. DECH conditioning and prophylaxis regimen

Disease in remission
- < 6 years, HLA-identical donors: BuCyMel - > 6 years, HLA-identical donors: BuFluMel - Haploidentical: BuFluMel and prophylactic DLI in the absence of GVHD
Active disease
- All patients: FLAMSA - Planned prophylactic DLI in the absence of GVHD
GVHD prophylaxis
- Related - CSA - Unrelated - ATG, CSA and MTX - Haploidentical – post-transplant Cyclophosphamide (D+3 and D+4), CSA and MMF

BuCyMel – Busulfan, cyclophosphamide and melphan; BuFluMel – Busulfan, fludarabine and melphalan; FLAMSA – etoposide, fludarabine and cytarabine, followed by busulfan and cyclophosphamide; CSA - cyclosporine; MMF - mycophenolate mofetil; DLI – donor leukocyte infusion; GVHD – graft versus host disease.

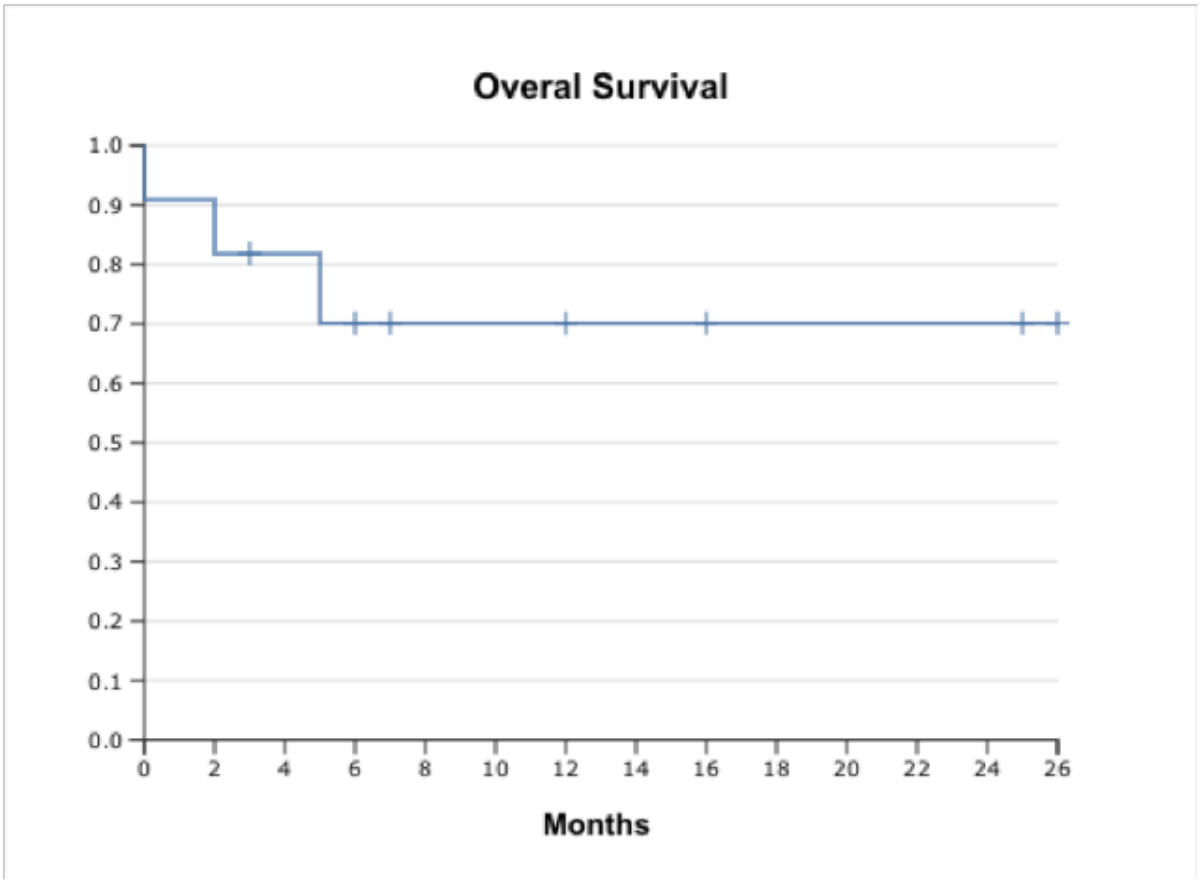
TABLE 2. Patient characteristics

Characteristics	**Median (variation)**	**Patients, n (%)**
Age	3 (1-15 years)	11
Gender Female Male		 4 (36%) 7 (64%)
Indications for HSCT High-risk cytogenetics AML secondary to MDS Relapse Refractory disease		 1 (9%) 1 (9%) 4 (36%) 5 (46%)
Disease status 1st CCR 2nd CCR Refractory disease		 2 (18%) 4 (36%) 5 (46%)

TABLE 3. Transplant characteristics

Transplants	Median (variation)	Patients, n (%)
Donor HLA-identical related Unrelated Haploidentical		 1 (9%) 1 (9%) 9 (82%)
Graft Peripheral stem cells Bone marrow		 5 (46%) 6 (54%)
Conditioning therapy BuCyMel BuFluMel FLAMSA		 1 (9%) 5 (45.5%) 5 (45.5%)
GVHD Acute Grade I-II Grade III-IV chronic * after planned DLI		 7 (63%) 4 (36%) 3 (27%) 3 (27%) 5 (71%)
Follow-up time	192 (22-772 days)	
Time from diagnosis to HSCT	162 (67-978 days)	
Time from indication to HSCT	60 (28-110 days)	

FIGURE 1. Overall survival



HIGH DOSE CHEMOTHERAPY WITH AUTOLOGOUS STEM CELL TRANSPLANTATION USING THIOTEPA IN EXTRAOCULAR RETINOBLASTOMAS - BRAZILIAN PEDIATRIC CENTER EXPERIENCE.

Renata Fittipaldi Da Costa Guimarães[1]; Karoline Helena Silva Da Silva[1]; Cintia Monteiro Lustosa[1]; Adriane Da Silva Santos Ibanez[1]; Jakeline Palmezano Crispim De S. Bufoni[1]; Virginio Climaco Araujo Fernandes Junior[1]; Laís Lima Quintino[1]; Patrícia Shimoda Ikeuti[1]; Carla Renata Pacheco Donato Macedo[1]; Luiz Fernando Teixeira[1]; Olga Margareth Wanderley De Oliveira Félix[1]; Victor Gottardello Zecchin[2].

Guimarães, RFC; Silva, KHS; Lustosa, CM; Ibanez, A.S.S; Bufoni, JPCS; Fernandes Junior, V.C.A;; Quintino, LL; Ikeuti, OS; Felix, O. M. W. O;

1. Instituto de Oncologia Pediátrica - IOP/GRAACC/Unifesp, São Paulo - SP - Brasil; 2. A Beneficiência Portuguesa de São Paulo, São Paulo - SP - Brasil.

Introduction: Retinoblastoma (RB) is the most frequent intraocular malignant tumor in children. While intraocular RB has excellent survival rate, extraocular RB has a worse prognosis. Autologous cell transplantation (HSCT) using thiotepa improves the survival of patients with advanced disease specially stage 4 and trilateral.

OBJECTIVE: Describe autologous HSCT using thiotepa performed in pediatric patients with extraocular Retinoblastoma from March 2005 to May 2021.

Material and Methods: Retrospective study of 33 patients submitted to autologous HSCT for RB in a single pediatric center. Peripheral stem cell (CTP) mobilization was performed with granulokine, followed by leukaphereses. Conditioning used thiotepa, carboplatin and etoposide. Infectious prophylaxis used sulfamethoxazole and trimethoprim, acyclovir and fluconazole and hepatic veno-occlusive prophylaxis used ursodeoxycholic acid. Neutrophil grafting was considered the 1st day of 3 days with N>500 and platelet grafting, the 7th day without platelet transfusion > 20,000.

Results: Age of patients varied between 1-18 years (median 4 years), 60% female and 40% male. Follow-up ranged from 48 to 4699 days (mean 993). Of the patients with stage 4 RB (22), 17 were in 1st remission (Rem) and 5 in 2nd Rem. 6 patients with trilateral disease, all 1st Rem. Four patients were relapsed (previous intra-ocular),3 in 2nd Rem and 1 in 3rd Rem. Eight had had CSF positive for neoplastic cells and 1 had active disease (CSF positive). Regarding the source of cells, 32 received CTP and 1 bone marrow due to mobilization failure. Regarding cellularity, the mean CD34 infused was 5.95x106/kg (min 2.2 and max 9.43). The mean time was 12 days for neutrophilic engrafting and 21 days for platelet engrafting. All evolved with grade 4 hematological toxicity, 3 with septic shock,87.8% had grade II-III mucositis requiring morphine, 75% required enteral diet and 18% parenteral nutrition. 33% required ICU. During the analysis period, seventeen patients were alive (14 in 1st Rem, including 5 trilaterals, and 3 in 2nd Rem), among them 2 with positive CSF. The main cause of death was recurrence (62,5% - 6 in 1st Rem, 3 in 2nd Rem, 1 3rd Rem), followed by MAT (9%, all by septic shock),1 head trauma (fall at home, D+227); 1 progression of active disease. OS in 2 years 66% for all groups, being RB 4 76%; Trilateral 67%; Positive CSF 33% (p0.21). DFS in 2 years 64% for all groups, being Trilateral 75%; RB 70%; Positive CSF 33% (p0.19).

Conclusion: Autologous HSCT containing thiotepa plays a significant role in the treatment of extraocular Retinoblastoma. Toxicity profile requires specialized team. Patients in 1st Rem and trilaterals seem to have better results. The involvement of the CNS continues with a worse prognosis and requires further studies to establish the best treatment approach.

Keywords: retinoblastoma; thiotepa; autologous stem cell transplant; pediatrics

IMPACT OF KIRMISMATCH VERSUS KIRMATCH DONOR USE IN PATIENTS WITH ACUTE LEUKEMIA UNDERGOING HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION

Cintia Monteiro Lustosa[1]; Adriane da Silva Santos Ibanez[1]; Jakeline Palmezano Crispim De S. Bufoni[1]; Virginio Climaco Araujo Fernandes Junior[1]; Karoline Helena Silva da Silva[1]; Laís Lima Quintino[1]; Patrícia Shimoda Ikeuti[1]; Olga Margareth Wanderley De Oliveira Félix[1]; Cristiane Menezes Vitoria Alferi[1]; Victor Zecchin[2;] Renata Fittipaldi da Costa Guimarães[1].

Lustosa, CM; Ibanez, A.S.S; Bufoni, JPCS; Fernandes Junior, V.C.A; Silva, KHS; Quintino, LL; Ikeuti, OS; Felix, O. M. W. O; Alferi, C.M.V; Zecchin V; Guimarães, RFC

1. Instituto De Oncologia Pediátrica Iop/Graacc/Unifesp, Sao Paulo - SP - Brasil; 2. A Beneficência Portuguesa de São Paulo, São Paulo - SP - Brasil. Instituto De Oncologia Pediátrica IOP/GRAACC/Unifesp – São Paulo, Brasil

Introduction: In patients with leukemia, relapse after allogeneic hematopoietic stem cell transplantation (HSCT) is still one of the main causes of mortality after HSCT. Despite attempts to promote alloreactivity of donor T cells, they are limited due to their ability to induce GVHD. Thus, donor choice may be promising, seeking those with killer immunoglobulin-like receptors (KIR) incompatibility to potentiate the effect of the graft against leukemia.

Objective: To describe the experience and compare the results obtained in patients with acute lymphoid leukemia (ALL) and acute myeloid leukemia (AML) undergoing Haploidentical HSCT using kirmismatch (G1) and Kir-match (G2) donors.

Methods: Retrospective cohort study of patients undergoing haplo-HSCT in a pediatric center.

Results: From January 2019 to June 2021, 44 HSCT Haploidentical –7% were being submitted to the second HSCT due to recurrence. 59% were male and with a median age of 9 years. 64% were LLA and 36% AML. Most patients were in CR2 (52%), CR1 (20%), active/refractory disease (16%) and CR3 (12%). All received myeloablative conditioning. As for the donors, 68% were male, with a median of 36 years. As a source, 64% used peripheral blood (PB) and 36% bone marrow (MO). G1 corresponded to 52% and G2 48%. In both groups, did not identify any primary and secondary graft failure. There was no statistical difference for the occurrence of GVHD between ALL-G1(79%) and ALL-G2 (71%), nor for LMA-G1 (75%) and LMA-G2 (57%), with a predominance of GVHD grade I for all groups. CGVHD was more frequent in both groups G1 LLA (43%) and for LMA (63%). As for the severity of cGVHD, there was a predominance of mild for all, except for LMA-G2 (67% moderate). 79% of ALL patients are alive in G1 and G2, p=1.00. While for LMA, 67% are alive in G1 and 87% in G2, p=0.58. There was less relapse of AML patients-G1 (13%) compared to AML-G2 (29%), which did not happen in the LLA (p = 0.56 and p = 1.00, respectively). Analyzing the factors that may contribute to less recurrence, use of PB (p=0.03) and presence of GVHDc (p=0.01) for the LMA-G1 group, which was not observed in the other groups. Recurrence was the main cause of death in ALL-G1 (100%), ALL-G2 (67%) and AML-G2 (100%). Only in AML-G1 that the causes occurred in the same proportion (33.3%): TRM, recurrence and infection. Among the two (4%) cases of TRM, one (50%) was undergoing the 2nd HSCT and both had active disease. On D+365 the OS was 78% in G1 and 80% in G2 (p=0.96) and the EFS was 69% in G1 and 62% in G2 (p=0.70). However, it is noteworthy that patients with AML had better long-term EFS when using Kir-mismatch donors. Conclusion: KIR alloreactivity seems to be more relevant for patients with AML, corroborating literature data. The use of PB and the development of cGVHD seem to contribute to lower relapse rates in this same group (AML-G1).

Keywords: Hematopoietic Stem Cell Transplantation. Haploidentical Transplantation. Acute Lymphoid Leukemia. Acute Myeloid Leukemia. Natural Killing Cells. Pediatrics.

OUTCOMES OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CHILDREN WITH ACUTE LEUKEMIA: SINGLE CENTER EXPERIENCE

Ana Maria Rahal Guaragna Machado[1], José Antonio da Silva Feitosa[1], Bruna Paccola Blanco[1], Tomas Marzagão Barbuto[1], Ana Beatriz Bechara Mafra[1], Julia Lopes Garcia[1], Alessandra Araujo Gomes[1], Lilian Maria Cristofani[1], Vicente Odone-Filho[1], Juliana Folloni Fernandes[1]

1. ITACI - Instituto de Tratamento do Câncer Infantil – Instituto da Criança – Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo

Introduction: Despite the increased availability of new drugs and immunotherapies, allogeneic hematopoietic stem cell transplantation (HSCT) still remains the stablished treatment for pediatric patients with high risk, relapsed or refractory acute leukemias. Objective: To analyze the outcomes of HSCT for pediatric patients with ALL and AML transplanted in a pediatric center.

Methods: Retrospective chart analysis.

Results: From May 2010 to April 2021, 107 consecutive children with ALL (n=59) and AML (n=48) received a first allogeneic HSCT in our institution. Median age was 9 years (10m–24y) and 58% were male. Median follow-up for survivors was 4 years. Fifty-nine patients had ALL, most (n=33) were transplanted in 2nd complete remission (CR) and without measurable minimal residual disease (MRD) by flow cytometry (n=49). Twenty-three patients were transplanted with matched sibling donors (MSD), 24 with matched unrelated donors (MUD) and 12 with haploidentical donors (Haplo). Cell source was BM (n=49), PBSC (n=5) or cord blood (n=5). Conditioning regimen was mostly myeloablative TBI-based (n=45), being either combined with cyclophosphamide (n=16), high dose etoposide(n=16) or fludarabine(n=13). Nineteen patients with MUD received ATG. Fourty-eight patients had AML, most in second CR(n= 21) and without MRD (n=31). Fourteen patients were transplanted with MSD, 27 MUD and 7 Haplo. Cell source was BM(n=35), PBSC(n=4) or CB(n=9). Most patients(n=23) received myeloablative busulfan based conditioning regimens and 21 patients with MUD donors received ATG. All patients received GVHD prophylaxis with cyclosporine A, associated with methotrexate, mycophenolate or steroids. All patients with Haplo donors received post-transplant cyclophosphamide. From the total 107 patients, 99 engrafted in a median of 19 days (11-39). All patients that did not engraft died early with infection (n=7) or toxicity (n=1). Fourty patients developed grades II-IV GVHD, 27 with ALL and 13 with AML. Twenty-seven patients had disease relapse. All 9 patients with AML that relapsed died from disease. From the 18 patients with ALL relapse, three are alive after chemotherapy treatment. Only 1 patient with relapsed ALL received a second transplant and died of infection. Four-year OS was 54+/-5% for the whole cohort, being 56+/-7% for ALL and 49+/-7% for AML. In an univariate analysis there was no difference in OS considering diagnosis, type of donor, cell source or conditioning regimen. Event-free survival (EFS) was 49+/-5%, 51+/-7% for ALL and 45+/-7% for AML. Fifty patients died (ALL, n=25; AML, n=25), mostly from disease relapse (n=23), infection (n=12) or GVHD (n=11).

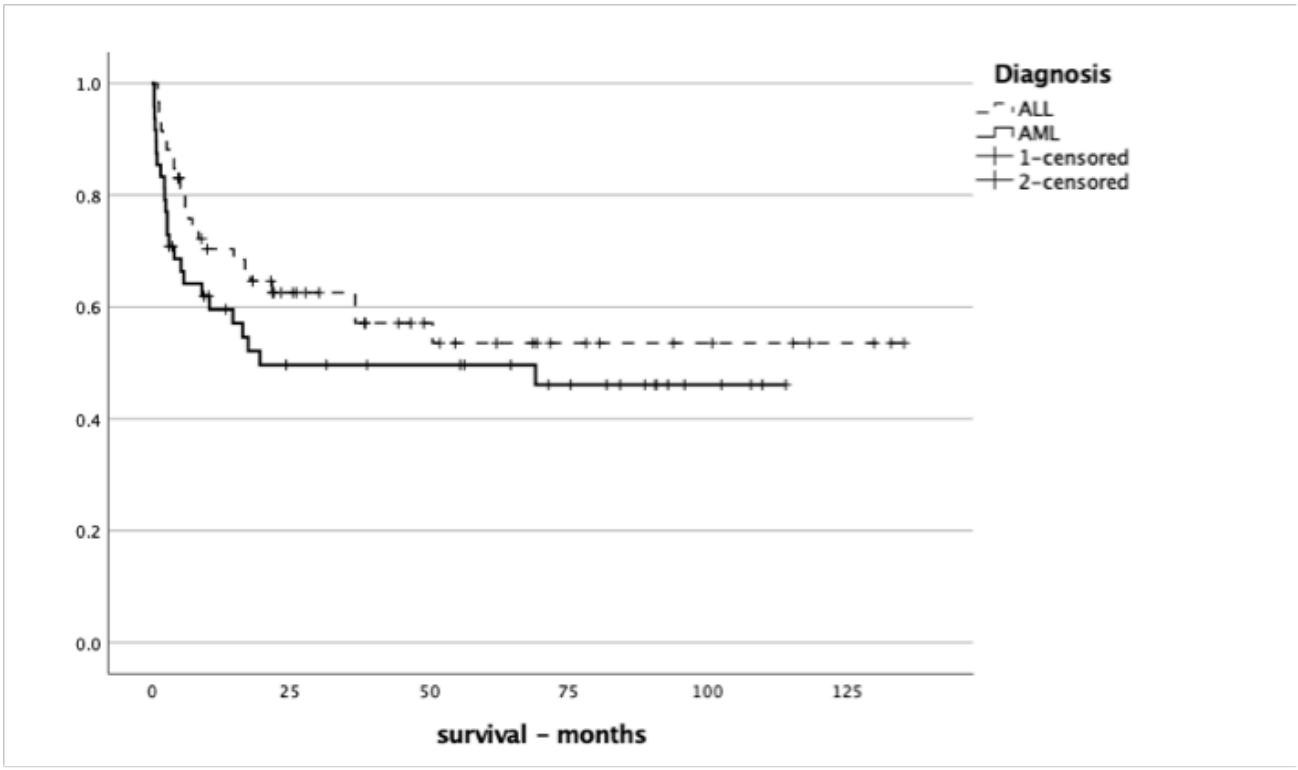
Conclusion: With an EFS of 49%, HSCT remains an important alternative for pediatric high risk, refractory or relapsed acute leukemia. A larger number of patients treated and multicentric prospective studies may be necessary to determine best treatment strategies concerning donor type, cell source or conditioning regimen.

TABLE 1. Disease characteristics prior to transplant

		ALL (n=59)	AML (n=48)
Disease status prior to transplant			
	First CR	10	14
	Second CR	33	21
	Third or more CR	12	10
	Active disease	4	3
MRD (flow cytometry)			
	negative	49	31
	0,01 – 0,1%	4	-
	0,1 – 1%	3	13
	> 1%	3	4

Abbreviations: CR, complete remission; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; MRD, minimal residual disease.

FIGURE 1. 4-year overall survival by diagnosis



PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) ACTIVITY BETWEEN 2008 AND 2019 IN BRAZIL: A REPORT OF THE BRAZILIAN SOCIETY OF BONE MARROW TRANSPLANT AND CELLULAR THERAPY (SBTMO)

Adriana Seber; Alessandra Araujo Gomes; Liane Esteves Daudt; Juliana Folloni Fernandes; Luiz Guilherme Darrigo Junior; Carmem Bonfim.

SBTMO - Grupo de TMO Pediatrico SBTMO/SOBOPE, Rio de Janeiro - RJ - Brasil.

HSCT is performed in Brazil since the 70's, most of them in public centers. Transplant numbers are regularly reported by most centers to the Brazilian Transplant Registry/ Brazilian Solid Organ Association (ABTO/RBT), Latin American Bone Marrow Transplant Group/ Worldwide Network for Blood and Marrow Transplantation (LABMT/WBMT), but transplant outcomes are not available in our country.

The objective of this work is to understand HSCT activity and outcomes of Brazilian children.

Methods: The SBTMO has developed the initiative to collaborate with the Center for International Blood and Marrow Transplant Research (CIBMTR) to receive back deidentified aggregate nationwide data reported by Brazilian transplant centers. This was approved by our national central IRB (Conep CAAE: 65575317.5.1001.0071) in 2019 as a research project including data from 2008 through 2027. This is the first report of the Brazilian Pediatric Hematopoietic Stem Cell Transplant activity prepared by the SBTMO Data Managers Working Group with the data reported to the CIBMTR and returned to the country as an enhanced Data Back to Center file.

Results: Between 2008 and 2019, 16 of the 19 institutions reporting to the CIBMTR also reported pediatric transplants. A total of 1,929 transplants were reported in children younger than 18 years of age and, different from the adult experience, most of them are allogeneic transplants (Figure 1). Within the past three years, the number of allogeneic transplants from unrelated and mismatched donors have increased and are now performed more often than transplants from matched sibling donors. Unrelated cord blood grafts are rarely used in the country (Figure 2). Marrow is the preferred graft source for all allogeneic transplants (Figure 3). Acute leukemias and severe aplastic anemia are the most common indications for HSCT (Figure 4). Infections cause 33% to 57% of the deaths within 100 days post HSCT (Figure 5). Overall survival after HSCT for acute leukemias is 37-62% without significant difference among different donor types (Figure 6). Pediatric myelodysplastic syndrome and chronic myelogenous leukemia have overall survival over 80% (Figure 7). Severe aplastic anemia is the most common non-malignant HSCT indication and the results with matched related and unrelated transplants are excellent, > 85% survival (Figure 8).

In conclusion, this is the first report on transplant outcomes in Brazilian children. The collaboration with the CIBMTR may be a feasible way for Latin American countries to know their transplant outcomes using a mature registry structure with several tools already in place to enhance the collaboration.

FIGURE 1

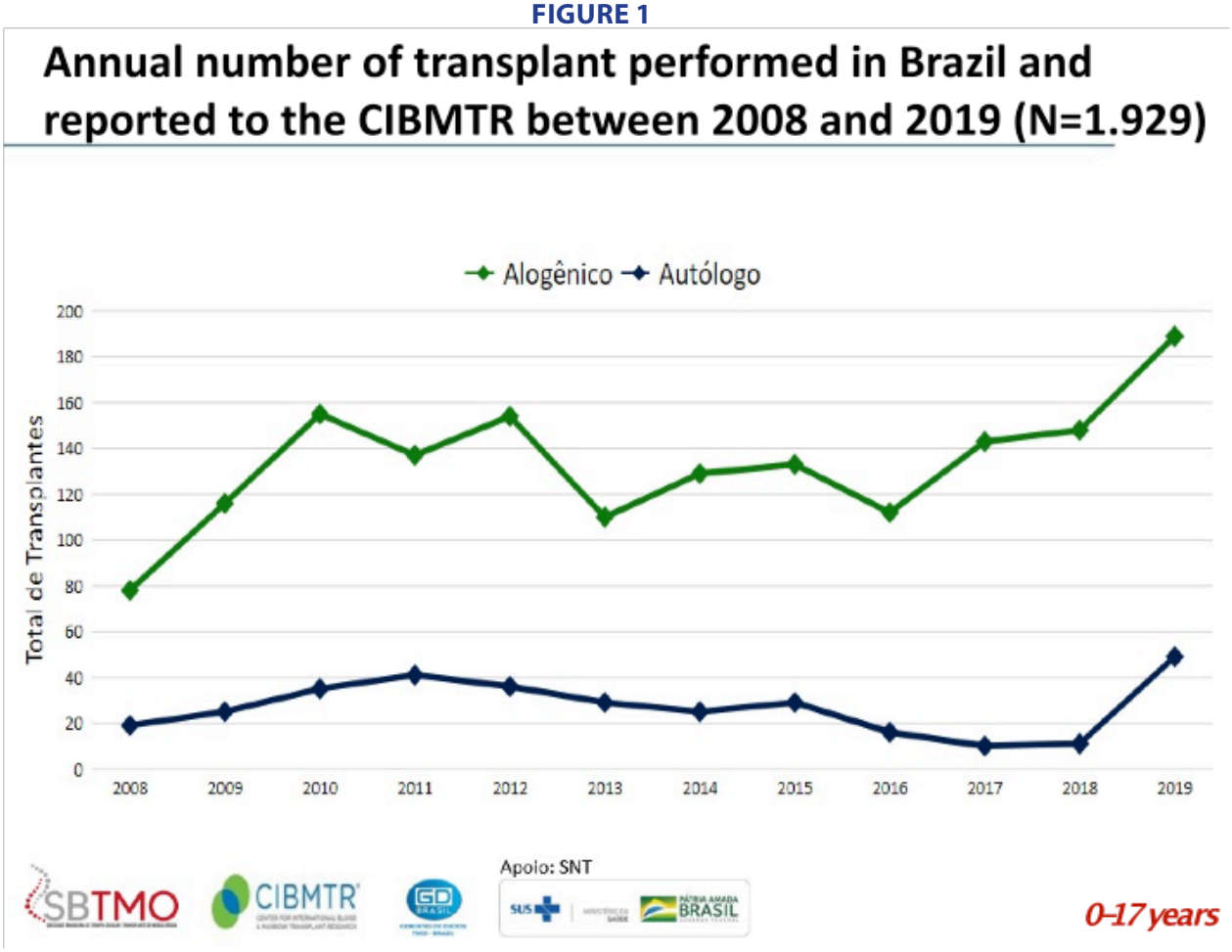
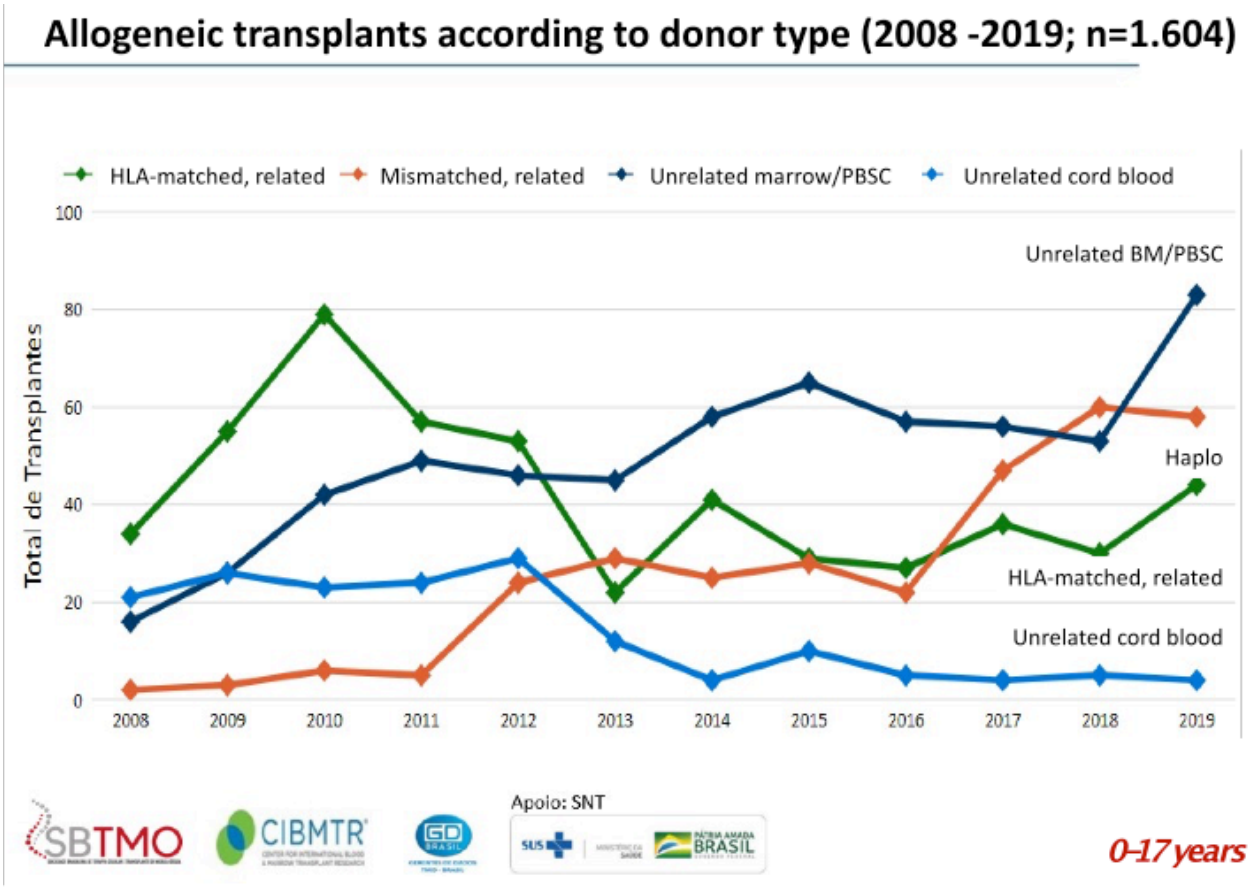


FIGURE 2



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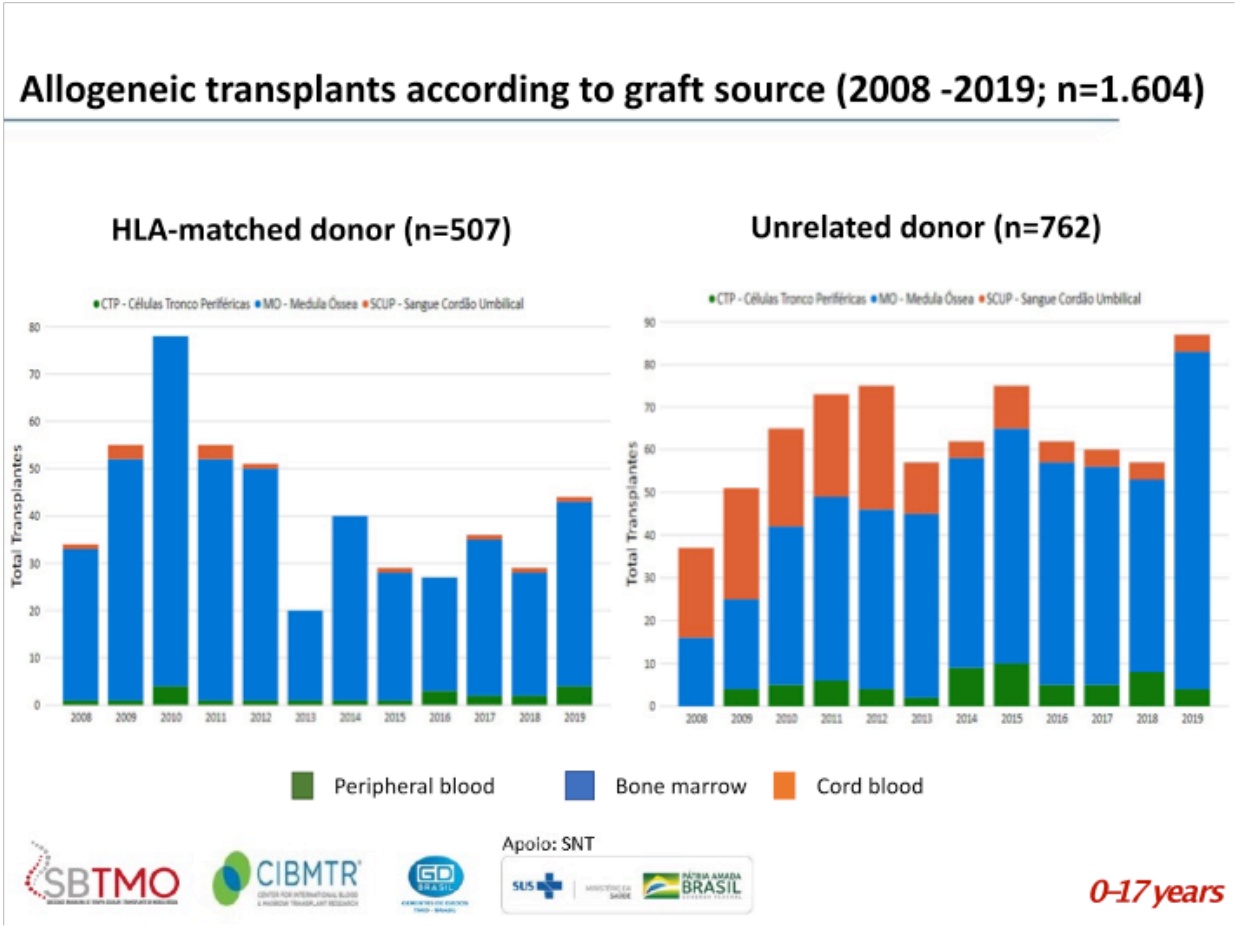

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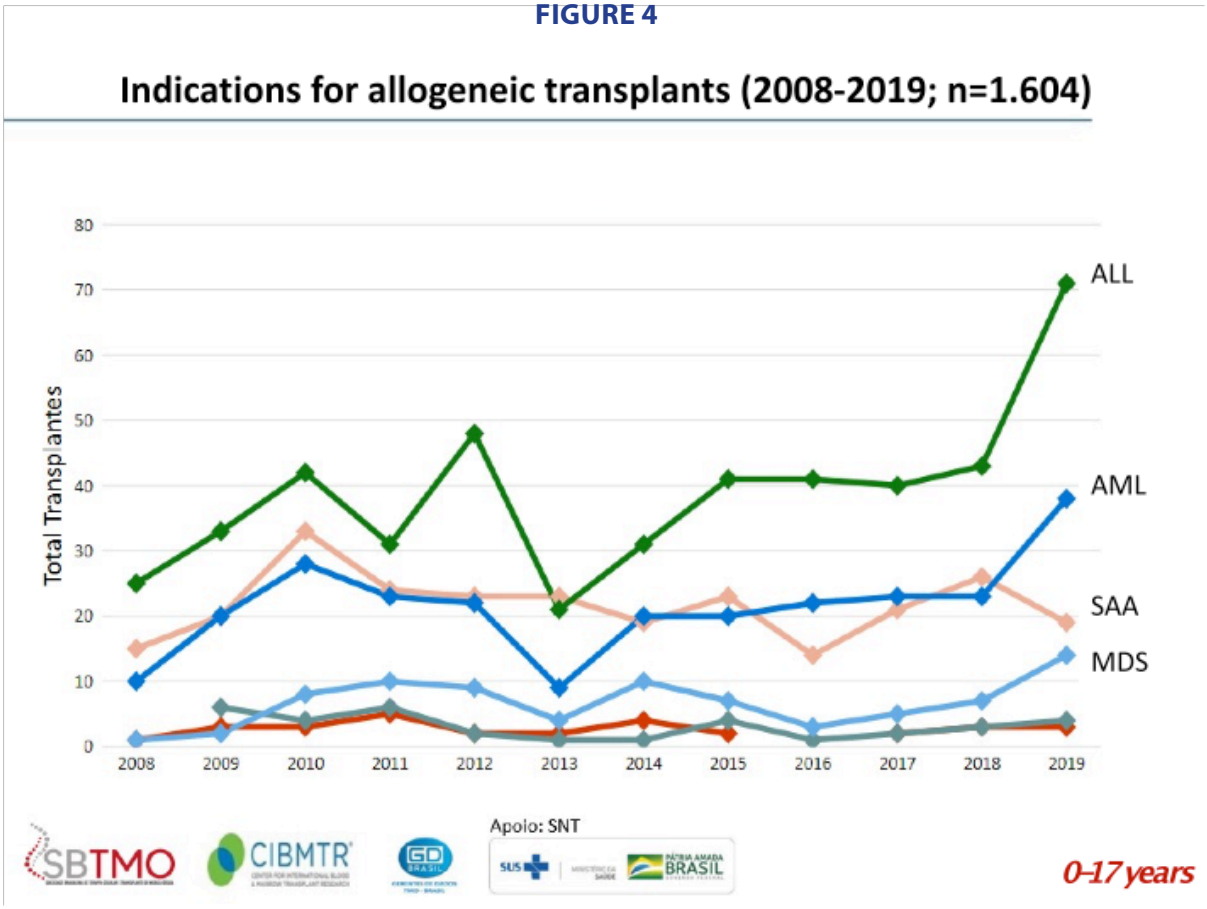

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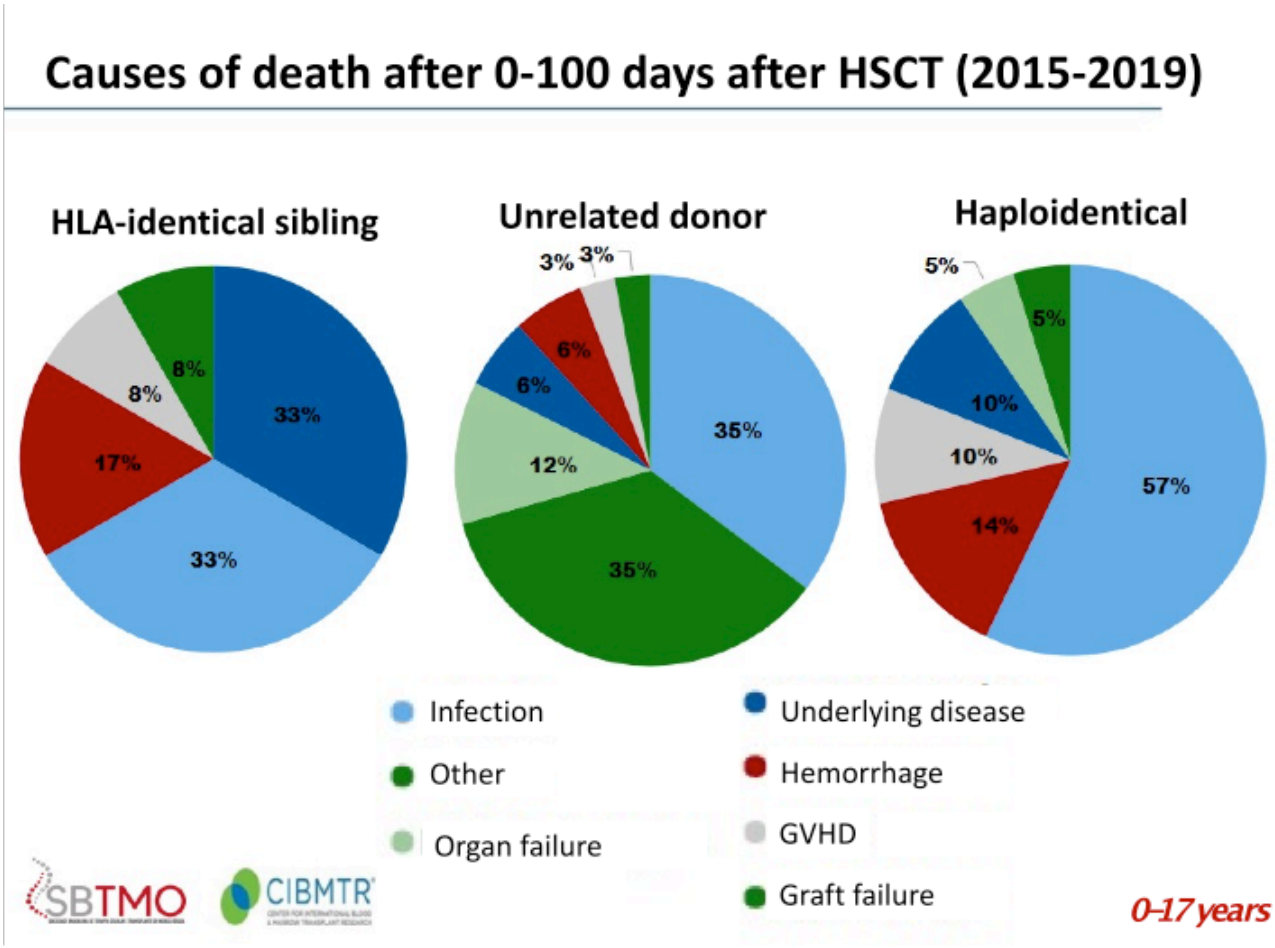

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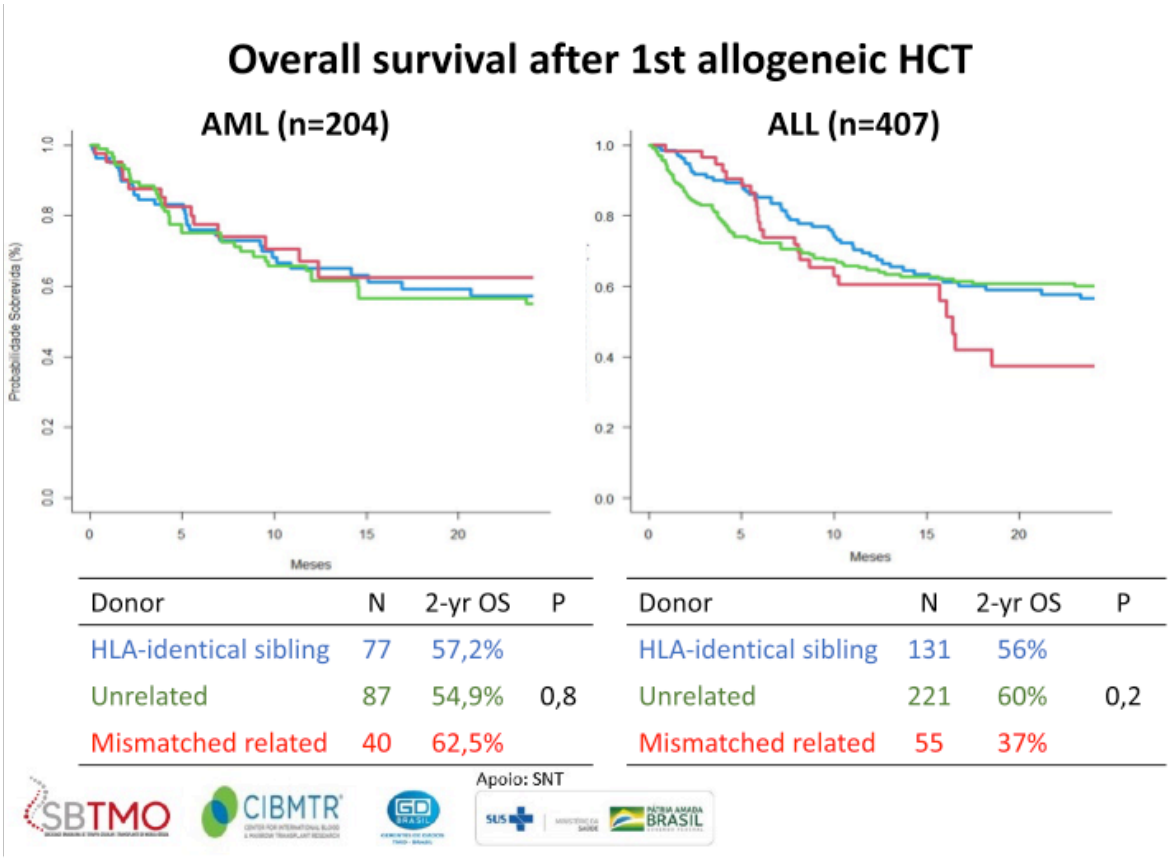


FIGURE 7

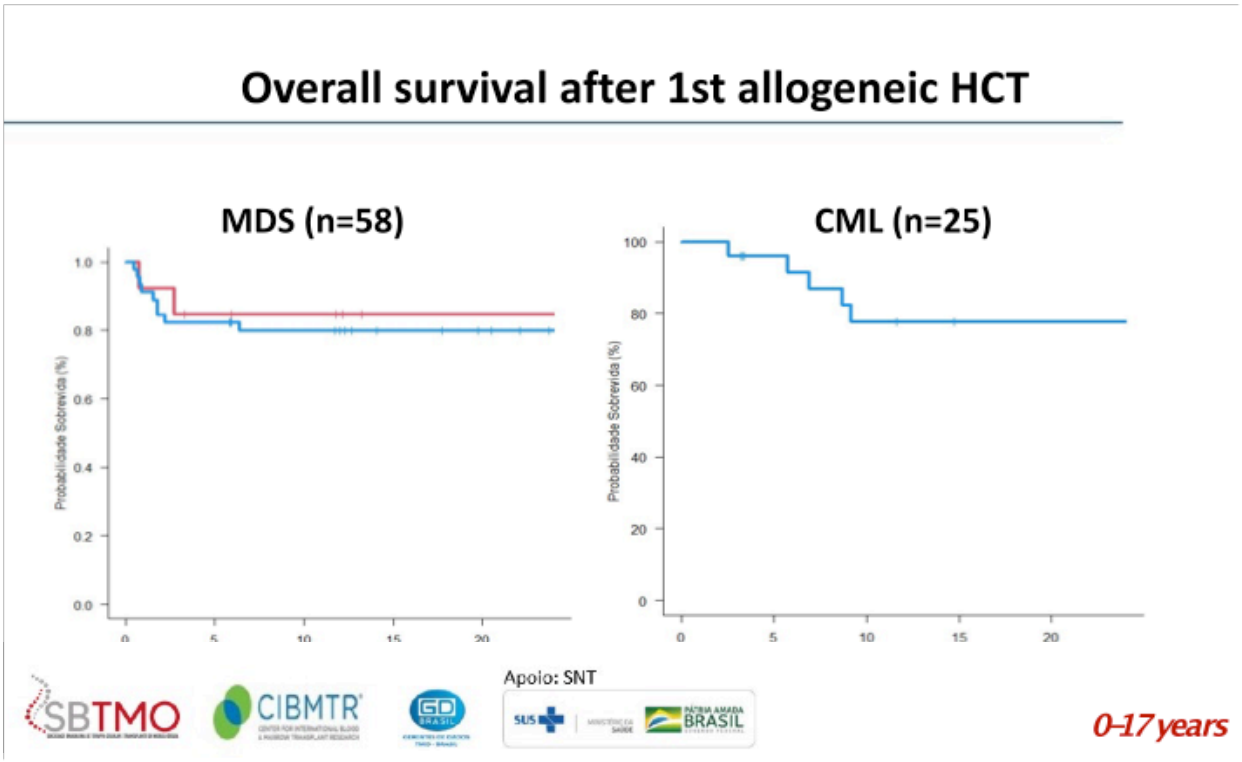
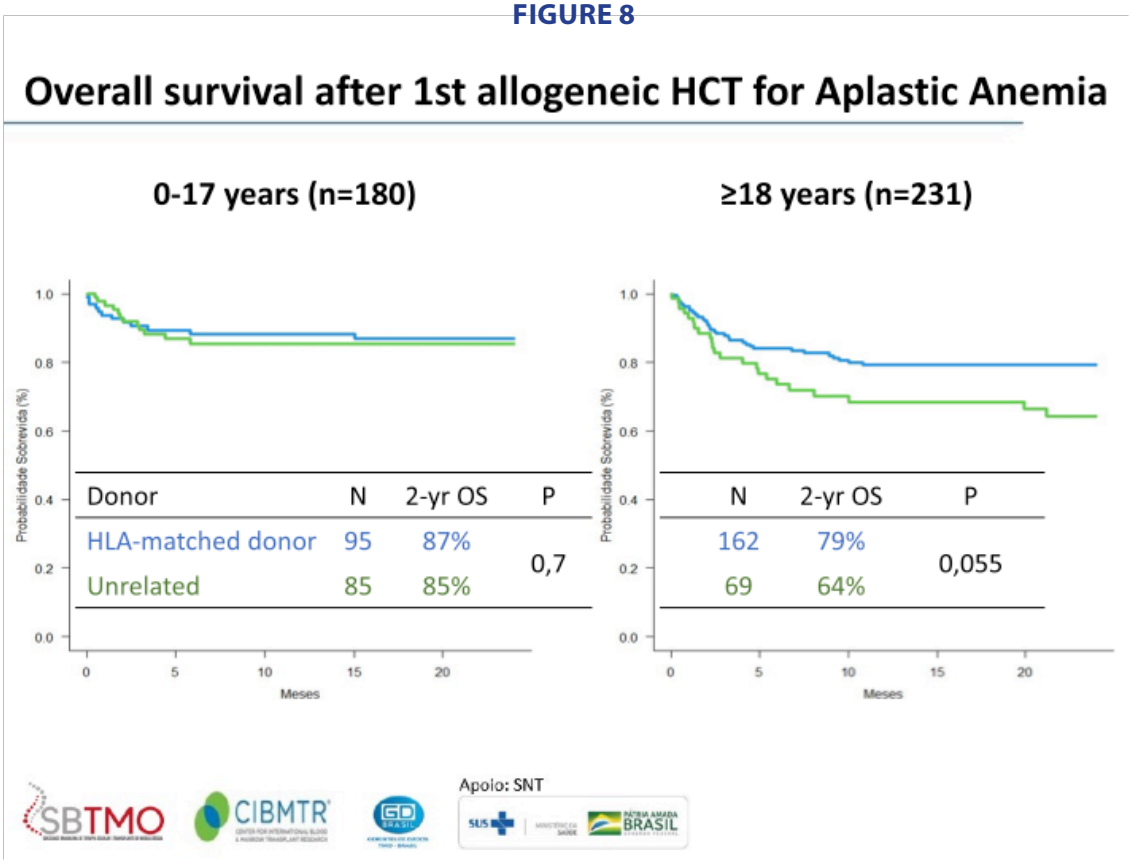


FIGURE 8



We would like to acknowledge Dr Nelson Hamerschlak, principal investigator of the National protocol, Dr. Marcelo Pasquini, for his help with the collaboration between CIBMTR and SBTMO, the Brazilian institutions reporting their data, the Data Manager Working Group and the Pediatric Working Group of the SBTMO and SOBOPE.

RELAPSE AFTER PEDIATRIC HEMATOPOIETIC CELL TRANSPLANTATION FOR CHILDREN WITH ACUTE LEUKEMIAS: A SINGLE CENTER EXPERIENCE IN 88 PATIENTS

Polliany Roberta Dorini Pelegrina[1], Cilmara Cristina Kuwahara Dumke[1], Gisele Loth[1], Fernanda Moreira de Lara Benini[1], Adriana Mello Rodrigues[1], Carolina Martins de Almeida Peixoto[1] (PEIXOTO,CMA), Juliana Luiza de Mello Bach[1] (BACH, JLM), Alberto Cardoso Martins Lima [2] (LIMA, ACM), Carmem Bonfim[1] (BONFIM,C)

1 Hospital Pequeno Príncipe
2 Immunogenetics Laboratory, Complexo Hospital de Clínicas, Federal University of Paraná

Introduction: Acute leukemias are the most common childhood cancer, and acute lymphoblastic leukemia(ALL) corresponds to 75% of cases. Hematopoietic cell transplantation(HCT) is indicated for selected cases, however relapse remains the major cause of treatment failure and death after this procedure.

Method: Retrospective, longitudinal, non-randomized, observational study. Database and medical records were analyzed, and statistics performed using the EZR program.

Results: 88 patients(pts) were transplanted from April/2013 to December/2019 in a single pediatric HCT unit. The median age was 8.1 years (0.2-17 years) and 67% were male. Pts had ALL (n=63; 82% B-ALL); acute myeloid leukemia (n=19) and biphenotypic leukemia(n=6) and were transplanted in remission (CR1=46; CR2=34; CR3+:7) and one in refractory disease. 88% had negative mensurable residual disease (MRD) pre-HCT and 7pts with ALL received blinatumomab before HCT. Bone marrow was the stem cell source in 69%, peripheral blood in 30% and one pt received a related cord blood HCT. Donors were related (n=24); unrelated (n=27) and haploidentical (n=37). Myeloablative conditioning was given to all pts and the most common regimen used was Cyclophosphamide + TBI (43%). The majority received cyclosporine+methotrexate (55%) or PTCY+ MMF+cyclosporine(41%) for GVHD prophylaxis. The median time to neutrophil and platelet engraftment was 20 days and 23 days, respectively. 22 pts relapsed at a median of 98 days after HCT (range: 20-800) and the 1-year cumulative incidence (CI) of relapse was 21%. According to the time of relapse after HCT, patients were treated with immunosuppression withdrawal, chemotherapy, immunotherapy, donor lymphocyte infusion or a 2 nd HCT. 16 pts had ALL, five received a 2nd HCT, three are alive, one in palliative care. Six pts had AML, one received a 2nd HCT and is alive, in remission. 11/22 pts did not receive a 2nd HCT and only one is alive in palliative care. Altogether 28 pts died at a median of 140 days after transplant (range: 15—1778) and relapse was the cause of death in 61%. With a median follow-up of 25 months, the 2-year overall survival for ALL was 69.6% (0.566-0.794) and for AML 63.2%(0.379-0.804). The 2-year event-free survival (without relapse or death) was 70% (0.596-0.787). In multivariate analysis, positive pre-HCT MRD (HR 2,97 p=0.009) and pts in CR2 (HR 5,30 p=0.003) or more advanced disease (HR 6,33 p=0.03) were risk factors (RF) for relapse, while the use of unrelated (HR 0.21 p=0.013) or haploidentical donors(HR 0.37 p=0.051) were protective for this complication.

Conclusions: In this single center retrospective study, relapse after HCT is associated with a dismal prognosis. As expected, we observed a higher relapse for those transplanted with a positive MRD and advanced disease. Although the numbers are small, this study highlighs the importance of identifying RF for relapse in order to guide strategies to prevent this complication.

SEVERE AND VERY SEVERE VOD AFTER HSCT: ANALYSIS OF 21 CASES IN PEDIATRIC PATIENTS.

Polliany Roberta Dorini Pelegrina[1]; Juliana Luiza de Mello Bach[1]; Adriana Mello Rodrigues[2]; Gisele Loth[3]; Cilmara Cristina Kuwahara Dumke[1]; Carolina Martins de Almeida Peixoto[1]; Fernanda Moreira de Lara Benini[1]; Rafaella Ribas Muratori[4]; Samantha Nichele[5]; Lara Maria Miranda de Gouvêa[6]; Lisandro Ribeiro[4]; Joanna Paula Trennepohl[4]; Paulo Ramos David João[1]; Mariana Faucz Munhos da Cunha[3]; Adriana Koliski[4]; Rebeca Amelia Toassa Gomes Mosquer[4]; Carmem Bonfim[7].

1. Hospital Pequeno Príncipe, Curitiba - PR - Brasil; 2. Hospital Pequeno Príncipe, Hospital De Clínicas - UFPR Curitiba - PR - Brasil; 3. Hospital Pequeno Príncipe, Hospital De Clínicas - UFPR Curitiba - PR - Brasil; 4. Hospital de Clínicas - UFPR, Curitiba - PR - Brasil; 5. Hospital Nossa Senhora das Graças, Hospital de Clínicas - UFPR Curitiba - PR - Brasil; 6. Hospital Nossa Senhora das Graças, Curitiba - PR - Brasil; 7. Hospital Pequeno Príncipe, Hospital Nossa Senhora das Graças Curitiba - PR - Brasil.

Introduction: Hepatic veno-occlusive disease(VOD) is a serious post-transplant complication with high morbi- mortality rates. The incidence of VOD is variable and pediatric patients have a higher risk of developing this disease. Although many risk factors have been described, severe and very severe VOD(s/vsVOD) may be unpredictable and associated with multiple organ failure and death.

Objective: Describe the cases of s/vsVOD in a cohort of pediatric patients(pts) undergoing hematopoietic cell transplantation(HCT) in three pediatric centers.

Method: Quantitative, cross-sectional study analyzing the medical records of pediatric pts who underwent HCT between 2018 and Jun/2021 and developed severe or very severe VOD.

Results: 378 transplants were performed during this period (allogeneic 90% and autologous 10%) and 21 pts were diagnosed with s/vsVOD according to criteria published by Corbacioglu(BMT,2017). The median age was 1.06years (3months–16.8years) and 52% were male. The diagnosis of primary immunodeficiencies(PID) was the most prevalent (SCID n=7;XIAP n=2; Chediaki-Higashi Syndrome n=1;Wiskott-Aldrich Syndrome n=1;HLH n=1), followed by malignant diseases (ALL n=4;NHL n=1;Neuroblastoma n=1), Sickle cell anemia n=1, Osteopetrosis n=1 and Amegakaryocytic purpura n=1. Donors were haploidentical(n=13), unrelated(n=6) or matched related (n=1). One patient received an autologous HCT. Stem cell source was bone marrow in 81% and all preparatory regimens were myeloablative (Busufan based:18 and TBI based:3). The first described symptom was weight gain(n=20), with a median onset on 16days(9-33). Regarding the severity criteria, all pts had weight gain, refractory thrombocytopenia and ascites. Increased bilirubin was present in 17 pts (maximum level of 12.9mg/dL and median of 3.84mg/dL) and 7 had coagulopathy, 14 pts required dialysis and intensive care. All pts were treated with supportive care, blood transfusions, fluid restriction and diuretics. Ten pts received corticosteroid pulse therapy (500mg/m2 12/12 hours for 3 days) and 5 are alive. Six pts received defibrotide associated with pulse therapy, and 2 received only defibrotide (5 are alive). Three pts received only supportive care, and all are alive and well. Eight pts died and in 7 VOD was the major cause of death. 13 pts are alive at a median of 1 year after HCT, without VOD recurrence. The incidence of s/vsVOD for the whole cohort was 6% but for pts with PID it was 16%.

Conclusion: Severe and very severe VOD is a serious post-HCT complication and clinical management remains challenging, especially for small babies transplanted for PID. Early detection or prediction of s/vsVOD could identify pts who could benefit from prophylactic measures and/or early treatment. It is essential to have an intensive care unit with experience in VOD to improve outcomes after this complication. Defibrotide, the only drug proved to treat this complication is not yet available for pts in the Brazilian public health system.

INFECTIOUS COMPLICATIONS

INFECTIVE ENDOCARDITIS INCIDENCE IN THE FIRST 100 DAYS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

Guilherme Fekete Chaim[1], Jéssica Fernandes Ramos[1,2], Lívia Caroline Mariano[1] e Vanderson Rocha[1,3,4]

1. Service of Hematology, Transfusion and Cell Therapy, Faculty of Medicine University of Sao Paulo, Sao Paulo, Brazil
2. Division of Infectious Diseases, Hospital das Clinicas, Faculty of Medicine University of Sao Paulo, Sao Paulo, Brazil.
3. Pro-Sangue Foundation Blood Donation Center, Sao Paulo, Brazil
4. Department of Hematology, Churchill Hospital, University of Oxford, Oxford, UK

Introduction: Patients undergoing HSCT are at high risk for infectious complications. Bloodstream infection (BSI) is one of the most common, with an incidence varying between 20 and 40% and Gram-positive bacteria accounting for approximately 40% of episodes. Despite so many episodes of bacteremia and the presence of long-term catheters, infective endocarditis (IE) seems to have a low incidence in this population, with few data in the literature.

Objectives: To determine the incidence of IE in patients undergoing HSCT, as well as to describe the incidence of BSI, identifying the most frequent pathogens associated with BSI and IE and their influence on early mortality (day+14). in a tertiary teaching hospital in Brazil

Methods: Retrospective, observational cohort study of all patients over 18 years of age transplanted in the period between January 1, 2014, and December 31, 2019, with a minimum follow-up until D+100, through analysis of institutional electronic medical records. Estimation of IE incidence and overall survival analyzes were calculated using the Kaplan-Meier method and compared with the Log-rank test.

Results: 649 HSCT recipients met the eligibility criteria, 58% male with a mean age of 48.8 years. The most common baseline condition was gammopathies (50.9%), followed by non-Hodgkin lymphoma (20.8%). Reviewing all blood cultures, echocardiography, and medical records we could identify 5 IE cumulative incidence of 0.74% (IC95% 0.24-1.72), with 1 death. Among the 5 cases, 4 occurred within the first two weeks of HSCT: 2 by Streptococcus, two by Gram-negative bacilli and one by coagulase-negative Staphylococcus. 3 occurred in the right vena cava/atrium and two in the left heart, as shown in Table 1. The incidence of BSI was 31.1% (95%CI 27.6-34.6) and its mortality in 14 days was 10% (95%CI 6.3-14.9). While in the total population the overall survival at D+100 was 91.1% (95%CI 88.6-93.0), in patients with BSI the survival was 82.4% (76.4-86.9).

Discussion: The incidence of BSI found in our study is comparable to that described in the literature. The largest series published in the last 20 years, has described an incidence of IE of 1.3% (20 cases), 15 of which were diagnosed post-mortem. Conclusion: Despite a high frequency of BSI in HSCT recipient and its association with early mortality incidence

TABLE 1- Clinical characteristics of five patients with infective endocarditis diagnosis after hematopoietic stem cell transplant

Gender Age	Baseline disease	HSCT	Blood culture	Clinical features	Transesophageal echocardiogram	Ophtalm	Antimicrobial therapy	Outcome
Male 44 y-o	Multiple myeloma	Auto	D+9 S. oralis	Neutropenia, Septic shock	Upper VC 5 x 8 mm.	Normal	Ceftriaxone\6 weeks	Cure
Female 57y-o	Multiple myeloma	Auto	D+8 S.haemolyticus;	Neutropenia	Right atrium 22 x 7 mm.	Not performed	Daptomycin 6 weeks	Cure
Male 24 y-o	Aplastic anemia	Full-match Allo	D+54 ESBL K.pneumoniae	Neutropenia. Septic embolism	TE: Upper VC 3 mm	Normal.	Ertapenem 4 weeks	Cure
Male 58 y-o	Hodgkin Lymphoma	Auto	D+6 S. viridans	Neutropenia Septic shock	Mitral valve 1,7 x 1,2 cm	Roth spots	Ceftriaxone 4 weeks	Death
Female 65 y-o	Multiple myeloma	Auto	D+9 ESBL E. coli	Neutropenia; Septic shock	Aortic valve	Normal	Meropenem 4 weeks	Cure

MONITORING HHV6 REACTIVATION IN UNRELATED AND HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION

Clarisse Martins Machado[1,2], Anderson João Simione[1], Ana Claudia Ferrari dos Santos[1], Juliana do Prado Moreno[1], Leila Cibele de Oliveira[1], Iago Colturato[1], Fernanda Barbieri[1], Mair P. de Souza[1], Vergilio Colturato[1]

1- Hospital Amaral Carvalho – Jaú/SP
2- Instituto de Medicina Tropical - São Paulo/SP

Human herpesvirus 6 (HHV6) is the main cause of encephalitis in allogeneic HSCT, and has been associated with other clinical manifestations, such as failure or delayed neutrophil/platelet engraftment, acute GVHD, manifestations of TGI, etc. Currently, HHV6 monitoring post HSCT is not recommended. However, a growing number of publications reports an increase in the rates of HHV6 reactivation and its complications in haploidentical HSCT. To evaluate the impact of HHV6 reactivation on haploidentical and unrelated (UD) HSCT. Weekly surveillance of HHV6 by quantitative PCR (Mobius) in whole blood was performed, up to d+120. Reactivation of HHV6 was defined by the detection of DNAemia. Chromosomal integration (HHV6-Ci) was defined by the detection of HHV6 in the hair follicle of asymptomatic patients with persistently high viral load. Variables analyzed were: Age, sex, type of donor, source of stem cells, underlying disease, type of conditioning, use of ATG, GVHD prophylaxis, acute GVHD, neutrophil and platelet grafts, overall survival and death. Ganciclovir IV was introduced for ≥2 weeks in patients with HHV6 DNAemia and appearance of neurological symptoms, or delay in leukocytes and/or platelets engraftment. In the presence of DNAemia and other clinical manifestations, the treatment was at physician's discretion. From 2016 to 2020, 167 HSCT NAP (60%) and 112 haploidentical (40%) were performed. The cumulative incidence of HHV6 reactivation was 41%, with 66% in haploidentical HSCT and 24% in UD HSCT (p<0.001). Reactivation occurred with a median of 24 (-3 to 765) days. The cumulative incidence of neutrophil and platelet engraftment was 91% and 85%, respectively. Frequency of neutrophil engraftment was lower when HHV6 reactivation occurred before engraftment (78% vs 93%, p=0.001). Recipients who reactivated HHV6 showed a delay in neutrophil engraftment in (19 vs 16 days; p=0.01). The same was observed with regard to platelet engraftment and previous HHV6 reactivation (74% vs 88%, p<0.001) and delay in platelet engraftment (26 vs 20 days; p=0.031). The cumulative incidence of acute GVHD II-IV was 25%, being higher in patients who reactivated HHV6 before the diagnosis of acute GVHD (44% vs 22%, p=0.011). Two of the 126 patients (1.6%) who reactivated HHV6 developed encephalitis 1-2 weeks after detection of HHV6 DNAemia. There was no difference in transplant-related mortality or overall survival in patients with or without HHV6 reactivation. HHV6-Ci was observed in two patients (0.7%). HHV6 monitoring demonstrated a higher frequency of reactivation in haploidentical HSCT. HHV6 reactivation affected neutrophil and platelet engraftment and increased the risk of acute GVHD. The frequencies of encephalitis (1.6%) and HHV6-Ci (0.7%) were similar to those described in the literature (1% and 1%, respectively). Monitoring of HHV6 HSCT may help the management of haploidentical HSCT complications.

Keywords: HHV-6. allo-HSTC. Haplo-HSCT

NON-INFECTIVE COMPLICATIONS

ANALYSIS DISEASE BURDEN, CLONAL EVOLUTION AND LONG TERM FOLLOW UP OF 167 PAROXYSMAL NOCTURNAL HEMOGLOBINURIA PATIENTS - ANOTHER NATURAL HISTORY

Ana Paula de Azambuja; Michel Michels Oliveira; Marco Antonio Bitencourt; Mariester Malvezzi; Ricardo Pasquini

Hospital de Clínicas da Universidade Federal do Paraná, Curitiba - PR - Brasil.

Introduction: Paroxysmal nocturnal hemoglobinuria (PNH) can occur as classical hemolytic disease or a small PNH clone found in a patient with bone marrow failure.

Purpose: To describe clinical features and long-term follow-up of 167 PNH patients and demonstrate differences between disease categories.

Methods: Multiparametric flow cytometry performed on 1025 patients referred from Jan/2000 to Dec/2019 found 167 (16.3%) confirmed PNH clone, 87M/70F. Clinical characteristics at first visit, and laboratory results, incidence of thrombosis, treatment and outcome during follow-up visits were considered for statistical analysis.

Results: Most patients (89.2%) had hypocellular bone marrow at diagnosis; 55(32.9%) developed hemoglobinuria, and 22(13.2%) developed thrombosis during monitoring. Mean age at aplasia diagnosis 28.4 years (range 5.6 - 71.2), and mean age at PNH clone detection 31.0 years (7.2 - 71.3 years). Clonal evolution occurred in 77 (46.1%) patients at a median of 4 years (range 6-281 months) after onset of cytopenia.

The cohort was divided into 15 Classic PNH, 55 hemolytic PNH with bone marrow hypoplasia (PNH/AA), and 97 definitive bone marrow disease with minor PNH clones - subclinical PNH (sc-PNH).

Subclinical patients had lower erythrocyte (2.0% vs 24.0% vs 57.8%) and granulocyte PNH clones (11.7% vs 58.8% vs 81.2%) than PNH/AA and Classic PNH, respectively. LDH, reticulocytes, absolute neutrophils and bone marrow cellularity were all lower in sc-PNH than hemolytic group. Pearson's analysis showed a statistically significant correlation ($p<0.001$) between PNH granulocyte clone and RBC clone (0.697), LDH (0.602), absolute neutrophils (0.310), platelet count (0.430), absolute reticulocytes (0.546), total bilirubin (0.330), and cell marrow biopsy (0.435). PNH granulocyte clone greater than 50% was found in 16/22 thrombotic patients. Median granulocyte clone was 89.1%(3.4%-99.2%) versus 12.3%(0.1%-34.0%), $p<0.001$, and erythrocytes 28.4%(3.4-99.8) versus 0.7%(0.1-14.0) in thrombotic versus the remaining 145 patients.

Treatment was highly heterogeneous during this 20-year follow-up: immunosuppressive therapy with CSA and/or thymoglobulin was given to 72 patients in the subclinical group (73.1%) and 45(64.3%) in the hemolytic group; 52 patients received HSCT (31.1%) of whom 40 in sc-PNH and 11 in PNH/AA; a total of 19 patients received Eculizumab after 2008 and 3 patients never received treatment.

The mean follow-up period was 74 months (1 - 330 months), with 31 deaths in total (80.4% OS). Sepsis was the main cause of sc-PNH mortality (16/18, 88.8%), and thrombosis in both hemolytic groups (11/13, 84.6%).

Conclusion: this study suggests clonal evolution in the long-term follow-up of aplastic patients and confirms the observation that high levels of PNH clones and LDH are associated with life-threatening hemolysis and thrombosis, whereas small PNH clones and young age are associated with the subclinical form of the disease.

Keywords: paroxysmal nocturnal haemoglobinuria, bone marrow failure, clonal evolution.

FIGURE 1: 1A: correlation between age of diagnostic and age at PNH clone confirmation; 1B: representation of PNH clone detection comparing to age at diagnostic in 40 pediatric patients; 1C: Kaplan-Meir overall survival curve showing no difference between PNH categories.

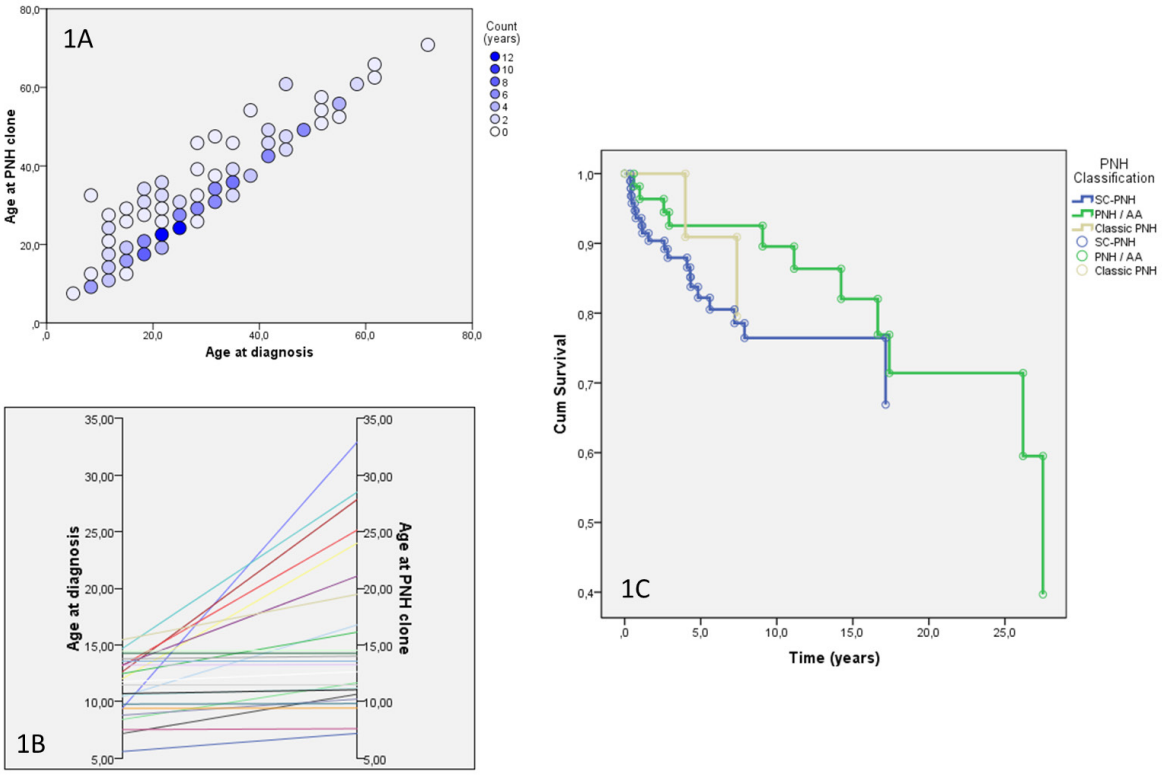


FIGURE 2: Correlation between LDH and PNH Clone in granulocytes (WBC) and erythrocytes (RBC), in different PNH categories. Pearson correlation was 0.595 and 0.602, respectively.

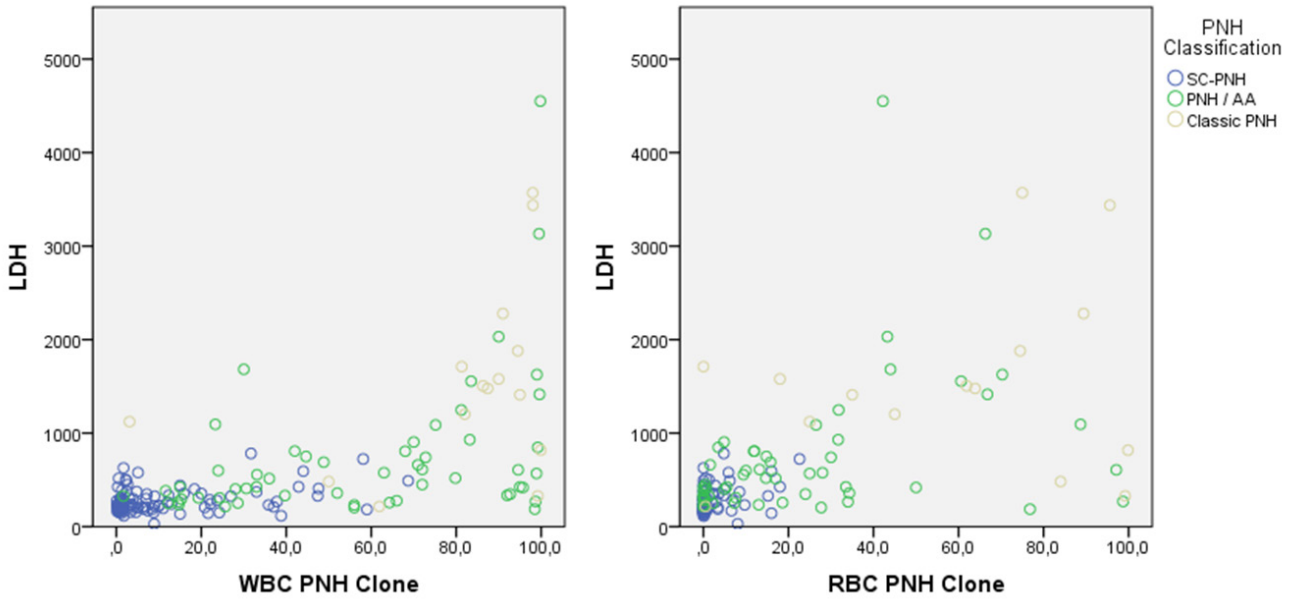
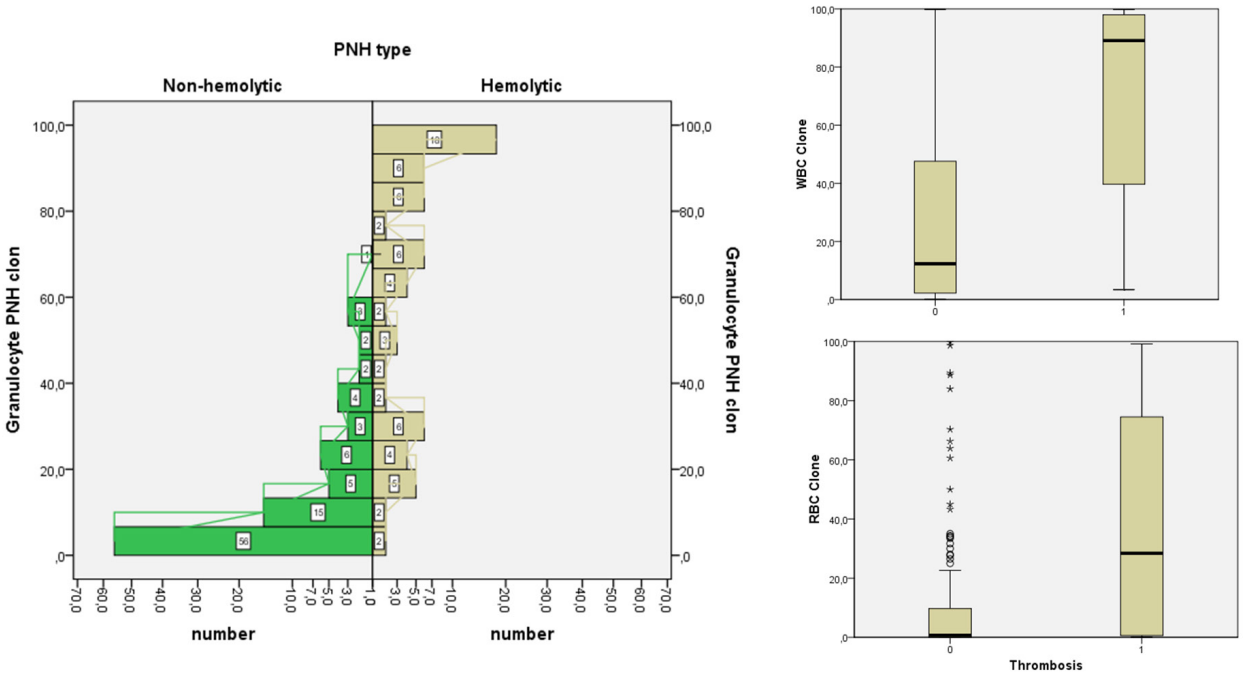


FIGURE 3: PNH clone predominantly <50% in Subclinical PNH patients (green) and heterogeneous but higher than 50% in Hemolytic patients (PNH/AA and Classic PNH together) (orange); WBC clone higher than 80% in thrombotic patients in contrast to less than 20% in non-thrombotic patients and RBC clone more heterogeneous in thrombotic and very low in non-thrombotic patients.



ASSESSMENT OF EFFICACY AND TOXICITY OF METHOTREXATE IN THE TREATMENT OF CHRONIC GRAFT-VERSUS-HOST DISEASE

Isabella Gonçalves Ramos, Giancarlo Fatobene, Ana Costa Cordeiro, Aliana Meneses Ferreira, Marina Fonseca, Livia Netto Chaer, Jhonny Manuel Carranza Jara Livia Caroline Barbosa Mariano, Vanderson Rocha

Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo - HCFMUSP

Introduction: Allogeneic hematopoietic stem cell transplantation (HSCT) is associated with several complications, including chronic graft-versus-host disease (cGVHD) in 30-70% of HSCTs. Chronic GVHD has impact on quality of life and mortality, often requiring multiple therapeutic lines. Among available therapeutic options, methotrexate is an attractive one as it is a potentially low-cost, effective alternative associated with reduced toxicity. However, previous studies were relatively small or included heterogeneous groups of patients. The aim of this analysis was to assess the impact of methotrexate on the treatment of cGVHD in adult patients.

Methods: Retrospective evaluation of electronic medical charts of patients. Eligible patients were those with diagnosis of cGVHD according to the 2014 NIH consensus criteria treated with methotrexate in second line or beyond between January 2014 and November 2020. Additionally, patients were required to have received at least 4 doses of methotrexate and have a minimum follow-up time of 3 months after starting this therapy. Best overall response (BOR) at 6 months was the primary endpoint, whereas secondary endpoints included failure-free survival, cumulative incidence of steroid withdrawal, overall survival, and toxicity.

Results: Twenty-one patients receiving methotrexate for treatment of cGVHD were identified; two of whom were excluded for having less than 3 months of follow-up period. Patients' characteristics and details of use of methotrexate are demonstrated in table 1. The analysis included 19 patients with a median follow-up of 18 months (range, 3 to71). The cumulative incidence of BOR at 6 months was 63% (11/19 patients), 16% of which (3/19 patients) corresponding to complete response, and 43% (8/19 patients) to partial response. Among patients with severe and moderate cGVHD, BOR were 37% (3/8 patients) and 45% (5/11 patients), respectively. The cumulative incidence of steroid discontinuation at 6 months was 60% (95% confidence interval [CI] 29-81%). Skin, mouth and liver were the most affected organs in evaluable patients; only two patients presented fascia/joint involvement. Failure-free survival at 6 months (figure 1) was 90% (95% CI 64-97%), and the overall survival at 1 year was 88% (95% CI 59-97%). Little methotrexate-attributable toxicity was observed, with only one case of renal toxicity and one case of liver toxicity, both at grade. One patient had disseminated adenoviral infection on methotrexate and other concomitant immunosuppressive drugs, which was not fatal. The median time between the start of methotrexate and BOR was 92 days (min-max17-180, n=11), and the maximum dose was 7.3 mg/m^2 (min-max3.2-13.4).

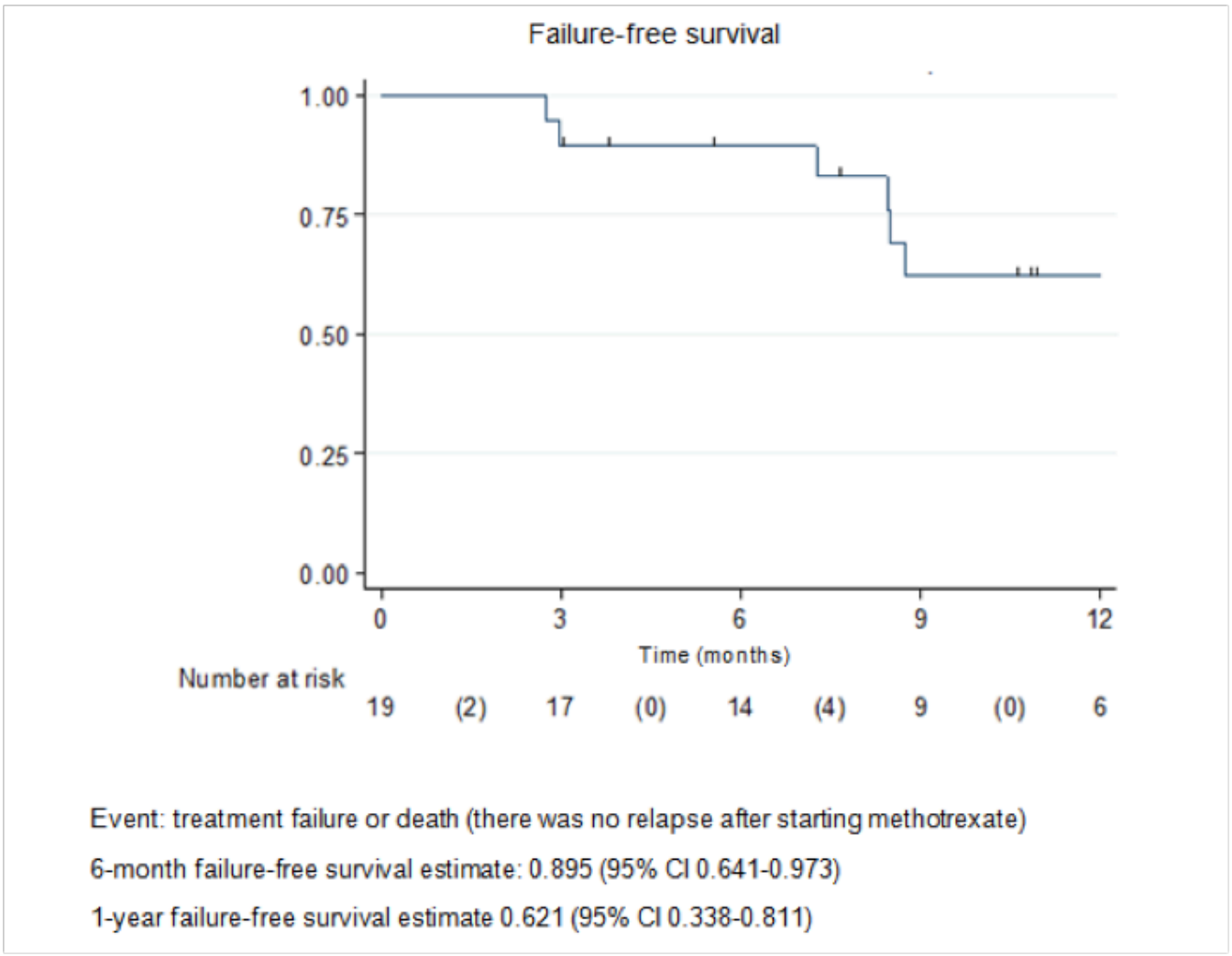
Conclusions: Patients receiving methotrexate for the treatment of cGVHD had an overall response rate comparable to previous studies in the literature and showed favorable toxicity and tolerance profiles. These advantages combined with its low cost make this medication an interesting option in resource-constrained countries. Apart from its retrospective nature, this analysis has relevant limitations: lack of a comparative group, organ-specific responses, and a formal evaluation of cost-effectiveness. Studies defining the ideal dose of methotrexate in cGVHD and encompassing a larger number of participants are necessary for a more accurate assessment of the role of this medication in the treatment of cGVHD.

Keywords: Hematopoietic stem cell transplantation. Graft-versus-host disease. Methotrexate.

TABLE1. MDS: myelodysplastic syndrome; CML: Chronic myeloid leukemia; CNI: calcineurin inhibitor; MMF: mycophenolate mofetil.

Table 1 **Characteristic**		**N=19**
Gender		
	Female sex — no. (%)	10 (52.6)
	Male sex — no. (%)	9 (47.4)
Primary desorder		
	Acute leukemia/ MDS/CML — no. (%)	16 (84.8)
	Lymphoproliferative disease — no. (%)	2 (10.6)
	Others — no. (%)	1 (5.3)
Age		
	Median (range) — yr	39 (19-65)
Stem cell donors		
	Haploidentical — no. (%)	2 (10.5)
	HLA-matched sibling — no. (%)	17 (89.5)
Stem cell sourcce		
	Bone marrow — no. (%)	4 (21.1)
	Peripheral blood stem cells — no. (%)	17 (78.9)
Grading of cGVHD		
	Moderate — no. (%)	11 (57.9)
	Severe — no. (%)	8 (42.1)
Sclerodermatous gvhd		
	Yes — no. (%)	8 (42.1)
	No — no. (%)	10 (52.6)
	Unknown — no. (%)	1 (5.3)
Number of previous tretment lines		
	2º line— no. (%)	10 (52.6)
	≥ 3ª line — no. (%)	9 (47.4)
Concomitant systemic therapy (maintenance for at least ≥ 30 days)		
	Yes — no. (%)	14 (73.7)
	No — no. (%)	4 (21.1)
	Unknown — no. (%)	1 (5.3)
Concomitant systemic therapy		
	Steroids — no. (%)	12 (80.0)
	CNI— no. (%)	8 (53.1)
	MMF— no. (%)	1 (5.3)
	Others— no. (%)	2 (11.8)
Discontinuation of methotrexate before the last follow up		
	Yes — no. (%)	10 (52.6)
	No — no. (%)	9 (47,4)
Reason to discontinue methotrexate (n=9)		
	Disease progression— no. (%)	3 (33.3)
	Patient decision (no response)— no. (%)	3 (33.3)
	Sustained response — no. (%)	3 (33.3)

FIGURE 1.



Event: treatment failure or death (there was no relapse after starting methotrexate)

6-month failure-free survival estimate: 0.895 (95% CI 0.641-0.973)

1-year failure-free survival estimate 0.621 (95% CI 0.338-0.811)

RISK FACTORS FOR GRAFT FAILURE AND OUTCOME OF SECOND HEMATOPOIETIC STEM CELL TRANSPLANTATION AS TREATMENT

Viviane de Jesus Torres Lima[1], Anderson Felipe da Silva[1], Lara Faria Souza Dias[1], Lucila Nassif Kerbauy[1], Mariana Nassif Kerbauy[1], Leonardo Javier Arcuri[1], Andreza Alice Feitosa Ribeiro[1] and Nelson Hamerschlak[1] - **Contributed equally*

1 Hospital Israelita Albert Einstein, Bone Marrow Transplantation Department, São Paulo, Brazil

Introduction: Graft failure (GF), primary or secondary, is a severe complication of hematopoietic cell transplantation (HCT). The incidence can reach 10% with alternative donors.1,2 Other risk factors are non-malignant diseases, HLA mismatch, non-myeloablative (NMA) conditioning and viral infections.3-7 There are some strategies in the prevention and management of GF, because the mortality of this complication is quite high (30-70%).8

Objectives: Describe incidence and outcomes in patients with GF.

Methods: Retrospective study that inclued patients with GF among allogeneic HCT performed from 2007 to 2021. Primary GF was defined as neutrophils < 0.5x109/L up to D+30, in the bone marrow as stem cell source (BM) or peripheral bood (PBSC), or up to D+42 in the umbilical cord blood source (UCB), and secondary failure such as loss of chimerism and cytopenias after initial engraftment.9 Total infused cells was defined as reduced when total nucleated cells (TNC) < 3x10E8/kg in the BM source, TNC < 3x10E7/kg and CD34+ < 1x10E5/kg in the UCB and CD34+ < 2x10E6/kg in the PBSC.2

Results: Among 397 allogeneic HCT (248 malignant and 149 non-malignant diseases), there were 18 GF (4,5%). The GF were: 15 (10% in non-malignant group) and 3 (1,2% in malignant group), with 3 adults and 15 children (<18 years). The source was BM in 50%; PBSC, 22% and UCB, 28%. GF occurred in 8.5% of all HCT with SCUP. Sixteen had a donor with HLA mismatch (9, unrelated and 7, haploidentical) and none had matched related donor. The conditioning was myeloablative in 39%, reduced intensity, 45% and NMA, 16%. There were 10 primary GF (55%) and 8 secondary GF (45%). The median time from primary GF to new HCT was 34 days and for secondary GF was 136 days. Among possible causes, 3 patients had viral infections (CMV, EBV and adenovirus); 1, reduced total infused cells. None of the 13 patients analyzed had anti-HLA specific donor. Seventeen of 18 patients underwent a second HCT, 8 of them with BM source, 6 with PBSC and 3 with UCB. In 14 (82.3%), another donor was used. Haploidentical donor (70%) and NMA conditioning were the most used (70%). Fourteen engrafted, with a median on D+15 (D+12 to D+22), and 3 patients had new primary GF (2 received UCB). Three of the 17 died after D+100 and 1 died in D+24. Three patients underwent a third HCT, with a median of 23 days, all with haploidentical donor and NMA conditioning. Two engrafted, and one failed again and died. Of the 18 patients with GF, 12 of them are alived. The 1-year overall survival of patients who had primary and secondary GF were 80% and 75%, respectively.

Conclusion: HCT for non-malignant diseases has a higher risk of GF. Second early HCT seems to be a good rescue strategy, but the use of UCB as a source should be viewed with caution. One of the main predictors of mortality in GF is the time to the second HCT and in our cohort the median for the second and third HCT were 34 and 23 days, contributing to good overall survival in 1 year.

Keywords: Graft failure. Allogeneic hematopoietic stem cell transplantation. Rescue treatment.

TABLE 1: Data related to disease, HCT and graft failure

	First HCT n: 18	Second HCT n: 17	Third HCT n: 3
Recipient age Median (Min-Max)	5 (1-63)	5 (1-63)	2 (1-11)
Recipient sex Male Female	14 4	13 4	2 1
Diseases Malignant* Benign+	3 15	2 15	1 2
Donor age Median (Min-Max)	37,5 (2-48)	31 (13-49)	36 (34-38)
Graft PBSC BM UCB	4 9 5	6 8 3	1 2 0
Anti-HLA Positive Unknown	0 5	0 5	0 0
Donor MRD MUD MMUD Haploidentical	0 2 9 7	0 1 4 12	0 0 0 3
Conditioning MAC RIC NMA	7 8 3	4 1 12	0 0 3
Engrafted		11	2
Primary graft failure Secondary graft failure	10 8	3 0	1 0
Time in days between primary graft failure and subsequent transplant Median (Min-Max)	--	34 (17-86)	23 (22-28)
Time in days between transplant and secondary failure Median (Min-Max)	136 (50-432)	--	--

*Malignant diseases: Acute lymphoblastic leukemia, Myelodysplastic Syndrome and Juvenile myelomonocytic leukemia +Benign diseases: X-linked adenoleukocytorofia (2 patients), Severe combined immunodeficiency (2 patients), Diamond Blackfan anemia (1 patient), Chronic granulomatous disease (2 patients), Primary immunodeficiency (1 patient), Mucopolysaccharidosis (1 patient), Chediaki Higashi syndrome (1 patient), Congenital diserytropoietic anemia (1 patient), Osteopetrosis (1 patient), Severe congenital neutropenia (1 patient), IPEX Syndrome - **Immunodysregulation polyendocrinopathy enteropathy X-linked** (2 patients). HCT: hematopoietic cell transplantation; PBSC: peripheral blood stem cell; BM: bone marrow; UCB: umbilical cord blood; HLA: human leukocyte antigen; MRD: matched related donor; MUD: matched unrelated donor; MMUD: mismatch unrelated donor; MAC: myeloablative; RIC: reduced intensity; NMA: non-myeloablative

TABLE 2: Data from total infused cells in HCT

	First HCT Median (Min-Max)	Second HCT Median (Min-Max)	Third HCT Median (Min-Max)
PBSC CD34+ (x106/Kg)	17,3 (4,5-24)	7,9 (2,8-28,1)	11
Viability	100% (90,6-100%)	99% (96,4-100%)	100%
BM TNC (x108/Kg)	4 (3,4-7,5)	6,7 (5,8-10,1)	34,9 (8,7-61)
Viability	94,8% (100-63,8%)	98% (96,5-100%)	96,2% (94,4-98%)
UCB CD34+ (x106/Kg)	0,5 (0,23-4,0)	0,25 (0,18-0,85)	
TNC (x107/Kg)	7,2 (0,1-71)	9,9 (2,9-11,2)	
Viability	96% (46-100%)	95% (92-98%)	

HCT: hematopoietic cell transplantation; PBSC: peripheral blood stem cell; BM: bone marrow; UCB: umbilical cord blood; TNC: total nucleated cells

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STUDY OF ACUTE KIDNEY INJURY IN PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Pastora Maria Araújo Duarte,[1] Beatrice Araújo Duarte[2] Fernando Barroso Duarte[1], Romélia Pinheiro Gonçalves Lemes[3]

1. Hospital Universitário Walter Cantídio (HUWC), Fortaleza, Brazil.
2. Centro Universitário Christus, Fortaleza, Brazil.
3. Universidade Federal do Ceará Research Laboratory in Hemoglobinopathies and Genetics of Hematologic Diseases, Fortaleza, Brazil

Introduction: Hematopoietic Stem Cell Transplantation (HSCT) is a procedure widely performed in patients with hematological autoimmune diseases and metabolic disorders, with an increase in overall survival. Despite this, Acute Kidney Injury(AKI) remains a frequent complication, affecting 10-70% of patients, contributing to an expressive mortality. Objectives: to analyze the occurrence of AKI in patients undergoing hematopoietic stem cell transplantation. Correlate the sociodemographic and clinical profile and variables related to HSCT with the onset and evolution of AKI, in addition to the impact on overall and event-free survival. Material and Methods: Retrospective cohort study, with descriptive and analytical approach, including all patients undergoing HSCT between Jan/2014 and Dec/2019 at Hospital Universitário Walter Cantídio(HUWC). Data were collected from multidisciplinary medical records and Master platform for laboratory tests and were tabulated in Microsoft Excel® 2016. For identification and stratification of AKI, the KDIGO method was used. Serum , creatinine was used as a marker of glomerular filtration rate (GFR) at time Zero, d30, d60 and d100 after HSCT, the CKD-EPI formula was used for estimation

Preliminary Results: 391 patients were included in the analysis, the most prevalent underlying disease was Multiple Myeloma (35.04%), followed by leukemia (31.20%). We had 264 autologous (67.52%) and 127 allogeneic (32.48%) HSCT. AKI was diagnosed in 129 patients (32.99%). In multivariate analysis, by logistic regression, the variables independently associated with AKI were: Allogeneic transplantation, diagnosis of leukemia and germ cell tumor, need for transfusion of packed red blood cells, use of three or more classes of antimicrobials, use of amphotericin B, polymyxin B, amikacin, voriconazole and teicoplanin, grafting time, BuFlu conditioning protocols, CyATG, FluCyATG, FluMel 140 and FluMel180, sepsis/septic shock, sinusoidal obstruction syndrome, cytomegalovirus infection, grade III mucositis and use of calcineurin inhibitors. The test post hoc showed that basal and early creatinines were different and higher than intermediate and late and that GFR in patients with AKI were lower than in those without AKI in all periods, except for baseline . The survival time of the group without AKI was higher than the group with AKI, and in these groups, the need to use renal replacement therapy (RRT) determined a higher risk of death . Among those who underwent conservative treatment, we found greater survival in those who recovered their kidney function. Conclusion: The incidence of AKI in patients undergoing HSCT at the HUWC was high, with classical association variables confirming its importance and impact on patient survival.

Keywords: INCIDENCE. ACUTE KIDNEY INJURY. HEMATOPOIETIC STEM CELL TRANSPLANTATION.

NURSING

SKIN TOXICITY ASSOCIATED WITH TIOTEPA: AN IMPLEMENTATION OF CARE BY THE NURSING TEA

Emanuele Christine dos Santos Pirolli[1], Laiane de Jesus Oliveira[1], Rebeca Almeida Ferrarese[1], Roberta Nomura[1], Renan Weber da Costa[1], Michele Jankovski Piloni[1], Juliana Luiza de Mello Bach[1], Adriana Mello Rodrigues[1], Carmem Bonfim[1]

1- Hospital Pequeno Príncipe, Curitiba - Paraná

Introduction: Thiotepa is an alkylating cytotoxic agent used during the conditioning regimen in Hematopoietic Stem Cell Transplantation (HSCT) for leukemia and some central nervous system tumors. This drug undergoes hepatic metabolism, and its active compound is Tepa. The drug has a half-life of 5 to 17 hours and acts by interrupting DNA bonds, combining antitumor and immunosuppressive effects. The physicochemical characteristic is lipophilic, which facilitates the passage through the blood-brain barrier. Urinary excretion is the majority; however, it can be found in high concentrations in the skin, which allows skin lesions.

Objective: Report the experience of the nursing staff in the specific care of pediatric patients who received Thiotepa during HSCT.

Method: Retrospective descriptive study of pediatric patients who underwent HSCT from October/2017 to June/2021 and who received Thiotepa in the conditioning regimen. Specific cares were adopted, and training with the nursing staff. The implemented care were: removing bracelets (including identification) and any other item that could cause pressure on the skin; wear loose cotton pajamas; leave open or loose diapers and change it with every diuresis or bowel movement; sanitize the intimate region with cotton and distilled water; perform three shower baths a day, never bed bath. Mainly sanitize the scalp, because the concentration of Thiotepa can lead to permanent alopecia; change the sheets every bath; do not use topical lotion while using Tiotepa, or balm for diaper rash; use simple and small bandage in central venous access, with daily change and avoid unnecessary bandage. All care was maintained for 48 hours after the end of the Thiotepa infusion.

Results: We performed a total of 224 HSCT (36 autologous and 188 allogeneic HSCT, totaling 224 HSCT during the study period. Of these, 12 (5.3%) patients used Thiotepa in their conditioning, 4 of them underwent autologous HSCT and 8 allogeneic HSCT. The dose ranged from 5 mg/kg (n=3) to 10 mg/kg (n=9), and the median time of use was 2.3 days (range: 1–3days). This drug was associated with Busulfan and Fludarabine in 8 patients (66.6%) and this was the most common conditioning regimen in this study. 91.6% of the patients were male, the median age at transplant was 2 years (8 months to 9 years) and the median body weight was 12.1 kg (6.8 kg to 35.1 kg). The care was implemented in all patients and only 1 had skin toxicity reactions, with hyperemia in the perineum region, solved in 7 days with local treatment with topical hydration and topical palm.

Conclusion: The adopted orientations and the training of the team allowed the identification of early signs of toxicity and ensured a reduction in cutaneous adverse effects during the use of Thiotepa. The standardization of this care in pediatric transplant centers can minimize medication risks to patients, in addition to favoring a better analysis of data related to the complication.

Keywords: Thiotepa, Skin toxicity, Hematopoietic Stem Cell Transplantation.

PHARMACY

IDENTIFICATION AND MANAGEMENT OF DRUG INTERACTIONS IN A PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT

Laiane de Jesus Oliveira[1], Thiago de Melo Costa Pereira[2], Ana Cristina dos Santos Machado[1], Juliana Luiza de Mello Bach[1], Adriana Mello Rodrigues[1], Polliany Roberta Dorini Pelegrina[1], Fábio Araújo Motta[1], Cilmara Cristina Kuwahara Dumke[1], Fernanda Moreira de Lara Benini[1], Carolina Martins de Almeida Peixoto[1], Gisele Loth[1], Carmem Bonfim[1], Heloisa Arruda Gomm Barreto[1],

1- Hospital Pequeno Príncipe – Curitiba, Paraná
2- Universidade Vila Velha – Vila Velha, Espírito Santo

Introduction: Hematopoietic Stem Cell Transplantation (HSCT) is used to treat both malignant and non-malignant diseases. Is a complex process that uses many drugs which can be classified into four groups: chemotherapy, immunosuppressants, supportive drugs and antimicrobials. Due to polypharmacy, the amount of drug interactions (DI) during transplantation is relevant. Therefore, the role of the clinical pharmacist in the identification, management and monitoring of these DI contributes to the safety and effectiveness of pharmacotherapy.

Objective: Identify the pharmaceutical interventions, involving DI, during pediatric HSCT in the pharmacotherapeutic follow-up.

Methods: Retrospective, descriptive study with a quantitative approach carried out from April/2020-June/21. During this period, pharmaceutical interventions with DI registered in the Clinical Pharmacy service spreadsheet were analyzed. Pharmacotherapeutic follow-up forms and electronic medical records were reviewed to identify DI with clinical repercussions. The checking of DI in clinical practice was performed with the aid of scientific literature (PubMed), also Drugx-Reax® (Thomson Micromedex TM, Greenwod Village) and Drugs (Drugs.com Statistics, Q4 2013) databases. Laboratory tests were evaluated to verify the DI as well as to analyze the management performed.

Results: During the study period, 86 patients were obtained. Of these, 71 were allogeneic and 15 autologous HSCT. Ten DI identified with clinical repercussions and with intervention by the pharmacist: 4 with immunosuppressants (cyclosporine [CSA] and sirolimus), 4 with antimicrobials (foscarnet, acyclovir, voriconazole, fluconazole, rifampicin, amphotericin B), 1 with antineoplastic (busulfan) and 1 with drugs of support (phenobarbital, furosemide). The interaction between sirolimus and fluconazole contributed to toxic levels of the immunosuppressant, and as an intervention was the suspension of sirolimus, return of the adjusted dose after collection of a new serum level and exchange of fluconazole for micafungin. Regarding the interaction between voriconazole x CSA, there was an increase in calcineurin inhibitor levels, requiring dose adjustment to minimize the adverse effects of the immunosuppressant. Also, DI that reduced CSA levels: rifampicin and phenobarbital, where the intervention was for dose adjustment as well as the exchange of anticonvulsant and interaction between phenobarbital and busulfan, which contributed to a reduction in the serum level of the chemotherapeutic, requiring adjustment of dose. Synergistic effects of nephrotoxicity were observed with: amphotericins, acyclovir, foscarnet, furosemide, implying the intervention of increased hydration and/or dose reduction according to the literature.

Conclusion: In view of the polypharmacy present in HSCT, DI are relevant. Pharmaceutical care contributes to its identification, management and monitoring, as well as the effectiveness and safety of pharmacotherapy.

Keywords: Drug–drug interactions; cyclosporine; fluconazole; sirolimus; fenobarbital hematopoietic stem cell transplantation; pediatric

IMPACT OF CHEMOTHERAPY TOXICITY IN HIGH DOSE CONDITIONING REGIME FOR AUTOLOGOUS HEMATOPOIETIC STEM CELLS TRANSPLANTATION IN OVERWEIGHT AND OBESE PATIENTS WITH MULTIPLE MYELOMA

Carolina Ferreira dos Santos[1], Leonardo Jun Otuyama[1], Bruna Del Guerra de Carvalho Moraes[1], Fernanda Carlos Nobrega[2], Lívia Carolina Mariano[1], Luiz Henrique dos Santos de Assis[3], Vanusa Barbosa Pinto[1], Vanderson Rocha[1]

1 Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo
2 Hospital Alemão Oswaldo Cruz
3 Hospital São Rafael

Introduction: Obesity is associated with an increased risk of complications during chemotherapy. Multiple myeloma (MM) is a frequent hematologic malignancy, and high-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (aHSCT) has been considered the first-line consolidation therapy in transplantation-eligible MM patients.

Objective: To evaluate the association between conditioning chemotherapy dose adjustment in aHSCT and clinical outcomes, including gastrointestinal (GI) toxicities (oral mucositis (OM), nausea, vomiting and diarrhea) and progression-free survival, in patients with MM.

Methods: This was an observational, retrospective, single-center study, including patients with MM who underwent aHSCT from january 2014 to july 2019, aged ≥18 years, in a Tertiary Public Hospital. Clinical criteria was used for chemotherapy dose adjustment, and from 2018 onwards, based on accumulated experience, our center established that for patients with weight ≥120% of the ideal weight, adjusted body surface (BS) should be used; and for patients with weight <120% of the ideal weight, BS should be calculated using real weight. Logistic and Cox regression models were used to assess potential risk factors for the presence of severe GI toxicities and for progression/death within 1 year of aHSCT.

Results: A total of 259 patients were included, from which 106 (41%) were female. As for BMI, 70 (27%) were eutrophic, 106 (41%) were overweight and 83 (32%) were obese. From the 83 obese patients, 63 (76%) had conditioning chemotherapy dosage based on real weight (RW) and 20 (24%) based on adjusted weight (AW). Patients were classified in two groups: RW and AW based conditioning. In the RW group (n=229), 168 (73%) had OM, 201 (88%) nausea, 109 (48%) vomiting and 196 (86%) diarrhea. In the AW group (n=30), 20 (67%) OM, 26 (87%) nausea, 17 (57%) vomiting and 23 (77%) diarrhea. There was no statistically significant difference between the two groups regarding GI toxicities. Both dose adjustment and BMI showed no statistically significant association with progression/death (p=0.607 and p=0.671, respectively). The risk for progression/death was significantly higher in patients transplanted after second line of treatment (p=0.025) compared to the first line. For severe GI toxicities, there was no difference for dose adjustment (p=0.481) and BMI (p=0.574). Male patients had a lower risk of GI toxicity than female patients (p=0.001).

Conclusion: The use of dose adjustment in melphalan dose calculation had no impact on disease progression/mortality in 1 year, and on incidence of severe toxicities, in patients with MM who underwent TCTHa.

PHYSIOTHERAPY

USE OF NON-INVASIVE MECHANICAL VENTILATION IN HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS

Andrea Cristina Gobus Becker[1], Carine Lumi[1], Claudia Caceres Astigarraga[1], Cristina Ungaretti de Campos Velho[1], Lisandra Della Costa Rigoni[1], Marcio Luiz Ferreira de Camillis[1], Nariane Roberta de França Guimarães[1], Paola Vicente Timotheo[1], Priscila Alves Perreira Cidade[1], Suelen da Silva de Vargas[1], Renata Hoffmann Longhi[1]

1 Hospital Moinhos de Vento

Hematopoietic stem cell transplantation (HSCT) is a curative care option for several onco-hematological diseases. HSCT is more than a procedure, it is a complex process divided into several stages with characteristic complications in each stage, among frequent complications, respiratory ones occur in 30 to 60% of patients. The Brazilian Consensus about Mechanical Ventilation has a grade B recommendation for the use of non-invasive mechanical ventilation (NIMV) in immunosuppressed and transplanted patients in general with respiratory failure. In such cases, we can offer oxygen supplementation and positive pressure ventilation to reverse the condition. NIMV in onco-hematologic patients, when properly indicated, is related to a lower rate of referral to ICU and lower risk of intubation.

Objectives: Identify the reason for using NIMV in patients undergoing HSCT, assess the duration of therapy and hospitalization and the need for orotracheal intubation (OTI). Check the reason for NIMV in patients who underwent and did not need OTI. Methodology: A retrospective cohort study, data were collected from the medical records of patients who underwent transplantation between 2019 and 2021. Results: The study included 57 patients with a mean age of 50.9 years +/- 14.1. Regarding the use of NIMV, out of the 57 patients who underwent HSCT, 18 patients (31.5%) needed its use during hospitalization period. The main reason for using NIMV was pulmonary congestion in 8 patients (14%), followed by atelectasis in 5 patients (10.7%). The duration of the NIMV was of 4 days on average. Success rate was 66.6%, because out of the 18 patients who needed NIMV, 12 did not need OTI. In the group of 12 patients who needed NIMV but did not progress to OTI, the main indications for use were: atelectasis in 6 patients (50%), congestion in 3 patients (25%), pneumonia in 2 patients (16.6%) and respiratory distress in 1 patient (8.33%). Patients who needed NIMV had a longer hospital stay, 23 days, when compared to patients who did not need NIMV ($p<0.001$).

Conclusion: The analysis in this specific group of patients suggests that the use of NIMV is an important therapeutic tool in the treatment of pulmonary congestion and atelectasis. The longer hospital stay in patients who underwent NIMV reflects the higher rate of clinical complications in this group. Complementary studies with a larger number of patients should be carried out to determine the impact of the use of NIMV in reducing the rate of OTI.

Keywords: hematopoietic stem cell transplantation, non-invasive mechanical ventilation, physiotherapy

NUTRITION

APPLICATION OF THE NUTRITIONAL RISK INDEX AS INSTRUMENT TO PREDICT EARLY COMPLICATIONS IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

Juliana Maria Faccioli Sicchieri[2], Bruna Silvestre Françoso[2], Barbara David dos Santos2, Thauany Nantes Guiráo[2], Isabela Laurencio Schiavoni[2], Thalita Cristina de Mello Costa[1], Renato Luiz Guerino-Cunha[1]

1 Department of Medical Images, Hematology and Clinical Oncology, Ribeirão Preto Medical School of University of São Paulo, Ribeirão Preto, SP, Brazil.
2 Internal Medicine Department, Ribeirão Preto Medical School of University of São Paulo, Ribeirão Preto, SP, Brazil.

Introduction: The Nutritional Risk Index (NRI) is an easy-to-apply and low-cost tool, consisting of the equation: NRI = (1.519 × serum albumin) + (41.7 × current weight / current weight index; values below a score of 97.5 are approximately clinically indicative of malnutrition. It presents a good correspondence between nutritional status and clinical outcome, and represents an interesting indicator in the scenario of allogeneic hematopoietic stem cell transplantation (HSCT-allo).

Objective:: To relate NRI scores before (NRI (B), referring to conditioning and NRI after (NRI (A), 30 days after HSCT to clinical outcomes.

Methodology: Retrospective descriptive and exploratory study, using data analysis of electronic medical records (gender, age, weight, serum albumin and body mass index (BMI), between the period of January 2015 to December 2019, in individuals of both genders, over 18 years old, diagnosed with neoplastic and non-neoplastic diseases and in the first HSCT-allo. The following variables were correlated: presence of graft-versus-host disease (GvHD), clinical outcomes, nutritional status, sex and age, applying Pearson correlation, with a significance level of $p \leq 0.005$.

Results: Among the 151 transplants performed, only 62 were included in the study due to inclusion criteria (Table 1). In the pre-transplant period, all patients achieved a score for malnutrition; in the post-transplant period, this score shows improvement, but still indicating malnutrition. For the descriptive variables, we observed that the BMI presented a strong and significant correlation with NRI(B) and NRI (A) (r=.596 and r=.875 p=0.001). The clinical outcomes did not show a significant correlation with NRI (B) and NRI (A) (r=-.590 and r=-.110 p=.556), and gender showed a strong and significant negative correlation only in the NRI (B) (r= -3.310 p=0.001).

Conclusion: The comparison between NRI (B) and NRI (A) showed a significant difference between the 2 periods, including patients with obesity and continued to signal clinical malnutrition after HSCT- allo, confirming the importance as a nutritional indicator. Thus, we suggest that more studies be carried out, with larger samples and in collaboration with several centers to validate these findings.

Keywords: Nutrition. Nutritional status. Nutritional risk index. Clinical outcome.

TABLE 1: patient characteristic and comparison of NRI (B) and NRI (A) scores

		N	%		
Sex	Female	28	45,2		
	Male	34	54,8		
Disease	Malignant	48	77,4		
	Non-malignant	14	22,6		
Stem cell source	Bone marrow	42	67,7		
	Peripheral blood stem cell	19	30,6		
	Umbilical cord blood	1	1,7		
Related donor	Yes	50	80,6		
	No	12	19,4		
GvHD	Yes	22	35,5		
	No	40	64,5		
Outcome	Relapse	9	14,5		
	Remission	53	85,5		
Death	Yes	14	22,6		
	No	48	77,4		
BMI	Underweight	4	6,5		
	Normal weight	29	46,8		
	Pre obesity	16	25,8		
	Obesity	13	21		
Albumin	≤ 3	2	3,2		
	> 3	60	96,8		
Comparison NRI					
NRI (B)	Score SD	49,7 (±8,3)	-		p=0.001
NRI (A)	Score SD	76,4 (±13,8)	-		

GVHD: graft-versus-host disease; BMI: body mass index; NRI: Nutritional Risk Index.

ODONTOLOGY

ORAL HEALTH CONDITION AND DENTAL TREATMENT IN ADULT PATIENTS PRIOR TO HSCT: RETROSPECTIVE STUDY

Augusto Arcemiro Bittencourt[1,2], Jorge Ferreira de Araújo[1], Cleber Nunes Alexandre[3], Juliana Bertoldi Franco[1], Maria Paula Siqueira de Melo Peres[1], Livia Mariano[4], Vanderson Rocha[4], Luiz Alberto Valente Soares Junior[1]

1. Department of Dentistry - Central Institute - Clinical Hospital of Medical School of the University of São Paulo – IC-HCF-MUSP, São Paulo – Brazil.
2. Postgraduate Program in Sciences Applied to Hematology, State University of Amazonas - PPGH-UEA, Manaus - Brazil.
3. Department of Dentistry of the Hospital Foundation of Hematology and Hemotherapy of Amazonas – FHEMOAM, Manaus - Brazil
4. Clinical Unit of Cell Therapy of the Hematology and Hemotherapy Service - Clinical Hospital of Medical School of the University of São Paulo – HCFMUSP, São Paulo - Brazil

Introduction: Specialized dentists play an important role in the identification and removal of oral infectious foci in patients who undergo a Hematopoietic Stem Cell Transplantation (HSCT). The main goal is to reduce the oral and dental complications that may occur during this procedure.

Objectives: To identify the main dental treatments and oral diseases present in adult patients prior to HSCT.

Methods: 153 dental records of patients prior to HSCT were evaluated, from January to December 2018, with 69 records being excluded due to incomplete or incorrect chart forms.

Results: Among the 84 patients who had medical records/radiographs, 43 were female (52%) and 41 male (48%) with a mean age of 50 years. The most prevalent hematologic malignancies were Multiple Myeloma n= 39 (46.42%) Non-Hodgkin's Lymphoma n= 23 (27.38%) and Hodgkin's Lymphoma n= 15 (17.85%). Autologous HSCT was predominant with n = 75 (89.3%). The decayed, missing, and filled teeth index (DMFT) was 19.22, with predominance of Missing Teeth = 1,105, followed by Filled Teeth = 433 and Decayed Teeth = 77, and n=63 (75%) was seen in the assessment of bone loss. It was observed that 75 (89.3%) patients needed dental treatment, with 192 dental procedures being performed (periodontal shaving n=54; dental restorations n=49; tooth extractions n=48). In addition to the dental demand, 29 patients (38.6%) had dental complaints, such as dry mouth (11 patients), fractured tooth (7 patients), gingival bleeding (6 patients), pain in the oral mucosa (4 patients), and toothache (2 patients).

Conclusion: This study shows the high demand for dental procedures prior to HSCT in adult patients, with the main procedures performed being periodontal scaling, restoration, and tooth extraction. These procedures are linked to dental caries and periodontal diseases, representing important infectious foci, even without patient's complaints of the oral cavity in most cases, which may have repercussions during and after HSCT. Thus, these data reinforce the importance of a vigilant evaluation by the dental surgeon before the HSCT, also the indispensable presence of a dentist in the multidisciplinary care team for this group of patients, in order to remove infection foci that can compromise the HSCT process and increase the risk of complications after HSCT.

Keywords: Oral Health

FIGURE 1: Selection of patients (Total included and excluded)

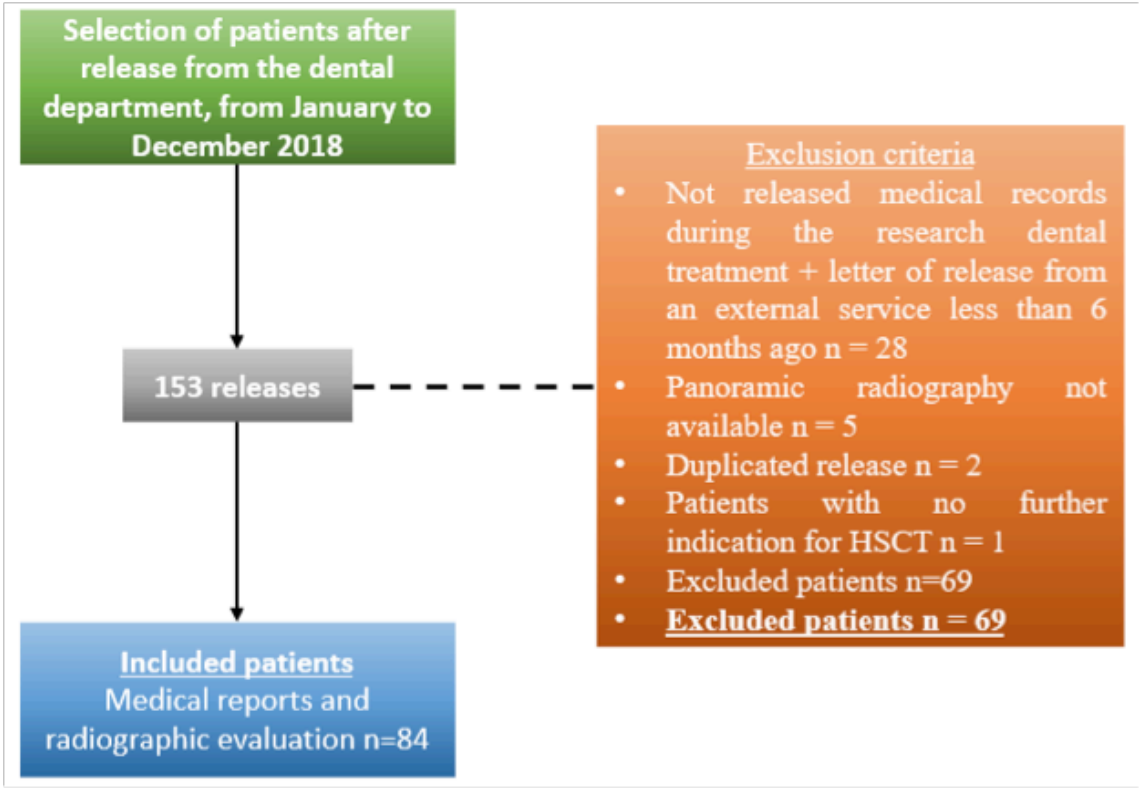
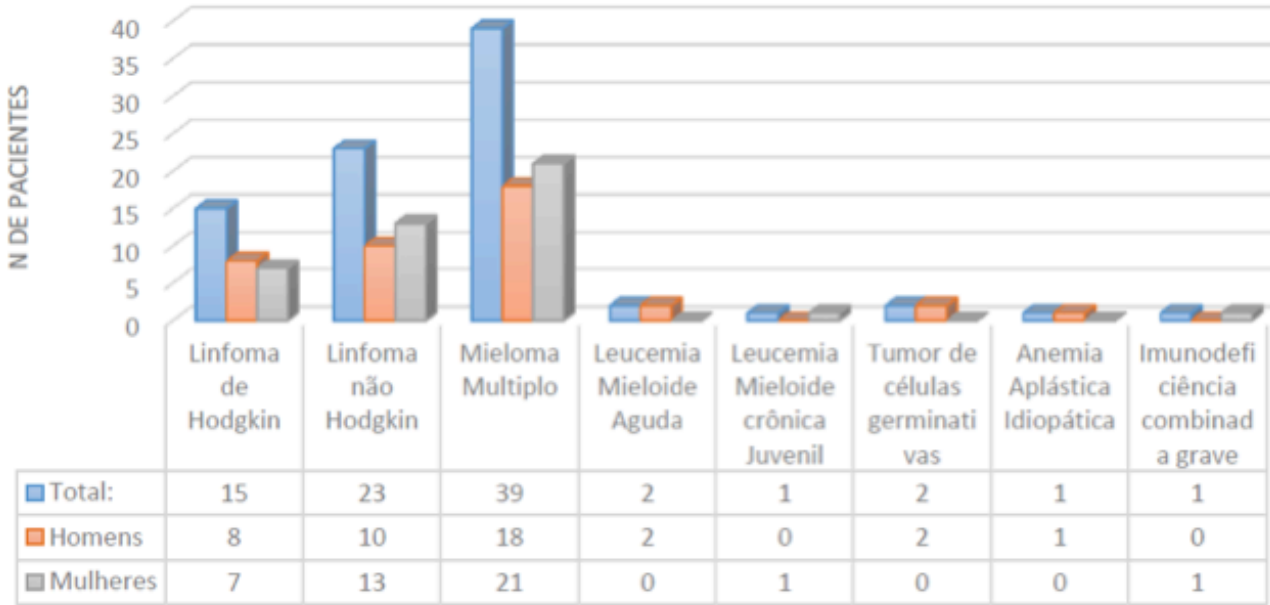
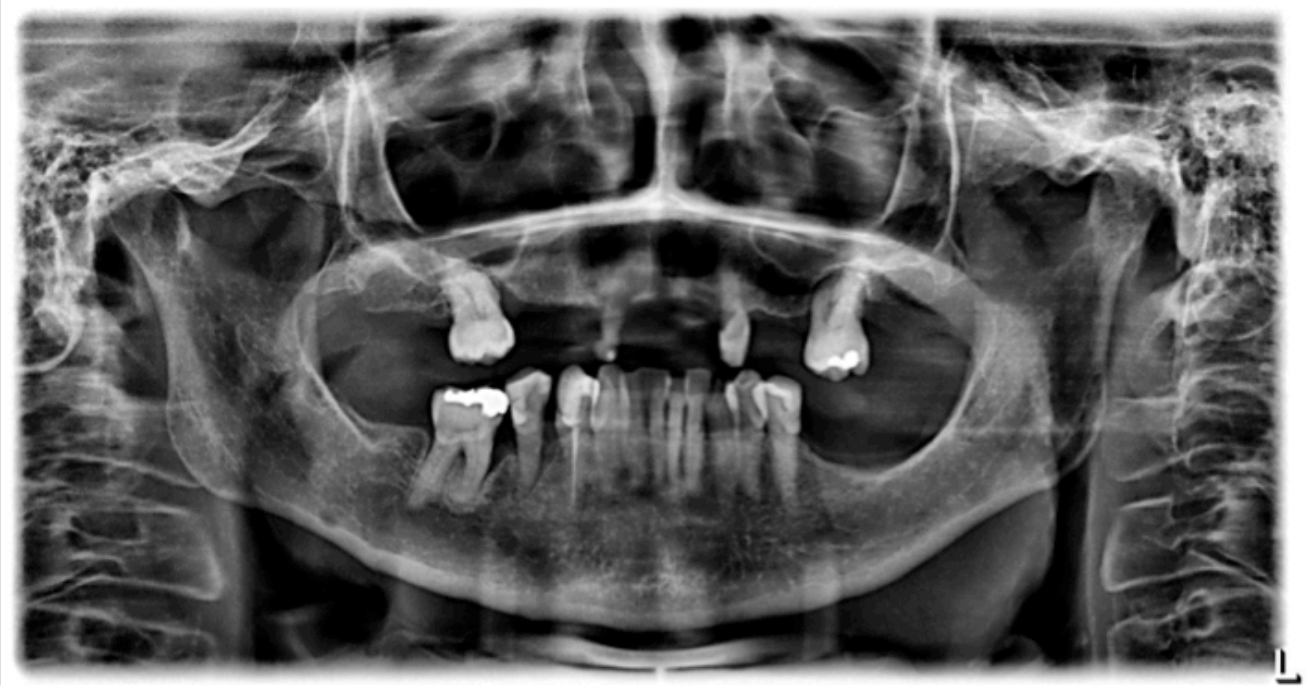


FIGURE 2: Prevalence of patients with hematological malignancies distributed by sex.



	Linfoma de Hodgkin	Linfoma não Hodgkin	Mieloma Multiplo	Leucemia Mieloide Aguda	Leucemia Mieloide crônica Juvenil	Tumor de células germinativas	Anemia Aplástica Idiopática	Imunodeficiência combinada grave
Total:	15	23	39	2	1	2	1	1
Homens	8	10	18	2	0	2	1	0
Mulheres	7	13	21	0	1	0	0	1

FIGURE 3: Exemplification of the assessment by means of panoramic radiography evaluating the following components: Decayed, Missing, Filled Teeth, and bone loss by sextant:



Legend Figure 3: D = Decayed Tooth; M = Missing Tooth; F = Filled Tooth; BL = bone loss

TABLE 1: DMFT: Data referring to decayed, missing, and filled teeth, divided by the total number of patients included.

Decayed Teeth	77
Missing Teeth	1,105
Filled Teeth	433
Total of Patients	84
DMFT	**19.22**

TABLE 2: Bone loss evaluated in six compromised sextants divided by the total number of patients

Number of compromised sextants	***n***	**%**
One Compromised Sextant	16	25.4
Two Compromised Sextants	11	17.46
Three Compromised Sextants	23	36.5
Four Compromised Sextants	5	7.94
Five Compromised Sextants	3	4.76
Six Compromised Sextants	5	7.94
Total	**63**	**100**

TABLE 3: Dental procedures performed prior to HSCT distributed by number of interventions and percentages.

Dental procedures performed	***n***	**%**
Periodontal scraping (session)	54	28.13
Dental restorations (tooth)	49	25.52
Dental extractions (tooth)	48	25
Dental prosthesis maintenance	13	6.77
Dental prophylaxis	12	6.25
Salivary management	11	5.73
Orthodontic appliance removal	3	1.56
Endodontic treatment (tooth)	1	0.52
Low Power Laser Photobiomodulation	1	0.52
Total	**192**	**100%**

TABLE 4: List of dental complaints per patient

Dental complaint	**Patients**
Dry mouth	11
Fractured tooth	7
Gingival bleeding	5
Pain in the oral mucosa	4
Toothache	2
Total	**29**

PSYCHOLOGY

EXPERIENCES OF PATIENTS IN POST-HSCT DURING THE COVID-19 PANDEMIC: EMOTIONAL SUFFERING AND POSSIBILITIES OF SUPPORT

Érika Arantes de Oliveira-Cardoso, Denise Maria Vendramini, Pamela Perina Braz Sola, Ana Clara Buson de Carvalho, Sandra Cristina Pillon, Thalita Cristina de Mello Costa, Jorge Henrique dos Santos, Maria Carolina de Oliveira, Renato Luiz Guerino Cunha, Manoel Antônio dos Santos

Patients undergoing Hematopoietic Stem Cell Transplantation (HSCT) during the COVID-19 pandemic, due to the recommended protective measures, need to adapt to a care routine, in many cases already surpassed, and undergo elaborated mourning, such as the loss of health, future plans, occupational and financial losses, among others. The aim of this study was to understand the experience of a pandemic in post-HSCT patients. This is a cross-sectional, descriptive-exploratory study with a quantitative approach. For data collection, an online form was used, the content of which was analyzed using the SSPS version 26.0 program. The convenience sample consisted of 30 individuals: most were female (n=19, 63.3%), with a mean age of 31.9 years (SD = 10.6), from eight Brazilian states, with at least one representative from each region of the country, most with single marital status and no children (n=19, 63.3%). The results show that 83% of patients said they believed that, in case of contamination, the disease would be fatal for them. 60% had doubts about the evolution of COVID-19 and its treatment in the post-HSCT. The majority (66%) were avoiding attending medical appointments, postponing routine exams. They refused to trust the effectiveness of the call center, opting to "wait for the pandemic to end", due to the fear of contamination. Due to this fear, 37% of patients opted for total isolation and 47% had a worsening in their quality of life, especially with changes in sleep and appetite. The most present feelings at that time were: anxiety (n=19), irritability (n=16), sadness (n=14), thoughts about death (n=13) and suicidal ideation (n=4). Before the pandemic, half of the sample did not recognize the need for emotional support. During the pandemic, 63.3% said they wanted psychological care. Another major impact of the pandemic is highlighted: the financial condition of the participants, with 44.8% of the sample having a family income of up to two minimum wages, 46.6% had reduced wages, and six were dismissed during this period. It is concluded that the pandemic triggered emotional suffering, financial difficulties, uncertainties regarding the evolution of the disease in transplant recipients and fear of seeking health care. Faced with these demands and the desire for emotional support, an online psychotherapy group was started, encouraging teleservices. Psychoeducation sessions and individual psychological care were also carried out. These data are important for planning intervention strategies that are sensitive to the particularities of vulnerable groups in the context of COVID-19.

Keywords: COVID-19; Hematopoietic Stem Cell Transplantation; quality of life

TALKING ABOUT DEATH WITH CHILDREN: THE PREPARATION OF A BOOK

Hellen Cristina Ramos Queiros, Érika Arantes de Oliveira Cardoso, Jorge Henrique Correa dos Santos, Lucas dos Santos Lotério, Ana Clara Buson de Carvalho, Livia Basso Alegre, Aline Guerrieri Accoroni, Manoel Antônio dos Santos

Introduction: Childhood illness and the need for intensive treatment, such as bone marrow transplantation, invite the child to prematurely come into contact with the issue of finitude itself. Talking about the processes of death and dying in the childhood scenario raises double anguish: in the child who listens and in the adult who talks about it. Objective: Thinking in this context, the objective of this study was to elaborate a children's book with a short story, which was structured from the theoretical framework of a multidimensional approach to the concept of death.

Method: The research has a qualitative design and was carried out according to the following steps: a) designing the project, b) content selection: a survey of the literature on the concept of death in childhood was carried out; c) elaboration of the story: choice of the scenario and Poli, a bee, as the protagonist of the book; d) elaboration of the pilot book; e) expert review: the material was analyzed by experienced psychologists; e) adequacy of language and content: the suggested adaptations were made; f) resubmission of material to specialists; h) storytelling for children to verify the understanding of the language used and the effectiveness of the material and i) completion of the book: the material was illustrated, cataloged and printed. Result: The book consists of the story of a single baby bee that survives the attack of a hungry bear on the hive, from the event she develops existential dialogues with a queen bee that are turned as questions to the children during the story. The book addresses four important categories for understanding the grieving process and that these are understood by children: a) finitude of life; b) temporality of dying; c) purpose of dying and d) continuity of life in the memory of those who remain.

Conclusion: The book proved to be an adequate and effective tool to talk about death, addressing the central concepts of this construct. An important fact was the children did not show discomfort during the telling, claiming that they enjoyed the story. The material produced can be used in different contexts, including in Bone Marrow Transplantation, and it can be an intermediary material that facilitates the expression of affection. of sick children, who will be able to talk in a playful and non-anxious way about terminality (PUB-USP).

Keywords: Death, Child, Termination.

SOCIAL SERVICE

OUT OF HOME TREATMENT PROGRAM IN THE STATE OF CEARÁ: FAVOR OR RIGHT OF USERS OF THE HUWC BONE MARROW TRANSPLANT SERVICE IN THE INTERIOR OF THE STATE OF CEARÁ?

Ana Caroline Freitas Do Monte E Silva Forte[1]; Ana Cristina Pereira Da Costa[2]; Naiane Zilma Da Silva[1].

1. Hospital Universitário Walter Cantídio, Fortaleza - Ce - Brasil;
2. INSS, Fortaleza - Ce - Brasil.

Introduction: The TFD (Out-of-Home Treatment Program) is an Ordinance of the Ministry of Health (No. 55, of February 24, 1999) which covers expenses related to air, land and river transport, daily for food. and cost allowance for patients whose distance from their home is more than 50km from their place of treatment. One of the greatest challenges for SUS users from the interior of the state of Ceará to perform HSCT in Fortaleza is the difficulty of getting around to undergo treatment in Fortaleza/CE. Objective: In order to discuss the challenges of the transplant patient, this study was carried out, which aims to answer the following question: how many patients treated by the Bone Marrow Transplant service have access to transport from their city for treatment in Fortaleza?

Method: The present work is the partial result of an ongoing research that was submitted and approved by the Ethics Committee of the HUWC. The weightings carried out derive from the social interview instrument, applied by social workers from the Bone Marrow Transplant Sector to 153 patients treated between the months of January 2019 to April 2021.

Results: Based on the survey carried out with 153 patients, they were evidenced the following data: of this quantity, 47 patients are from Fortaleza/CE; 26 are from the Metropolitan Region, and 80 are from the interior (more than half with 52%). With regard to access to transport, 77 of these patients reported accessing transport on their own; 38 reported that they have access via municipal transport, via the health department; 11 reported that they have difficulties in accessing the city's transport and that, therefore, they sometimes do it on their own; and 5 reported that they cannot get transportation through the city.

Conclusions: The results of this research show a difficult social reality of patients in the interior of the state who face numerous difficulties to perform their treatment in the capital. The results reveal that only 29% of patients have access to transport in their municipality (it should be noted that, according to the MS Ordinance, the TFD includes, in addition to transport, accommodation and allowances). It is intended to raise with this work debates about the realization of the GT in the cities in order to provoke discussion about the reality of the transplanted in an attempt to expand citizenship rights that guarantee dignity and social equity. The population's lack of understanding about GT in its entirety can be a factor that hinders its implementation in practice (SILVA, 2018). Thus, it is necessary that this policy can be discussed again in municipalities in the interior of the State so that users can effectively access it, not from the perspective of "favor", but as a right of the assisted population.

QUALITY AND DATA MANAGEMENT

THE CHALLENGES IN MANAGING TWO MULTICENTER STUDIES USING THE CENTER FOR INTERNATIONAL BLOOD AND MARROW TRANSPLANT RESEARCH (CIBMTR) DATABASE, CONSIDERING THE BRAZILIAN LAW.

Cinthya Corrêa da Silva[1], Mariana Clapis Bello Veloso[1], Ana Claudia Machado Urvanegia[1], Anderson Felipe da Silva[1], Leonardo Javier Arcuri[1], Nelson Hamerschlak[1]

1Hospital Israelita Albert Einstein, Bone Marrow Transplantation Department, São Paulo, Brazil.

Introduction: The scientific research is important for the hematopoietic stem cell transplantation (HSCT). In order to preserve the rights of research participants, regulations were created in the country (law) and the Central Institutional Review Board (CIRB), which established the Institutional Review Board (IRB). Since Resolution 466, the regulatory process now occurs electronically, through Plataforma Brasil (PB). Today, there is the General Law of Data Protection-(No. 13,709) that aims to preserve the individual's sensitive data. Based on this, two works were developed and submitted to the IRBs and CIRB to develop a unified database in the country that uses the CIBMTR' infrastructure.

Objective: To describe the challenges in managing the approval process of two Brazilian multicenter HSCT studies using the CIBMTR structure.

Method: Historical analysis in the management of the ethical approval process of two studies in Brazil.

Results: From the initiatives of the Brazilian Society of Bone Marrow (SBTMO) to develop a registry of HSCT, a multicenter study was approved in 2017 and regularized the uploading data from the country to the CIBMTR and in the same year another study comparing haploidentical transplantation versus related and unrelated. The centers had to join the platform and currently there are in the overall project 56 centers approved by CIRB, representing 86%(3195) of the transplants performed in 2020 in Brazil. It was observed that some professionals were not aware of the regulatory process and that many centers had no investigator support center. Over the years, the number of centers that adhered to the overall project has increased, resulting in an increased number of amendments submitted to the IRB/CIRB. The lack of submission of these amendments in some participating centers was one of the challenges, resulting in actions from the SBTMO to avoid this drawback. For the projects to be successful, communication between the research manager and the participating centers was important, especially when the center did not have an investigator support center. Difficulties with the regulatory process and handling of the PB occurred frequently and the proponent center helped in the orientation of this process. In order to simplify and disseminate the information, the SBTMO media was used, in which the data were updated for the centers within minutes. Using the analysis of the local IRBs, content adjustments were proposed to the proponent center, resulting in the alignment of the project with the local laws.

Conclusion: The support of the principal investigator of each center was fundamental for the local IRBs to approve the project. Some adaptations in the project benefited all the centers. The proponent center's awareness of the different research practices in Brazil has greatly aided the process, which has driven greater adherence to the CIBMTR, and increased the number of centers in the overall design of the country's data reservoir.

Keywords: HEMATOPOIETIC STEM CELL TRANSPLANTATION. ETHICS. DATABASE.

HEMOTHERAPY AND CELL THERAPY

PROCESSING LOGISTICS OF DONOR LYMPHOCYTES DOSES FOR THE TREATMENT OF MINIMAL RESIDUAL DISEASE AND MIXED CHEMEIRISM

Mayara Regina Alves Gomes; Olga Margareth Wanderley de Oliveira Félix; Ana Caroline de Lima Alves; Adriane da Silva Santos Ibanez; Cintia Monteiro Lustosa; Jakeline Palmezano Crispim de S. Bufoni; Cristiane Menezes Vitoria Alferi; Danielle Vitorassi Barbosa Cruz; Erika Martins; Karoline Helena Silva da Silva; Laís Lima Quintino; Patrícia Shimoda Ikeuti; Virginio Climaco Araujo Fernandes Junior; Camila Marquezini Moraes de Oliveira; Paula Gracielle Guedes Granja; Renata Fittipaldi da Costa Guimarães.

Gomes, MRA[1]; Félix, OMWO1; Alves, ACL[1]; Ibanez, ASS[1]; Lustosa, CM[1]; Bufoni, J PCS[1]; Alferi, C.M.V[1] ; Cruz DVB[1]; Martins, E[1]; Silva, KHS[1]; Quintino, LL[1]; Ikeuti, PS[1]; Fernandes Junior, V[1]; Oliveira, CMM1; Granja, PGG[1]; Guimaraes, RFC[1].

1. Instituto de Oncologia Pediátrica IOP/GRAACC/Unifesp – São Paulo, Brasil

Donor lymphocyte infusion (DLI) is used to treat minimal residual disease (MRD) after allogeneic transplantation and for reversal of mixed chimerism. The efficacy of DLI is limited, with substantial risk of graft-versus-host disease (GVHD). The ideal is to slowly increase small doses of lymphocytes based on the patient's chimerism. DLI infusion is an alternative if cells are available, and efficacy depends on the type of disease and dose of CD3 infused. However, it is important to consider the costs of the procedure, the space available in freezers – 80°C and also the logistics of release. Another alternative, which also requires logistics, is the collection and infusion of fresh DLI.

Objective: To describe the logistics of DLI processing in a cellular processing center (CPC).

Method: Retrospective evaluation of the medical records of twenty-seven donors and their recipients from March 2006 to June 2021. All donors performed CD3 dosage. The DLI bags of leukoapheresis products were cryopreserved in doses. For the infusions, the bags were thawed in warm water at 37°C and the cellularity to be infused was calculated. The volume was aspirated in syringe and directed to infusion. Peripheral blood (PB) was collected in a bag with anticoagulant adjustment and referred to infusion. All patients were monitored for one hour.

Results: There were 14 DLIs for adult and 13 for pediatric patients. As for donor type, 16 were related and 11 were unrelated, 3 of them collected for REDOME. For adult patients the median CD3/kg was 104x106 (6-425) and for pediatric patients 383x106 (0.105-3,895). For cryopreserved products, the storage median was 3 bags (1-5). All adult patients received the first fresh dose with 14 x106CD3/kg (0.5-266), 10 received a second dose with 28x106 (5-58), 4 received third of the with 50x106 (10-54), 2 received a fourth dose with 60 x106 (12-108) and 1 patient received a fifth dose with 12.2 x106 /kg. Seven of the eight pediatric patients received a fresh first dose with a median of 10x106 (0.105 -455), 5 received the second dose of 1.1 x106 (0.9-2.1), 4 received the third dose with 4.4 x106 (1.1 to 5.1), 2 patients received a fourth dose with 1.1 (1-1.1) and 1 patient received a fifth dose with 1x x106. We performed the infusion of fresh DLI from PB only for 2 patients, one patient received four staggered doses of 1.04 x106CD3, 2.56 x106CD3, 4.56 x106CD3 and 10.6 x 106CD3/kg. The second patient received two with 1.06 x106/kg. The yield of the three unrelated DLI collections for REDOME was 342x x106, 150 x106 and 76 x106CD3/kg.

Conclusion: Logistics was essential to make available the number of doses of clinical protocols, without compromising the space of freezers, without increasing costs and without impact on the protocols of the cell processing center.

Keywords: Donor lymphocytes. Allogeneic transplant. DLI doses.

PRODUCTION OF UMBILICAL CORD NK CELLS IN A GMP ENVIRONMENT FOR ADOPTIVE IMMUNOTHERAPY AGAINST ACUTE MYELOID LEUKEMIA: A PRECLINICAL STUDY

Lucila N. Kerbauy[1,2,3*], Larissa L. Co[a1*], Andrea T. Kondo[1], Juliana A. P. de Godoy[1], Isabel C. Bello[1], Oswaldo Keith Okamoto[1,3], José Mauro Kutner[1], Nelson Hamerschlak[1,2], Raquel M. A. Paiva[1]

1 Department of Hemotherapy and Cell Therapy, Hospital Israelita Albert Einstein, São Paulo, Brazil
2 Department of Hematology and Stem Cell Transplantation, Hospital Israelita Albert Einstein, São Paulo, Brazil
3 Human Genome and Stem Cell Research Center, Department of Genetics and Evolutionary Biology, Biosciences Institute, University of São Paulo (USP), São Paulo, Brazil.

**Authors contributed equal to this work*

Background: Natural Killer (NK) cells are lymphocytes of the innate immune system presenting an ability to recognize and kill tumor cells. The application of NK cells from the umbilical cord is attractive. It is an allogeneic source, readily available since the product is already frozen, easily obtainable, with no need to submit donors to the risks of blood collection. However, due to the small volume of blood in an umbilical cord unit, obtaining a number of adequate NK cells for clinical use is a challenge.

Aims: expand ex vivo NK cells from umbilical cord blood (NK-CORD) in a GMP (Good Manufacturing Practice) environment and evaluate the total number of cells after expansion, purity, cytogenetics, cytotoxic function in vitro and in vivo. Determine in a preclinical study the feasibility of using NK-CORD for adoptive immunotherapy.

Methods: NK cells were isolated from umbilical cord blood and expanded in co-culture with feeder cells (mbIL21) in GREX 100 and IL2 supplementation. On day 14 (D14+), cells were characterized for cytotoxic activity in vitro by calcein methodology in the following cell lines: HL60, OCI-AML2, and OCI-AML3. Additionally, the cytotoxic potential of NK cells was evaluated in vivo in NOD-Scid (IL2rgnull) mice.

Results: we observed a high number of NK cells after expansion, median of 9.3x1010 (2.3x1010 - 19x1010, N=4), the viability median was 96.5% (93.7 - 99.0%, N=3), and the purity with CD56+/CD3- was 93.2% (90.9 - 96.1%, N=3). The cytotoxicity of NK cells in different myeloid cell lines was above 90% from the 1:20 dose (target cell: effective cell). In vivo studies demonstrated that NK cells (10x106/animal) are safe for in vivo administration as animals were followed up to D99+ without any toxicity (n=6). After in vivo infusion, NK cells were distributed to bone marrow and spleen, with no sign of toxicity. Preliminary in vivo cytotoxicity studies have shown that animals treated with NK-CORD cells have a lower tumor growth rate than control animals (treated with Molm13 tumor lineage only). The overall survival of animals treated with NK cells is higher than control animals (n=5).

Conclusion: we demonstrate that NK cells can be expanded with a high degree of purity, viability, and yield from umbilical cord blood. The in vitro activity defines that NK cells are cytotoxic to different tumor myeloid cell lines, and the in vivo activity showed NK-CORD cells might delay tumor growth. Therefore, we showed that NK cells are safe and effective and have the potential for clinical application.

Keywords: NK cells, umbilical cord blood, acute myeloid leukemia

SUSTAINED REMISSION WITH ANTI-CD19 CAR-T CELLS AS SIXTH LINE THERAPY IN A RELAPSED/REFRACTORY DIFFUSE LARGE B CELL LYMPHOMA (DLBCL) PATIENT AND IMMUNE RECONSTITUTION: A CASE REPORT

Aliana Meneses Ferreira[1], Samuel Campanelli Freitas Couto[2,3], Theo Gremen Mimary de Oliveira[2,3], Livia Caroline Barbosa Mariano[1], Rodrigo Nalio Ramos[2] , Nelson Hamerschlak[4], Marcos de Lim[a5], Vanderson Rocha[1,2,3]

1. Division of Hematology, Transfusion Medicine and Cell Therapy, Hospital das Clínicas - HCFMUSP, University of Sao Paulo, SP , Brazil - 2. Laboratory of Medical Investigation in Pathogenesis and targeted therapy in Onco-Immuno-Hematology (LIM-31) - Department of Hematology - Hospital das Clínicas - HCFMUSP, University of Sao Paulo, Sao Paulo, Brazil - 3. Pro Sangue Hemocentro SP Foundation, Sao Paulo, Brazil - 4. Bone Marrow Transplantation Unit, Hospital Israelita Albert Einstein, Sao Paulo, Brazil - 5. Ohio State University, Columbus, Ohio, USA

Introduction: Anti-CD19 CAR-T cell therapy has been associated with improved outcomes in R/r DLBCL. In Brazil, management of patients treated with this therapy can be cumbersome due to the lack of experience with this therapeutic product in most centers.

Objective: Describe a case of successful anti-CD19 CAR-T cell treatment as salvage therapy in a patient previously exposed to 5 therapy lines, including autologous HSCT, as well as detail the patient's follow-up post CAR-T cell infusion.

Methods: Case description, with patient's laboratory and imaging results during follow-up.

Results: A 62-year-old male patient with a 7-year history of DLBCL, previously treated with 5 lines of therapy, was referred to Cleveland (Dr Marcos de Lima) to receive anti-CD19 CAR T-cells in March 2020 following disease relapse after autologous transplant and refractoriness to later therapeutic lines. Referral was due to the lack of available therapies with curative intent in Brazil, associated to the availability to enroll in an anti-CD19 CAR-T cell therapy clinical trial (CASE 2417) at the Seidman Cancer Center in Cleveland, Ohio, USA. PET-CT results before CAR-T cell treatment are shown in Figure 1. The infused cell product was manufactured with the automated CliniMACS® Prodigy platform using a commercial lentiviral vector. As pre-infusion lymphodepletion therapy, the patient received cyclophosphamide 60mg/kg on D-6 and fludarabine 25mg/m2 on days D-5 to D-3. The infusion of the CAR T cells occurred on 20/02/2020 – cellular dose: 2 x 106 /kg. As early complications, the patient had grade II CRS and severe neutropenia related to the use of sulfamethoxazole-trimethoprim for pneumocystis prophylaxis. There was no neurotoxicity. Patient remained hospitalized for a month, and returned to follow-up at HC/FMUSP in May 2020. During patient follow-up, regular evaluation of immune reconstitution is being performed – table 1. Analysis of immune reconstitution by flow cytometry after CAR-T cell therapy showed reconstitution of CD3+, CD8+ and NK (CD3-CD16+CD56+) lymphocytes, reduced levels of CD4+ lymphocytes and absence of CD19+ B cells (Table 1). Given the old age of the patient, exposure to multiple lines of therapy and lack of consensus in the literature, we opted for monthly immunoglobulin replacement in the first year. Patient is receiving infectious prophylaxis with acyclovir and monthly pentamidine. There have been no infectious complications so far. Disease reassessment with PET-CT 6 and 12 months after therapy demonstrated a complete response (CR) (Figure 2). Although we do not have available data regarding CAR-T cell persistence, the serial evaluation of lymphocyte subpopulations confirms persistent B cell aplasia.

Conclusions: Anti-CD19 CAR T-cell therapy is efficient therapy in R/r DLBCL, with manageable late toxicities. This patient's persistent B cell aplasia associated with CR from disease 16 months post-infusion suggests persistence of circulating CAR-T cells.

Keywords: CAR T cells; anti-CD19; refractory lymphoma

FIGURE 1: PET-CT after 5 lines of therapy (R-CHOP, R-ICE, high dose chemotherapy followed by autologous hematopoietic stem cell transplant, R-DHAOx and R-lenalidomide) and before therapy with Anti-CD19 CAR-T Cells.

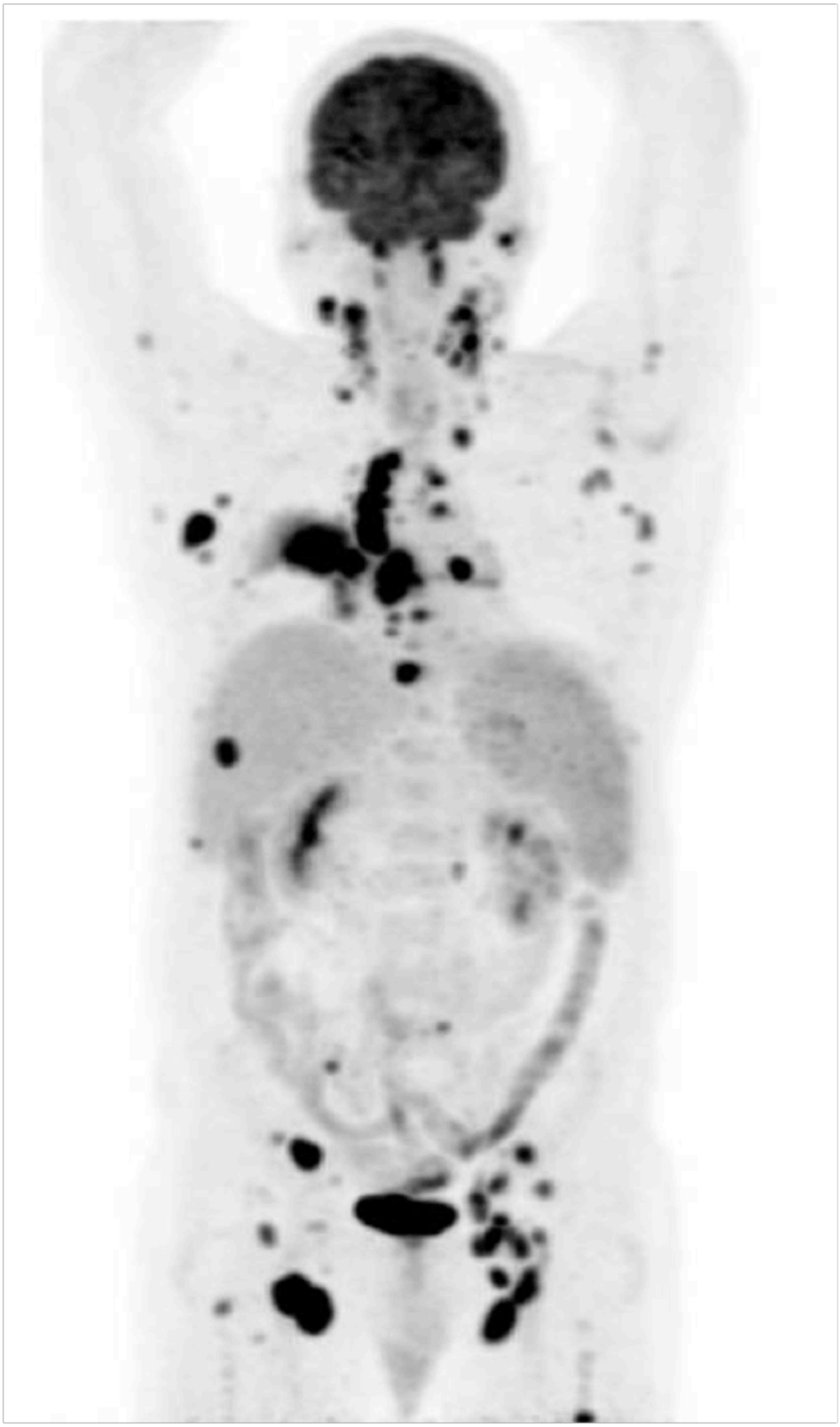


FIGURE 2: PET-CT 12 months after Anti-CD19 CAR-T cells infusion

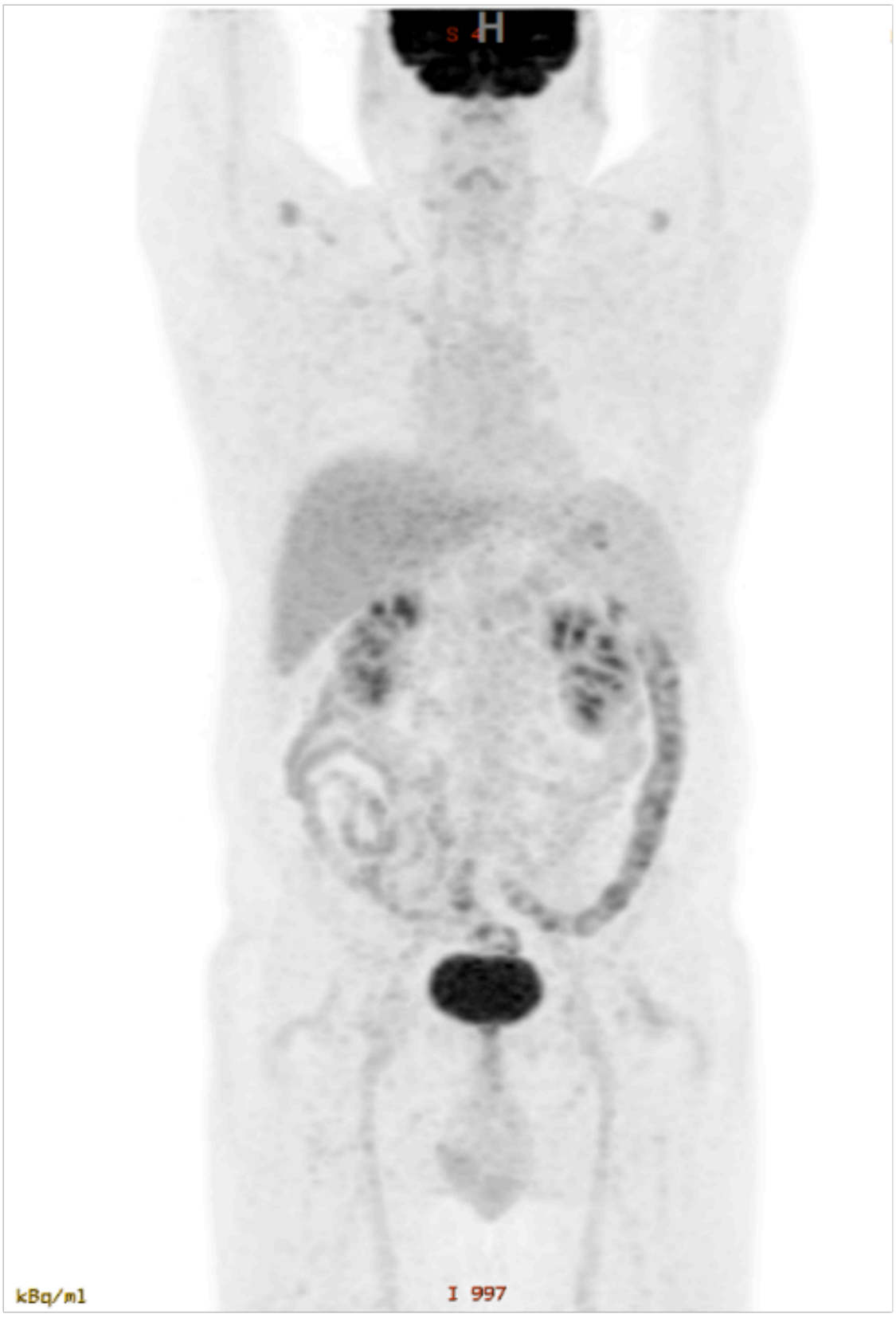


TABLE 1: Evaluation of lymphocyte subpopulations and immunoglobulin G levels after CAR-T cell therapy. (1) Values obtained from Haematologica 84:499-504, 1999 and J. of Allergy Clin. Immunol 112:973-980, 2003.

	20/05/20 (2m)	19/08/20 (5m)	12/11/20 (8m)	11/02/21 (11m)	20/05/21 (14m)	Heathy donors' references (1)
CD45+CD3+ (cells/mm3)	631	687	578	711	1018	605-2460 cells/mm3
CD45+CD3+CD4+ (cells/mm3)	122	156	116	160	240	493-1666 cells/mm3
CD45+CD3+CD8+ (cells/mm3)	447	489	370	504	669	224-1112 cells/mm3
CD45+CD19+ (cells/mm3)	0	0	0	0	0	72-520 cells/mm3
CD45+CD3- CD16+CD56+ NK cells (cells/mm3)	232	253	200	------	359	73-654 cells/mm3
IgG (mg/dL)	403	450	687	651	614	700-1600 mg/dL
Immunoglobulin Replacement (IVIg)	Monthly - first year after CAR-T cell therapy Presently, every 3m					

POSTERS PRESENTATIONS

ALLOGENEIC HSCT

ACUTE MYELOMONOCYTIC LEUKEMIA WITH INV(16) WITH EXTRAMEDULLARY RELAPSE AND PERICARDIAL EFFUSION AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

Aline Sinhorelo Ribeiro[1], Júlia Plentz Portich[1], Lisandra Della Costa Rigoni[1], Sheila Nogueira do Amaral[1], Marina de Almeida Furlanetto[1], Fernanda Fetter Scherer[1], Liane Esteves Daudt[1], Lúcia Mariano da Rocha Silla[1], Claudia Caceres Astigarraga[1] & Alessandra Paz[1].

1. Bone Marrow Transplantation and Hematology Department from Hospital de Clínicas de Porto Alegre, Brazil.

Introduction: Acute myeloid leukemia (AML) with inv(16)(p13q22) or t(16;16)(p13;q22) is generally associated with an overall good prognosis, although relapses occur in about 30% of cases.Some of these patients may benefit from a more aggressive treatment strategy,including hematopoietic stem cell transplantation (HSCT) depending on treatment response.

Objective: We aim to describe a case of a patient with AML with inv(16)(p13q22), treated with HSCT,with an early relapse also treated,and posterior extramedullary relapse.

Results:The patient is a 25 years old male with acute myelomonocytic leukemia with inv(16) diagnosed in October 2017.He was submitted to induction treatment with 7+3 and achieved a partial remission,underwenting a reinduction with 7+2, achieving a complete remission.He consolidated with 3 cycles of HIDAC.He was classified as high risk due to induction failure.He was submitted to a matched 12x12 related HSCT in november 2018,conditioning with BuCy, graft versus host disease (GVHD) prophylaxis with cyclosporine and methotrexate, peripheral blood graft source.He had a Grade 1 acute gastrointestinal GVHD. He was on complete remission,with negative minimal residual disease and with 100% donor chimerism on D+100.On D+180 evaluation,he had a diagnosis of bone marrow and CNS early relapse, with 24% blasts on bone marrow and 64% donor chimerism.He was submitted to 8 cycles of azacitidine,5 doses of donor lymphocytes,in addition to 5 intrathecal chemotherapies with cytarabine, methotrexate and dexamethasone, achieving complete remission, with 98% donor chimerism and negative CNS,finishing in January 2020.In June 2020, he had a new CNS relapse. He then went to a 18Gy CNS radiotherapy, with complete response, until october 2020.In february 2021 he reached to the emergency department because of a dry cough,which worsened at bedtime,associated with weight loss and fever.He had reduced murmurs on cardiorespiratory auscultation, and cervical and axillary palpable lymphonodes.Chest x-ray revealed an enlarged cardiac silhouette, and echocardiogram showed a massive pericardial effusion without signs of tamponade.Full body CTs revealed nodular lesions in abdominal organs, retroperitoneum and other soft tissues and bones,even in the fat located between the piriformis muscle.He had a pericardiocentesis with drainage of 1.1L of sero-hematic pericardial fluid,with 29.4% of myeloid blasts on immunophenotyping.On bone marrow analysis, he had 0,3% of myeloid blasts.Due to performance status and unavailability of other treatment options in the public health system,the patient was treated with palliative oral etoposide.He had disease progression and died after 40 days of palliative care, in April 2021.

Conclusion: Extramedullary relapse of AML following allogeneic HSCT remains a poorly understood outcome.AML with inv(16)(p13q22) can behave as an aggressive disease, although relapse can occur in later times,as exemplified by our case report.

Keywords: allogeneic stem cell transplantation. Acute myelomonocytic leukemia with inv(16). Extramedullary relapse.

ALLOGENEIC BONE MARROW HEMATOPOIETIC STEM CELL TRANSPLANTATION - UNRELATED: COMPARATIVE ANALYSIS BETWEEN THE STATES OF PARANÁ AND SÃO PAULO REGARDING THE AVERAGE HOSPITAL STAY AND ASSOCIATED COSTS, IN THE PERIOD FROM 2016 TO 2020

Débora Fontenele Alves[1], Carol Leal de Miranda[1], Nickolas Souza Silva[1], Ana Caroline de Moraes Mittri[1], Brenda Meneses Santos[1]

1 Federal University of Ceará, Ceará, Brazil

Introduction: Bone Marrow Transplantation (BMT) is a proposed treatment for some disorders that affect hematopoietic cells, such as leukemia. The procedure can be divided into two subtypes: allogeneic, in which the medullary precursor cells come from another person, related or not to the patient; and, autologous, when precursor cells are extracted from the patient's own marrow, or from peripheral blood. Knowing the costs associated with these procedures and the average length of stay of patients is essential to outline strategies for the distribution and encouragement of these procedures homogeneously in Brazil. Objective: To perform a comparative analysis between the states of Paraná (PR) and São Paulo (SP), in relation to the average hospital stay and associated costs, from 2016 to 2020 for allogeneic BMT of unrelated hematopoietic stem cells.

Method: Descriptive, quantitative and retrospective research. Secondary data, in the public domain, collected in July 2021, at the Department of Informatics of the Unified Health System (DATASUS) were used. Allogeneic BMT hematopoietic stem cell was selected - unrelated - and the following variables were analyzed: hospitalization; average length of stay; amount; period from January 2016 to December 2020.

Results: According to the data obtained in the period analyzed, there were 781 hospitalizations for allogeneic BMT of hematopoietic stem cells - unrelated - across the country. Of these hospitalizations, the states of PR and SP had the highest national percentages, 20% (158) and 43% (335), respectively. The year 2020 was the one with the lowest number of hospitalizations, only 11% (86) throughout Brazil. As for the average hospital stay, it corresponded to approximately 35.1 days in PR and 30.8 days in SP. Both represent the states whose total hospital expenses were the highest in the country: around 18 million reais in PR and almost 39 million reais in SP.

Conclusion: Only two of the 26 brazilian states concentrate approximately 63% of hospitalizations for allogeneic BMT of hematopoietic stem cells - unrelated. The state of SP occupies the first position among the Brazilian states with the highest number of hospitalizations for allogeneic BMT - not related. The state of PR, however, compared to the state of SP, leads the average hospital stay for the same procedure. Both represent, together, 64% of the total expenses with hospitalizations throughout the country. It is necessary to observe this pattern and raise the reasons why this distribution occurs.

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR THE TREATMENT OF SICKLE CELL DISEASE (SCD): DISTINCT STRATEGIES AND COMPLICATIONS, BUT SIMILAR RESULTS WITH HAPLOIDENTICAL (HAPLO) AND HLA-IDENTICAL SIBLING HSCT

Carla Maria da Costa Zanchetta Oliveira, Roseane Vasconcelos Gouveia, Gustavo Zamperlini, Valéria Cortez Ginani, Maria Gabriela Matos Alves Dias, Carla Nolasco Monteiro Breviglieri, Luciana dos Santos Domingues, Marcia Vieira Pupim, Paola Soriano, Juliana Francielli Marques, Francisca Vanóide Brito, Adriana Seber

Onco-TMO em Pediatria; Hospital Samaritano – SP

Despite the newborn screening, clinical support and early introduction of hydroxyurea, the morbidity and mortality of SCD is still high in our country. The only curative treatment available is HSCT, indicated for patients with severe complications of the disease. There is a greater risk of graft rejection when transplanting SCD. Most children do not have a HLA-compatible healthy donor, so several groups have been developing strategies to improve the results with Haplo HSCT.

Objective: To present our experience with Haplo and HLA-identical HSCT for the treatment of SCD with the strategies developed by USP-Ribeirão Preto group and by the Vanderbilt multi-institutional learning collaborative group.

Method: For HLA-matched sibling donors transplants, conditioning was with ATG (rabbit), Busulfan and Fludarabine (Flu) and GVHD prophylaxis with CSA-MTX. For Haplo transplants, Flu, Cyclophosphamide, ATG, Thiotepa and TBI 200 cGy were used. Only one patient in this group did not receive Thiotepa: her TBI dose was increased to 400 cGy, a conditioning option developed by the international consortium based on Johns Hopkins Oncology Center's experience. GVHD prophylaxis was with PTCy, Sirolimus-MMF. The only allowed graft source was bone marrow. Before Haplo, patients remained on hypertransfusion regimen for at least 2 months, with reticulocytes <10%, HbS <20% and patients had to be using hydroxyurea at least 20 mg/kg/day. Before HSCT, patients received ganciclovir until D-1 and prophylactic acyclovir during hospitalization. During HSCT, platelets were kept >50.000/mm3, hemoglobin between 9-10 g/dL, strict blood pressure control and anticonvulsant during the entire period of Sirolimus or CSA use.

Results: Between 2016 and 2021, 6 HSCT were performed for girls ages 3 to 18 years. Two of them had HLA-matched sibling donor and 4 of them an Haplo donor. The CD34 dose ranged from 4 to 10x10(6)/kg. The median time to neutrophil recovery was 22 days after Haplo, versus 18 days after HLA-identical siblings transplants. Two of 4 Haplo patients had acute skin GVHD and 1 had chronic moderate GVHD, all of them responsive to steroids. After HLA-identical HSCT, 1 patient had dry eyes, and another had moderate chronic skin and GI GVHD and still receives imunossupression almost 5 years after HSCT. One patient in each group had mixed chimerism. The patient who did not receive Thiotepa had decreasing mixed chimerism, coinciding with low adherence to sirolimus. It was reverted with medication adjustment and donor lymphocyte infusion. With a median follow-up of 563 days, all patients are healthy. All children had successive viral reactivations that required appropriate treatment.

Conclusions: We observed promising results in this small cohort, and similar outcomes after Haplo and HLA-identical donor transplants. It is important that the medical team has experience in Haploidentical transplantation to deal with the complications. Thiotepa seems to be important for engraftment.

Keywords: Allogeneic Hematopoietic Stem Cell Transplantation; Sickle Cell Disease; haploidentical HSCT; HLA-identical sibling HSCT

Patient	1	2	3	4	5	6
Age (years)	18	10	3	14	15	4
HSCT	HLA-identical sibling	HLA-identical sibling	Haploidentical	Haploidentical	Haploidentical	Haploidentical
Conditioning	ATG/Bu/Flu	ATG/Bu/Flu	Flu/Cy/ATG/TT/ TBI 200	Flu/Cy/ATG/ TBI 400	Flu/Cy/ATG/TT/ TBI 200	Flu/Cy/ATG/TT/ TBI 200
GVHD prophylaxis	CSA/MTX	CSA/MTX	PTCy/Sirolimus	PTCy/Sirolimus	PTCy/Sirolimus	PTCy/Sirolimus
Bone marrow stem cells source	Bone marrow	Bone marrow	Bone marrow	Bone marrow	Bone marrow	Bone marrow
CD34 dose/kg	4x10(6)	6,81x10(6)	10x10(6)	9x10(6)	4,74x10(6)	7,81x10(6)
Neutrophil recovery	D+16	D+20	D+23	D+24	D+22	D+19
GVHD	yes	yes	yes	yes	yes	no
Chimerism	Stable mixed	complete	complete	Decreasing mixed	complete	complete
Viral reactivation	yes	no	yes	no	no	yes

BONE MARROW TRANSPLANTATION IN MYELOFIBROSIS: HIGH INCIDENCE OF GRAFT VERSUS HOST DISEASE IS AN OBSTACLE TO CLINICAL OUTCOMES

Lara Faria Souza Dias[1], Fabio Pires de Souza Santos[1], Mariana Nassif Kerbauy[1], Lucila Nassif Kerbauy[1], Andreza Alice Feitosa Ribeiro[1], Leonardo Javier Arcuri[1], Viviane de Jesus Torres Lima[1], Anderson Felipe da Silva[1], Carolina Leme de Moura Pereira[1], Newton de Freitas Centurião[1], Carolina Perrone Marques[1], Ana Carolina Vieira de Lima[1], Luana Nobrega da Costa[1], Jade Zezzi Nascimento[1], Nelson Hamerschlak[1]

1Hospital Israelita Albert Einstein, São Paulo, Brazil

Introduction: Despite the availability of new agents in the therapeutic arsenal of myelofibrosis (MF), the only potential curative treatment is allogeneic bone marrow transplantation (BMT). Unfortunately, BMT in MF is associated with a mortality of around 50%, whether related to transplant (TRM) or to relapse. Determining the risk factors and the main causes of TRM in MF is of paramount importance to prevent adverse outcomes.

Objective: Analyze clinical, laboratorial and characteristics of the BMT of patients with MF transplanted in a single service.

Methods: This is a retrospective study with 16 patients diagnosed with MF undergoing BMT between 2010 and 2020.

Results: The median follow-up was 2.4 years and the overall survival at 2 years was 80% (CI95 62-100%). Eleven of the sixteen patients were women (68%). The median age at diagnosis was 54 years. Half of the participants were asymptomatic at diagnosis and were referred for investigating an abnormal blood count. At diagnosis, 8 patients had splenomegaly (50%), 4 had night sweats (25%) and 2 presented with weight loss (12.5%). From the 14 patients who had the result of the karyotype, 11 were normal (78%) and 3 had alterations (21%; del5, n=2, and del20, n=1, were the alterations found). Ten patients had the JAK2 V617F mutation (83%), 1 had CALR mutation and 1 had MPL (8%). Other mutations found were: ASXL1 (33%), SRSF2 (16%), TET2 (16%), ETV6, EZH2, U2AF1. Primary MF corresponded to 60% of cases and MF secondary to essential thrombocythemia occurred in 40%. Of the 16 transplants performed, 5 were matched-sibling, 5 full matched unrelated donor, 2 mismatched unrelated, 1 cord blood, and 3 haploidentical. Seven patients (43%) had previously used JAK2 inhibitor. Peripheral blood cell source was used in 9 patients (56.25%), followed by bone marrow (37.5%) and 1 umbilical cord blood (6.25%). Reduced intensity transplantation was done in 9 patients (56%) and myeloablative in 7 patients (44%). The association of Busulfan, Fludarabine and Antithymocyte Globulin (BuFlu±ATG) was the most common conditioning regimen. The busulfan serum level target was 4000 AUC, associated with ATG in unrelated cases (43.75%). All patients had neutrophil engraftment, with a median of 15 days (9-22). Six patients died. The causes of death were: cerebral ischemia (n=1), infection (n=1) and transformation to acute myeloid leukemia (n=1). Of the 16 patients, 2 had grade IV acute GVHD (12.5%), 3 patients had grade III (18.75%) and 4 had grade II (25%).

Conclusion: Despite the small number of cases, our results were similar to those in the literature using the BuFlu regimen with the proper dosage of Busulfan. Optimizing the conditioning regimen and the use of JAK2 inhibitors appears to have contributed to the improvement of the BMT engraftment rate for myelofibrosis. However, new strategies are needed to decrease the incidence of GVHD and thus improve clinical outcomes in this transplanted population.

Keywords: Allogeneic stem cell transplantation. Myelofibrosis. GVHD.

COMPREHENSIVE GERIATRIC ASSESSMENT IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN OLDER THAN 50 YEARS: A MULTICENTRIC STUDY

Yara Ceres E Silva Ferreira Lima[1]; Ana Claudia Ferrari Dos Santos[2]; Vergilio Antonio Rensi Colturato[2]; Mair Pedro De Souza[2]; Anderson João Simioni[2]; Sarah Emanuelle Viana Campos[1]; Fernando Barroso Duarte[1].

1. Hospital Universitário Walter Cantidio, Fortaleza - CE - Brasil;
2. Hospital Amaral Carvalho, Jau - SP - Brasil.

Introduction: The allogeneic hematopoietic stem cell transplant (HSTH) emerged as important strategy in acute leukemia, lymphomas, and solid neoplasms treatment, in addiction to benign disease, for example aplastic anemia. This treatment requires myeloablative chemotherapy therapy followed by the infusion of hematopoietic stem cell from the donor. Furthermore, this processing has any risks, since infections, graft versus host disease (GVHD) to death. Over the decades, the cases of hematologic disease that needs allogenic transplant is growing, requiring a comprehensive geriatric assessment as a mechanism to choose the better treatment option.

Objective: To apply a clinical frailty score and Karnofsky score in allogeneic hematopoietic stem cell older than 50 years old for three years in Walter Cantídio University Hospital (Fortaleza/Ceará) and in Amaral Carvalho Hospital (Jaú/São Paulo), expecting to recognize the profile of this patients and to demonstrate the relation between the clinical frailty score and overall survived, besides to estimate the contribution of GVHD prophylaxis and relapse in overall survival.

Methods: Multicentric, retrospective, descriptive, analytical and quantitative study, acquiring dates by means of exams and medical record from Walter Cantídio University Hospital in Fortaleza/Ceará and Amaral Carvalho Hospital in Jaú/São Paulo.

Results: The study selected 252 patients, 147 males and 105 females, sort in gender, disease, HCTCI score, CFS and KPS. In three years, the overall survival in FIT score is 2,46 years, while in FRAILTY score is 1,82 years. About the prophylaxis, the combination of cyclosporine, mycophenolate mofetil, cyclophosphamide had worse results than others prophylaxis. As expected, in case of relapse, there is shorter survival.

Conclusion: The elderly population require a geriatric score in order to evaluate the profile of this patients once the allogeneic transplant must happen, then FIT patients has longer survival than FRAILTY patients.

DONOR CELL-DERIVED CHRONIC MYELOMONOCYTIC LEUKEMIA DEVELOPING 25 YEARS AFTER ALLOGENEIC BONE MARROW TRANSPLANTATION IN A PATIENT WITH CHRONIC MYELOID LEUKEMIA

Marcia Quiroga[1], Marco Antonio Bitencourt[2], Ana Paula Azambuja[1,2], Ana Teresa Braz[1], Joselito Getz[1], Luciana Nasser Dornelles[1], Roseli R. Silva[1], Rafael Marchesini[2], Vaneuza Araújo Moreira Funke[2], Samir Nabhan[2], Ricardo Pasquini[2], Alberto Cardoso Martins Lima[1]

1 Immunogenetics Laboratory, Complexo Hospital de Clínicas, Federal University of Paraná
2 Bone Marrow Transplantation Unit, Complexo Hospital de Clínicas, Federal University of Paraná

Donor Cell Leukemia (DCL) is a rare cause of leukemia relapse after allogeneic HSCT, occurring in approximately 0.1% of transplants. Although the DCL pathogenesis is still unclear, it seems to involve intrinsic and extrinsic factors to the recipient and donor. Moreover, advanced molecular methods have revealed a gradual increase in reported cases. Here we describe a unique case of donor cell-derived chronic myelomonocytic leukemia (CMML) developing 25 years after BMT for chronic myeloid leukemia. In 1993, a 40-years old female patient underwent BMT with an HLA-identical brother (52 years old). Conditioning regimen was busulfan 16 mg/kg and cyclophosphamide 120 mg/kg; GVHD prophylaxis was cyclosporine, methotrexate, and methylprednisolone. On day +24, the patient had a neutrophil count of 2,535/µL, with evidence of donor cell chimerism by cytogenetic analysis (46,XX[9]//46,XY[25]). In 2018, the patient was 65-years old and returned to the service presenting leukocytosis (20,000/µL) with neutrophilia and left shift, associated with sustained monocytosis (>3,800 monocytes/µL) and signs of dysplasia in peripheral blood. Bone marrow evaluation showed neutrophilia with cytoplasmic degranulation/abnormal nuclei, dysplastic monocytes, and 1.5% immature cells, suggestive of Myeloproliferative/Myelodysplastic Syndrome. Peripheral blood flow cytometric immunophenotyping confirmed the presence of 3.4% of myeloid blasts in addition to abnormal neutrophilia/monocytosis (CD56 positive). Bone marrow karyotype showed male cells and inversion of chromosome 7, //46,XY,inv(7)(q22q31). Real-time PCR detected no BCR-ABL transcripts. Next, chimerism testing was performed with Short Tandem Repeats (STR) markers by capillary electrophoresis and analyzed with GeneMapperTM software, which showed 100% of donor cells in total leukocytes. The chimerism analysis was repeated three years after with cell subpopulations (T-cells, B-cells, and granulocytes) and confirmed the persistence of 100% of donor STR markers, thereby validating the DCL occurrence. Altogether, clinical investigation and laboratory tests were consistent with a diagnosis of donor-derived CMML. In 2021, the patient had marked leukocytosis (197,000/µL), and thrombocytopenia and expired three days after hospitalization due to disease progression. Interestingly, the BMT donor was also diagnosed with Myelodysplastic Syndrome after 23 years. He showed a similar phenotype to that of the patient and cytogenetics with 7q deletion and passed away in 2020. We speculate that the development of CMML in the recipient could be related to clonal hematopoiesis in donor cells that were infused 25 years earlier. In conclusion, the present case highlights the importance of a comprehensive evaluation to identify DCL in patients undergoing allogeneic HCT. Our report also underscores the need for frequent monitoring by STR chimerism testing to confirm donor-derived leukemia and distinguish it from primary disease relapse.

Keywords: Donor cell leukemia. Clonal hematopoiesis. Bone marrow transplantation. Chimerism. STRs.

EFFECTIVENESS AND SAFETY OF HIGHER TOTAL DOSES OF ATG COMPARED WITH LOWER TOTAL DOSES IN PATIENTS UNDERGOING ALLOGENEIC HSCT IN A TEACHING HOSPITAL

Bruno Mateus de Castro[1], Joice Zuckermann[2], Thiago Almirante Cunha[1], Alessandra Paz[2], Leila Beltrami Moreira[1]

1 Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brasil
2 Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, Brasil

Introduction: Rabbit anti-thymocyte immunoglobulin (ATG) is used during allogeneic hematopoietic stem cell transplantation (Alo-HSCT) as prophylaxis of graft-versus-host disease (GVHD). The total doses of ATG (based on mg/kg) and infusion days vary between transplant centers without a standard dose.

Objectives: To compare higher total dose of ATG with lower total doses in patients undergoing allogeneic HSCT for clinical outcomes of transplantation.

Methods: retrospective observational study based on the analysis of medical records of patients undergoing allogeneic HSCT between the years 2015-2020. High ATG dose (greater than or equal to 10 mg/kg) was considered as exposure.

Results: From 152 allogeneic HSCT in the period, 73 patients who used ATG were included, divided into two groups: low total dose (less than 10 mg/kg; 31 patients) and high total dose (greater than or equal to 10 mg/ kg; 42 patients). In the high-dose group, 69% of patients were male, in the low-dose group 58% (p 0.33) with a median age of 11 and 17 years, respectively. Among the diagnoses, the most prevalent were Acute Lymphoblastic Leukemia, Acute Myeloid Leukemia, Myelodysplastic Syndrome and Aplastic Anemia. Among leukemias, the frequency of early leukemia was higher in the high-dose group, whereas advanced leukemia was more prevalent in the low-dose group (52.6% and 30.8%; 47.4% and 69.2%, p 0.22, high and low dose, respectively). Cell source was predominantly bone marrow with myeloablative conditioning modality (88.1% and 64.5%; 71.4% and 54.8% high and low dose, respectively). Donors were mostly unrelated (90.3% and 74.2%, high and low dose, respectively) with no statistical difference between the types of mismatch in HLA between groups. The median of CD34+ cells count infused between the groups was 3.5 x 10^6/kg and 4.8 x 10^6/kg and total nucleated cells count were 3.9 10^8/kg and 6.1x 10^8/kg. The median time to neutrophil recovery was 20 and 18 days (high and low dose group, respectively). There was no statistical difference between the groups for the evaluated outcomes of acute GVHD (I-II; III-IV), chronic GVHD (mild, moderate and severe), Cytomegalovirus (CMV) reactivation, EBV (Epstein-barr virus) reactivation, sepsis, graft failure and mortality.

Conclusion: There was no association between higher or lower total doses of ATG and the incidence of HSCT clinical outcomes in the studied sample.

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PAROXYSMAL NOCTURNAL HEMOGLOBINURIA - EVALUATION OF TWO DIFFERENT TIME PERIODS

Ana Paula de Azambuja; Michel Michels Oliveira; Marco Antonio Bitencourt; Vaneuza Funke; Ricardo Pasquini.

Hospital de Clínicas da Universidade Federal do Paraná, Curitiba - PR - Brasil.

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired clonal disease of hematopoiesis that presents with hemolysis or thrombosis and can develop bone marrow failure with severe aplastic anemia (SAA). Although the development of new drugs with anti-complement activity may help decrease hemolytic activity in most patients, treatment with allogeneic hematopoietic stem cell transplantation (HSCT) remains the only curative approach to PNH.

Objective: to report the experience of 24 related and 6 unrelated bone marrow transplants in the treatment of patients with hemolytic PNH in the classical form and to compare the outcome in the period 1988-2000 with the most recent experience (2001-2021).

Methods: 14 patients (46.6%) with PNH diagnosed by Ham-saccharose test undergoing BMT until the year 2000 and 16 (53.3%) diagnosed by flow cytometry analysis and transplanted after the year 2001 were included.

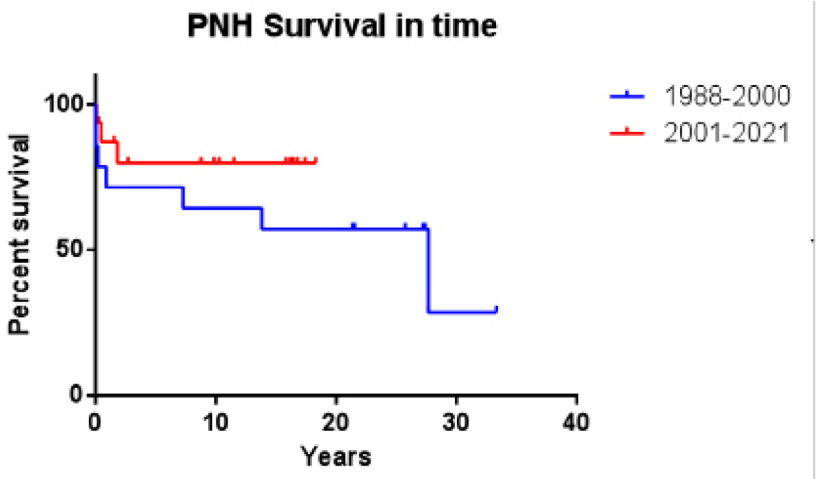
Results: There were 11F/19M, with a mean age at diagnosis of 25 years (13-57) and age at transplantation of 29.5 years (14-58 years). The mean time from diagnosis to HSCT was 2,5 years (range: 1-4). All patients were transfusion dependent, had some degree of cytopenia, and had received various therapies prior to transplantation such as cyclosporine (CyA), prednisone, and thymoglobulin. There were three recent patients who received Eculizumab for 1, 2 and 3 years prior to transplantation.

Results: Stem cell sources were bone marrow (n=28) or peripheral blood (n=2), from compatible donor (n=23), incompatible donor (n=1) and six unrelated incompatible donors (n=6). Conditioning consisted of busulfan 11, cyclophosphamide 120 mg in 24 patients and busulfan and fludarabine in six. GVHD prophylaxis consisted of methotrexate and cyclosporine.

Overall survival was 33.3% (10/30), with 7/14(50%) patients diagnosed and transplanted between 1988-2000 dying, with a median survival of 27.7 years, while 3/16 (18.75%) of the 2001-2021 group died, median survival not reached (p=0.24).

Most of the patients (5/8) who died had been transplanted before 2002. Two of them died before neutrophil implantation due to transplant-related toxicity, three patients died due to acute GVHD complications two, six and eleven months after HSCT, and one patient died due to disease relapse 7 years after transplantation. There was one premature death in 2007 and one death 7 months after transplant in 2009 due to sudden death of unexplained cause. The only patient who died in 2015 had received a bone marrow related mismatch and relapsed with hemolytic disease and large PNH clone two years after transplant.

Conclusion: Related or unrelated HSCT are curative approaches to PNH and can be used in classic hemolytic PNH when immunosuppression and Eculizumab are not sufficient to control cytopenia and hemolysis. Morbidity and mortality have decreased over time, showing that this is a safe and effective therapy.



IMPACT OF THE COVID-19 PANDEMIC ON THE RELEASE AND CRYOPRESERVATION OF PRODUCTS FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A CELL PROCESSING CENTER IN SOUTHERN BRAZIL

Melissa Helena Angeli, Gabrielle Dias Salton, Anelise Bergmann Araújo, Juliana Gonçalves Constante, Tissiana Schmalfuss, Juliana Monteiro Furlan, Liane Marise Röhsig

Centro de Processamento Celular, Hospital de Clínicas de Porto Alegre, Rio Grande do Sul, Brasil

Introduction: Since COVID-19 has been recognized as pandemic worldwide, hematopoietic stem cells (HSC) for use in allogeneic transplants, which were usually collected and fresh infused, started to be cryopreserved, following national and international guidelines. Many transplant centers have adopted this practice to avoid complications, such as donor infection by SARS-COV-2 and logistical difficulty in transporting the product, ensuring the donor and the recipient's safety and graft availability on the day of transplantation. Objective: Evaluate the impact of the COVID-19 pandemic on HSC received and released for allogeneic transplantation by the cell processing center (CPC) from a southern Brazil hospital and the impact on the number of cryopreserved HSC prior transplantation.

Methodology: A retrospective analysis through electronic records was performed of received, released and cryopreserved allogeneic HSC from bone marrow and peripheral blood stem cells. The data were compared considering the 14-month interval of the pandemic period (May/2020 to June/2021) and the same time interval in the pre-pandemic period (January/2019 to March/2020). Results: In the pre-pandemic period, HSC were collected from 40 donors, of which 20 were transplanted at the center, 9 were sent to national destinations and 11 to international destinations. During the pandemic period, the number of collections at the center was 28, with 24 transplanted at the hospital, 1 released for national destination and 3 for international destinations. Regarding the receipt of material collected outside the transplant center, in the pre-pandemic period, 7 international and 6 national donations were received, while in the pandemic period, 6 international and 6 national donations were received. Assessing the impact on the cryopreservation of products, it was found that in the pre-pandemic period, of the 33 materials processed at the CPC for allogeneic transplantation in the institution, 26 were released for fresh transplantation (78.8%) and 7 were cryopreserved (21,2%). Thirty six allogeneic products were processed and all (100%) were previously cryopreserved for transplantation during the pandemic period.

Conclusions: There was no impact on the number of allogeneic transplants performed at the institution, either by donations made at the own institution, or by donations received from national or international centers. However, it was possible to observe a decrease in the release of HPC products to national and international destinations. Data showed a significant increase in cryopreservation procedures for allogeneic transplantation in the pandemic period, resulting in changes on the CPC logistics and increasing the financial costs associated with this procedure. In addition, the possible impacts on the quality of the material and the clinical adjustments necessary for the transplantation of cryopreserved material must be considered.

Keywords: Allogeneic Transplantation. Hematopoietic Stem Cells. Cryopreservation. COVID-19. Cell Processing Center. Bone Marrow. Peripheral Blood Stem Cells.

PANORAMA OF INCIDENCE, DISTRIBUTION AND EFFICACY OF HEMATOPOIETIC STEM CELL TRANSPLANTS PERFORMED IN THE NORTHEAST REGION OF BRAZIL IN THE LAST DECADE.

Carol Leal de Miranda[1], Nickolas Souza Silva[1], Débora Fontenele Alves[1], Ana Caroline de Moraes Mittri[1], Brenda Meneses Santos[1]

1 Federal University of Ceará, Ceará, Brazil

Introduction: Hematopoietic stem cell transplantation (HSCT) is one of the main therapeutic alternatives for some hematologic malignancies. HSCT is subdivided into autologous, in which the patient's own cells are used, and allogeneic, when the cells come from a compatible donor, which may or may not be related. In addition, stem cells can come from bone marrow, peripheral blood, or umbilical cord blood.

Objective: To realize an analysis of the incidence, distribution and effectiveness of hematopoietic stem cell transplants, over the last 10 years, in the Northeast (NE) region of Brazil.

Method: Descriptive, quantitative and retrospective research. Secondary data, in the public domain, collected in July 2021, at the Department of Informatics of the Unified Health System (DATASUS), in the Hospital Procedures section of the SUS, were used. For the analysis of the registered HSCT, frequencies and percentages of the following variables were used: hospitalizations per year of service, period from January 2011 to December 2020; in Brazil, by state.

Results: According to the data obtained in the analyzed period, there were 2,924 hematopoietic stem cell transplants in the Northeast region of Brazil, concentrated in the states of Pernambuco (56.1%), Ceará (18.9%), Rio Grande do Norte (15.1%) and Bahia (9.9%). Of this total number of transplants, 65.4% were autogenic and 34.6% were allogeneic, being 81.8% related and 18.2% unrelated. As for post-transplant complications, Pernambuco stood out with the highest number of notifications (2,371), of which 61.8% corresponded to autogenic HSCT and 38.2% to allogeneic HSCT. Also for the state of Pernambuco, 6,944 admissions for treatment of post-HSCT complications were computed, with approximately 99.97% of the related allogeneic type.

Conclusion: The Northeast region of Brazil, made up of nine states, has an unequal distribution in terms of HSCT. Only the four states mentioned above have any record of this procedure in DATASUS, predominantly the autogenic and related type - when considering those of an allogeneic character. Pernambuco stands out as the main contributing state to this statistic in the NE region. However, PE also presents a marked number of post-autogenic HSCT complications, paradoxically to the data analyzed regarding the treatment of complications, which were predominantly related to allogeneic HSCT. In this context, further studies are needed to investigate the factors associated with the uneven distribution of HSCT in the NE and the high rate of complications related to HSCT - allogeneic in PE.

QUANTITATIVE ANALYSIS OF ALLOGENEIC BONE MARROW HEMATOPOIETIC STEM CELL TRANSPLANTATION - UNRELATED IN TIMES OF PANDEMIC IN NORTHEASTERN BRAZIL

Ana Caroline de Moraes Mittri[1], Carol Leal de Miranda[1], Nickolas Souza Silva[1], Débora Fontenele Alves[1], Brenda Meneses Santos[1]

1 Federal University of Ceará, Ceará, Brazil

Introduction: Allogeneic hematopoietic stem cell transplantation (HSCT-A) from bone marrow is a procedure that aims to replace the deficient hematopoietic cells of its recipient with healthy cells from a donor, whether a close relative or an unrelated person, since that there is histocompatibility between them. Therefore, it is necessary that the donor is available to undergo certain hospital procedures so that their hematopoietic stem cells are collected and transfused in the proper recipient.

Objective: To assess whether the COVID-19 pandemic negatively interfered with the amount of HSCT-A in the bone marrow by unrelated individuals performed in the Northeast region of Brazil.

Methods: Observational, transversal and retrospective research. Data from the public domain, collected in July 2021, at the Department of Informatics of the Unified Health System (DATASUS) were used together with the Hospital Information System of the SUS (SIH/SUS). For the analysis, the frequencies and percentages of the following variables were evaluated: procedures; Hospital Admission Authorization (AIH) approved by year of care according to Federation Region, from January 2011 to December 2020, with the values for the Northeast region of the country being studied.

Results: From the data obtained, it was found that in the period analyzed, in the Northeast region of Brazil, 245 hospitalizations for HSCT-A of bone marrow - unrelated - were performed. Over the years 2011 to 2019, there is a progressive annual increase in the number of transplants and in 2020, there is a reduction of 72.5% (a drop of 28 procedures) compared to the previous year. The biggest drop, 85%, could be noticed in the state of Pernambuco, ranging from 16 procedures performed in 2019 to 3 in 2020.

Conclusion: Thus, a significant reduction in HSCT-A was noted in 2020 compared to In the previous year, despite the annual growth trend, it is important to carry out a careful analysis to understand the reasons that justify such an event and the possibility of a relationship with the context of the pandemic caused by COVID-19 which began that same year. Having identified the factors, it is valid to seek ways to restore the annual growth of procedures performed, such as through campaigns aimed at clarifying the safety and care of bone marrow donation in the context of a pandemic, for example.

READMISSIONS AND SURVIVAL IN A COHORT OF PATIENTS UNDERGOING HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A TEACHING HOSPITAL FROM 2015-2021

Joice Zuckermann[1], Bruno Mateus De Castro[2], Thiago Almirante Cunha[2], Priscila De Oliveira Da Silva[1], Alessandra Aparecida Paz[1], Fernanda Fetter Scherer[1], Lisandra Della Costa Rigoni[1], Marina De Almeida Furlanetto[1], Claudia Caceres Astigarraga[2], Liane Esteves Daudt[1], Lucia Mariano Da Rocha Silla[1], Leila Beltrami Moreira [2]

1 Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, Brasil
2 Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brasil

Introduction: Haploidentical hematopoietic stem cell transplantation (HSCT-Haplo) has increased significantly in recent years and has become a viable alternative for patients without compatible donors. This strategy allows universal availability and faster donor acquisition, along with accessibility and provision of immunotherapy in the post-transplant period. The main disadvantages are the increased risk of graft vs. host disease (GVHD), the need for T cell depletion in vivo or ex vivo, leading to a higher incidence of infection by low immune reconstitution and a high incidence of recurrence.

Objective: To describe the clinical characteristics of patients undergoing HSCT-Haplo, the reasons for readmissions and survival.

Methods: Retrospective analysis of medical records of patients undergoing HSCT-Haplo from 2015 to 2021.

Results: 32 patients (35 haploidentical transplants), 12 adults (mean 36.8 years; SD 12.4; 69.2%% female) and 20 pediatric patients (mean 8.8 years; SD 5.9) were evaluated ; 63.6% male). The main diagnoses were Acute Myeloid Leukemia (21.9%), Acute Lymphoid Leukemia (21.9%) and Combined Immunodeficiency (9.4%). The donors were father (25.7%), mother (25.7%), sister (22.9%) and brother (20%). Cell sources were bone marrow (71.4%) and peripheral blood (28.6%). Most conditionings were non-myeloablative (51.4%), followed by myeloablative (31.4%) and RIC (17.1%).Most patients did not have pre-transplant comorbidities (57%), in patients who did have comorbidities, the most frequent was pneumopathy (12.5%). Two patients (6.25%) underwent previous allogeneic HSCT and 1 patient underwent previous autologous HSCT. The main causes of readmission were: infection (60%), recurrence (20%) and acute GVHD (20%).The readmission rate at 1 year was 62.5% (20 patients), with a median of readmissions of 1 (p25 0 ; p75 3). The time between HSCT and the first readmission ranged from D+38 to D+539. The median survival was 12 months (p25 3.5 p75 18.7), with 17 deaths (53.1%) in the period observed.

Conclusion: Haploidentical HSCT is a potentially curative procedure. In the cohort, readmission rates within one year were frequent, which characterizes the complexity of the procedure, with infection being the most common cause. The median survival in the cohort was one year, with high rates of acute GVHD and relapse.

RETROSPECTIVE EVALUATION OF THE INCIDENCE OF CYTOKINE RELEASE SYNDROME AND INFECTIONS IN PATIENTS SUBMITTED TO ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH HAPLOIDENTICAL DONOR

Rodrigo C Bonardi[1], Livia Mariano[1], Leonardo Otuyama[1], Bruna Moraes[1], Vanderson Rocha[1]

[1]Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brasil

Introduction: Allogeneic hematopoietic stem cell transplantation (HSCT) from HLA-identical related donors has historically had the best results; however, this donor is only available in 30% of cases. Haploidentical HSCT using post-cyclophosphamide (Haplo-PTCy) has emerged as an alternative, showing results similar to those of HLA-compatible donors. In haploidentical HSCT with in vivo T cell depletion, fever and inflammatory signs have been observed without the presence of active infection in the first days after the infusion of progenitor cells, a condition called cytokine release syndrome (CRS) and may be associated with longer neutrophil/platelet graft time in severe cases. The graft-versus-host disease (GVHD) prophylaxis with PTCy demonstrated an increase in the number of viral infections in this setting.

Objectives: To describe the incidence of CRS and infections (bacterial, fungal, viral) in Haplo-PTCy in the period from onset of conditioning to D+180.

Casuistry: Patients undergoing Haplo-PTCy from January 2014 to April 2020.

Methods: Single-center, retrospective, observational study. Retrospective evaluation through analysis of medical records. Evaluate the outcomes - CRS incidence, grafting time, acute GVHD (100 days) and mortality until D+180.

Results: A total of 34 patients met the eligibility criteria. The median age was 35.6 years; 18 were male (52.9%);14 patients had AML (41.1%), 10 ALL (29.4%), 8 other hematologic malignancies (13.5%). The conditioning performed was myeloablative (MAC) in 20 patients (58.8%), and reduced intensity in 10 patients (29.4%). The source of cells was bone marrow (BM) in 20 (58.5%). CRS occurred in 22 patients (64.7%, CI 46.4-80.25%), and severe (greater than equal grade II) in 4 patients (18.2%); in these 22 patients the source was peripheral blood in 13 patients and the MAC conditioning regimen in 13 patients. The median time of neutrophils recovery was 15.9 (??) days. Graft versus host disease (GVHD) grade II-IV occurred in 19 patients (55.8%) and III-IV 4 patients (11.7%). At D+180, 11 patients died (32.3%). Regarding infections, 31 (91.1%) patients had bacterial infection up to D+180 - being 19 (59.3%) bloodstream infections, 6 urinary tract infections (19.3%); 31 of viral infections (91.1%), being the main reactivations by CMV (31 patients, including 3 cases of CMV disease), and 11 BK Polyomavirus; 7 patients had fungal infections (20.5%) - 4 classified as probable aspergillosis. The mean follow-up of patients alive was 9.4 months, with estimate overall survival of 71.8% at 6 months.

Conclusions: the incidence of CRS in patients undergoing Haplo-PTCy was comparable to previous reports. Also already described there is a high incidence of CMV reactivations - that reflects a high prevalence of CMV seropositivity in Brazilian population.

Keywords: haploidentical allogeneic transplantation; cytokine release syndrome; infection

THE ROLE OF THE CLINICAL PHARMACIST IN A MULTIDISCIPLINARY TEAM FOR THE USE OF IMMUNOSUPPRESSANTS IN POST ALLOGENEIC HSCT PATIENTS

Vanessa Oliveira[1], Joice Zuckermann[2]

1. Farmacêutica residente do Programa de Residência Multiprofissional em Saúde do Hospital de Clínicas de Porto Alegre, Porto Alegre, Brasil
2. Farmacêutica do Hospital de Clínicas de Porto Alegre, Porto Alegre, Brasil

Introduction: Immunosuppressants are widely used in patients after allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for prophylaxis of Graft versus Host Disease (GVHD). This class of drugs requires strict monitoring, as its toxicity is associated with a narrow therapeutic range, so the supervision of adherence will guarantee its efficacy and safety in rational use from admission to hospital discharge. In this sense, the clinical pharmacist can occupy a central place in the multidisciplinary team to provide adequate treatment management.

Objective: To describe the importance of the presence of a clinical pharmacist in the guidance of patients undergoing allogeneic HSCT using immunosuppressants.

Method: This is a retrospective cross-sectional study, in which clinical pharmacists belonging to a protected environment unit of a tertiary hospital, where adult and pediatric allogeneic HSCT are performed, started a program to monitor the use of immunosuppressants. Pharmacists provide a playful and complete education on access, dosage, drug-drug and drug-food interactions and possible adverse reactions, aimed at both patients and caregivers. The guidelines are also delivered at hospital discharge, in a table containing dosage and possible drug-drug and drug-food interactions.

Results: From March to July 2021, pharmacists treated twelve patients undergoing allogeneic HSCT, with nine patients receiving GVHD prophylaxis with Tacrolimus and the others with Cyclosporine, the measurement of blood concentration of these immunosuppressants is useful for dose adjustment and obtaining adequate immunosuppression with minimal toxicity. The drug Tacrolimo has a reduction of up to 27% of its absorption in the presence of food, so the proper fasting orientation for patients is important.

Conclusions: The clinical pharmacist's approach to patients undergoing allogeneic HSCT was an important factor to promote safety and adherence to treatment with immunosuppressants. This reinforces the importance of these professionals in a multidisciplinary team involved in the health care of these patients and their caregivers.

Keywords: Hematopoietic Stem Cell Transplantation. Immunosuppressants. Clinical pharmacy.

THE USE OF CYCLOPHOSPHAMIDE 50 MG/KG IN REDUCED TOXICITY CONDITIONING REGIMENS PROVIDES ENGRAFTMENT OF ALL CHILDREN WITH SEVERE APLASTIC ANEMIA UNDERGOING ALLOGENEIC TRANSPLANTS FROM UNRELATED AND HAPLOIDENTICAL DONORS.

Maria Gabriela Alves Dias Matos; Luciana dos Santos Domingues; Roseane Vasconcelos Gouveia; Juliana Francielle Marques; Gustavo Zamperlini; Valéria Cortez Ginani; Carla Maria da Costa Zanchetta Oliveira; Carla Nolasco Monteiro Breviglieri; Adriana Seber.

Equipe ONCO-TMO Hospital Samaritano, São Paulo - SP - Brasil.

Allogeneic hematopoietic stem cell transplantation (HSCT) with a HLA-identical related donor is the treatment of choice for severe aplastic anemia in children and adolescents. Immunosuppressive therapy is still used in the absence of an identical donor, however, the chance of responding to immunosuppression with rabbit ATG in our country is only 17% within three months (Clé, 2018), increasing mortality associated to infections, in addition to the risk of late disease relapse and secondary myelodysplasia. In the absence of an identical donor, transplantation with unrelated and haploidentical alternative donors has been increasing considerably. The major obstacles to its success are the high risk of graft failure, graft-versus-host disease (GVHD), and transplant-related mortality (TRM). Years ago, our team chose to increase the dose of cyclophosphamide in the conditioning regimen to 50 mg/kg to reduce the chance of rejection, but it is essential to evaluate the effectiveness of this strategy. Our objective is to evaluate the results of transplants in children and adolescents with severe aplastic anemia using 50 mg/kg in the conditioning therapy.

Method: All patients received reduced toxicity conditioning regimen: for patients with HLA-identical sibling donors, cyclophosphamide 200 mg/kg and thymoglobulin; unrelated and haploidentical donors used fludarabine, cyclophosphamide, thymoglobulin and total body irradiation 200cGy. We increased the dose of cyclophosphamide from conditioning from 14.5mg/kg/day x 2 days to 25mg/kg/day x 2 days from 2018 on due to the report of primary and secondary graft failure observed in other Brazilian transplant services. For GVHD prophylaxis we used cyclosporine and methotrexate for the related and unrelated transplants and calcineurin inhibitor, mycophenolate mofetil and cyclophosphamide post-transplant in haploidentical transplants.

Results: Between March 2013 and March 2021 our team transplanted 17 patients with severe aplastic anemia, 8 with related haploidentical donors, 6 unrelated donors and 3 HLA-identical siblings. Eleven children were transplanted with cyclophosphamide 50 mg/kg in conditioning: 7 with haploidentical donors and 4 unrelated. The mean age was 10.5 years, 8 females. The graft source was bone marrow in all but one patient. There were no primary or secondary graft failures and no transplant-related death. There was no difference in transplant morbidity with increased dose of cyclophosphamide in the conditioning therapy. With a median follow up of 86 months, all patients are alive, with complete donor chimerism, independent of transfusions and without severe GVHD.

Conclusion: Allogeneic transplantation is a safe option to cure severe aplastic anemia, with few complications during and after transplantation. The increase in the cyclophosphamide dose did not modify the morbidity and mortality of transplantation and can be considered as an option to decrease the risk of graft failure.

THE USE OF IMMUNOTHERAPY BEFORE AND AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Anderson Felipe da Silva[1], Viviane de Jesus Torres Lima[1], Lucila Nassif Kerbauy[1], Mariana Nassif Kerbauy[1], Juliana Folloni Fernandes[1], Gabriele Zamperlini Netto[1], Andreza Alice Feitosa Ribeiro[1], Nelson Hamerschlak[1]

1 Hospital Israelita Albert Einstein, São Paulo, Brazil.

Introduction: Patients diagnosed with refractory or relapsed acute lymphoid leukemia (ALL) are typically treated with conventional chemotherapy, associated with several toxicities and low complete response (CR)[1]. Immunotherapies have emerged as a new therapeutic advance not only able to offer better CR and less toxicity than conventional chemotherapies (QT) but also as bridge therapy to HSCT or rescue of relapsed patients after HSCT, with the most prominent being blinatumomab (BLIN) and inotuzumab ozogamicin (INO)[2].

Objective: Compare data from patients with B-ALL treated with immunotherapy in a Brazilian center with the current literature.

Methods: A retrospective observational study that included all patients with B-ALL treated with BLIN or INO in the service from January 1, 2015, to May 31, 2021. Data were obtained from medical records and chart analysis.

Results: In this period, 8 patients used immunotherapy, 4 children and 4 adults, with median age of 17 years (0-42). Five patients (4 BLIN and 1 INO) used immunotherapy before an allogeneic hematopoietic stem cell transplantation (HCT). 4 out of these 5 had only positive minimal residual disease (MRD+), reaching negative MRD (MRD-) in 3 (75%); 1 patient had active disease and used BLIN after the 4th relapse, obtaining partial response (PR) after 2 cycles, followed by rescue with Hyper-CVAD, reaching CR; before HCT, he had an extramedullary relapse and underwent 1 cycle of INO and radiotherapy with complete remission of the lesions, proceeding to HCT with MRD+ without active disease. Considering these 5 patients, the median number of cycles for a response was 1; 3 out of these 5 patients had chemotherapy pre-immunotherapy as a rescue attempt, achieving morphologic response, followed to immunotherapy with MRD+ (table 1). Except for one patient who died with sinusoidal obstruction syndrome (INO pre-HCT), none of the others showed significant acute toxicities. As post-HCT therapy, 4 used immunotherapy (3 BLIN and 1 INO). Of these, 1 had MRD+ and reached MRD- after BLIN and donor lymphocyte infusion (DLI) and 3 had active disease, 2 of which achieved CR with MRD- without use of QT (one remained in remission for 4 months, dying of COVID-19 and the other has remained in remission for 3 years without a 2nd HSCT) and 1 patient underwent rescue QT achieving morphologic remission with MRD+, followed by BLIN reaching MRD- and proceeded to a 2nd HCT. All 4 patients (100%) had MRD- at the end of treatment. As post-HCT therapy, the median number of cycles for response was 2.5 cycles and the median number of cycles of immunotherapy used was 3 cycles (Table 2).

Conclusion: It is known that patients with only MRD+ can reach MDR- at a rate of about 78% with BLIN3, which is similar to the 75% found in this study in pre-HCT use. In post-HCT use, published data show CR with INO of 76%4 and with BLIN of 40-45%5,6. In this study, all 4 patients achieved MRD- with the use of immunotherapy post HCT, although it is worth noting that one patient made combined use of BLIN with DLI and another of INO with Hyper-CVAD. In conclusion, the data presented demonstrates the feasibility of using immunotherapy in the Brazilian context with very good results in patients with R/R ALL comparable to the current literature.

Keywords: Allogeneic hematopoietic stem cell transplantation. Refractory or relapsed acute lymphoid leukemia. Immunotherapy.

TABLE 1. Description of patients submitted to immunotherapy before allogeneic hematopoietic stem cell transplantation

Patient	Time to relapse after HCT	Immunotherapy +/- Concomitant treatment	Active disease pre-immunotherapy	MRD Positive	Total Cycles	Morphologic Response	Respose: MRD negative	Followed by HCT / Outcome
1	-	Blinatumomab	No	Yes	1	NA	Yes	Yes
1	1 year and 10 months after HCT	Blinatumomab	Yes	Yes	1	Yes	No	No
1	2 years and 1 month after HCT	Inotuzumab + HyperCVAD + Dasatinib	Yes	Yes	2	Yes	No	Death from VOD after 2 Cycles of Inotuzumab
2	-	Blinatumomab	No	Yes	1	NA	Yes	Yes
3	1 year after HCT	Blinatumomab	No	Yes	3	NA	Yes	Yes – 2º HCT
3	1 year and 6 months after 2º HCT	Blinatumomab + DLI	Yes (extramedullary)	No	3	No	NA	Remission with chemotherapy after failure of Blinatumomab/ DLI
3	2 years and 11 months after 2º HCT	Inotuzumab + 1 cyclo of mini HyperCVAD	Yes (extramedullary)	No	4	Yes	NA	Death from COVID-19 with disease in remission
4	-	Blinatumomab	No	Yes	1	NA	No	Yes – Followed by HCT with MRD positive
4	60 days after HCT	Blinatumomab + DLI	No	Yes	2	NA	No	MRD negative after 8 cycles of DLI
5	-	Inotuzumab	Yes (extramedullary)	Yes	1	Yes - partial	No	HCT in remission after radiotherapy. Death on D+263 due to infectious complications with disease in remission

NA: not applicable

TABELA 2. Description of patients submitted to immunotherapy after allogeneic hematopoietic stem cell transplantation

Patient	Time to relapse after HCT	Immunotherapy +/- Concomitant treatment	Active disease pre-immunotherapy	MRD Positive	Total Cycles	Morphologic Response	Respose: MRD negative	Followed by HCT / Outcome
3	1 year after HCT	Blinatumomab	No	Yes	3	NA	Yes	Yes – 2º HCT
3	1 year and 6 months after 2º HCT	Blinatumomab + DLI	Yes (extramedullary)	No	3	No	NA	Remission with chemotherapy after failure of Blinatumomab/ DLI
3	2 years and 11 months after 2º HCT	Inotuzumab + 1 cyclo of mini HyperCVAD	Yes (extramedullary)	No	4	Yes	NA	Death from COVID-19 with disease in remission
6	1 year and 3 months after HCT	Blinatumomab + DLI	No	Yes	3	NA	Yes	Remain in remission without 2º HCT
7	6 months after HCT	Blinatumomab	Yes	Yes	8	Yes	Yes	Remain in remission without 2º HCT
8	12 months after HCT	Inotuzumab	Yes	Yes	2	Yes	Yes	Death from COVID-19 during treatment with disease in remission

NA: not applicable

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TIME TO TRANSPLANT: NO IMPACT OF DONOR SELECTION IN PEDIATRIC PATIENTS WITH ACUTE LEUKEMIA

Francisco Barriga, Catherine Gutierrez, Veronica Jara, Angelica Wietstruck.

Seccion de Hematologia Oncologia, División de Pediatria, Pontificia Universidad Catolica de Chile. Centro de Cancer, Red de Salud UCChristus.

Introduction: The time that lapses between indication and donor search to transplant (time-to transplant, TTT) may impact outcome in patients with acute leukemia (AL). Longer periods from donor search to transplant may interfere with timely initiation of conditioning regimen, allowing for leukemia progression or relapse. It has been postulated that related donors (RD) are at advantage to unrelated donors (URD) due to immediate availabity. Objective: To test this hypothesis we compared TTT in pediatric patients with AL between related and unrelated donor transplants.

Methods: We analyzed children with AL transplanted at our center between 2014-2021. Donor selection algorithm was (fig 1): a)Matched sibling; b) URD 10/10 or 9/10 permissive DPB1 mismatch; c) cord blood 5-8/8 high resolution >3x10e7 TNC/kg; d)haplo. All patients received standardized induction or reinduction-consolidation protocols before transplant. TTT was defined as the days between the medical indication for transplant and initiation of donor search to graft infusion. TTT was compared between related and unrelated donor transplant. (paired t test, two tailed)

Results. 47 patients were included in the analysis: 36 ALL, 11 AML; 32 Early disease (CR1, CR2), 15 advanced disease (CR3 or active leukemia) RD: 22 (13 MSD, 9 haplo) URD: 25 (16 adults, 9 UCB). Median TTT was 46 days for RD (23-155) and 63 days for URD (50-132), (two tailed p=0,9, fig 2.)

Conclusion: We found no impact of donor choice in TTT for pediatric patients with AL. This is likely because all patients receive variable weeks of chemotherapy before transplant, allowing for timely URD search. This has implications in criteria used for donor selection, which should be based in expected outcome for each disease, stage and donor type.

FIGURE 1. Donor selection algorithm

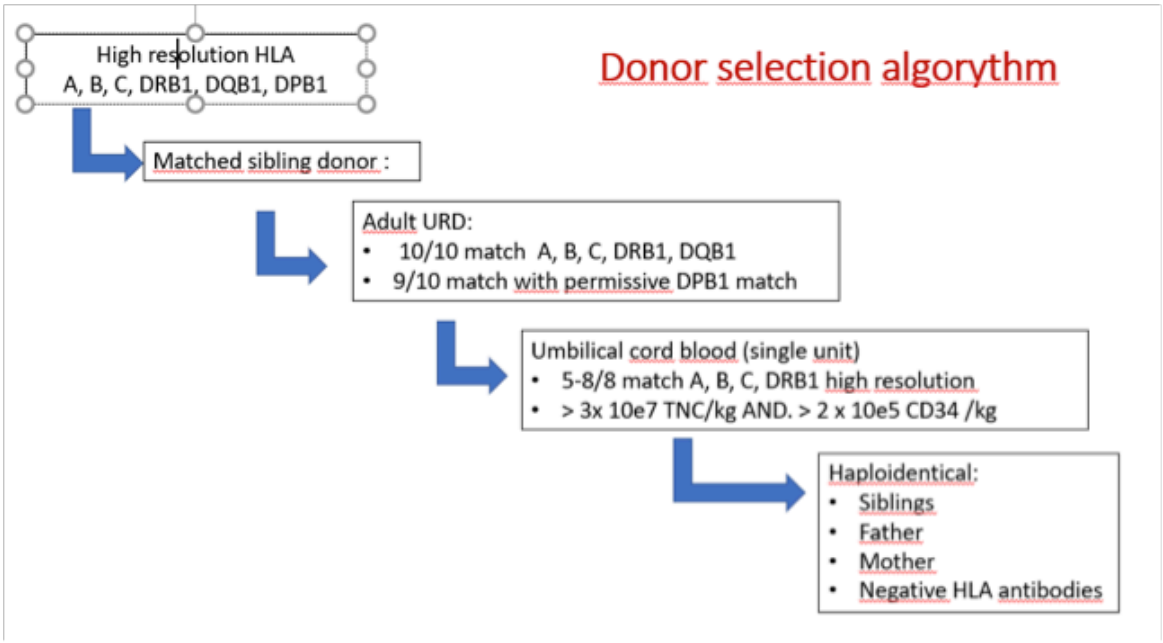
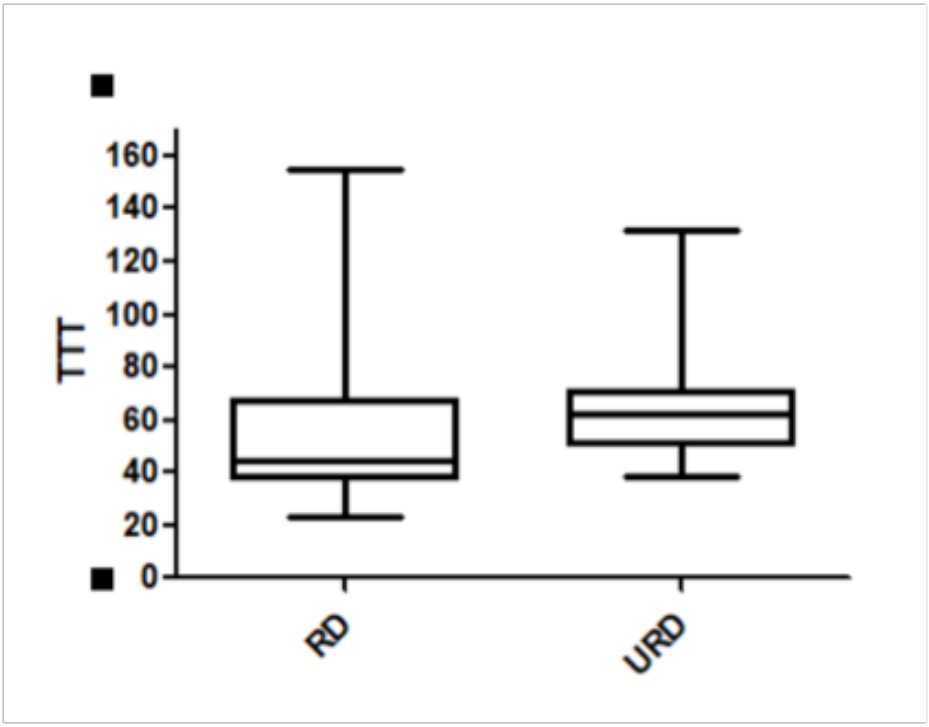


FIGURE 2. TTT comparison. RD related donors. URD: (unrelated donors)



AUTOLOGOUS HSCT

AUTOLOGOUS BONE MARROW TRANSPLANTATION IN ACUTE LYMPHOBLASTIC LEUKEMIA PH POSITIVE: CASE REPORT.

Karine Sampaio Nunes Barroso[1], Lívia Andrade Gurgel[1], João Paulo Vasconcelos Leitão[1], Talita Vaz de Queiroz[1], Beatriz Stela Gomes De Souza Pitombeira Araújo[1], Geísa Ferreira Gomes Peixoto[1]

1 Hospital Regional da Unimed, Fortaleza, Brasil

Introduction: The Acute Lymphoblastic Leukemia (ALL) Philadelphia (Ph) positive is a high risk leukemia and the bone marrow transplantation (BMT) was indicated after the first remission. When the allogeneic BMT was not feasible, like the absence of an eligible donor, the autologous BMT is an option to ALL high risk with negative minimal residual disease (MRD). The maintance with tirosine kinase inhibitor (ITK), preferred the new generation of ITK.

Objective: description of a unique case of autologous BMT in ALL PH positive in a private hospital from Fortaleza Ceará.

Methods: description analyses/ report case.

Results: Female, 30 years old, without disease previous, was diagnosis of acute lymphoblastic leukemia B PH positive (p190) in April 2019. The treatment was CALGB and imatinib 600mg. The minimal residual disease (MRD) was negative after induction and Central Nervous System (CNS) prophylaxis phases and before BMT. The Philadelphia p190 was negative after CNS prophylaxis phases and before BMT. She did not have brothers or unrelated donor in REREME (Receptor National Registry). In this moment, after a literature review, the autologous BMT is a good option. The patient was had mobilized with vinorelbine and Granulocites Grow Factor. The apheresis occurred at D10 and D11 after chemotherapy in December 2019. The conditioning was Carmustine, Citarabine, Etoposideos and melphalan. The carmustine had imported. The infusion occurred in February 20th 2020. The patient had febrile neutropenia with Klebsiella pneumoniae ESBL, without instable hemodynamic. The engraftment occurred at D+10. D+30 imatinib was restarted because ponatinib was denied. The patient realized minimal residual disease and BCR-ABL every 3 mouths. Six month after BMT, BCR-ABL was positive. Ponatinib was denied again and we began Dasatinib. After 18 months the patient persists with MRD and BCR-ABL negatives. Conclusion: the autologous BMT is an option feasible and safe to Ph+ ALL with MRD negative in the absence of donors.

Keywords: Acute Lymphoblastic Leukemia Philadelphia, autologous bone marrow transplantation.

AUTOLOGOUS TRANSPLANTATION WITH NON-CRYOPRESERVED CELLS: EXPERIENCE OF THE GSH GROUP

Aline Miranda de Souza[1], Talita Ferreira de Almeida[1], Marília Valvasori[1], Leandro Felipe Figueiredo Dalmazzo[1]

Introduction: Cryopreservation of cells is a high-cost procedure and the reinfusion of cells containing cryopreserving solution, especially dimethyl sulfoxide (DMSO), is related to toxicities, which are sometimes severe. As an alternative to cell cryopreservation for patients who are submitted to short conditioning regimens, some services have adopted infusion with cooled cells.

Methods: In compliance with the requirement of RDC No. 508/2021, the infusion must occur within 48 hours after the end of the collection. To achieve this, the multi-professional team specialized in apheresis procedures of the GSH Group monitors the evolution of mobilization, together with the medical team that will perform the transplant. The beginning of the procedure for collecting progenitor cells by apheresis occurs in the morning of D-2, and the cell processing laboratory of the GSH Group releases the report of the CD34+ cell count of the product on the same day. When the cellularity obtained is sufficient to perform the transplant, the conditioning is started at the following day (D-1). If there is a need for a second cell collection the following day, either to complete the desired cellularity for transplantation, or to maintain cryopreserved hematopoietic progenitor cells for future use, a second collection is performed on the morning of D-1, and after the end of the apheresis procedure, conditioning chemotherapy is infused. In the case that the desired cellularity is not obtained after 2 collections, the cells from the first collection are cryopreserved and the third day of collection is performed. The cryopreserved cells can be used for infusion or kept stored for future use. The infusion then occurs in D0 after 24 hours after the end of conditioning chemotherapy. The collected cells are kept stored at a cooler temperature (2 -10°C) until the moment of infusion.

Results: Between July 2020 and July 2021, 19 transplants with an infusion of non-cryopreserved cells were performed in hospitals served by the GSH Group in the metropolitan region of São Paulo. Three patients were submitted to 2 days of collection by apheresis, and only 1 patient was submitted to 3 days of collection. All patients received infusion only with non-cryopreserved cells. No patient presented severe adverse events during the infusion, or in the following 60 minutes, and the most frequent event was grades 2 and 3 of arterial hypertension, according to the CTCAE. All patients had engrafted, and the period until neutrophilic graft varied from D+09 to D+15. All patients were independent of red blood cell and platelet transfusion in D+30.

Conclusion: To perform autologous TCPH with non-cryopreserved cells is a low-cost procedure and exposes the patient to a lower risk of adverse events related to transplantation; however, the success of this procedure depends on an adequate team and structure so that the entire process occurs within the validity period of the hematopoietic progenitor cells.

Key words: stem cell infusion. fresh stem cell infusion. autologous peripheral stem cell collection.

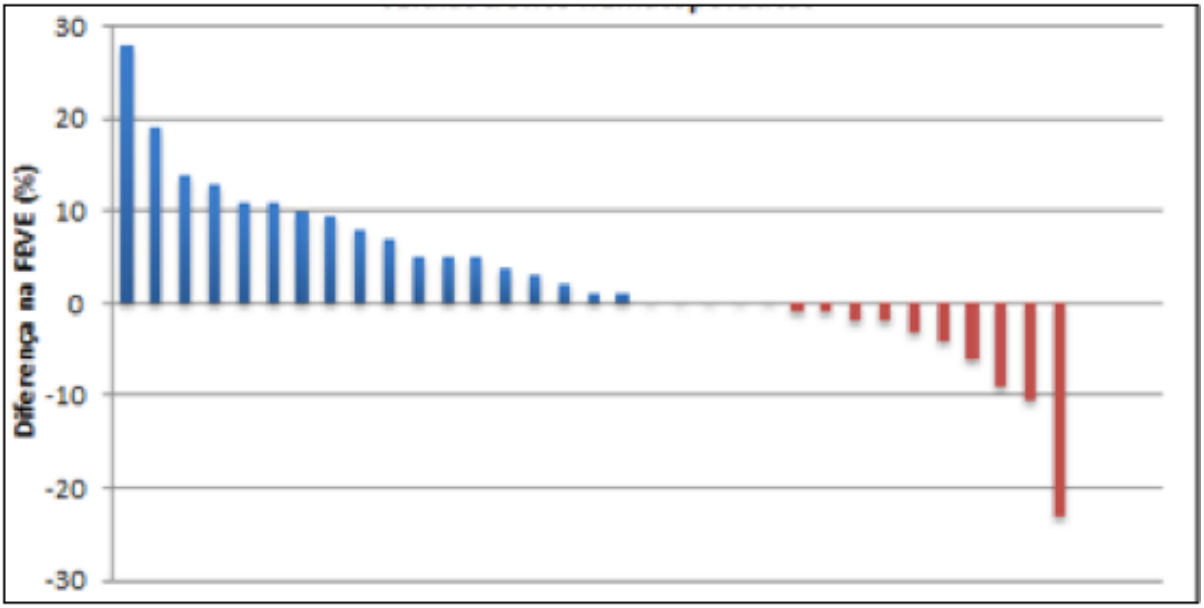
CARDIOTOXICITY AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION: A REAL-LIFE ASSESSMENT

Kátia Regina Lopes Alves[1], Author Abrahão Elias Hallack Neto[1], Author Kelli Borges dos Santos[1], Author Angelo Atalla[1], Author Erich Vinícius de Paula[2], Author Paulla Rayane Chaves Utsch[1], Author Isabela Lopes Pena[4]

1. University Hospital, Federal University of Juiz de Fora, Juiz de Fora, Minas Gerais, Brazil
2. Department of Internal Medicine, University Hospital, State University of Campinas, Campinas, São Paulo, Brazil
4. Department of Statistics, University Hospital, Federal University of Juiz de Fora, Juiz de Fora, Minas Gerais, Brazil

Introduction: Patients undergoing hematopoietic stem cell transplantation (HSCT) involve cardiovascular complications, which risk factors are associated with conditioning regimens, pre-transplant therapy and previous cardiovascular diseases. Goals: Evaluate the incidence and degree of early cardiotoxicity after autologous hematopoietic stem cell transplantation (AHSCT). Casuistry: This is an on-demand sample of all patients undergoing AHSCT at two centers between March 2018 to May 2019 and October 2019. Methods: Data from pre- and post-conditioning physical examination and propaedeutic examinations, such as troponin-I dosage and echocardiogram before and after conditioning chemotherapy, were evaluated. Changes were classified according to the Brazilian Guidelines on Cardio-Oncology. Results: Seven (21.2%) patients had cardiotoxicity on echocardiography, with a reduction from 71.53% to 64.75% in the mean pre- and post-conditioning left ventricular ejection fraction (p = 0.00013). Clinical cardiovascular alterations demonstrate a relationship with advanced staging and more than one year between diagnosis and AHSCT (p=0.01 in both). Specific clinical signs of congestion were correlated with radiotherapy in the mediastinum and dose >400mg of doxorubicin before AHSCT (p=0.02 and p=0.01, respectively). Conclusions: In this real-life study, it was possible to notice a higher incidence of cardiac injury after AHSCT, which was related to the type of therapy performed before transplantation. Better pre-AHSCT assessment and recognition of patients with subclinical myocardial dysfunction can prevent clinical heart failure and reduce morbidity and mortality related to myocardial damage in these patients. This fact, in a real-life study, reflects our limitations and makes us seek proposals to improve cardiovascular assessment in patients who will undergo AHSCT and, consequently, reduce morbidity and mortality related to myocardial lesions in these patients.

FIGURE 1 – Graph of the relationship between the use of cyclophamide and left ventricular ejection fraction before and after autologous hematopoietic stem cell transplantation



Source: Prepared by the author (2020).

CENTRAL NERVOUS SYSTEM PRIMARY LYMPHOMA IN IMMUNOCOMPENTENT PATIENTS

Matheus Navarrina Trindade[1]; Diniz Brum Lamaison[2]; Flávia Céspedes Gurki[1]; Manoella Silva dos Santos[1]; Victor Júlio Balestrin[1]; Vitória Xausa Bosak[1]; Fabrizio Fianco Valenti[1]; Guilherme Beust Amador[1]; Dani Laks[1]

1 Universidade do Vale do Rio dos Sinos – UNISINOS
2 Hospital de Clínicas de Porto Alegre – HCPA

Introduction: Central nervous system primary lymphoma (CNSPL) are extranodal and aggressive malignancies that develop in the brain, meninges and spinal cord in the absence of systemic involvement at diagnosis. The incidence of CNSPL in Western countries is 5/1,000,000 people per year and the prevalence is higher among men, caucasians and >60 years. Currently, it is estimated that CNSPL accounts for up to 1% of non-Hodgkin lymphomas (NHL) and 3% to 5% of primary brain tumors. In immunosuppressed patients, such as HIV+, HTLV+, EBV+, the incidence is 3600 times higher.

Objective: To clarify the CNSPL nature that is still not so well understood just as the pathogenesis. The CNS does not contain physiologically resident lymphocytes that cross the blood-brain barrier. However, there are evidences that T and B cells enter the CNS under physiological conditions, and CNSPL can originate from B cells of systemic lymphoid tissues that cross this barrier. The clinical presentation of CNSPL is often focal or multifocal symptoms, increased intracranial pressure and neuropsychiatric changes. TC and MRI have single or multiple homogeneous lesions that extands for the frontal lobe, basal ganglia, thalamus and corpus callosum, which is justified by their clinical presentation. The Dx is made through biopsy of the lesion and immunohistochemistry. The treatment, due to the infiltrative nature of the lesion, is adjuvant brain chemotherapy and radiotherapy.

Materials And Methods: Search performed in the patient's electronic medical record in a retrospective analysis of the collected data.

Results: Female patient, 34 years old, with sudden loss of consciousness, temporospatial disorientation, dysarthria, paresthesia, complex seizures. History of progressive left temporal region headache starting 2 months ago. Laboratorials without changes and negative sorologies. MRI showed an expansive lesion in the left frontal lobe affecting the contiguous corticals of the superior and middle frontal gyrus, restriction to contrast diffusion, measuring about 3.8 cm in the longest axis, in addition to an area of hypersignal suggesting vasogenic edema. Upon complete resection, the anatomopathological examination revealed the presence of a poorly brain parenchyma differentiated neoplasia. Immunohistochemistry, CD20+, PAX-5+, CD10+, BCL6+, and P56+, compatible with large B-cell CNSPL. PET-CT did not evidentiated systemic changes. Due to the difficulty of penetration into the CNS through the blood-brain barrier, therapies for the treatment of non-Hodgkin's lymphoma (NHL) do not have the same effectiveness. The R-MAD and autologous HSCT protocol were performed in order to consolidate the therapeutics. It showed improvement, but the patient keeps in follow-up without evidence of relapse.

Considerations: The earlier the diagnosis, the better the prognosis despite the aggressiveness of the disease. Autologous stem cell transplantation adjunct to chemotherapy and radiotherapy has lower morbidity and mortality, as well as curative possibility.

PEDIATRIC AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION EXPERIENCE AT A COMPREHENSIVE CANCER CENTER OF SÃO PAULO DURING THE SARS-COV-2 PANDEMIC.

Jessica Talita Mariana Wicthoff Raniero, Marjorie Vieira Batista, Elaine Cristina Breves, Milena de Freitas Rodrigues, Luciana Mariana Palanchi Piotto

Background: In February 2020 in Brazil, the first case of respiratory infection by the new coronavirus, SARS-COV-2, an extremely contagious virus that causes severe disease, especially in the elderly population and those with comorbidities, was confirmed. Additionally, patients with hematologic malignancies and those undergoing Hematopoietic Stem cell Transplantation (HSCT) are at high risk of complications due to the high degree of immunosuppression caused by chemotherapy treatment regimens.

Objective: To describe the experience of a Pediatric Autologous Hematopoietic Cell Transplantation (HCT) during the last 18 months of the SARS-CoV-2 pandemic in a Cancer Center.

Methods: This is a descriptive, retrospective study of a case series of patients under 18 years old who underwent HCT during the SARS-COV-2 pandemic. The patient and guardian perform a swab for SARS-COV-2 test via an outpatient service before implantation of the central catheter and harvest of stem cells, as well as more two swabs for SARS-COV-2 test before HCT. Paper submitted and approved by the Institutional Ethics Committee CAEE 41490720.8.0000.5432.

Results: We identified 4 patients with Hodgkin's Lymphoma for HCT, aged between 9 and 14 years, 03 patients from the state of São Paulo, and 01 from Amazonas. Through the "Protected Flow Protocol" aimed at cancer patients and their families, all results should have been negative for SARS-COV-2 and had not previously had contact with the virus. The patient and his guardian were confined to the apartment after the neutrophil engraftment, and the care team was reduced. But even with the care implemented to prevent infections, 50% needed intensive care in the first days after stem cell infusion and another 25% after grafting. However, they remained negative for SARS-COV-2 and followed a hospital discharge within 30 days after engraftment.

Conclusion: We did not observe a drop in transplants in our service, even in the face of an uncontrolled pandemic worldwide. Moreover, we had no patient infected with SARS-COV-2, showing that the protocols and intra-hospital preventive care were effective. No transplant patient and guardian returned with any complications/ infection for 6 months after the HCT.

Key-words: Hematopoietic Stem cell Transplantation, Pediatric, SARS-COV-2

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IMPACT OF CHEMOTHERAPY AND AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION ON THE REVERSAL OF NEUROLOGICAL SYMPTOMS IN A PATIENT WITH SPORADIC LATE-ONSET NEMALINE MYOPATHY RELATED TO MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE: CASE REPORT

Germano Glauber de Medeiros Lima[1], Guilherme Carneiro Barreto[1], Giselle Groetares de Lima[1], Livia Mariano[1], Gracia Aparecida Martinez[1] e Vanderson Rocha[1]

1 Hospital das Clinicas da Faculdade de Medicina da USP, São Paulo, Brazil

Introduction: Nemaline myopathy is a rare neurodegenerative disease that involves the formation of intracytoplasmic rods and disruption of muscle fibber architecture. Sporadic cases of the disease are even rarer. In this subgroup, the course of the disease is dramatic, with rapid and fatal progression. The association with monoclonal gammopathy of undetermined significance (MGUS) enables treatment with chemotherapy and autologous hematopoietic stem cell transplantation (auto-HSCT), with promising results in enhancement of muscle strength and increasing survival rate.

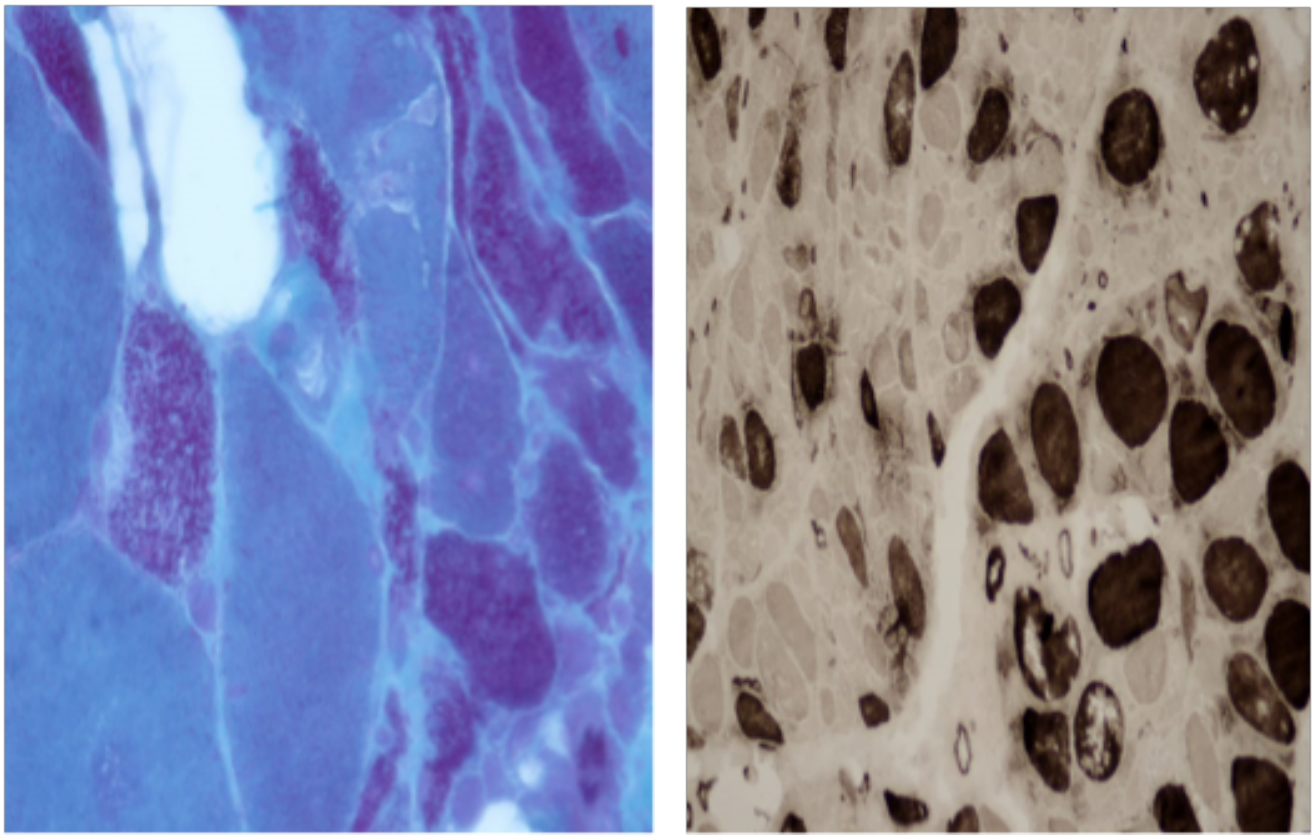
Objective: Report a case of a patient with SLONM associated with MGUS with regression of neurological signs and symptoms after treatment with chemotherapy followed by auto-HSCT.

Results: 40-year-old male, active smoker, with a 1-year history of weight loss of 15kg and progressive muscle weakness, initially affecting the scapular waist and upper limbs, followed by lower limbs and bulbar muscles, dysphagia for liquids, weak cough, dysphonia and choking, thus configuring severe progressive myopathy with a predominance of proximal and bulbar muscles. Etiological investigation showed unaltered inflammatory and muscle injury markers, as well as negative HIV and viral hepatitis serology. Electroneuromyography showed a myopathic pattern in proximal musculature. There was no suspicious mass or lymphadenomegaly on computed tomography scans. During investigation, positive serum immunofixation for IgG kappa was found, with no measurable monoclonal peak in protein electrophoresis. A biopsy of the biceps musculature was then performed, showing architectural disorganization of the muscle fibbers and also the presence of cytoplasmic bodies without amyloid deposits or inflammatory characteristics (Figure 1). Therefore, the diagnosis of SLONM associated with MGUS was established. The patient evolved with worsening of symptoms and need for tracheostomy, in addition to nutrition through gastrostomy. Initial treatment with corticosteroids and intravenous immunoglobulin failed to respond. Four cycles of the VCD protocol (bortezomib, dexamethasone and cyclophosphamide) were performed in sequence, with the achievement of negative serum immunofixation. Afterwards, the patient was admitted for high-dose chemotherapy with melphalan followed by auto-HSCT. After 9 months of follow-up, the patient evolved with exponential improvement of deficits, with no more dysphagia and able to walk without support, undergoing rehabilitation without the need for any medication.

Conclusion: This case represents a rare sporadic myopathy associated with MGUS in an adult patient. The literature is categorical in stating that such patients usually have an unfavourable outcome and survival of 1-5 years after diagnosis. In this context, auto-HSCT appears as one of the few therapeutic alternatives leading to a satisfactory response.

Key words: nemalinic myopathy, monoclonal gammopathy, hematopoietic stem cell transplantation

FIGURE 1. Left biceps musculature biopsy with a large amount of intracytoplasmic stick-shaped aggregates in more than 50% of them



OUTCOMES AFTER MOBILIZATION FAILURE OF HAEMATOPOIETIC STEM CELLS FOR AUTOLOGOUS STEM CELL TRANSPLANTATION

Livia Netto Chaer[1], Diego Vinicius Santinelli Pestana[1], Debora Toshie Hamasaki[1], Isabella Gonçalves Ramos[1], Jhonny Manuel Carranza Jara[1], Samuel Campanelli Freitas Couto[1], Livia Mariano[1], Vanderson Rocha[1,2]

1 Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo
2 Churchill Hospital - Oxford University Hospitals, CH/England.

Introduction: Autologous haematopoietic stem cell transplantation (ASCT) is currently the long-term consolidation treatment for various haematological malignancies. Collection of adequate haematopoietic stem cell yield is critical to a successful ASCT but not always achieved due to haematopoietic stem cell mobilization failure (HSCMF). Despite broad understanding of factors involved in the process of HSCMF and available rescue measures to improve success rates, details regarding cell collection and outcomes of those patients are still lacking.

Objectives: This study aimed to yield data about clinical outcomes of patients after HSCMF and cellular products collected by aphaeresis in those patients.

Population: Patients older than 18 years of age at the time of mobilization and HSCMF.

Methods: We performed a retrospective, unicentric study that assessed overall and relapse free survival following HSCMF, clinical outcomes, and median peripheral CD34+ before and after collection, whenever collection occurred. Data were collected from patients' databases and medical records. Results were reported in median, rates and percentages, and absolute values.

Results: Five hundred eighty-six patients underwent at least one mobilization protocol while preparing for ASCT. Twenty-nine of them (5%) failed mobilization. Fourteen (48%) patients died during the studied period. Median time to death was eight months, varying from one to thirty months. Disease progression was responsible for ten deaths, and infection was responsible for four deaths. Twenty patients (69%) had relapsed, with a median relapse free survival of 6.5 months (1-29mo). Seven (24%) patients among the survivors were receiving salvage therapy, and five (17%) were being followed clinically. Eight participants (27.5%) underwent peripheral stem cell collection by apheresis, with insufficient cell collection. The median peripheral CD34+ cells in those patients was 10.9/mm3 and 1.7/mm3 in patients who did not undergo apheresis. Among those who underwent collection (8 participants), the median CD34+ collected was 0,81 x 106 CD34+ cells/kg.

Conclusions: These results reinforce the hypothesis that patients who failed mobilization of peripheral CD34+ cells during ASCT may experience limited overall survival rates and relapse free survival. Nonetheless, the results obtained from analysis of the material collected via apheresis offer some perspective of future advances such as ex vivo expansion. Further studies should investigate the feasibility of expanding low number of collected CD34+ cells to use as a HSC graft for ASCT.

Keywords: haematopoietic stem cell mobilization failure, autologous stem cell transplantation,

Financial support: none.

TABLE 1: Characteristics of patients and collected cells.

	Disease	Peripheral (CD34+/mm³)	Nº of Collections	Mobilization protocol	Total collected cells (x 106 CD34+/kg)	Outcome
1	MM	21,2	1	GCSF + Plerixafor	0,42	Death 3 months after mobilization
2*	NHLDLBC (CNS)	6,7	2	GCSF + Plerixafor	1,79	Alive QT + RDT + follow up (last contacted 14 months after mobilization)
3	NHLDLBC	1,7	1	GCSF + Plerixafor	0,28	Death 11 months after mobilization
4*	AML	10,7	2	GCSF	1,73	Alive QT + follow up (last contacted 24 months after mobilization)
5*	NHLDLBC	11,8	3	QT + GCSF	0,42	Returned to original health care institution (last contacted 3 months after mobilization)
6	MM	10,3	1	GCSF	0,72	Death 14 months after mobilization
7	MM	11,2	1	GCSF	1,01	Alive Follow up (last contacted 34 months after mobilization)
8	MM	27,1	1	GCSF	1	Alive QT + follow up (last contacted 10 months after mobilization)

MM = multiple myeloma; NHLDLBC = non-hodgkin lymphoma of diffuse large B cells; CNS = central nervous system; AML = acute myeloid leukemia; QT = chemotherapy; RDT = radiotherapy; *patients who had ≥2 collections.

PROCÉLULA – HEMATOPOIETIC PROGENITOR CELL PROCESSING CENTER: NINE YEARS AND SEVEN MONTHS EXPERIENCE AT CLÍNICA DE HEMOTERAPIA LTDA, NITERÓI RJ, BRAZIL

Gustavo Correa Mussel Tavares do Prado[1], Calos Henrique de Carvalho Ribeiro[1], Juliana Jardim Saldanha[1], Gabriel Alves Costa Veranio Silva[1], Catarina Maria Balbi Finkel[1], Márcia Maria Lisbôa[1], Juliana Pessoa Rivello de Azevedo[1]

1 Procélula – Terapia Celular

Keywords: Hematopoietic Progenitor Cells (HPC), Cryopreservation and Autologous Transplantation.

Since its implementation, Procélula has contributed to the growing number of autologous transplants performed in the private sector of the State of RJ. We present our experience over nine years. For the harvest of HPC, patients were mobilized with different protocols. Apheresis were started on the first day these patients had more than 10 CD34+ cells/mm3 in their peripheral blood. An average of 4 volemias were collected by apheresis for mononuclear cells in Cobe Spectra or Optia. Leukometry was performed in an ABX Micros ES60 automatic counter. Products were cryopreserved using a solution composed of hydroxyethyl starch at a concentration of 5.83%, human albumin at 4% and Dimethylsulfoxide (DMSO) at 5% of the final volume, divided into fractions of 60 to 115mL, with a target cell concentration of 2-3x108 total leukocytes/ml. These fractions were stored at -80°C and kept at constant temperature until the date of transplantation. Cell viability was defined by light microscopy and trypan blue exclusion. For HPC quantification, we used flow cytometry for CD34+/CD45low cells, according to the methodology defined by ISHAGE, in a FACScalibur cytometer (B&D). We performed a clonogenic assay with MACSMedia system (Miltenyi Biotech) of methylcellulose culture with recombinant factors for growth of granulocyte and monocyte colony-forming units (CFU-GM) that were observed under inverted light microscopy 14 to 16 days after incubation at 37oC. From December 2011 to June 2021, 967 patients were analysed (542 myelomas, 389 lymphomas and 36 other diseases) with a median age of 55 years (17 pediatric patients aged 0.6 to 14 years; 950 adults aged 15 to 74 years), who performed 1055 mobilizations with G-CSF (53 associated with chemotherapy, 314 with Plerixafor and 13 with chemotherapy and Plerixafor; 994 with harvest and 61 mobilization failures without harvest) and 1,486 total apheresis. The average of HPC circulating before the first apheresis was 23 CD34+/mm3 (0-410), with an average of 4.01x106 CD34+/Kg (0.11-50.5) harvested by apheresis. Frozen products had a mean cell concentration of 2.60x108/mL (0.35-6.61) with a recovery of 116.41% after thawing (36.4-283.3). They presented cell viability >99% before cryopreservation, and recovered an average of 92.9% (68-99.8) of the viability and 80.4% (5.5-830.5) of the CFU-GM in the thawing period. 2,972 functional assays were performed, and the ratio between them (CD34/UFC-GM) was 2.5 (0.7-88.9) in the fresh sample and 3.3 (0.7-91.1) in the sample thawed. Transplants were performed in 915 of these patients, with a mean of 3.63x106 CD34+/Kg (1.20-19.79) and 1.68x106 CFU-GM/Kg (0.04-10.60) infused in each patient. The time to engraftment of granulocytes averaged 10 (8-17) days. These data demonstrate, with large sampling, that mechanical cryopreservation at -80°C with a low concentration of DMSO results in excellent clinical outcomes for autologous HPC transplantation.

RETROSPECTIVE ANALYSIS OF ORAL MUCOSITIS PRESENCE IN PATIENTS UNDERGOING HEMATOPOIETIC CELL TRANSPLANTATION USING MELPHALAN

Marcella Ferreira Gobbi; Michele dos Santos Lima; Cristiane Santos da Rocha; Mariana Henriques Ferreira; Fabiola Germano de Castro; Camila de Moura Gatti; Celso Mitsushi Massumoto; Maria Cristina Martins de Almeida Macedo; Roberto Luiz da Silva; Danielle Lima Corrêa de Carvalho

Hospital 9 De Julho, São Paulo - SP - Brasil.

Hematopoietic stem cell transplantation (HSCT) can lead to several toxicities, including an oral mucositis (OM), leading to an impact on the nutrition and quality of life of patients. Some conditioning protocols uses high dose Melphalan (Mel) in their composition, which can lead to neutropenia, thrombocytopenia, diarrhea, vomiting and mucositis. The Dental Surgeons (DS) on the HSCT care team prevent and treat these changes in the oral cavity. The aim of the study was to describe de incidence of OM in HSCT patients with Mel as conditioning and its duration. Patients and Methods: Patients undergoing HSCT (n = 38) were retrospectively evaluated from January 2016 to May 2020 taking into account the degree of OM, photobiomodulation protocol and cryotherapy. Results: All patients underwent photobiomodulation protocol using 660nm, 100mW, 1J, 10J/cm2 and cryotherapy (5 minutes before infusion, during infusion and 30 minutes after Mel administration). Low level laser therapy was performed daily starting on the second day of conditioning until bone marrow engraftment and an cryotherapy performed on the day of Mel infusion. All patients were in autologous HSCT for Multiple Myeloma. The gender prevalence was male (57.89%), the mean age was 58.79 years and showed mild OM (grade 0: 44.73%; grade 1: 21.05%; and grade 2: 31.57 %) and low frequency of severe OM (grade 3: 2.63%). Regarding the duration of OM days, 5 days were the most frequent duration, corresponding to 23.81% of patients, with signs and/or symptoms starting on D+4 (21.05%) and HSCT engraftment occurred more frequently at D+11 (38.23%). Conclusion: The presence of CD, photobiomodulation and cryotherapy during Mel infusion and the daily follow-up of patients undergoing HSCT minimized the expected risk of severe OM, and none of the evaluated patients had grade IV OM.

USE OF ALTERNATIVE REGIMENS TO BEAM IN AUTOLOGOUS BONE MARROW TRANSPLANTATION FOR LYMPHOMAS: EXPERIENCE IN A CENTER IN VOLTA REDONDA RJ.

Juliana Orcini Matias; Juliana Annete Damasceno Rodrigues; Andreia Cristina Fortes Bassani; Christine Desiree Militão Guedes; Cristiane Silveira Cunha; Flavio Henrique Paraguassu Braga; Livia Rachid; Rafael Ono Furukawa; Renata Sarkis Alves Ávila; Luis Fernando da Silva Bouzas

Hospital Unimed Volta Redonda, Volta Redonda - RJ - Brasil.

Introduction: Most patients with intermediate and high-grade Hodgkin's and non-Hodgkin's Lymphomas are cured with first-line treatment. In refractory or relapsed cases, in the presence of chemosensitivity, treatment with high-dose chemotherapy followed by autologous bone marrow transplantation is the gold standard.

The BEAM protocol (carmustine, etoposide, cytarabine and melphalan) is the most commonly used conditioning in autologous BMT in patients diagnosed with lymphoma.

With the discontinuation of the sale of carmustine in the country and the shortage of melphalan that occurred in Brazil, alternative schemes emerged that use only one or none of these drugs.

Objectives: Describe the lymphoma subtype, age, gender, tolerability (based on the presence of mucositis and/or diarrhea), number of days until marrow engraftment, length of stay (based on the date of marrow infusion until the day of hospital discharge) and treatment-related mortality (TRM) one hundred days after autologous BMT of 17 patients undergoing autologous bone marrow transplantation at Hospital Unimed Volta Redonda after conditioning protocols: CBV (carmustine, cyclophosphamide and etoposide), LEAM (lomustine, etoposide, cytarabine, melphalan) and LACE (lomustine, cytarabine, cyclophosphamide and etoposide).

Methods: Retrospective analysis of a series of 17 cases diagnosed with Hodgkin's lymphoma and non-Hodgkin's lymphoma submitted to autologous bone marrow transplantation at Hospital Unimed Volta Redonda with conditioning alternative to BEAM.

Results: Of the 17 cases evaluated: 8 patients had a diagnosis of classic Hodgkin's Lymphoma, 2 patients with Mantle Cell Non-Hodgkin's Lymphoma, 4 patients with Diffuse Large B-Cell Lymphoma, 1 patient with Anaplastic ALK-negative Non-Hodgkin's T Lymphoma, 1 patient with angioimmunoblastic non-Hodgkin T lymphoma and 1 with lymphoblastic T non-Hodgkin lymphoma.

Ten patients were female and eight males.

The average age was 34 years (17 to 52 years).

The average number of days for marrow engraftment was 12 days (8 to 16 days).

As for tolerability, 10 patients had grade 1 mucositis, 4 patients had grade 2 mucositis and 12 patients had self-limited diarrhea.

The average length of stay was 17 days (10 to 25 days).

Treatment-related mortality (TRM) one hundred days after autologous BMT was 5.8% (1 death in a patient with Angioimmunoblastic T Lymphoma occurred on D18 after autologous BMT due to sepsis).

Conclusion: Alternative regimens to BEAM as conditioning for Autologous Bone Marrow Transplant in Hodgkin and Non-Hodgkin's Lymphoma patients are an alternative with good tolerability, attachment time, hospital stay and TRM acceptable in patients of both genders and of varying ages.

HSCT PEDIATRIC

ALTERNATIVE DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) AFTER BLINATUMOMAB IN CHILDREN WITH RECURRENT OR REFRACTORY (R/R) B-ACUTE LYMPHOID LEUKEMIA (B-ALL)

Gustavo Zamperlini[1,2]; Roseane Vasconcelos Gouveia[1,2], Valéria Cortez Ginani[1,2], Carla Maria da Costa Zanchetta Oliveira[1,2], Maria Gabriela Matos Alves Dias[1,2] , Carla Nolasco Monteiro Breviglieri[1,2], Luciana dos Santos Domingues[1,2] , Marcia Vieira Pupim[1,2], Paola Azenha Milani Soriano[1,2], Juliana Francielli Marques[2], Claudinéia Farias Andrade[2], Francisca Vanóide Brito[2], Priscila Mendes Paiva[2], Marçal Cavalcante Andrade Silva[3], Alex Freire Sandes[3], Roberta Pasianotto Costa Trofo[3], Lélia Bolonha[2], Paula Mara Assis Ceia[2], Adriana Seber[1,2]

1 Equipe Onco-TMO em Pediatria;
2 Hospital Samaritano – SP/Brazil;
3 Laboratório Fleury – SP/Brazil

The survival of children with B-ALL that is primary refractory, relapsed or refractory is very poor. Successive attempts to achieve complete remission with chemotherapy directly impact the treatment results due to chemotherapy toxicity and progressive blast resistance. Blinatumomab, a bispecific antibody that engage CD3 in T lymphocytes to CD19 blasts, has documented efficacy in chemo refractory disease, allowing patients to start HSCT with no measurable disease, contributing significantly to a better survival. This strategy has been well described, but we do not know its effectiveness in our country. Objective: To evaluate the response and survival of children with relapsed/refractory B-ALL (R/R) treated with blinatumomab followed by allogeneic HSCT. Method: Children with R/R B-ALL referred to our Pediatric HSCT team still with active disease underwent central nervous system and medullary evaluation to quantify the disease by flow cytometry and to determine blast positivity for the CD19 (target of blinatumomab) and CD22 (target of inotuzumab) antigens. For children with hematological disease, chemotherapy with mini-HyperCVD (Jabbour E, personal communication) was associated with blinatumomab at the recommended package insert dose. All patients received prophylactic or therapeutic intratecal chemotherapy. The conditioning for unrelated HSCT was TBI 1200-VP (Forum Protocol) and for Haploidentical HSCT, Fludarabine-TBI1200 and prophylaxis of DECH with cyclosporine (CsA)-mini-methotrexate and post-transplant cyclophosphamide, CsA, MMF, respectively. Result: 19 children were treated with blinatumomab followed by allogeneic HSCT with alternative donors, 11 boys, with median age of 6 years. Of the 19 patients, 11 required only one blinatumomab cycle; 6 had blinatumomab and conventional chemotherapy and 3 required inotuzumab due to persistency of the disease and CD22 expression. Only one child did not reach pre-HSCT morphological remission, continued with the procedure to be referred for CAR-T therapy after transplantation but died of transplant-related complications. Pre-HSCT measurable residual disease was negative in 8 patients and positive in 11. HSCT was performed with a haploidentical donor in 9 children and unrelated donors in 10. None of the children who underwent HSCT with negative MRD had disease recurrence; one of them died due to transplant-related toxicity. Of the 11 children undergoing HSCT with positive MRD, two are alive receiving prophylactic DLI and blinatumomab after HSCT. In total, 7 patients are alive and in remission with a median follow-up of 5.3 months after HSCT. Conclusions: B-ALL refractory to chemotherapy is a uniformly fatal disease without immunotherapy. With the use of blinatumomab we were able to rescue 9 of the 19 children, an excellent result when we consider that no other form of treatment is available in our country. For children transplanted with positive MRD, the use of post-HSCT blinatumomab associated with prophylactic lymphocyte infusion is a promising curative strategy.

Keywords: ALL, blinatumomab, DLI, MRD, haploidentical

TABLE 1. Patient Characteristics

Characteristics	Median and variantion; patients, n (%)
Age	6.26 (1.32 – 15.85 years)
Gender	
- Male	12 (64%)
- Female	7 (36%)
Number of blinatumomab cycles before HSCT	
1	11 (57%)
>1	8 (43%)
Minimal Residual Disease	
- Negative	8 (43%)
- <0.1%	2 (10%)
- >0.1%	9 (47%)
Donor	
- Haploidentical	9 (47%)
- Not related	10 (53%)
Survival	
- Alive	9 (47%)
- Death	10(53%)
Survival based on MRD	
- Negative	7 (87%)
- Positive	2 (18%)
Follow Up	151 dias (8 – 1518)

ASSESSMENT OF THE OUTCOME OF HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRICS: PERIPHERAL VERSUS BONE MARROW GRAFT

Cintia Monteiro Lustosa[1]; Adriane da Silva Santos Ibanez[1]; Jakeline Palmezano Crispim de S. Bufoni[1]; Virginio Climaco Araujo Fernandes Junior[1]; Karoline Helena Silva da Silva[1]; Laís Lima Quintino[1]; Patrícia Shimoda Ikeuti[1]; Olga Margareth Wanderley de Oliveira Félix[1]; Cristiane Menezes Vitoria Alferi[1]; Victor Zecchin[2]; Renata Fittipaldi da Costa Guimarães[1].

1. Instituto De Oncologia Pediátrica Iop/Graacc/Unifesp, Sao Paulo - Sp - Brasil;
2. A Beneficência Portuguesa De São Paulo, São Paulo - Sp - Brasil.

Introduction: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) has been even more used in this period of pandemic by SARSCOV2, being a curative option for children with hematological diseases due to the easier access to the donor and, consequently, the possibility of HSCT in less time. Thus, it is essential to carefully evaluate the results, defining the best graft option, especially with regard to transplant-related mortality (TRM), GVHD, overall survival (OS) and disease-free (EFS), in order to indicate it safely and aiming at the best clinical results.

Objetives: To compare the results obtained in patients undergoing haplo-HSCT using bone marrow (BM) as the stem cell source versus peripheral blood.

Methods: Retrospective cohort study of patients undergoing haplo-HSCT in a pediatric center.

Results: From January 2019 to Juny 2021, 53 haplo-HSCT were performed – six (11%) of these patients were undergoing the second HSCT due to relapse. 57% were male and the median age was 9 years. There was a predominance of ALL (53%), AML (30%), lymphomas (8%), MDS (6%) and SAA (4%). Myeloablative conditioning was used in 85%. As for donors, 70% were male and the median age was 34 years. The group that used BM (G1) as graft corresponded to 38% and PB (G2) 62%. There were no primary or secondary graft failure in both groups. aGVHD occurred in 78% in G1 and 75% in G2 and, cGVHD in 28% in G1 and 47% (p =0.75 and p = 0.24, respectively). G1 presented 93% of cases of aGVHD grade I and 7% grade II and, G2 67% grade I, 13% grade II and 21% grade III (p=0,06). The severity of cGVHD, was predominantly mild (G1: 100% and G2: 53%) 33% moderate and 12% severe in G2 (p = 0.06). Third-nine percent of patients in G1 relapsed and only 21% in G2 (p = 0.20). There was a higher incidence of patients alive in G2 (G2: 85% and G1: 55%) (p = 0.02), with a median follow-up of 266 and 226 days, respectively. Among the causes of death, recurrence in G1 was the main cause (n=6; 67%), TRM (n=2; 22%) and infection (n=1; 11%), and in G2 40% (n=2) by recurrence, 40% (n=2) TRM and 20% (n=1) infection (p=0.42). At D + 365, OS was 54% (G1) and 90% (G2) (p = 0.02), and EFS was 61% (G1) and 78% (G2) (p = 0.13).

Conclusion: We observed that the group that used PB had a greater number of patients alive and had better rates of OS, with a statistical difference. In addition patients who used PB as a graft source showed higher incidence of GVHD, appearing to be a protective factor for recurrence, since this group was observed best OS and EFS indices.

Keywords: Hematopoietic Stem Cell Transplantation. Haploidentical Transplantation. Bone Marrow. Peripheral Stem Cells. Pediatrics.

EVOLUTION IN THE NUMBER OF HEMATOPOIETIC STEM CELL TRANSPLANTS (HSCT) DURING THE FIRST AND SECOND WAVE OF THE COVID-19 PANDEMIC - EXPERIENCE OF A BRAZILIAN PEDIATRIC CENTER.

Karoline Helena Silva da Silva; Patrícia Shimoda Ikeuti; Virginio Climaco Araujo Fernandes Junior; Laís Lima Quintino; Adriane da Silva Santos Ibanez; Cintia Monteiro Lustosa; Jakeline Palmezano Crispim de S. Bufoni; Cristiane Menezes Vitoria Alferi; Olga Margareth Wanderley de Oliveira Félix; Fabianne Altruda de Moraes Costa Carlesse; Renata Fittipaldi da Costa Guimarães.

Instituto de Oncologia Pediátrica IOP/GRAACC/UNIFESP, São Paulo - Sp - Brasil.

Introduction: The COVID-19 pandemic had a major impact on the health of the general population. At the beginning of 2020, we were faced with a difficult-to-control scenario, without specific antiviral treatment and without a vaccine perspective. In this panorama of the COVID-19 pandemic, a adaptation in the transplant planning occurred in our center. Initially we underwent changes and adaptations that consequently impacted the reduction of transplanted patients. Some of the alternatives adopted were the replacement of donors not related to haploidentical and performing PCR test for COVID-19 pre-admission of patients and their parent regardless of symptomatology. For patients from other cities or states, we request the patient and parent/companion test before coming to our center. In cases where the patient tested positive for COVID-19, the schedule was postponed up to 28 days and two new negative tests confirmed the negativity, with a minimum interval of 24 hours between them.

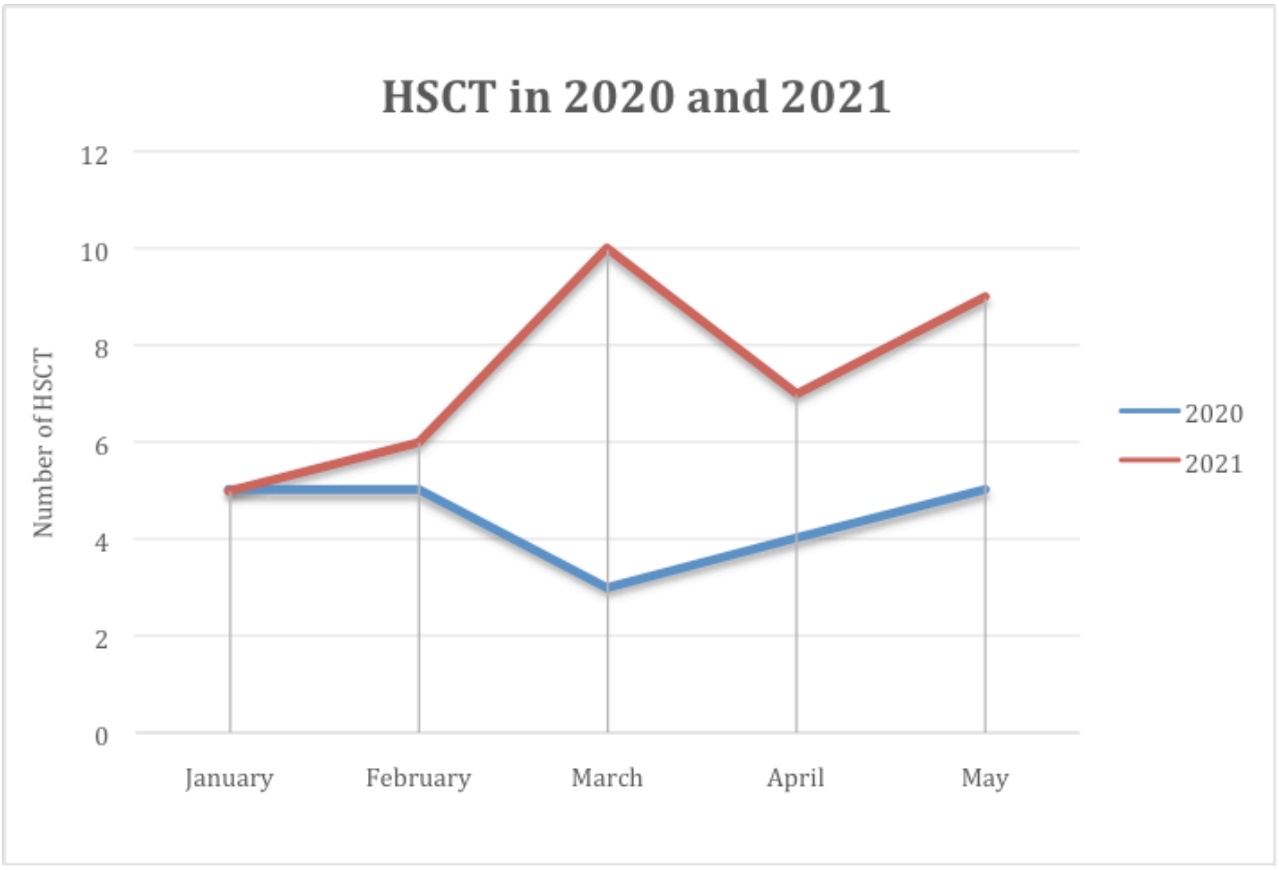
Objective: To evaluate the evolution in the number of hematopoietic stem cell transplants during the first and second wave of the COVID-19 pandemic.

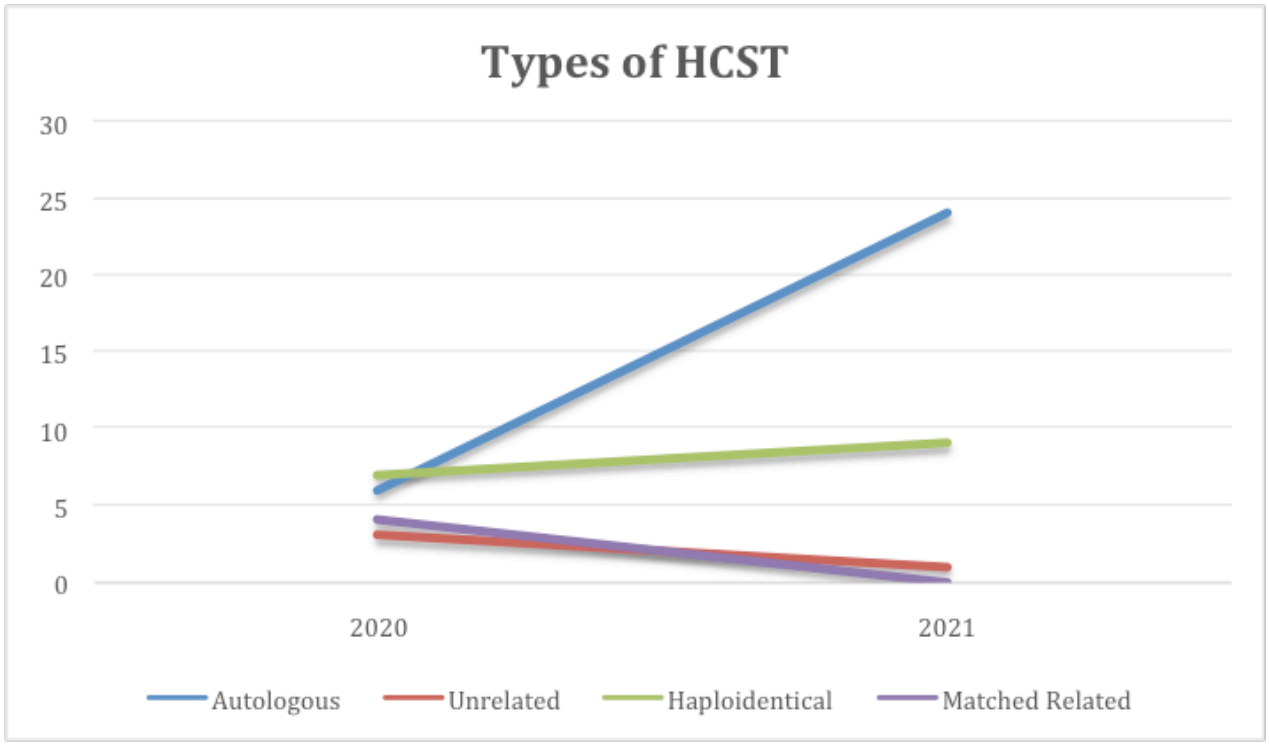
Material and method: Retrospective cohort study of patients programmed to perform HSCT (autologous, matched related, unrelated, haploidentical) during the COVID-19 pandemic in a pediatric HSCT center.

Results: In a comparison in the number of HSCT performed from January to May 2020 and January to May 2021, 22 HSCT were performed in 2020 and 37 in 2021 (68.2% more). We performed 5 HSCT in January/2020 and 5 in January/2021 (there was no change in %); 5 HSCT in February/2020 and 6 in February/2021 (20% more); 3 HSCT in March/2020 and 10 in March/2021 (233% more); 4 HSCT in April/2020 and 7 in April/2021 (75% more); 5 HSCT in May/2020 and 9 in May/2021 (80% more). Regarding the type of transplant, in the period studied: 6 autologous HSCT were performed in 2020 and 24 in 2021; 3 unrelated in 2020 and 1 in 2021; 9 haploidentical in 2020 and 12 in 2021; and 4 matched related in 2020 and none in 2021.

Conclusion: In a general comparison of the impact of the number of HSCT in the period from January to May in the years 2020 and 2021 we had an increase of 68.2% in the total number of transplants performed. This increase may have been a reflection of the learning curve in the management of HSCT planning in the pandemic scenario. In addition to performing a greater number of autologous transplants due to the suppressed demand in 2020, combined with the prioritization of haploidentical transplants, which allowed the non-postponement of HSCT and greater safety in the serological status of the pre-transplant donor.

Keywords: COVID-19; Stem Cell Transplant; paediatrics


HSCT in 2020 and 2021
Number of HSCT
12
10
8
6
4
2
0
January
February
March
April
May
2020
2021


Types of HCST
30
25
20
15
10
5
0
2020
2021
Autologous
Unrelated
Haploidentical
Matched Related

EXPERIENCE WITH RUXOLITINIB IN THE TREATMENT OF GRAFT VERSUS HOST DISEASE (GVHD) IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

Roseane Vasconcelos Gouveia[1], Valéria Cortez Ginani[1], Gustavo Zamperlini[1], Carla Maria da Costa Zanchetta Oliveira[1], Carla Nolasco Monteiro Breviglieri[1], Maria Gabriela Alves Dias Matos[1], Luciana dos Santos Domingues[1], Marcia Vieira Pupim[1], Paola Azenha Milani Soriano[1], Juliana Francielle Marques[1], Claudineia Faria de Andrade[1], Francisca Vanoide de Brito Santos[1], Priscila Mendes Paiva[1], Adriana Seber[1]

1 Equipe Onco-TMO em Pediatria; Hospital Samaritano, São Paulo, Brasil

Chronic GVHD is one of the major causes of late mortality related to allogeneic HSCT. Prolonged use of systemic corticosteroids leads to numerous deleterious effects, especially in children. There is no second-line treatment of choice for cortico-refractory disease. The experience of the transplant center and the availability of medications often guide the therapy, in addition to the organs involved and the pattern of toxicity of each strategy. The management of chronic GVHD is difficult and systemic immunosuppression should be the minimum to control the disease until immunological tolerance between the recipient and the donor is achieved. Ruxolitinib has been used as a second line in the treatment of acute GVHD, but experience in chronic GVHD is still limited.

Objective: To evaluate the use of ruxolitinib in children with refractory chronic GVHD as a second line of treatment.

Method: Evaluation of medical records of children with chronic GVHD refractory to steroids who used ruxolitinib as a 2nd-line treatment.

Results: Three pediatric patients received ruxolitinib as a 2nd-line treatment.

1st patient: Presented with moderate chronic GVHD affecting skin and gastrointestinal tract one month after CsA discontinuation, used in the treatment of acute GVHD. Corticosteroids and CsA were restarted, but the patient remained with diarrhea and melena. Ruxolitinib was associated at 2.5mg PO 12/12h with good response, and corticosteroid reduction could be initiated. There was no toxicity associated with ruxolitinib. Five months later, still using ruxolitinib, he had another reactivation of intestinal GVHD with pneumatosis and ocular involvement. He received four infusions of mesenchymal cells with resolution of the GVHD. Currently, there is not any GVHD activity, and the child is slowly tapering steroids on alternate days, with good tolerance.

2nd patient: chronic GVHD with involvement of the skin, eye, mouth, and gastrointestinal tract despite using sirolimus, oral steroids and entocort, in addition to topical treatments for skin and eyes. Ruxolitinib was associated in at 10mg/day. He had significant improvement in chronic GVHD involvement in all organs and is tolerating a slow steroid taper. There was, however, worsening of thrombocytopenia after the introduction of ruxolitinib.

3rd patient: acute GVHD of the skin (grade 3) despite being on methylprednisolone 2mg/kg/day for severe hepatic venocclusive disease. He also had severe pharmacodermia, positive PCR for herpes 6 and 7, ocular and lichenoid cutaneous GVHD. He started ruxolitinib at 5mg/day, increased to 10mg/day after 45 days due to incomplete skin response. As there was worsening of thrombocytopenia, PUVA was also associated 3x/week, with significant improvement of GVHD, allowing weaning of steroids with good tolerance.

Conclusion: Ruxolitinib was well tolerated, but we observed hematological toxicity in two of the three patients. There was an improvement in chronic GVHD in all patients, however, in one of the patients the response was transient, with worsening when the steroid taper was restarted. In two patients it was possible to decrease steroid dose with the initiation of ruxolitinib, without recrudescence of the GVHD.

TABLE 1: Demographic data

Patient	1	2	3
Age (Years)	3	16	14
HSCT	Haploidentical (father)	Unrelated 10x10 with permissive PD	Haploidentical (brother)
Underlying disease	MPN/refractory M5-AML	T-ALL in 3rd remission with CNS relapse after radiotherapy	Refractory Hodgkin lymphoma + Sβ thalassemia
Conditioning	Fludarabine, busulfan and melphalan	Fludarabine, busulfan, thiotepa and ATG	Fludarabine, cyclophosphamide and TBI 400cGy
GVHD prophylaxis	PT-Cy, CsA, MMF	CsA, Mtx 10mg/m^2 D+1,+3 e +6	PT-Cy, sirolimus and MMF
Stem cell source	Bone marrow	Peripheral blood stem cells	Peripheral blood stem cells
Graft: CD34/kg	10x106	3,8x106	9,17x106
Acute GVHD			
Onset	D+37	D+15	D+26
Organ involvement	Skin and gastrointestinal tract	Skin and gastrointestinal tract	Skin and gastrointestinal tract
Treatment	Methylprednisolone 2mg/kg/day	Methylprednisolone 2 mg/kg unresponsive; Extracorporeal photoapresis one session	Methylprednisolone 2 mg/kg unresponsive; Sirolimus (prophylactic)
Chronic GVHD			
Organ involvement	Skin and gastrointestinal tract	Skin, eyes, mouth, and gastrointestinal tract	Skin and eyes
Treatment	Cyclosporine and corticosteroid	Sirolimus, corticosteroid and entocort	Sirolimus, corticosteroid
Indication of ruxolitinib association	No response in cutaneous and intestinal GVHD after 1 month of corticosteroids	Worsening of dry eye and lichenoid skin lesions	Onset of GVHD and progression to overlap syndrome despite the use of corticosteroid

HAPLOIDENTIC HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH GENDER MISMATCH: CLINICAL OUTCOME OF PATIENTS AT A PEDIATRIC BONE MARROW TRANSPLANTATION CENTER

Jakeline Palmezano Crispim de S. Bufoni; Adriane da Silva Santos Ibanez; Cintia Monteiro Lustosa; Laís Lima Quintino; Karoline Helena Silva da Silva; Virginio Climaco Araujo Fernandes Junior; Patrícia Shimoda Ikeuti; Olga Margareth Wanderley de Oliveira Félix; Cristiane Menezes Vitoria Alferi; Maite Freire Cardoso; Erica Almeida Viana; Débora Prestes Rehme; Renata Fittipaldi da Costa Guimarães

Instituto de Oncologia Pediátrica IOP/GRAACC/UNIFESP, São Paulo - SP - Brasil.

Introduction: Haploidentical hematopoietic stem cell transplantation (HSCT) has been an alternative and curative option for children with hematological diseases due to greater ease of access to the donor and, consequently, the possibility of HSCT in less time.In the absence of an identical HLA related donor, choosing a young, unrelated male donor without comorbidities would be the best option, but with the clinical urgency of the patient and in the current context of the new coronavirus pandemic, choosing a haploidentical donor is an attractive option and in the presence of two or more donors, other factors such as kir calculation and gender mismatch should be considered.

Objective: To review the results obtained in male patients undergoing Haploidentical HSCT, being the donor (mother). Material and method: Retrospective cohort study of patients undergoing Haploidentical HSCT in a pediatric center.

Results: From January 2019 to June 2021, 53 HSCT Haploidenticals were performed, 10 with the characteristics of the study. Recipients with a median age of 13 years, 7 were diagnosed with ALL, 2 with AML and 1 HL. 20% of patients entered 1st complete clinical remission (RCC); 50% in 2nd RCC, 10% in 3rd or more RCC, 20% with active disease and 20% had already done the 1st HSCT (1 autologous and 1 Haploidentical/father). The conditioning used in 90% of patients was Flu+TBI and 10% was Bu+Flu+Mel. The median age of the donors is 39 years, with 70% being Kirmismatch, 10% match in both directions and 20% Mismatch in the HVG. The choice of the donor (mother) was selected in 70% by the Kir calculation and 30% by social conditions, family structure or clinical impossibility of the father. The graft source of choice was 50% MO and 50% CTP, with a median of cellurity of 10.28x10^6 CD34/Kg of the recipient. Regarding ABO incompatibility, 80% were compatible and 20% with minor incompatibility. The median number of pregnancies of the donors was 2. Neutrophil take-up was at the median of D+14, without graft failure or rejection. 2 patients died (1 associated with the 2nd HSCT and 1 due to disease relapse after 8 months of HSCT). 90% progressed to acute GVHD (grade I or II) with a median time on D+34 and 60% progressed to chronic GVHD (20% mild; 40% moderate and 40% severe) with a median time on D+164.

Conclusion: Haploidentical HSCT has been increasing in Brazilian centers. Haploidentical HSCT results, as well as other HSCT, depend on some variants, which make it impossible to estimate the percentage of people who will or will not succeed in coping with the disease after the procedure. Although the number of the study is not statistically significant, 80% of patients are alive after Haploidentical HSCT with gender mismatch (female to male),

Keywords: Hematopoietic Stem Cell Transplantation. Haploidentical Transplantation. Pediatrics.

HEMATOPOIETIC STEM CELL COLLECTION BY APHERESIS IN CHILDREN UNDER 10KG FOR AUTOLOGOUS TRANSPLANTATION

Aline Miranda de Souza[1]; Sanny Marcele da Costa Lira[1]; Andreza Alice Feitosa Ribeiro[2]

1 Grupo Gestor de Serviços de Hemoterapia – GSH, São Paulo-SP
2 Bone Marrow Transplantation Department, Hospital and Maternity Brasil, Santo André-SP

Introduction: The hematopoietic progenitor cell collection (HPC) by apheresis in children is challenging due to the higher risk of complications because of the low total blood volume and poor venous access, especially those below 10kg. The extracorporeal volume of the apheresis equipment system, the impossibility of peripheral venous access and the metabolic complications resulting from the toxicity secondary to citrate are the main factors that should be considered at the time of planning the collection procedure. In addition, the impossibility of effective communication between the patient and the team performing the procedure and the stress on the family dynamics related to the sick child require an adequate interaction between the apheresis team, family, bone marrow transplant team and pediatricians for success of the procedure.

Objective: To review the literature on the collection of hematopoietic progenitor cells by apheresis in young children and to report the data regarding the procedures performed by the GSH Group at the Hospital and Maternity Brasil.

Methods: Between 01/11/19 and 31/06/21, 3 patients weighing up to 10kg were treated for HPC collection by apheresis. The age range of these patients at the time of the procedure was from 7 to 19 months, and weight between 6.9 and 10kg.

Results: Two were female, 2 had neuroblastoma as diagnosis and 1 had a theratoid tumo. All patients were submitted to inguinal central venous catheter implantation without complications. All procedures took place in a intensive care unit under monitorization. All patients were mobilized with GCSF 10-15µg/Kg and the peripheral blood CD34+ range before the collection was 36 to 87. The circuit of the apheresis equipment was filled with red blood cell concentrate compatible with the ABO, Rh and Kell systems. The total blood volume processed was between 2,8 and 3 and the time of the procedure was between 200 and 300 minutes. To prevent electrolyte disorders related to citrate anticoagulation, prophylactic replacement of calcium, magnesium, and potassium was performed. No patient presented signs or symptoms of hypocalcemia, and the results of the laboratory electrolyte control tests after the end of the procedure were within the normal range, whin platelets count above 50.000/mm3. All patients reached a total number of collected CD34+ cells greater than 3x106/kg in only 1 procedure. The collection efficiencies were above 50%, and no patient presented any adverse event related to the procedure. Two of the patients have already been referred for transplantation, obtaining neutrophilic grafts after 11 and 12 days.

Conclusion: The procedure for collecting HPC by apheresis in young children is a safe procedure when performed by a specialized and experienced multidisciplinary team, and in a hospital institution that offers the necessary structure to deal with possible complications.

Keywords: stem cell collection by apheresis, pediatric cell collection, pediatric BMT

IMPACT OF POSITIVE MINIMAL RESIDUAL DISEASE IN THE OUTCOME OF PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC OR BIPHENOTYPIC LEUKEMIA WHO UNDERWENT ALLOGENEIC HEMATOPOETIC STEM CELL TRANSPLANTATION - A SINGLE-CENTRE EXPERIENCE

Raisa Machado Amaral; Thábata Cristina Paradas Moreira da Silva; Maite Freire Cardoso; Débora Prestes Rehme; Karoline Helena Silva da Silva; Virginio Climaco Araujo Fernandes Junior; Laís Lima Quintino; Patrícia Shimoda Ikeuti; Cintia Monteiro Lustosa; Adriane da Silva Santos Ibanez; Jakeline Palmezano Crispim de S. Bufoni; Victor Zecchin; Renata Fittipaldi da Costa Guimarães.

Instituto de Oncologia Pediátrica -IOP-GRAACC/UNIFESP, São Paulo - SP - Brasil

Introduction: In patients with acute lymphoblastic leukemia (ALL), negative residual disease (MRD) pre hematopoietic stem cell transplantation (HSCT) is one of the main factors related to better outcomes. Patients who cannot achieve negative MRD, even after intensifying chemotherapy, are still a challenge, since the level of pre-HSCT MRD is inversely related to event-free survival. However, patients submitted to allogeneic HSCT with positive MRD that achieve post-HSCT molecular remission still can be cured. There are limited data in the evaluating their prognostic value in pediatric patients. Objective: To evaluate the impact on outcome of pediatric patients diagnosed with ALL and biphenotypic leukemia submitted to allogeneic HSCT with positive MRD.

Method: Retrospective cohort study of patients submitted to allogeneic HSCT with positive MRD between October 2014 and March 2021.

Results: 10 patients with positive MRD were transplanted and MRD levels ranged from 0.03% to 0.9%. The median age was 10.6 years, 80% of female and 20% male patients. In 80% the diagnosis was ALL-B, 10% of ALL- T and 10% of biphenotypic leukemia. Four of the 10 patients (40%) spinal cord recurrence after HSCT in evaluations performed between D+30 and six months. Of these, three died (30%), one due to sinusoidal obstruction syndrome, one due to sepsis and the other due to early recurrence. One patient is alive and evaluating therapeutic possibilities.. One patient had D+30 positive DRM, and treatment with Blinatumomab was started associated with lymphocyte infusion from the donor and is in molecular remission 10 months after HSCT. At the present time, six of the 10 patients (60%) are in post-HSCT remission, with follow-up raged from 10 months to five years.

Conclusion: Despite the limitation of the sample, some patients seem to benefit from allogeneic HSCT even with positive MRD, since 60% are in remission. Close monitoring of post-HSCT MRD may be interesting to start early approaches if positive MRD, such as reduction of immunosuppression, use of DLI or monoclonal antibodies (eg. Blinatumomab). However, more studies are needed to determine the real prognostic impact of pre- and post-HSCT MRD in pediatric population.

Keywords: acute lymphoblastic leukemia, pediatric hematopoietic stem cell transplantation, measurable/minimal residual disease.

INTERVAL BETWEEN TIME OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (ALLO-HSCT) AND THE ONSET OF ACUTE GRAFT-VERSUS-HOST DISEASE, IN A SINGLE PEDIATRIC HSCT CENTER

Adriane da Silva Santos Ibanez; Virginio Climaco Araujo Fernandes Junior; Karoline Helena Silva da Silva; Laís Lima Quintino; Patrícia Shimoda Ikeuti; Cintia Monteiro Lustosa; Jakeline Palmezano Crispim de S. Bufoni; Cristiane Menezes Vitoria Alferi; Olga Margareth Wanderley de Oliveira Félix; Débora Prestes Rehme; Maite Freire Cardoso; Erica Almeida Viana; Raisa Machado Amaral; Renata Fittipaldi da Costa Guimarães.

Instituto de Oncologia Pediátrica IOP/GRAACC/UNIFESP, São Paulo - SP - Brasil

Introduction: Acute graft-versus-host disease (GVHD) is an adverse immunologic phenomenon following allogenic hematopoietic stem cell transplant.and may contribute to increased HSCT-related morbidity and mortality. The main the risk factors for GVHD are: disparity in HLA compatibility, donor age and gender, intensity of conditioning regimen, GVHD prophylaxis, source of progenitor cells and CMV serological status of patient and donor.

Goal: To describe the time interval between allo-HSCT and the onset of acute GVHD.

Material and method: A retrospective cohort study of patients undergoing allo-HSCT who developed acute GVHD.

Results and discussion: We analyzed 38 patients who underwent allogeneic HSCT between June 2020 and March 2021 in a pediatric HSCT unit. Of these, 25 were male (66%), with a median age of 9.5 years. Of the 38 HSCT, 22 were with haploidentical donor (58%), 12 with unrelated donor (32%) and 4 with HLA compatible sibling (10%). The source of the graft was peripheral progenitor cells in 18 HSCT (47.3%), bone marrow in 17 (44.7%) and umbilical cord blood in 3 (8%). There was a gender disparity between donor and recipient in 16 (42%) of hSCT, of these, 8 (21%) had female donor with male recipient. The age of the donors ranged from 4 to 44 years, with a median of 31 years. In 25 HSCT (65.8%), donor and recipient had IgG reagent serology for Cytomegalovirus (CMV) and, in 4 (10.5%), the recipient had non-reactive IgG serology with igg reagent donor for CMV. GVHD prophylaxis varied according to the type of transplant, and tacrolimus associated with mycophenolatom was used in 50% of patients. 26 patients (68%) presented clinical manifestations of acute GVHD, beginning between D+14 and D+151, with the median in D+45. Of these, 24 patients (92%) had skin involvement - grades I (10 = 42%), II (11 = 46%), III (3 = 12%), and 2 (8%), had liver involvement - grades II and III (1 patient each = 4%).

Conclusion: The time between the allo-HSCT and the onset of acute GVHD is variable. In this study, the interval ranged from D+14 to D+151, with the median in D+45 (92,3% during the first 100 days after allo-HSCT). This wide range reinforces the need for frequent follow-up of these patients in the first 100 days after HSCT, as well as the guidance of family members and pacients on the early recognition of clinical manifestations of GVHD, aiming to reduce the morbidity and mortality of these patients.

Keywords: Acute graft-versus-host disease, hematopoietic stem cell transplantation, pediatrics

MINIMIZING THE IMPACT OF LONG-TERM HOSPITALIZATION: THE HUMANIZATION OF HEALTH CARE IN A PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT

Ariane Piovan Ribeiro[1], Livia Cristina Ferreira de Oliveira[1], Regina Célia da Silva Dias[1], Vânea Lucia dos Santos Silva[1], Paula Moreira da Silva Sabaini[1], Luara Sandrin Engracia Garcia[1], Neysimélia Costa Villela[1], Luiz Fernando Alves Lima Mantovani[1], George Mauricio Navarro Barros[1], Nayara da Silva Santos Cardozo[1], Claudia Adriana Fernandes[1], Simone Cristina Germano de Oliveira[1], Luiz Fernando Lopes[1]

1. Barretos Cancer Hospital, Barretos, Brasil

Introduction: Hematopoietic Stem Cell Transplantation (HSCT) is a treatment consisting of several distinct phases marked by a long-term hospitalization, a condition that can be very distressing to both patient and family. Having in mind that in the health care field humanization means valuing the individual itself, its essential to empower the patient autonomy and his choices regarding his own treatment. This action may turn the treatment a less traumatic experience.

Objective: To describe actions that may promote humanization in the health care assistance to children undergoing stem cell transplantation.

Methods: This is a descriptive study, an experience report based in several actions implemented in a HSCT Unit with focus in health care humanization.

Results: A partnership involving the multi-professional team involved in the treatment of children undergoing HSCT was responsible for a series of actions with the goal to minimize the hospitalization impact. In our institution there are several projects with the intend to improve humanization in patient care. When a patient is admitted in the Pediatric HSCT Unit we collect several informations, like personal preferences (TV shows, cartoons, toys and favorite activities). Our goal is to create an affective record that may turn possible different individualized actions like developing a personalized identification plate at the patient room´s door containing his name, parents name and favorite character (figure 1). Each patient bedroom is individual and has an adjacent bedroom and bathroom for his parents, making possible to maintain the family bond intact during the hospitalization period (figure 2). With the prospect to stimulate the normal child developing and also patient's entrainment, the unit has a playroom equipped with HEPA (High Efficiency Particulate Arrestance) filters (figure 3). This allows our patients to perform several activities outside his room. Before the hematopoietic stem cell infusion, the Blood Bank Department offers the patient the possibility of customize his own stem cell bag (figure 4). After the confirmation of the marrow recovery we make a celebration nicknamed "Engraftment Party" (figure 5). The patient´s room is decorated by the patient and his family to celebrate what this special moment seem by the family as rebirth. When the patient is discharged he receives a "Bravery Certificate" with the idea to congratulate the patient for his efforts during the long period of time in the hospital (figure 6).

Conclusion: Actions respecting the concept of humanization in the health care field may help not only the treatment as well the recovery of children undergoing HSCT. This could prevent traumatic experiences only by offering an individualized and personal patient care allied to the current health care technologies currently available.

Keywords: Humanization

FIGURE 1: Patient room´s door identification

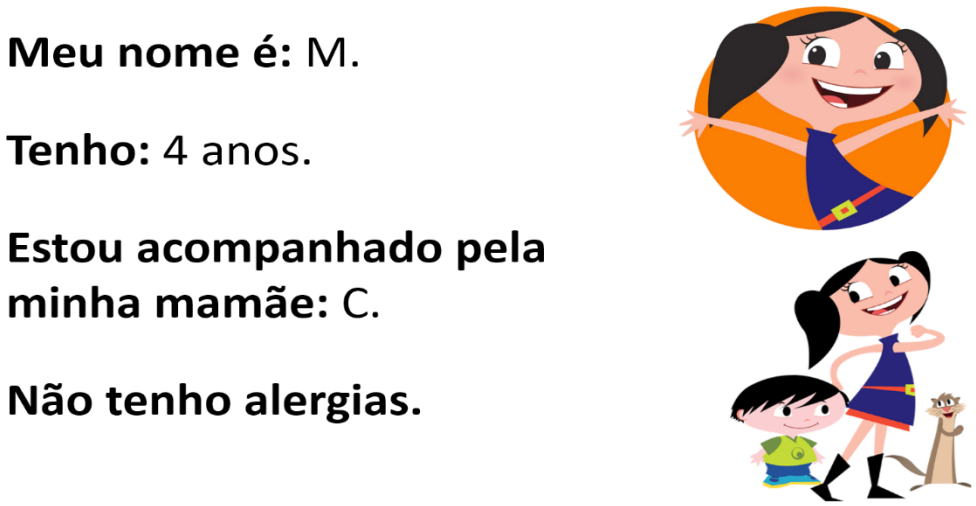


FIGURE 2: Parent and patient room

FIGURE 3: Playroom

FIGURE 4: Customized stem cell bag

FIGURE 5: Engraftment Party

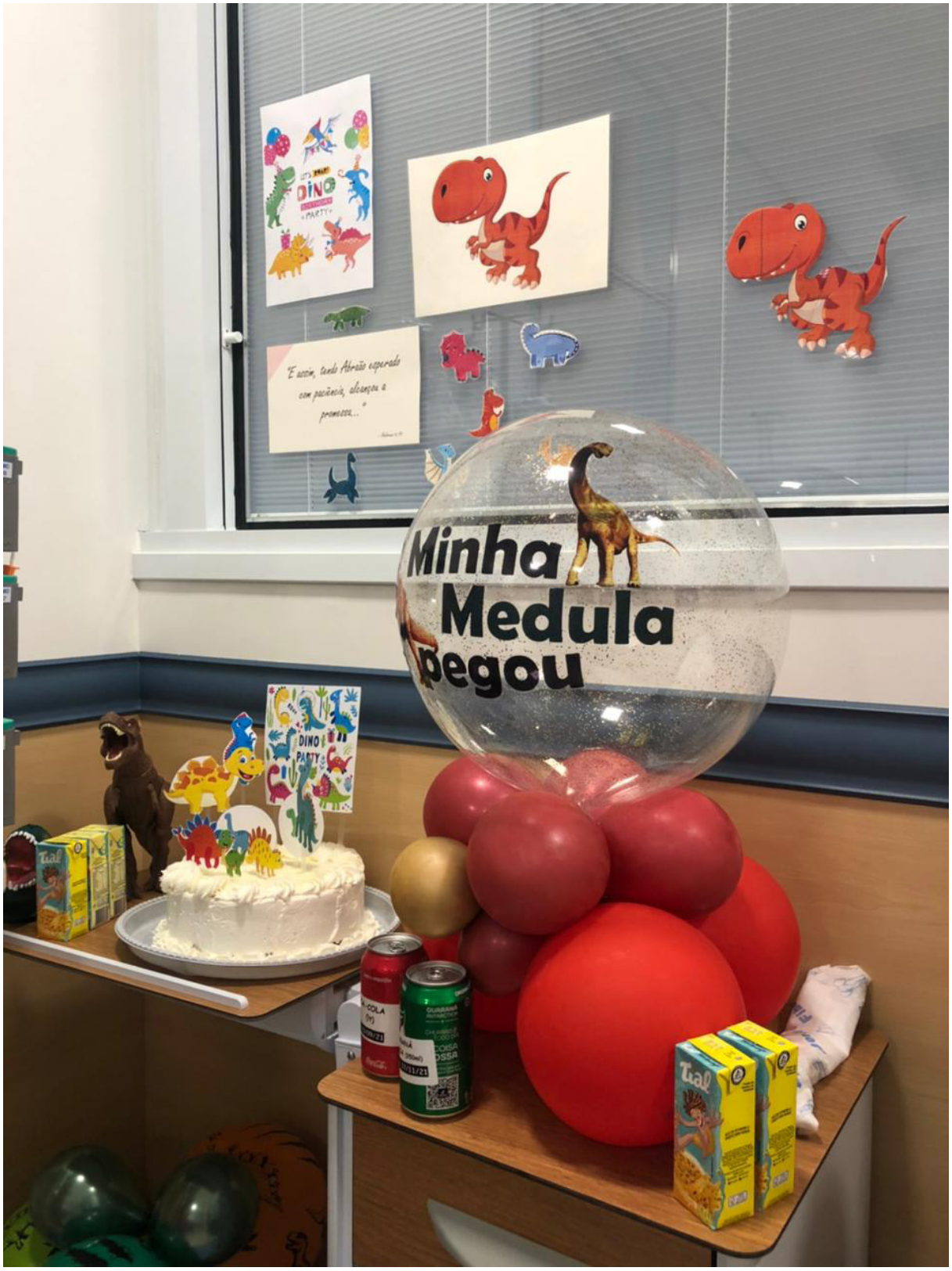
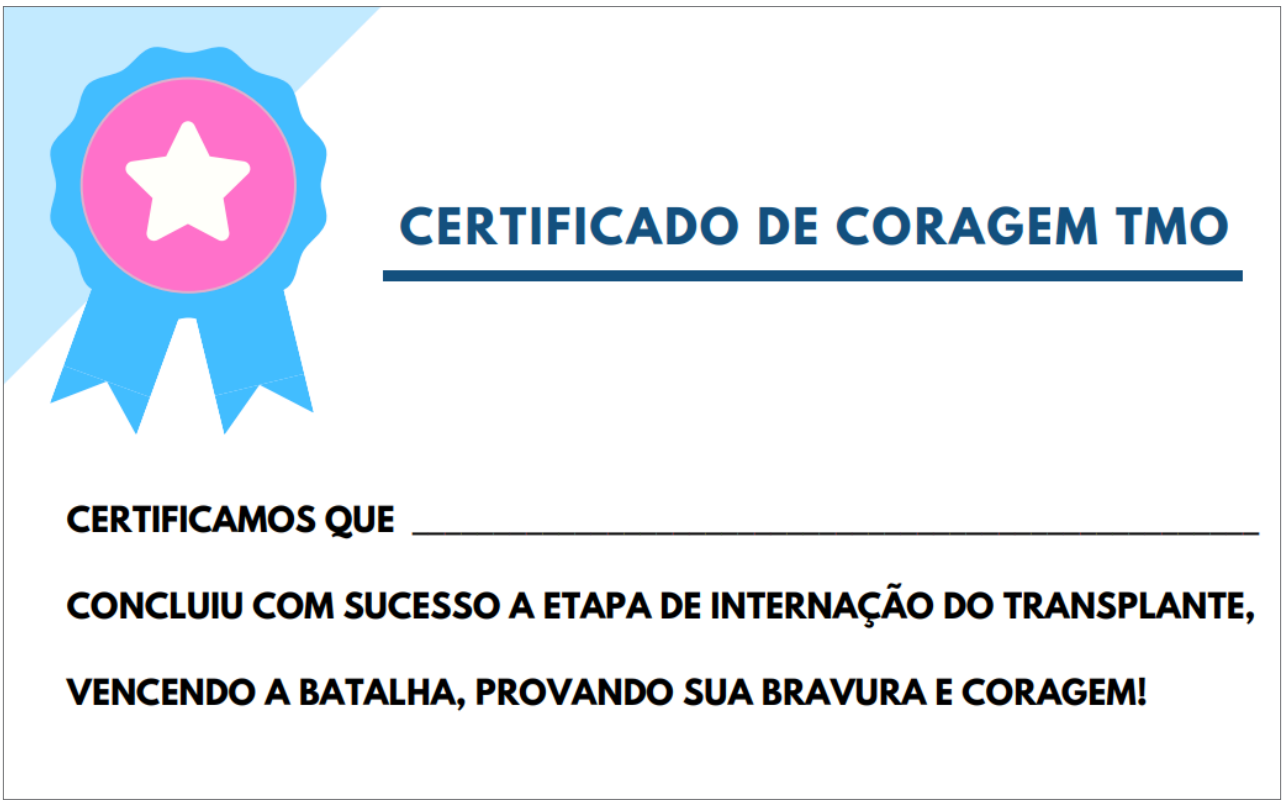


FIGURE 6: Bravery Certificate



MOLECULAR PROFILE AND SURVIVAL OF PATIENTS WITH JUVENILE MYELOMONOCYTIC LEUKEMIA SUBJECTED TO HEMATOPOIETIC STEM CELL TRANSPLANTATION

Rafaela de Souza Ferreira[1], Patrícia Shimoda Ikeuti[2], Neysimélia Costa Ville[la1], Luiz Fernando Lopes[1], Angela Mandelli Venancio[1], Luiz Fernando Alves Lima Mantovani[1], George Maurício Navarro Barros[1]

1. Hospital de Câncer de Barretos, Barretos, Brasil
2.Instituto de Oncologia Pediátrica IOP/GRAACC/Unifesp, São Paulo, Brasil

Introduction: Juvenile Myelomonocytic Leukemia (JMML) is a rare aggressive disease, with its most effective treatment consisting of hematopoietic stem cell transplantation (HSCT). In about 90% of cases, patients present somatic or germinal mutations in the NF1, PTPN11, KRAS, NRAS and CBL genes. Ages above 2 years old, blood platelets count below 33 thousand and fetal hemoglobin above 10% upon diagnosis, as well as PTPN11 mutations are bad prognosis' factors.

General objective: To describe the molecular profile of JMML patients subjected to hematopoietic stem cell transplantation in a pediatric HSCT service.

Specific objective: To evaluate the global survival and event-free survival rates for pediatric JMML patients subjected to hematopoietic stem cell transplant in a pediatric HSCT service, according to their molecular profile.

Case selection: A retrospective cohort study was performed with 27 patients who had received molecular profile analysis upon diagnosis and undergone HSCT between January 2014 and July 2019. METHOD: Along with descriptive analysis, a measurement was done on the global survival of each molecular marker and of event-free survival. The survival probability was estimated by a Kaplan-Meier curve and the comparisons were made by the Logrank test. The chosen significance level was 0.05 and the data was analyzed by the SPSS software, version 2.1.

Results: Nine patients had PTPN11 mutations, 4 had KRAS, 4 had NRAS, 1 had 2 marker mutations (PTPN11 and NRAS), 6 had been diagnosed with Neurofibromatosis type 1 (NF1) and 3 didn't have any molecular markers. Upon full-group evaluations, the global survival rate in 3 years was 65% and the event-free survival rate was 59,3%. No statistically relevant differences were found in the survival related to the molecular marker (P=0,153).

Conclusions: The casuistry epidemiology was similar to the one described in readings, predominantly PTPN11, followed by NRAS and KRAS alterations and clinical diagnosis of NF1. No survival differences related to molecular markers were found, most likely due to the sample size.

Keywords: Juvenile myelomonocytic leukemia; hematopoietic stem cell transplantation; molecular biology.

OUTCOMES AFTER AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION (AUTO-HCT) IN CHILDREN AND ADOLESCENTS WITH MALIGNANT DISEASES: EXPERIENCE FROM A SINGLE CENTER

Juliana Luiza de Mello Bach[1], Polliany Roberta Dorini Pelegrina[1], Cilmara Cristina Kuwahara Dumke[1], Gisele Loth[1,2], Fernanda Moreira de Lara Benini[1], Adriana Mello Rodrigues[1,2], Carolina Martins de Almeida Peixoto[1], Alberto Cardoso Martins Lima[2], Carmem Bonfim[1,2]

1 Hospital Pequeno Príncipe
2 Immunogenetics Laboratory, Complexo Hospital de Clínicas, Federal University of Paraná

Introduction: Autologous hematopoietic stem cell transplantation (auto-HSCT) is an important consolidation treatment of malignant diseases. The most common indications are central nervous system tumors (CNSTu), neuroblastomas and lymphomas. Survival after auto-HSCT depends on the stage and type of disease. Although results have improved during the past decades, in Brazil, the delay in referral, lack of specialized hospitals and specific chemotherapies lead to a worse survival for these patients.

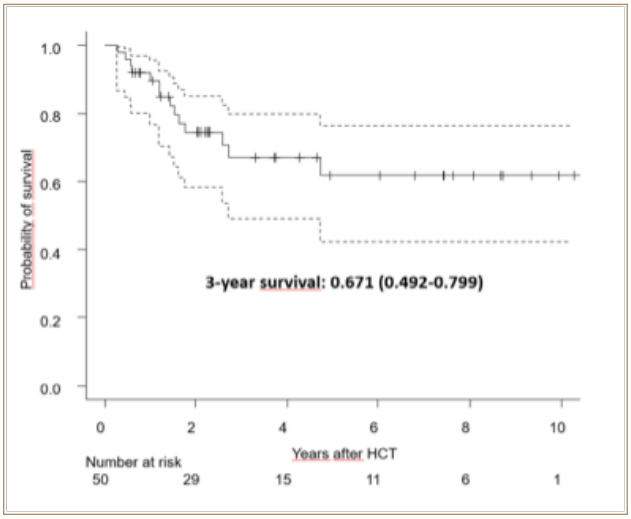
Objective: To analyze survival outcomes after auto-HSCT for children transplanted over a 10-year period in a Brazilian pediatric HSCT institution.

Method:Quantitative cross-sectional study analyzing the medical records of patients aged between 0-17 years who underwent auto-HSCT between Apr/2011 and Dec/2020.

Results: During this period, 228 transplants were performed, of which 17% (n=50) were auto-HSCT, with a median age of 6,9 years (1-17yeas) and 64% were male. The primary diagnoses were: High-risk neuroblastoma (n=19), Hodgkin's lymphoma post relapse/disease progression (n=13), CNSTu: Choroid plexus carcinoma, Pinealoblastoma and Rhabdoid teratoid tumor (n=7), Burkitt lymphoma (n=4), Germ cell tumor with poor response to initial treatment or relapse (n=3), M3 acute myeloid leukemia in remission (n=2), Multiple myeloma (n=1) an Ewing`s tumor (n=1). All patients receive myeloablative conditioning, 23 with busulfan (BU) and melphalan (MEL), 9 with BU, MEL and gemcitabine, only 1 has received tandem transplant. Stem cell sources were peripheral blood (n=48), bone marrow (n=1) and umbilical cord (n=1). The median number of infused CD34 cells was 6,06x10^6/kg (0,69x10^5/kg-12,2x10^6/kg). Patients remained hospitalized for a median of 29 days (20-105days). All patients had hematologic recovery, with a median neutrophil engraftment of 11 days (9-25days) and platelet engraftment of 17 days (12-45days). Twenty-two patients (44%) relapsed at a median of 8 months after transplant (1 month– 2.7years). Of these, 12 (54%) had the diagnosis of neuroblastoma. Out of the relapsed patients, one received a haploidentical transplant (multiple myeloma) and one received a matched sibling transplant (Hodgkin's lymphoma) and the other 20 patients received palliative care. Fourteen out of the 22 patients died at a median of 1.1 year after transplant (6months– 4.7 years) including the patients who received a 2nd transplant for multiple myeloma. Relapse was the only cause of death and no patient died due to transplant related mortality. With a median follow-up of 3 years (7months–10years), 36(72%) patients are alive including 8 patients in palliative care with evidence of disease. The overall survival rate is 67,1% at 3 years.

Conclusion: Solid tumors in the pediatric age group represent a great challenge, despite the success of transplant, relapse is still very prevalent. Difficulty in accessing new strategies to avoid relapse has made it difficult to improve the overall survival rate.

Keyword: Autologous, Transplant, Pediatric.



RETROSPECTIVE EVALUATION OF NEUROBLASTOMA PATIENTS UNDERGOING SINGLE-CENTER AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION FROM 2007 TO 2017

Aina Henriques Melgaço; Simone Cunha Maradei Pereira.

Instituto Nacional do Cancêr - CEMO, Rio De Janeiro - RJ - Brasil.

Introduction: Neuroblastoma (NB) is the most common extracranial solid tumor in childhood, with high clinical heterogeneity. Patients stratified as high risk undergo cycles of chemotherapy and surgery at induction and have an indication for consolidation therapy with high doses of chemotherapy followed by cell rescue with autologous hematopoietic cell transplantation (TACH). Despite all the developments in the treatment of patients, high-risk neuroblastoma is still a challenge due to its high mortality.

Objective: To analyze patients undergoing TACH with a diagnosis of neuroblastoma.

Casuistry: Clinical and epidemiological data collected by consulting the medical records of 24 patients were analyzed. There were 3 excluded patients.

Method: Retrospective cohort study of pediatric patients diagnosed with advanced stage neuroblastoma undergoing TACH. Analysis performed by the R program and Kaplan-Meier and log-rank method for survival analysis.

Results: Data survey showed that 71.4% of patients were under 4 years of age. (Table 1). Median survival was 36 months, with an overall 5-year survival of 56% (Figure 1). When patients were divided into 2 groups (<4 years and >5 years), the probability of overall survival was higher in children under one year and there were no survivors in those over 5 years (p. 0.0698) in the 60-month period.(Figure 2) Conclusions: With this study, it was possible to confirm the high mortality of NB, despite therapy with TACH, showing that more studies on this pathology are needed in order to improve its survival.

Keywords: High risk neuroblastoma; Autologous bone marrow transplantation, Infant neoplasm; Global Survival.

TABLE 1 — Patient data

	n (21)	%
Gender		
Feminino	9	42,9
Masculino	12	57,1
Age		
0-4 anos	15	71,4
> 5 anos	6	28,5
Protocol		
Neuro IX	19	90,5
Outros	2	9,5
INRG		
Alto	19	90,5
Intermediário	2	9,5
INSS		
4	17	81
3	4	19
N-MYC-N		

Amplified		5	23,8
Not amplified		3	14,3
Not avaliable		13	61,9
Relapses before TACH			
1	14		66,7
2	6		28,6
>2	1		4,8
Pre BMT irradiation			
Sim	0		0
Não	21		100
relapse location			
Local	14		66,7
Metástatica	3		14,3
Ambos	4		19
MIBG before TACH			
Sim	8		38,1
Não	10		47,6
Terapeutico	3		14,3
Status before TACH			
RC	7		33,3
RP	14		66,7

TABLE 2 — Transplant-related data

	n (21)	%
Conditioning		
CEM	20	95,2
BuMel	1	4,8
cell source		
Medula óssea	5	23,8
Sangue periférico	14	66,7
Ambos	2	9,5
Use of ATRA		
Sim	20	95,2
Não	1	4,8
Death		
Sim	15	71,4
Não	6	28,6

TABLE 3 — Data related to post-transplantation

	Days (D+)
Average survival after HSCT	
mean	757,6
average	711

FIGURE 1- Overall survival

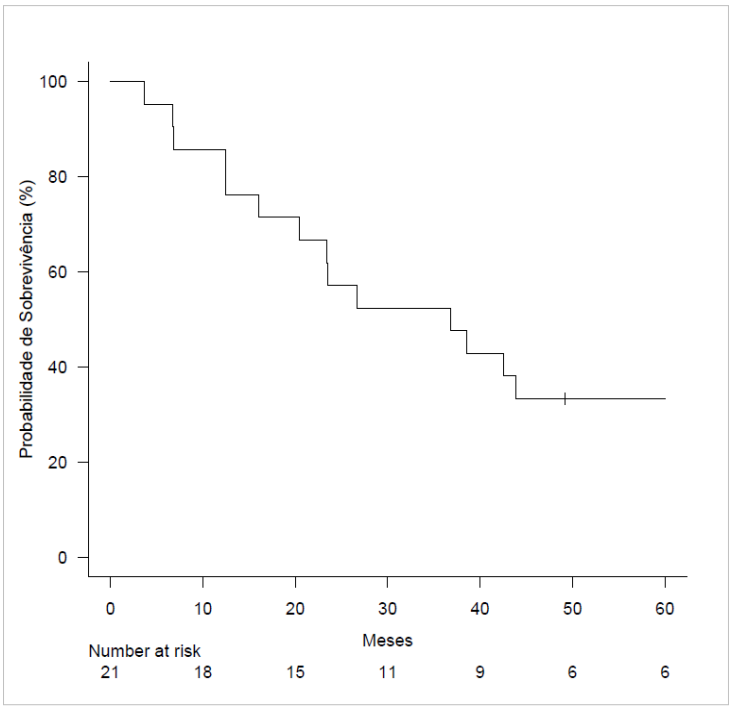
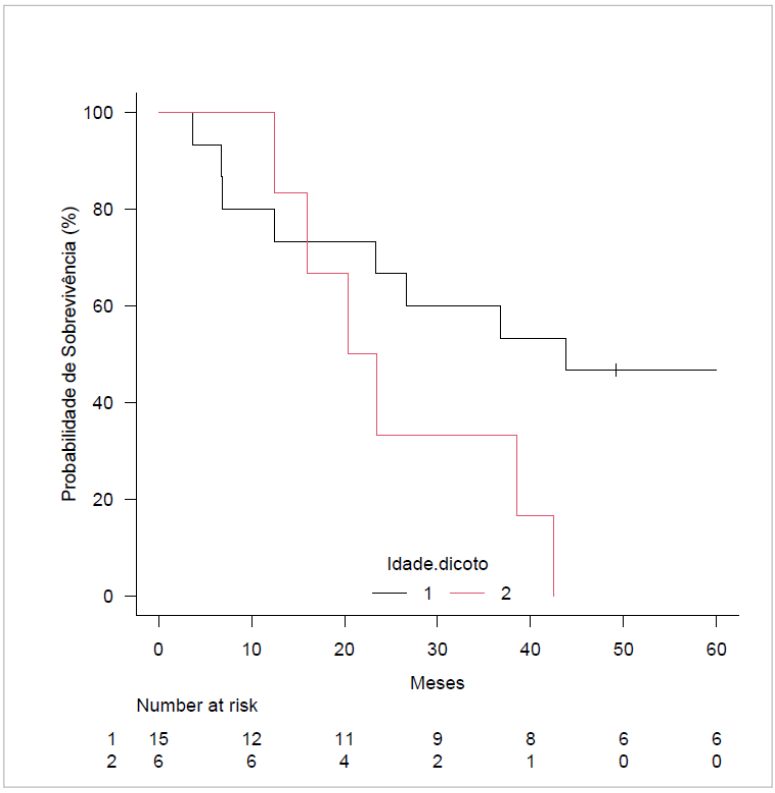


FIGURE 2- Overall survival by age



REVERSAL OF MIXED CHIMERISM WITH INFUSION OF DONOR LEUKOCYTES IN CHILDREN UNDERGOING HAPLOIDENTICAL HEMATOPOIETIC STEM TRANSPLANTATION (HSCT)

Roseane Vasconcelos Gouveia[1], Valéria Cortez Ginani[1], Gustavo Zamperlini[1], Maria Gabriela Alves Dias Matos[1], Carla Maria da Costa Zanchetta Oliveira[1], Luciana dos Santos Domingues[1], Carla Nolasco Monteiro Breviglieri[1], Marcia Vieira Pupim[1], Paola Azenha Milani Soriano[1], Juliana Francielle Marques[1], Claudineia Faria de Andrade[1], Francisca Vanoide de Brito Santos[1], Priscila Mendes Paiva[1], Adriana Seber[1]

1. Equipe Onco-TMO em Pediatria; Hospital Samaritano, São Paulo, Brasil

Introduction: Donor leukocyte infusion (DLI) may be a therapeutic option for patients with baseline disease recurrence after HSCT. The cellular dose varies according to the underlying disease, indication, type of donor and the presence of graft-versus-host disease (GVHD). The activity of donor lymphocytes against receptor hematopoiesis to reverse mixed chimerism after HSCT is not well established.

Objective: To evaluate the efficacy and safety of DLIs performed in children with mixed chimerism.

Methods: Description of the use of DLI in patients with mixed chimerism after haploidentical HSCT to avoid rejection and, in patients with leukemia, also to prevent recurrence of the disease.

Results: Three patients received leukocyte infusion as a treatment for mixed chimerism:1st, 15 years old, haploidentical HSCT with his mother's peripheral blood stem cells (PBSC) in 2014 for treatment of Ph+ ALL in 3rd remission. Conditioning was fludarabine and 1200cGy TBI and GVHD prophylaxis cyclophosphamide (Cy), cyclosporine (CsA), mycophenolate (MMF). Acute GVHD in the skin and intestine (GI) resolved with steroids. Nine months after HSCT, he presented with molecular BCR-ABL recurrence, treated with DLI every 4 weeks 104CD3/kg, 105CD3/kg and 106CD3/kg. Despite the DLIs, disease evolved to positive minimal residual disease as measured by flow cytometry, with up to 2.5% blasts. The disease had a complete response to blinatumomab, but he presented with mixed chimerism (198 XX,2XY) after the 4th cycle, without measurable disease. DLI 3x107CD3/kg and 108CD3/kg were associated to the blinatumomab without GVHD. Few months later, a severe Coxsackie encephalitis triggered acute and chronic sclerodermoid GVHD in the mouth and skin. He is currently 7 years after HSCT in remission of the disease, with complete chimerism and still on immunosuppressors for the treatment of moderate chronic GVHD.

2nd, 13 years old, haploidentical HSCT with father's marrow for sickle cell anemia in 2019. Conditioning: fludarabine, Cy, rabbit ATG and TBI 400cGy; prophylaxis of GVHD: Cy, sirolimus, MMF. She received 9x106 CD34/kg. Four months after HSCT, even having already achieved complete chimerism, she had decreasing chimerism with nadir 9 months after HSCT of 66% allogeneic cells at the VNTR. Poor adherence to sirolimus was documented at this time. She received two DLIs with one month interval, 106CD3/kg and 5x106CD3/kg with progressive improvement of chimerism, stable around 90% of allogeneic cells, despite chronic lichenoid GVHD of the skin, responsive to steroids.

3rd, 13 years of age, haploidentical HSCT with PBSC from his sister in February 2021 for treatment of refractory B-ALL that went into remission only with blinatumomab. Conditioning included fludarabine and TBI (1200cGy), prophylaxis of GVHD, Cy, CsA, MMF. Mixed chimerism was present since the 1st post-HSCT marrow evaluation, reaching 39% of allogeneic cells 3 months after HSCT, but repeatedly evaluated with no recurrence of the underlying disease. He received DLI 1x106CD3/kg and 5x106CD3/kg with a one-month interval. He achieved complete chimerism three months after the 1st DLI, also presented with moderate chronic lichenoid DECH of the skin and GI tract.

Conclusion: DLIs reversed the mixed chimerism in the three patients without severe adverse events, but the presence of mild or moderate GVHD in all, responsive to corticosteroids. DLI was shown to be safe and with potentially promising results to reverse mixed chimerism after haploidentical HSCT.

ROTAVIRUS INFECTIOUS ENTERITIS ASSOCIATED WITH ACUTE GASTROINTESTINAL TRACT GRAFT DISEASE IN A HAPLOIDENTICAL POST-HSCT PATIENT

Maite Freire Cardoso; Débora Prestes Rehme; Raisa Machado Amaral; Karoline Helena Silva da Silva; Virginio Climaco Araujo Fernandes Junior; Laís Lima Quintino; Patrícia Shimoda Ikeuti; Cintia Monteiro Lustosa; Adriane da Silva Santos Ibanez; Jakeline Palmezano Crispim de S. Bufoni; Fabianne Altruda de Moraes Costa Carlesse; Renata Fittipaldi da Costa Guimarães.

Instituto de Oncologia Pediatrica (IOP/GRAACC)/ UNIFESP, Sao Paulo - SP - Brasil.

Introduction: Abdominal complications affect more than 80% of patients who undergo hematopoietic stem cell transplantation (HSCT). Diarrhea is one of symptoms of digestive tract mal- function. In case of patients who have undergone allo-geneic HSCT, after conditioning regimen-associated mucositis, the most common cause attributed to diarrhea is graft-versus-host disease (GvHD), and in 40% of cases the cause is infectious, with viruses being the main agents. Rotavirus is one of the most common causes of diarrhoea worldwide, but one of the least studied causes of diarrhoea post SCT. The incidence of rotavirus in stool samples from patients undergoing HSCT is about 10%. In these immunosuppressed patients its course may be more severe.

Objective: To describe a clinical case of a patient submitted to haploidentical HSCT who developed post-HSCT acute diarrhea, diagnosed with rotavirus enteritis.

Method: Review of the index case medical record.

Results: A 2-year and 4-month-old female patient diagnosed in July 2020 with acute myeloid leukemia with KMT2A t(10;11)(p12;q23) rearrangement, treated with AML Protocol BFM 2004-AR and referred for haploidentical HSCT in first remission. The donor was the mother, and the source, bone marrow. She received myeloablative conditioning with busulfan, fludarabine, and melphalan, with GVHD prophylaxis with cyclophosphamide, mycophenolate mofetil, and cyclosporine. She presented an episode of clinical sepsis on D+4, and broad-spectrum antibiotic therapy was started, maintained until neutrophilic grafting, on D+12. On D+13, the patient suddenly developed gastrointestinal symptoms (vomiting, diarrhea and abdominal distension), associated with a diffuse maculopapular rash affecting more than 70% of the body surface, compatible with grade 2 acute skin GVHD. It continued with progressive worsening of abdominal distension, liquid and bloody stools, in addition to weight gain, anemia and thrombocytopenia. Imaging exams showed large distension of the small loops and colon, with mild and diffuse parietal thickening, suggestive of infectious enterocolitis. Among the main diagnostic hypotheses, GVHD of the gastrointestinal tract (GIT), hepatic veno-occlusive disease and viral infection were considered. Initiated methylprednisolone 2mg/kg/day. TGI biopsy was not performed due to the patient's clinical condition. Concomitantly, we investigated Clostridium difficile toxins and PCR for adenovirus and rotavirus in feces, isolating rotavirus. Thus, with isolation of the agent and suggestive images, a patient diagnosed with rotavirus enterocolitis, with probable GVHD – due to clinical and response to systemic corticosteroid therapy. The patient evolved well, with progressive improvement, tolerance to rapid corticoid reduction, and hospital discharge on D+44.

Conclusion: Although there are more frequent diagnoses in the HSCT scenario, when thinking about possible causes of acute diarrhea, it is important to remember common causes in the general population, especially in preschoolers.

THE ASSOCIATION OF BLINATUMOMAB (BLINA) AND INOTUZUMAB (INO) MAY INDUCE COMPLETE RESPONSE OF REFRACTORY B-LINEAGE ACUTE LYMPHOCYTIC LEUKEMIA (B-ALL) AND ALLOW HEMATOPOIETIC STEM CELL TRANSPLANTATION (TCTH) IN COMPLETE REMISSION

Luciana dos Santos Domingues[1]; Claudineia Farias Andrade[2]; Roseane Vasconcelos Gouveia[2]; Valéria Cortez Ginani[2]; Maria Gabriela Alves Dias Matos[2]; Carla Maria da Costa Zanchetta Oliveira[2]; Carla Nolasco Monteiro Breviglieri[2]; Marcia Vieira Pupim[2]; Paola Azenha Milani Soriano[2]; Daniela Lutti[2]; Evandro Jose Carneiro Fernandes Souto[2]; Roberto Luiz da Silva[3]; Maria Cristina Martins de Almeida Macedo[3]; Adriana Seber[2].

1. Equipe ONCO-TMO Hospital Samaritano, São Paulo - SP - Brasil;
2. Equipe ONCO-TMO em Pediatria; Hospital Samaritano, São Paulo - SP - Brasil;
3. Hospital Nove de Julho-DASA, São Paulo - SP - Brasil.

Even with the recent advances in the treatment of childhood B-ALL, at least 10-15% of children have a relapse of the disease. Currently, the therapeutic regimens used to treat relapse result in suboptimal disease-free survival rates, and these rates are even lower when children are in 2nd and 3rd relapses or have refractory disease. CD19 and CD22 are widely expressed in B-ALL blasts, making them excellent targets for immunotherapy. Despite the remarkable efficacy in relapsed/refractory (R/R) disease and Ino approval in adults, the development of this agent for children did not start until 2016. Regimens with fractionated doses of Ino have the similar efficacy, but less hepatotoxicity than single dose regimens. Blina is a bispecific antibody that binds the CD3 of T-lymphocytes to cells expressing the CD19. Blina would not have action, therefore, in severely aplastic or lymphopenic patients, because its action depends on the patient's own normal T-lymphocytes. CAR-T anti-CD19 and CD22 (dual CAR-T) cells are in development, but sequential use of the two immunotherapy drugs is not described in pediatrics.

Objective: To describe the effectiveness and low toxicity of the association of the two immunotherapy drugs for induction of remission of B-ALL totally refractory to chemotherapy, allowing HSCT in complete remission.

Method: Mini-Hyper CVD: Cycle 1 - Cyclophosphamide 150 mg/m2, 12/12h, 3 days + Dexamethasone 5 mg IV 6/6h (20 mg/day) 14 days, total 32 doses + Vincristine 2 mg/m2, 2 doses. Pegfilgrastim 6 mg, SC, D9, total 1 dose; Inotuzumab 0.6 mg/m2 D2 and 0.3 mg/m2 D8.

Methotrexate 12 mg IT D2, Cytarabine 30 mg IT D7.

Cycle 2 - Methotrexate 250 mg/m2 D1, Cytarabine 0.5 g/m2 12/12h D2 and D3, total 4 doses; Inotuzumab 0.3 mg/m2 D2 and D8, total 2 doses, Ara-C IT D2 and Mtx-IT D7.

Blinatumomab 15mcg/m2/day in continuous infusion until the beginning of the conditioning therapy.

Result: A 10-year-old child with B-ALL diagnosed in 2017 relapsed at the end of maintenance of the GBTLI-2009 protocol. Since then, the disease had been fully refractory to UKR3-ALL, FLAG (2 cycles) and one cycle of blinatumomab. The patient was then treated by us with mini-HyperCVD + Ino, but after two cycles she remained with 28% blasts that lost the CD22, but regained expression of the CD19. We restarted her on blinatumomab and, although severely aplastic, she presented with cytokine release syndrome, with anasarca and fever. On D11 of blinatumomab the bone marrow aspirate and spinal fluid were in remission. She continued on blinatumomab until D15, when she started the myeloablative conditioning with TBI 1.200 cGy and fludarabine. He received bone marrow from her haploidentical brother and GVHD prophylaxis with cyclosporine and MMF. She received ursodiol, acetylcysteine and heparin prophylaxis and had no sinusoidal occlusion syndrome.

She engrafted on D+28. Due to the aggressiveness of the disease, she is receiving maintenance blinatumomab and prophylactic donor leukocyte infusions with neither GVHD nor disease relapse, in excellent health condition 5 months after HSCT.

Conclusion: Blina and Ino can be used sequentially to achieve remission of refractory disease, allow HSCT, and hopefully cure the patients.

Keywords: Inotuzumab. Blinatumomab. leukemia. transplantation. child. immunotherapy.

USE OF KIRMISMATCH VERSUS KIRMATCH DONOR IN HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC PATIENTS: EXPERIENCE OF A SINGLE CENTER

Cintia Monteiro Lustosa[1]; Adriane da Silva Santos Ibanez[1]; Jakeline Palmezano Crispim de S. Bufoni[1]; Virginio Climaco Araujo Fernandes Junior[1]; Karoline Helena Silva da Silva[1]; Laís Lima Quintino[1]; Patrícia Shimoda Ikeuti[1]; Olga Margareth Wanderley de Oliveira Félix[1]; Cristiane Menezes Vitoria Alferi[1]; Victor Zecchin[2]; Renata Fittipaldi da Costa Guimarães[1]

1. Instituto de Oncologia Pediátrica IOP/GRAACC/UNIFESP, Sao Paulo - SP - Brasil;
2. A Beneficência Portuguesa de São Paulo, Sao Paulo - SP - Brasil.

Introduction: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) is emerging as an alternative and curative option for children with hematological diseases, especially in this period of pandemic by SARSCOV2. Studies show that the incompatibility killer immunoglobulin-like receptors (KIR) potentiates the effect of graft versus leukemia, reducing relapses. Thus, this factor can help in choosing the best haploidentical donor to improve the effectiveness of this modality.

Objetives: Describe the experience and compare the results obtained in patients undergoing haplo-HSCT using a kirmismatch (G1) and non-kirmismatch (G2) donor.

Methods: Retrospective cohort study of patients undergoing haplo-HSCT in a pediatric center.

Results: From January 2019 to June 2021, 53 Haploidentical HSCT were performed – six (11%) of these patients were undergoing a second HSCT due to recurrence. 57% were male and with a median age of 9 years. There was a predominance of ALL (53%), AML (30%), Lymphomas (8%), MDS (6%) and SAA (4%). Most patients were in CR2 (54%), followed by CR3+ (18%), CR1 and active/refractory disease – both with 14%. Myeloablative conditioning was used in 85%. As for donor, 70% were male and the median age was 34 years. 62% used peripheral blood (PB) as a graft source and 38% used bone marrow (MO). G1 corresponded to 47% and G2 53%. In both groups, did not identify any primary and secondary graft failure. There was more GVHDa (G1: 79% and G2: 73%) and GVHDc (G1: 46% and G2: 35%) in G1, with no statistical difference (p=0.74 and p=0.56, respectively). G1 had 74% of the cases of GVHD grade I, 10% grade II and 16% grade III, and G2 80% grade I, grade II and III 10% each (p=1.00). As for the severity of cGVHD, there was a predominance of mild (G1:73% and G2: 56%), followed by moderate - 18% (G1) and 33% (G2) and severe 9% (G1) and 11% (G2) (p=0.63). There was no statistical difference (p=0.75) for recurrence, G1 25% (median 112 days after HSCT) and G2 31% (median 135 days). However, there was less recurrence when using PB in G1 (PB 15% and BM 31%) (p=0.37) and when the patient had cGVHD in both G1 (9%) and G2 (zero) (p=0, 18 and p=0.06, respectively). In addition, 76% of patients are alive in G1 and 71% in G2 (p=0.76). Among the causes of death, recurrence was the main cause in both groups (G1 67% and G2 50%), but G2 had higher TRM (G1 n=1; 17% and G2 n=3; 38%) (p =0.42). It is noteworthy that among the four (7% of the sample) TRM cases, two were undergoing the 2nd HSCT. On D+365 the OS was 77% in G1 and 74% in G2 (p=0.74) and the EFS was 72% in G1 and 69% in G2 (p=0.77).

Conclusion: There was no statistically significant difference between groups in the outcomes analyzed. G1 had a lower recurrence rate, especially when using CTP as a graft source. Furthermore, cGVHD seems to be a protective factor against relapse of the underlying disease in both groups. However, there is a limitation in the analysis of this study due to the small sample size.

Keywords: Hematopoietic Stem Cell Transplantation. Haploidentical Transplantation. Natural Killing Cells. Pediatrics.

INFECTIOUS COMPLICATIONS

ANALYSIS OF THE INCIDENCE OF BLOOD CURRENT INFECTION ASSOCIATED WITH CENTRAL VENOUS CATHETER IN PATIENTS SUBMITTED TO HEMATOPOETIC STEM CELL TRANSPLANTATION IN A PRIVATE HOSPITAL IN PORTO ALEGRE

Janaina da Silva Flôr[1], Valesca Scalei Cezar[1], Claudia Cáceres Astigarraga[1], Cristhiane de Matos Vieira[1], Taiana Kessler Gomes Saraiva[1], Gabriela Pereira Flores[1]

1 Hospital Moinhos de Vento, Porto Alegre, RS, Brasil;

Introduction: Hematopoietic Stem Cell Transplantation (HSCT) is a treatment for onco-hematologic diseases and for autoimmune diseases, demonstrating the possibility of cure and/or significant increase in disease-free survival. For HSCT to occur and maintenance1 For this treatment, it is necessary that the patient has a central venous catheter (CVC), whether it is a short- or long-term catheter. This catheter has a high number of manipulations by the care team, as it is from this catheter that several fundamental treatments are performed. Thus, there is a high relationship between CVC and healthcare-related infections, and patients undergoing HSCT who have bloodstream infection related to venous devices present worsening of their clinical condition, evolving to septic conditions2.

Objective: To verify the incidence of CVC catheter-associated bloodstream infection (CLABSI) in a hematopoietic stem cell transplant unit in a private hospital in Porto Alegre, from January 2017 to June 2021. Describe the main measures used for CLABSI prevention in this unit. Results: Catheters are classified as temporary and long-term. Of the 130 transplants performed between January 2017 and June 2021, all patients needing to use a CVC, a total of 15 CLABSI were counted. Of these, 8 occur in temporary catheters and 7 in long-term catheters. The incidence was 1.13/1000 temporary catheter day and 0.60/1000 permanent catheter day. Among the measures to prevent CLABSI are constant inspection of the catheter insertion site, observation of the 5 moments of hand hygiene during catheter manipulation, evaluation of the integrity of dressings, validity of equipment, cannulas and extenders. Training aimed at better hand hygiene practices, insertion and handling of these catheters are also offered periodically to the teams. The observation of the 5 moments of hand hygiene is performed by a member of Infection Control. The incidence of CLABSI and adherence to hand hygiene is calculated monthly, with all data being shared with the team.

Conclusion: With a continuing education program and with observations and guidance during the daily practice of professionals, it is possible to establish solid and consolidated routines for safer care for transplant patients. The multidisciplinary team, especially the nursing team, has a fundamental role in the prevention of CLABSI. In the hematopoietic stem cell transplant unit, there is an absence of CLABSI in long-term catheters for 14 months, and in temporary catheters for 6 months. Checking and sharing CLABSI incidence data and hand hygiene are important to help the team and senior management to identify the measures to be adopted, for a safer outcome for the patient.

Keywords: Bone Marrow Transplantation; Infections; Catheters.

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BONE MARROW TRANSPLANTATION IN MULTIRESISTANT BACTERIA: RESULTS IN A SINGLE CENTER.

Karine Sampaio Nunes Barroso; Livia Andrade Gurgel; João Paulo de Vasconcelos; Beatriz Pitombeira; Fernando Barroso Duarte

Hospital Universitário Walter Cantidido, Fortaleza - Brasil

Introduction: The multiresistant bacteria (MRB) is a big challenge in a bone marrow transplantation (BMT) unit. The colonization of Gram negatives resistant for carbapenem or gram positive resistant for vancomycin previous BMT increases the risk of septic shock and dead in the early phases of BMT. We made BMT in patient of all the general hospital and hematologic services of all state and we recognized different previous infections. It is important to investigate previous infections and colonization to correct isolation into the unit and determined the use of antibiotic in the febrile neutropenia and shock septic, the preemptive diagnosis of colonization into the hospitalization, through once a week rectal swab to Klebsiella pneumonia carbapenamase (KPC) and Vancomycin resistant enterococci (VRE). In our service we reduced the intensity of conditioning in patients with previous infections or colonization to MRB and the patient assigned consent term about the major risk of complication related.

Objective: described the results in early phase of BMT in patient colonization of MRB.

Methods: We included data of BMT realized in our service in 2020 until June 2021 with KPC and VRE colonization and infections and another infecctions of MRB and all the patients with blood culture positive of MRB.

Results: We realized 66 autologous BMT. All the patients had KPC and VRE negative before BMT, 4 (6%) became positive to VRE into the hospitalization and 6 were positive to KPC (9%) in the same period. Just one patient had febrile neutropenia with blood culture positive to KPC (16,6%). He recovered. One patient had blood culture positive to Pseudomonas aeruginosas with just colistin sensitivity. She is alive too. In the allogeneic BMT: 28 BMT were realized (17 related donor (60%), 9 haplo (32%) and 2 unrelated donor (7%). Two patients had colonization previous BMT (7,14%), both were KPC. After BMT: 3 patient s had VRE 3 (10,7%), 3 (10,7%) new colonization from KPC, total 5 (17,8%). Two patients had KPC and VRE (7,14%). Two patients (40%) colonized had culture positive to KPC and 1 died to septic shock and febrile neutropenia. Two other patients had culture positive to Pseudomonas aeruginosas with just colistin sensitivity. Both died to septic shock and febrile neutropenia.

Conclusions: in our service VRE positive is not associate to infection and mortality. In autologous: 16,6% of KPC patients had infection without dead. In allogeneic 40% of positive KPC had infection and the mortality was 20% of total KPC positive. The Pseudomonas aeruginosas with just colistin sensitivity occurred in 3 cases (1 autologous and two haplos). In allogeneic the mortality was 100%. And is the actual major danger in our service.

Keywords: bone marrow transplantation, KPC, VRE.

COVID-19 IN A POST-TRANSPLANT PATIENT: CASE REPORT

Natalia Naome Oshiro[1]; Fernanda Rackes da Silva Fagundes[2]; Alzira Maria Stelmatchuk[2]; Simone Martins Nascimento Piubello[1]; Luciana Puchalski Kalinke[1]

1. UFPR, Curitiba - PR - Brasil;
2. CHC/UFPR, Curitiba - PR - Brasil.

Introduction: COVID-19 has represented a global challenge to health systems due to its high infectivity and pathogenicity. Patients with pre-existing conditions are more likely to have complications, which can lead to a higher mortality risk. Post-transplant patients are usually on immunosuppressive therapy and this state of immune deficiency can result in opportunistic infections.

Objective: To report the case of COVID-19 in a patient who was submitted to a transplantation.

Method: Case report.

Result: A 23-year-old male patient, diagnosed with peripheral T-cell lymphoma in December 2017, started treatment with CHOP. In October 2018 he had a relapse of the disease, started treatment with GDP without response and the therapeutic strategy was changed to R-ICE protcol with partial response. In January 2020, he underwent autologous stem cell transplant (aHSCT) with the expectation that he would later perform haploidentical stem cell transplant (hHSCT). The BuCyE protocol was used for conditioning. On D+2 he developed fever, positive blood culture for a Coagulase-Negative Staphylococci in a double-lumen catheter. Chest CT scan shown signs of an inflammatory and infectious process in the left lung base. On D+18, he had neutrophilic attachment and was discharged from the hospital without platelet attachment. On April 15 he was admitted for haploidentical HSCT-matched sibling, source of peripheral blood. The patient evolved with grade IV haematological toxicity, grade III mucositis, febrile neutropenia, Cytomegalovirus pneumonitis, desaturation and shortness of breath associated with changes in the chest CT showing ground-glass opacity and tree-in-bud appearance. He developed polyomavirus haemorrhagic cystitis and grade III GVHD of the liver and skin. Treatment with methylprednisolone 1mg/kg which improved the alterations. Neutrophil attachment occurred on D+20 and platelet attachment on D+44. On 7/05 he developed runny nose and fever, nasal swab collection for multiple viruses was carried out on 7/06, which detected COVID-19. Chest CT was performed in the following day, reporting ground-glass opacities and centrilobular lung nodules bilaterally. He was treated with Ciclosporin, Tamiflu-Ribavirin and oral prednisone; Ganciclovir was suspended. On 10/15 the he was admitted due to post-COVID-19 lung GVHD manifestations; therefore, endoscopy was performed which showed oesophageal candidiasis, biopsy ulcers with the presence of herpes and infection with cytomegalovirus (CMV). Bronchoalveolar lavage was performed due to worsening of the chest tomography, however, it was not possible to identify an infectious agent. PCR test for tuberculosis and mycological tests gram were negative. On 12/09, he was admitted to the Respiratory Intensive Care Unit due to septic shock associated with Gram-Negative bacillary bacteraemia. Management in the ICU with invasive mechanical ventilation, vasoactive drugs, dialysis and broad-spectrum antibiotic therapy. On 12/12, he had refractory shock and death.

Conclusion: The prognosis of COVID-19 in patients with complications after transplantation is not optimistic and remains cautious. The development of pulmonary GvHD after SARS-Cov-2 infection is also worthy of investigation.

INVASIVE DEMATIACEOUS FUNGAL SINUSITIS IN A PATIENT WITH PAROXYSMAL NOCTURNAL HEMOGLOBINURIA SUBMITTED TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

Júlia Plentz Portich[1], Aline Sinhorelo Ribeiro[1], Lisandra Della Costa Rigoni[1], Sheila Nogueira do Amaral[1], Marina de Almeida Furlanetto[1], Fernanda Fetter Scherer[1], Liane Esteves Daudt[1], Lúcia Mariano da Rocha Silla[1], Claudia Caceres Astigarraga[1] & Alessandra Paz[1]

1. Bone Marrow Transplantation and Hematology Department from Hospital de Clínicas de Porto Alegre, Brazil.

Introduction: Paroxysmal nocturnal hemoglobinuria (PNH) is characterized by destruction of hematopoietic cells through activation of the complement system, manifesting as hemolytic anemia, thrombosis and marrow failure.Allogeneic hematopoietic stem cell transplantation (HSCT) remains the unique cure. Invasive fungal infections are an important cause of morbimortality in patients undergoing HSCT.Although Aspergillus spp. is the most frequently isolated microorganism, rare species are becoming prevalent with the use of prophylaxis. Dematiaceous fungi are characterized by the presence of melanin.Invasive dematiaceous fungal sinusitis (IDFS) is a rare disease.

Objective: We aim to describe a case of IDFS in a patient with PNH submitted to HSCT.

Results: The patient is a 21 years old female, with a history of marrow failure diagnosis in 2013, treated with cyclosporine (withdrawn due to encephalopathy) and thymoglobulin,without response.In 2014 she was diagnosed with PNH,with thrombotic abdominal manifestations.She started intermittent anticoagulation, due to thrombocytopenia.PNH initial clones were present in 45% of neutrophils, 50,9% of monocytes and 8,3% of erythrocytes.She had multiple new abdominal thrombosis.Eculizumab was not available, despite a court order, which was denied. She was submitted to a matched unrelated HSCT with permissive DPB1 mismatch.Conditioning was FluCy TBI 2Gy and graft versus host disease (GVHD) prophylaxis thymoglobulin, methotrexate and tacrolimus.The graft source was thawn bone marrow with a total number of 5x10ˆ6/kg CD34 and total nucleated cells of 5x10ˆ8/kg.Neutrophil engraftment occurred in D+13 and platelet in D+33.In D+9 she started with a holocranial and facial headache.Sinuses CT showed a mucosal thickening of the maxillary sinus, compatible with inflammatory sinusopahty. Nasofibroscopy revealed a blackish area on medium turbinate,covered with white dots. She did a middle turbinate extraction with septoplasty.Anatomopathological revealed fungal elements with spore and septate hyphae and sprouting,with extensive angioinvasion.Direct search was positive for hyaline hyphae and culture displayed a dematiaceous fungus -Colletotrichum sp.She used amphotericin B lipid complex for 14 days, followed by voriconazole with complete response.On D+31 she had a diagnosis of acute skin GVHD stage II Grade 2, starting prednisone 1mg/kg/day and posteriorly progressing for methylprednisolone 2mg/kg/day, with complete response in 14 days. She had the necessity of tacrolimus suspension because of microangiopathy, exchanged for sirolimus.On D+51 she was diagnosed with volcano-like gastric erosions, immunohistochemistry was compatible with cytomegalovirus infection.She used ganciclovir for 15 days, with severe hematological toxicity, and changed to foscarnet until 21 days of treatment, with complete response. She has a 100% donor chimerism and no detectable PNH clone on D+60.

Conclusion: She is currently on D+86, with no relapse of the IDFS.

Keywords: allogeneic stem cell transplantation. Paroxysmal nocturnal hemoglobinuria. Invasive dematiaceous fungal sinusitis.

PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION AND PROFILE OF HEALTHCARE ASSOCIATED INFECTIONS CAUSED BY RESPIRATORY VIRUSES

Paula Krys[1], Heloisa Ihle Garcia Giamberardino[1], Carmem Bonfim[1], Cilmara Cristina Kuwahara[1]

1 Hospital Pequeno Príncipe, Curitiba, Brasil.

Introduction: Hematopoietic stem cell transplantation (HSCT) is a procedure used as treatment for many malignant and non-malignant diseases. Patients undergoing HSCT have higher risk of developing healthcare associated infections (HAIs), because of immunosuppression, repeated and long-term hospitalizations and use of invasive devices. Respiratory virus (RV) infections in this population show varying levels of morbidity and mortality – although these viruses usually cause upper respiratory tract infections, these infections can progress to viral pneumonia, with average mortality rates of 10%1,2,3.

Objective: to understand the epidemiological profile of HAIs caused by RV (RV-HAIs) in patients hospitalized in the HSCT Service, in a pediatric quaternary care hospital.

Method: retrospective and descriptive study analyzing RV-HAI data from the Epidemiology and Infection Control Service. All RV-HAIs which were diagnosed from January 2016 to June 2021 through RT-PCR by nasopharyngeal swab collection in patients that underwent HSCT were analyzed.

Results: RV-HAIs represented 13,4% of all HAIs during the time period, occurring in 38 (15,8%) of all transplanted patients (n=241). The 40 RV-HAIs episodes represent an incidence rate of 15,5% considering the total of transplants (n=258), of which: 102 (39,5%) were haploidentical, 69 (26,7%) related donor, 46 (17,8%) unrelated donor and 41 (15,9%) autologous HSCT. All HAI cases were classified according to epidemiological criteria and identified as upper respiratory tract infections (70%, n=28), lower respiratory tract (27,5%, n=11) and rhinovirus pneumonia (2,5%, n=1). Most HAIs (87,5%; n=35) occurred in a median of 12 days after transplantation, during the neutropenia period (60%; n=24). Assessing seasonality, 65% (n=26) of cases happened between March and September. The year with most cases of RV-HAIs was 2019 (30%, n=12). In 2020 there were 3 cases of SARS-CoV-2 infection, with favorable clinical outcomes and chest tomography with no pulmonary impairment. 8 (20%) out of the total 40 RV-HAIs were cases of viral co-infection. The main identified agents were rhinovirus (40%; n=16), human coronavirus (12,5%; n=5), SARS-CoV-2 (7,5%; n=3), parainfluenza (5%; n=2), respiratory syncytial virus (5%; n=2) and human metapneumovirus and rhinovirus co-infection (5%; n=2).

Conclusion: RV-HAI incidence was 15,5%, concurring with previous reports from literature that show varying incidence of 5 to 22,5%1,2,3,4. The predominance of rhinovirus and human coronavirus as the etiological agents was also identified by Stelmatchuk (2017) and Lee, et. al. (2012). However, other studies have identified parainfluenza virus1,3 as the main RV in nosocomial infections. This study shows how variable and dynamic respiratory virus circulation is and how these viruses should be investigated routinely concomitant with other infectious diseases in post-HSCT patients.

Keywords: Respiratory virus; HSCT; HAI.

FIGURE 1: Respiratory viruses agents of RV-HAIs from January 2016 to June 2021. Subtitles: Rhi: rhinovirus. hCoV: human coronavirus. MPVh: human metapneumovirus. PIV: parainfluenza virus. RSV: respiratory syncytial virus. Ad: adenovirus. HboV: human bocavirus. Flu B: influenza B.

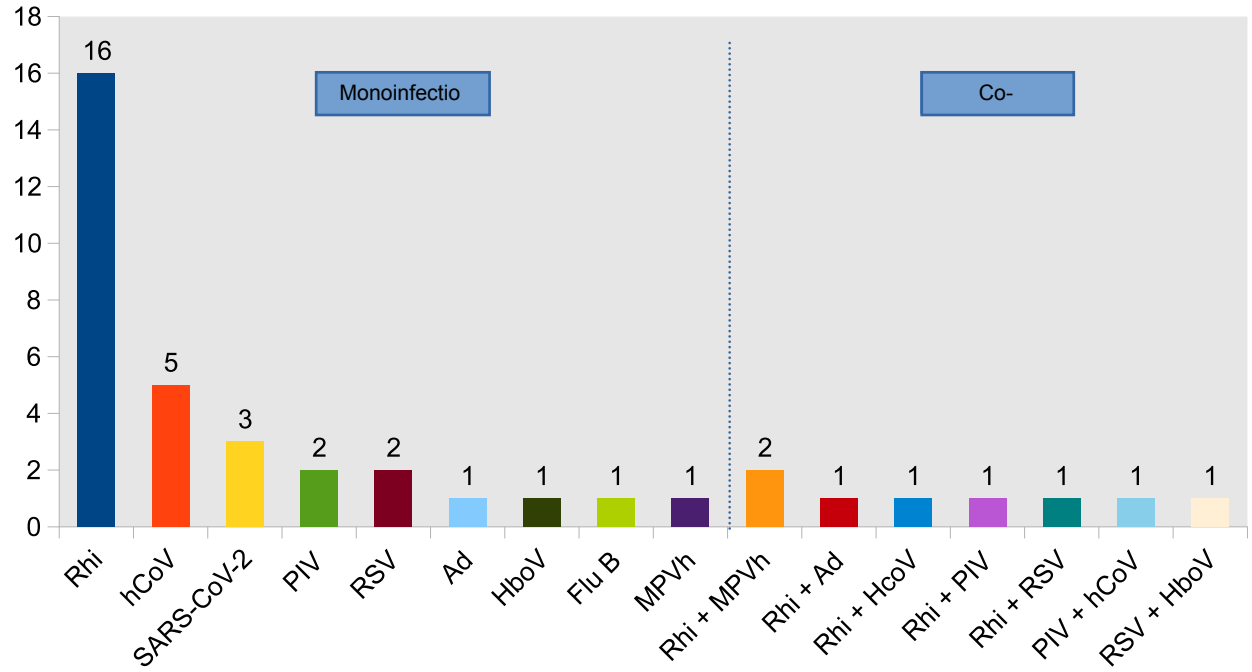
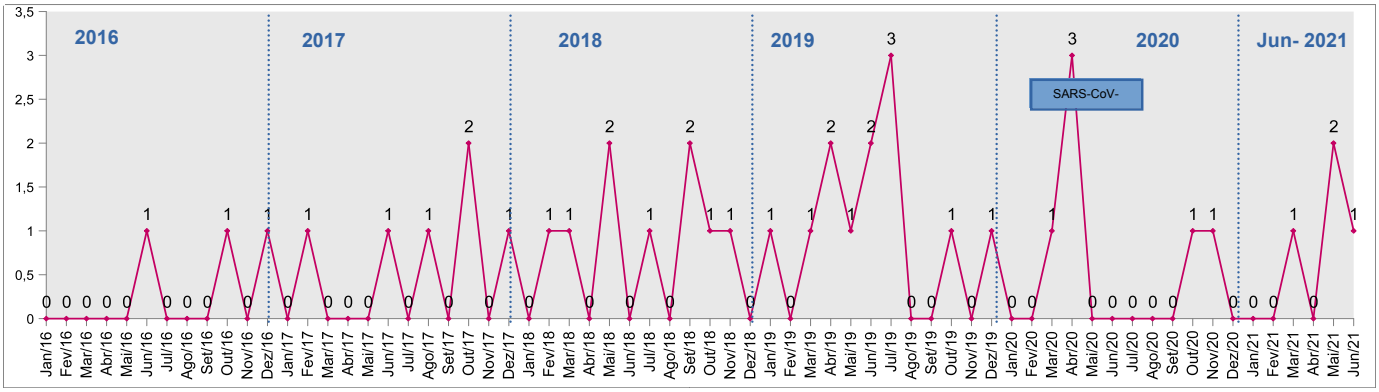


FIGURE 2: Temporal RV-HAI distribution in the Hematopoietic Stem Cell Transplantation Service, from January 2016 to June 2021.



PROFILE OF ONCOHEMATOLOGICAL PATIENTS DIAGNOSED WITH COVID-19 IN A HEMATOLOGICAL THERAPY CENTER IN BRAZIL

Janaina da Silva Flôr[1], Valesca Scalei Cezar[1], Claudia Cáceres Astigarraga[1], Cristhiane de Matos Vieira[1] ,Taiana Kessler Gomes Saraiva[1]

1 Hospital Moinhos de Vento, Porto Alegre, RS, Brasil;

Introduction: The new coronavirus pandemic still affects a large portion of the world population and puts vulnerable individuals on alert. The literature has shown that cancer patients are more likely to develop the disease in its most severe form, placing these individuals as susceptible to severe complications and even death1.

Objective: to describe the profile of onco-hematological patients diagnosed with COVID- 19 from March 2020 to December of the same year, admitted to an onco-hematological therapy center in southern Brazil.

Material and methods: This is a descriptive, retrospective study carried out in an onco-hematological inpatient unit of a hospital in southern Brazil, covering the period from March to December 2020. Data collection occurred through analysis from the medical records of patients admitted to this unit who were diagnosed with COVID-19. It was submitted to the research ethics committee of the Hospital Moinhos de Vento, under the opinion number 1.910.843 CAAE: 63004716.6.1001.5330.

Results: We had a total of eleven patients diagnosed with COVID-19 in this period. There were six (55%) female patients and five (45%) male patients. The average age was 62 years. Among the types of hematological diseases, the most prevalent was acute leukemia, with four cases (36%). After diagnosis and progression of COVID-19, seven patients (64%) required intensive care, six of which underwent orotracheal intubation. Of the patients referred to the Intensive Care Unit, 85% died, a total of six deaths. With regard to the overall outcome, we had a total of 55% of deaths due to COVID-19, which corresponds to six patients, the others (45%) were discharged to their homes. Discussion: among individuals affected by COVID-19, onco-hematological patients need greater care in order to prevent infections because as they receive immunosuppressants, they become more susceptible to infectious conditions, becoming a high-risk population in this pandemic2. Patients who were intubated and received advanced life support were victims of the most severe form of the disease and because they were already part of a risk group, they were in line with the literature that highlights a large number of deaths in this population. The global outcome is well above the national average with regard to deaths from coronaviruses, showing us that more protective measures should be instituted for onco-hematologic patients.

Conclusion: Cancer patients are in the risk group for developing the severe form of COVID-19 and thus become the patients with the worst prognosis of the disease. Due to neutropenia and the already compromised health status due to the high doses of chemotherapy received by onco-hematological patients, they are more fragile, leading to more severe complications of the two diseases.

Keywords: COVID-19, Hematology, Mortality.

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PROSPECTIVE COHORT STUDY OF SARS COV-2 INFECTION AND COVID-19 IN HEALTH CARE WORKERS FROM A HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) UNIT: POST-VACCINATION ANALYSIS

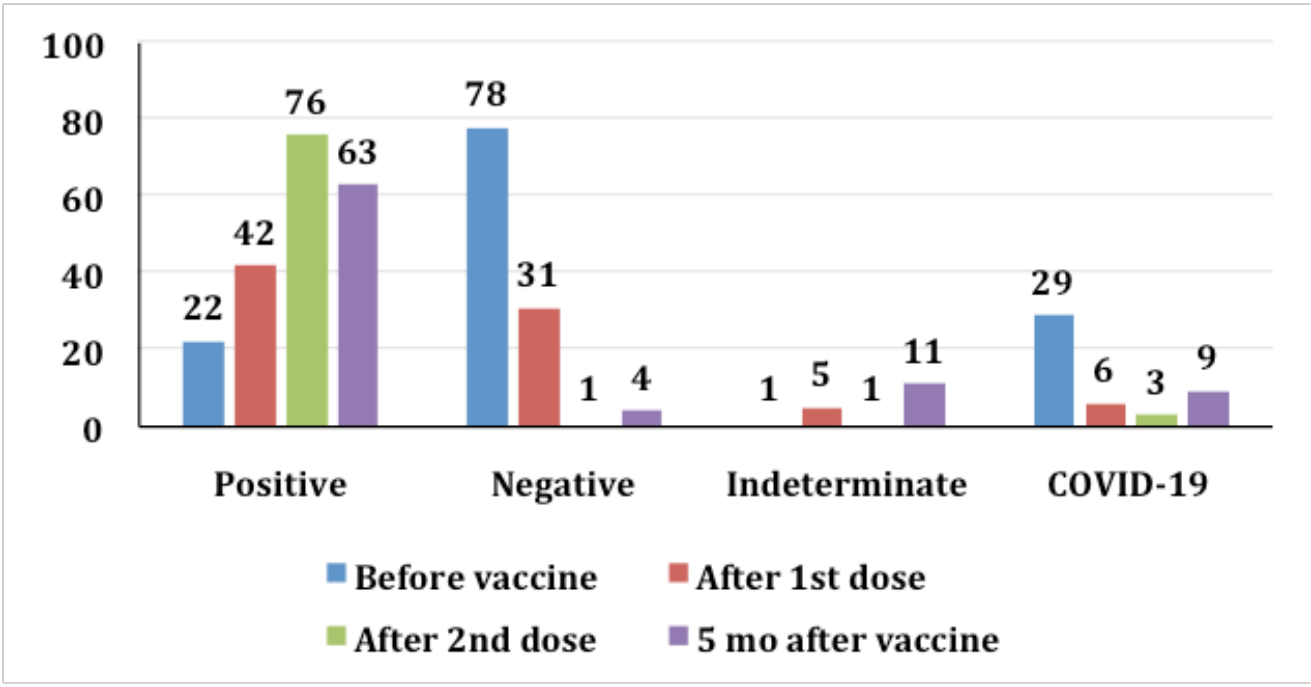
Ana Claudia Ferrari dos Santos[1], Juliana do Prado Moreno[1], Lilian Perílio Zanetti[1], Leila Cibele de Oliveira[1], Lúcia Helena de Almeida Testa[1], Anderson José Simione[1], Mair P. de Souza[1], Vergilio Colturato[1], Clarisse Martins Machado[1,2]

1- Hospital Amaral Carvalho – Jaú/SP
2- Instituto de Medicina Tropical - São Paulo/SP

Vaccination against COVID-19 started in Brazil in January 2021, as one of the strategies to control the pandemic. It was initially prioritized for groups at higher risk of exposure to SARS CoV-2, such as health care workers (HCWs). In this study, we evaluated the serologic response and the occurrence of COVID-19 cases post-vaccination in health professionals from HSCT unit. Study participants received the 1st dose of COVID-19 vaccine between January and March, and the 2nd dose between February and June 2021. Serological response was defined by seroconversion in HCW seronegative before vaccination. Diagnosis of post-vaccination SARS CoV-2/COVID-19 was made by PCR (RealStar SARS-CoV-2, Altona Diagnostics/Germany). Detection of anti-SARS CoV-2 antibodies was done by ELISA (Anti-SARS CoV-2 ELISA, Euroimmun/Brazil). The cumulative probability of SARS CoV-2/COVID-19 was estimated by cumulative incidence. Between December 30, 2020 to July 5, 2021, 109 HCWs were included for evaluation of COVID-19 incidence. From inclusion up to vaccination start, 29 HCWs acquired SARS CoV-2/COVID-19. At follow-up, 7 individuals dropped out of the study and one was not vaccinated, so 101 HCWs were included in the present study. Eight PAS (8%) received chAdOx1 (Oxford/Astrazeneca/Covishield) and 93 (92%) Sinovac (Butantan). The median post-vaccine follow-up was 153 (91-165) days. At pre-vaccine evaluation, 22 of 101 (21.8%) HCWs who received the vaccine already had anti-SARS CoV-2 antibodies and 1 HCW had an indeterminate result. Of the 78 susceptible PAS, 42 (53.8%) seroconverted after the 1st dose, 31 (39.7%) remained negative and 5 (6.4%) had an indeterminate result. After the 2nd dose, 76 tested positive (97.4%), 1(1.3%) had an indeterminate result, and 1(1.3%) had a negative result. Among those vaccinated, 6 (6%) had COVID-19 between the 1st and 2nd dose, and 3(3%) after the 2nd dose, the remaining 92(91%) remained negative. Graph 1 shows the evolution of antibodies and the occurrence of COVID-19. The median duration of symptoms was 10(5-25) days and according to the WHO classification, 5 (55.6%) had mild, 3(33.3%) moderate, and 1(11.1%) had severe symptoms with no need for hospitalization. Three (33.35) had positive serology before the episode of COVID-19 and 6 (66.7%) were negative. The median time off work was 15 (13-24) days. As for the symptoms reported by the HCWs, 8(88.9%) reported headache, 7(77.7%) coryza, 7(77.7%) fever, and 6(66.7%) miscellaneous symptoms. The serological response to the COVID-19 vaccine was 97.4%. The decrease in seropositivity and increase in negative and indeterminate results five months after vaccination indicate short-term post-vaccine immunity. Despite vaccination and protective measures, COVID-19 occurred in 9 PAS (9%) post-vaccine, despite the presence of specific antibodies in 3 of them. Considering the vaccines used in this study, the data suggest the need for periodic revaccination.

Keywords: SARS-CoV-2 vaccine. COVID-19. Health care worker

GRAPH 1 - Evolution of specific antibodies and occurrence of COVID-19



PROSPECTIVE COHORT STUDY OF SARS COV-2 INFECTION AND COVID-19 IN HEALTH CARE WORKERS FROM A HEMATOPOIETIC STEM CELL TRANSPLANT UNIT (HSCT): PRE-VACCINATION ANALYSIS

Ana Claudia Ferrari dos Santos[1], Juliana do Prado Moreno[1], Lilian Perílio Zanetti[1], Leila Cibele de Oliveira[1], Lúcia Helena de Almeida Testa[1], Anderson José Simione[1], Mair P. de Souza[1], Vergilio Colturato[1], Clarisse Martins Machado[1,2]

1- Hospital Amaral Carvalho – Jaú/SP
2- Instituto de Medicina Tropical - São Paulo/SP

In Brazil, health care workers (HCWs) continue acquiring COVID-19 and 27% of those who hospitalized with severe disease have died. HSCT recipients are profoundly immunosuppressed and HCWs of transplant units need to be tested periodically to ensure patient safety. We conducted a prospective cohort study with periodic sampling of nasal wash (NW) and serum to estimate the cumulative incidence of COVID-19 in health professionals from HSCT units. In addition to periodic sampling, from inclusion (dzero) onwards, HCWs were daily surveyed for the presence of symptoms. NW was taken if symptoms and/or exposure to a confirmed or suspected case of COVID-19. If tested positive by PCR, they were away for 14 days and returned to work with at least 1 negative PCR test. Detection of SARSCoV-2 was performed by PCR (RealStar® SARSCoV-2, Altona Diagnostics/Germany) and monthly serology by ELISA (Anti-SARSCoV-2 ELISA, Euroimmun/Brazil). The cumulative incidence of SARSCoV-2/COVID-19 was estimated by cumulative incidence. Between May 13, 2020 and March 22, 2021, 109 HCWs were included, 96 female, 13 male, median age of 37(20 - 58) years and median of 5.9 years of experience in the area. The median follow-up was 259(79-309) days. 29 cases of SARSCoV-2/COVID-19 were diagnosed at a median of 53(0-258) days, for a cumulative incidence of 30 %. 13 cases (11.9%) were detected at inclusion and 16 during follow-up. Of the 13 cases detected at inclusion, 5 (19.2.5%) were diagnosed by PCR and 8 (30.8%) by serology, showing previous infection. During follow-up, 13 new cases of SARSCoV-2/COVID-19 were diagnosed by PCR and 3 cases of SARSCoV-2 infection were retrospectively detected by serology performed at the end of the study. Duration of positive PCR was 15(7-28) days. Seroconversion was detected in 15 of the 18 cases (83.3%) diagnosed by PCR with a median antibody persistence of 152(1-247) days. Of the 29 cases, 16 were asymptomatic. The cumulative incidence of asymptomatic and COVID-19 cases was 16.8% and 16.2%, respectively. The duration of symptoms was 11(1-35) days, with 6 cases (46.1%) of mild symptoms, 3(23.1%) moderate and 4 (30.8%) of severe symptoms. One HCW (7, 7%) required hospitalization and oxygen therapy. The median time of medical leave for HCWs with COVID-19 was 16(13-33) days. One case of reinfection was diagnosed seven months after the 1st episode of asymptomatic infection without appearance of specific antibodies. The cumulative incidence of SARSCOV-2/COVID-19 in this study was 30%, being similar in asymptomatic cases or COVID-19 (about 17%), demonstrating the importance of periodic testing, in addition to symptom surveillance. About 30% developed severe forms of COVID-19 with persistence of symptoms for more than 10 days. The current scenario represents a great challenge in the management of HSCT units to ensure patient safety.

Keywords: COVID-19. SARS-CoV-2. Health care workers

SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2) SEROPREVALENCE IN A HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT

Livia Mariano (Mariano, L)[1], Priscila Tavares Musqueira (Musqueira, PT)[1], Bruna Del Guerra Carvalho Moraes (Moraes, BGC)[1], Lea Campos Oliveira (Oliveira, LC)[1], Leonardo Jun Otuyama (Otuyama, LJ)[1], Silvia Figueiredo Costa (Costa, SF)[1], Vanderson Rocha (Rocha, V)[1]

1 Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brasil

Introduction: The coronavirus disease 2019 (COVID-19) pandemic has become an increasing challenge for the Brazilian healthcare system, with over 550 000 deaths reported due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by July 2021. It has been an unprecedented stress in the health system, including hematopoietic stem cell (HSCT) transplant programs. Respiratory virus (RV) infections are important causes of mortality in patients undergoing HSCT and frequency of oligo-symptomatic patients is unknown.

Objective: To evaluate the seroprevalence of COVID-19 in patients in a HSCT center.

Casuistic: Patients and donors evaluated at outpatient unit and before admission for HSCT or mobilization protocol and healthcare workers.

Methods: This was a cross-sectional study conducted at the TCTH center between June and December 2020 evaluating the presence of anti–SARS-CoV-2 immunoglobulin IgG/IgM antibodies (rapid chromatographic immunoassay) in patients from the outpatient care. PCR and Serology tests for COVID-19 were collected from all patients 48 hours before admission. Serologies were performed using the Camtech, Luxus and Thermogenesis tests, which have the same sensitivity and specificity profile. A survey about symptoms and epidemiologic questions was sent to all patients. The data were collected and stored on the REDCap platform.

Results: There were evaluated 156 individuals, 113 patients, 39 health professionals and 4 donors. The seroprevalence for Sars-cov-2 was 29.5%. There was no difference in seroprevalence between patients and healthcare workers. Among patients, 40% have already been transplanted and 42.5% were pre transplant patients whose serology was collected before admission. The remainder were patients who collected pre-mobilization but were not transplanted yet. Median age of 48 years, with a predominance of males (62%), 60% with a high school education level or higher. Sixty-five patients answered the survey and seroprevalence in this subgroup was 32%. No viral symptoms previously in 2020 was reported by 54% of patients. Most common symptoms reported were fever (35,4%) and nasal symptoms (33,8%). All transplanted patients (n=45) were allogeneic with a median of 15.8 m post-transplant, 44% with comorbidities, 58% with a diagnosis of chronic GVHD and 58% using immunosuppression. Of them, twenty-seven percent have lymphopenia, and seroprevalence in this group was 38%. Of these patients, 4 had previously documented infection with another coronavirus, and three of them came with positive serology. Ten patients were evaluated in a second moment, with only 1 seroconverted. Two patients had positive sars-cov-2 PCR months after the initial serology and one of them was IgG reagent, but the serology was not repeated at the time of the PCR.

Conclusion: Patient's Covid-19 seroprevalence was similar to healthcare workers, higher among allogeneic transplanted patients and preceded by mild flu-like symptoms.

Keywords: Hematopoietic stem cell transplantation, Covid-19, Serology

SUCCESSFUL BONE MARROW TRANSPLANTATION FOR CD40 LIGAND DEFICIENCY WITH CONCURRENT PARACOCCIDIOIDOMYCOSIS INFECTION

Rafaella Ribas Muratori[1]; Flávio de Queiroz Telles Filho[1]; Débora Carla Chong e Silva[1]; Herberto José Chong Neto[1]; Samantha Nichele[1]; Gisele Loth[1]; Adriana Mello Rodrigues[1]; Adriana Koliski[1]; Joanna Paula Trennepohl[1]; Rebeca Toassa Mousquer[1]; Lisandro Ribeiro[1]; Ricardo Pasquini[1]; Carmem Bonfim[2]

Muratori RR[1], Filho FQT[1], Silva DCC[1],2, Neto HJC[1], Nichele S[1], Loth G[1],2, Rodrigues AM[1],2, Koliski A[1], Trennepohl JP[1], Mosquer RATG[1], Ribeiro L[1], Pasquini R[1], Bonfim C[1],2.

1. Hospital de Clinicas da UFPR, Curitiba - PR - Brasil
2. Hospital de Clinicas da UFPR, Hospital Infantil Pequeno Príncipe Curitiba - PR - Brasil

Introduction: Paracoccidioidomycosis (PCM) is a systemic endemic mycotic infection that may cause acute/subacute disease in children that are usually responsive to prolonged antifungal therapy. However, in immunosuppressed hosts, the disease may evolve into disseminated and chronic forms with pulmonary sequelae and lung fibrosis. CD40 Ligand deficiency often presents in infancy with increased susceptibility to recurrent sinopulmonary infections and opportunistic infections. Here we present a case of a 7-year-old boy diagnosed with CD40L deficiency, PCM and obliterative bronchiolitis who underwent a successful bone marrow transplant (BMT).

Case report: This child was admitted to our hospital in 2019 with a history of chronic diarrhea, recurrent otitis and upper respiratory infections, since 1 year of age. At presentation he had a new onset of multiple lymphadenomegalia and respiratory distress and required mechanical ventilation. A lymph node and duodenal biopsies revealed Paracoccidioides spp and chest CT showed multiple abnormalities. Amphotericin B was initiated without improvement, then switched to trimethoprim-sulfamethoxazole and voriconazole with good clinical response. A diagnosis of immunodeficiency was suspected and confirmed with a molecular diagnosis of CD40L deficiency. During follow-up, he had multiple episodes of respiratory infections, requiring ventilatory support. The patient was referred to our BMT unit and pre-BMT, images revealed multiple mesenteric lymph nodes, probably related to PCM infection and obliterative bronchiolitis. The patient underwent a matched sibling BMT after a Busulfan (13 mg/kg), Fludarabine (180 mg/m^2) and Thymoglobulin 5mg/kg regimen. Cyclosporin and MMF were given as GVHD prophylaxis. At the time of the BMT the patient was receiving TMP-SMT and voriconazole for PCM treatment, diuretics for pulmonary edema and IGIV replacement. Voriconazole was switched to Isavuconazole due to a better toxicity profile. Hematological engraftment was fast, and the only complication was an early (D+26) and recurrent CMV reactivation, treated with gancyclovir. Donor chimerism at D30 and D90s were 69% and 75% respectively. Lineage-specific donor chimerism showed reduced T lymphocytes with 15% at D30 and 23% at D90. Donor myeloid and B lymphocytes were 89% and 96% at D90. Immune reconstitution after BMT was evaluated at D60 and D90 with stable values of both CD4+ (310 and 359/ul) and CD8+ (299 and 222/ul). At last follow-up, 108 days post-BMT, the patient was still receiving monthly IGIV, presenting occasionally with acute bronchospasms but otherwise asymptomatic, with no evidence of infections.

Conclusions: Careful decisions regarding conditioning, time of the transplant and antifungal therapy should be taken into account in this type of patient, alongside a multidisciplinary team, to achieve the best result possible. To our knowledge, this is the first BMT performed concurrent with PCM infection.

THE IMPACT OF THE COVID-19 PANDEMIC ON A HEMATOLOGICAL THERAPY CENTER IN SOUTHERN BRAZIL

Valesca Scalei Cezar[1], Janaina da Silva Flôr[1], Claudia Cáceres Astigarraga[1], Cristhiane de Matos Vieira[1] ,Taiana Kessler Gomes Saraiva[1], Gabriela Pereira Flores[1].

1 Hospital Moinhos de Vento, Porto Alegre, RS, Brasil;

Introduction: Hematopoietic stem cell transplantation (HSCT) requires a considerable period of immunosuppression, thus leaving the patient susceptible to opportunistic infections1. In February 2020 in Brazil, there was confirmation of an outbreak of infection by the new coronavirus, SARS-CoV-2 , whose disease was called COVID-19. It is characterized by conditions that can vary from asymptomatic to severe respiratory conditions, the transmission of the virus happens from person to person, through droplets of respiratory secretion, body fluids or indirect contact with contaminated surfaces2. In the context of HSCT, the prevention of transmission, rapid diagnosis and isolation of suspected cases has a direct impact on the morbidity and mortality of patients1.

Methodology: Experience report from a hematological therapy center in southern Brazil.Results:In addition to the institutional protocols adopted, based on ANVISA recommendations, the routines of the hematological therapy unit had as reference the SBTMO publications on and COVID-19 and HSCT. The first change was the reduction in the number of hospitalizations of patients for HSCT, hospitalized only patients considered at high risk. For admission to the unit, patients must collect RT-PCR for COVID-19 within 96 hours of admission to the home, with rapid RT-PCR collected upon arrival at the inpatient unit. Patients transferred from other sectors, or suspects, collect rapid RT-PCR for COVID-19 and, in case of a positive result, are transferred to the hospital's referral unit for COVID-19. In addition, visits and companions were permanently suspended. released upon evaluation by the care team, they must have a negative RT-PCR test for COVID-19 to enter the unit, and must remain for at least 7 days and wear a surgical mask full time. , if symptoms are removed and they collect at least two tests to return to work. Another necessary adaptation was the pre-hospitalization reception, HSCT and discharge guidance through video calls through the Google Meet application. Hand hygiene maintained a good adherence rate during the period. Discussion: Studies have shown that the patient with cancer has a higher risk of infection by SARS-CoV-2, as well as that it can deteriorate faster than individuals without the disease. In the context of HSCT, characterized by the complexity and vulnerability of the patient, the effort must be even more effective, with the joint action of the hospital infection control service, the health institution as a whole, in addition to the engagement of the entire care team2.Conclusion : During these 18 months of pandemic, 11 patients were infected. Comparing the year 2019, with 26 transplants and the year 2020, with 25, a total of 38 HSCT were performed in these 18 months, showing that the greatest impact happened in the structuring of the processes and not in the numbers of the center.

Keywords: Bone Marrow Transplant; Hematology; COVID-19.

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NON-INFECTIVE COMPLICATIONS

ACQUIRED HYPOFIBRINOGENEMIA ASSOCIATED WITH STEROID THERAPY FOR GRAFT VERSUS HOST DISEASE AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION: A CASE REPORT

Patrícia Oliveira da Cunha Terra[1], Camila Dermínio Donadel[1], Lucas Oliveira[1], Camila Campos Mesquita[1], Patrícia da Silva Laurindo[1], Ana Carolina de Jesus Vieira[1], Nattália Araújo Alves[1], Isabela Rozatte da Silva[1], Juliana Bernardes Elias Dias[1], Fabiano Pieroni[1], Ana Beatriz Pereira Lima Stracieri[1], Thalita Cristina de Mello Costa[1], Juliana Maria Faccioli Sicchieri[1], Gil Cunha De Santis[1], Luciana Corrêa Oliveira[1], Renato Luiz Guerino-Cunha[1]

1 Department of Medical Images, Hematology and Clinical Oncology, Ribeirão Preto Medical School of University of São Paulo, Ribeirão Preto, SP, Brazil.

Introduction: Acquired hypofibrinogenemia (AH) is mainly caused by liver disease, disseminated intravascular coagulation (DIC) and hemophagocytic lymphohistiocytosis. Here we describe a patient who has been diagnosed with AH during the treatment of acute graft-versus-host disease (GvHD).

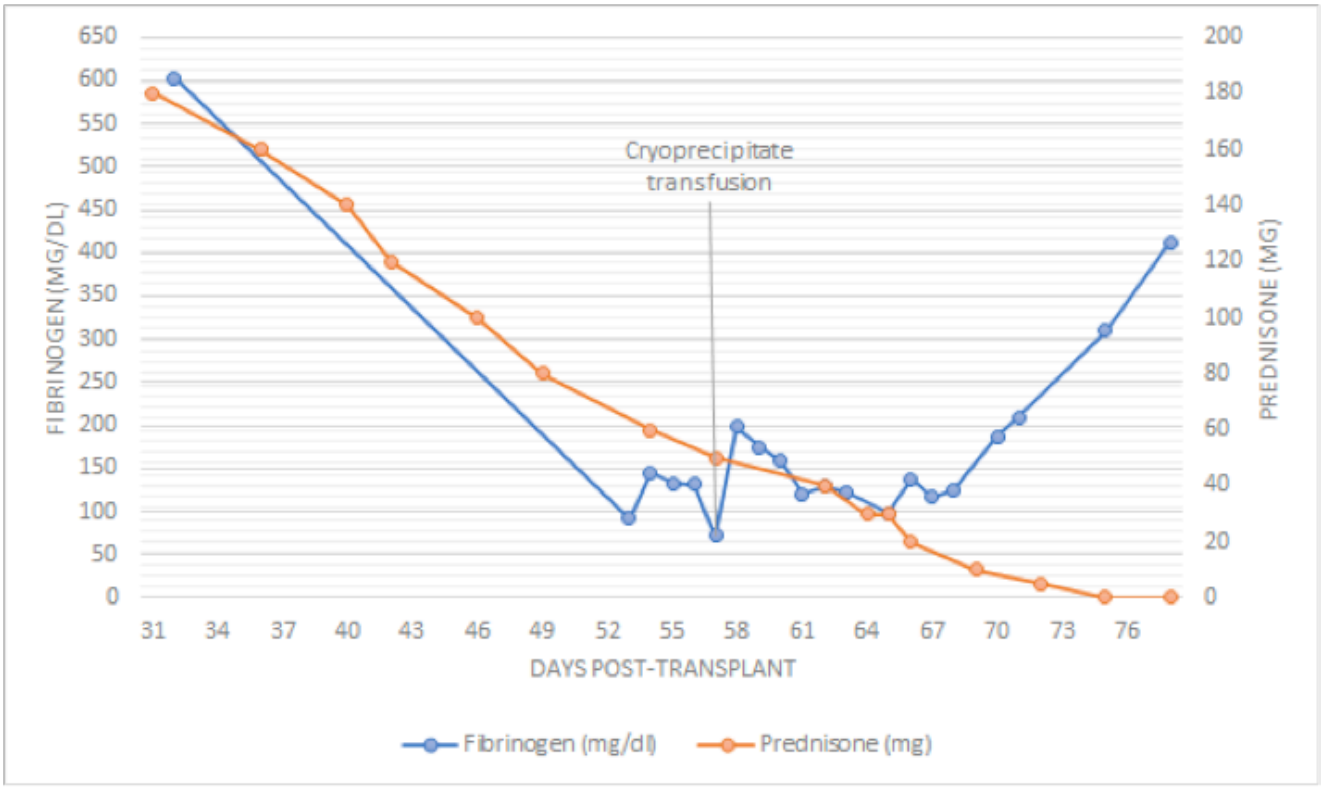
Case Report: A 60-year-old male underwent HLA-identical unrelated donor hematopoietic stem cell transplantation (HSCT) for acute myeloid leukaemia in second remission. Reduced intensity conditioning regimen consisted of fludarabine, busulfan (FluBu2) and antithymocyte globulin. The source of hematopoietic progenitor cells was peripheral blood and the GvHD prophylaxis was based on mycophenolate mofetil with cyclosporine. At day 31 post-HSCT he was diagnosed with acute GvHD involving skin and gut (global stage III according to MAGIC classification) and received prednisone 2 mg/kg/day. After five days, anticoagulation with enoxaparin was introduced to treat a catheter-associated right subclavian vein thrombosis, but was discontinued on day 53 due to upper gastrointestinal bleeding caused by gastric ulcers, with no histological evidence of GvHD or CMV infection. At that time the exams demonstrated hemoglobin 8,5 mg/dl, platelets 66x109/L, fibrinogen 92 mg/dl, prothrombin time (PT) and activated partial thromboplastin time (aPTT) within normal limits. At day 57, fibrinogen level was 72 mg/dl, with prolongation of PT and normal aPTT, and the patient received cryoprecipitate transfusion. He persisted with low fibrinogen levels, prolonged thrombin time (corrected with a mixture test) and normal TP and aTTPA, with no new bleeding episodes. Clinical and laboratory evolution made the diagnosis of liver disease and DIC unlikely. Based on the hypothesis of AH related to the use of high-dose corticosteroids, a rapid reduction of prednisone was performed up to day 75 and fibrinogen increased until normal levels (figure 1).

Discussion: Few studies correlate AH with hematologic neoplasms (acute lymphoblastic leukaemia and chronic lymphocytic leukaemia) and GvHD treatment. A case series demonstrated 8 cases of AH in 15 post-HSCT patients treated for GvHD with methylprednisolone (1 to 2 mg/kg/day). The mean diagnosis time was 20 days after the beginning of the treatment with 2 mg/kg/day. In our report, the diagnosis of AH occurred 22 days after starting prednisolone 2 mg/kg/day with no evidence of other underlying causes. AH might be correlated to prolonged use of steroids, however if it translates into higher risk of bleeding disorders is uncertain. Since GvHD is frequent after HSCT and requires the use of steroids, AH can be an underdiagnosed event.

Conclusion: We demonstrated that high-dose corticosteroids use might be correlated to AH, in accordance with previous results from scarce literature. Further studies are needed to investigate if prolonged high-dose steroids treatment may alter steps in fibrinogen kinetics and its impact on HSCT patients.

Keywords: hypofibrinogenemia; graft versus host disease; hematopoietic stem cell transplantation.

FIGURE 1. Fibrinogen levels and prednisone dose post-HSCT.



COVID-19 AS A POSSIBLE TRIGGER TO ACUTE GRAFT-VERSUS-HOST DISEASE AFTER AUTOLOGOUS TRANSPLANTATION IN HODGKIN'S DISEASE PATIENT

Fernanda Batista Rosa Pinto[1], Anita Cassoli Cortez[1], Fernanda Aline Moreira de Oliveira[1], Vanessa dos Anjos Bovolenta[1], Jaqueline Sapelli [1], Thais Fischer[1], Jayr Schmidt-Filho[1]

1 Hematology Department, A.C.Camargo Cancer Center, São Paulo, SP, Brazil.

Introduction: Acute graft-versus-host disease (aGVHD) is a rare complication on autologous hematopoietic stem cell transplantation (auto-HSCT). The current study reports a case of a patient who presented aGVHD after auto-HSCT following Coronavirus Disease-19 (COVID-19). A literature review was performed to describe patients diagnosed with concomitant GVHD and COVID-19.

Case report: We report the case of a 31 years-old female, diagnosed with unfavorable classic Hodgkin's Lymphoma, early stage IIB, during pregnancy. She was treated with ABVD chemotherapy regimen, without response to treatment. She underwent three salvage regimens IGEV, DHAP and brentuximab, without response, maintaining a stable disease. Auto-HSCT was performed GemBuMel conditioning with complete response after that. Two months after the transplant, she developed COVID-19, with no need for hospitalization, use of corticosteroids or oxygen therapy. After recovery from COVID-19, the patient lost 9 kg. She underwent upper digestive endoscopy with a biopsy showing apoptotic cells, neutrophilic infiltrate and eosinophilic globules compatible with GVHD, histological grade 1.

Discussion: A literature review was carried out in order to report cases of GVHD possibly triggered by COVID-19 infection or with concomitant occurrence. Two cases were raised between 2020 and 2021 and both were from patients with COVID-19 and GVHD who underwent allogeneic stem cell transplantation and were already being treated for chronic GVHD before the infectious diagnosis.

Although there isn`t any case of aGVHD diagnosed after SARS-CoV-2 infection until the present time, there are descriptions of the association between other viral infections and the development of GVHD. The herpes simplex vírus, cytomegalovirus and human herpes vírus, are related to an increased risk for development of a GVHD. Other viruses such as rhinovirus, parainfluenza and Bk virus were described as a trigger in flares of aGVHD disease. Regarding the SARS-CoV-2 infection preceding the diagnosis of aGVHD, we believe it may have been an infectious trigger for the development of the disease.

It is hypothesized that aGVHD and SARS-CoV-2 infection share pathophysiological features. Both conditions have cytokine storm playing an important role further driving and amplifying disease pathogenesis. Thus the increase in the inflammatory response to any viral pathogen may be related to an increase in the occurrence of GVHD, without a necessary relation with a specific virus.

Considering the temporal relation between the COVID-19 infection and the emergence of aGVHD, as well as the studies reports of viral infection as a possible trigger, our hypothesis is that in this case the secondary activation of pro-inflammatory pathways due to the activation of the immune response to a viral antigen may be implicated as the cause of GVHD. However, it is important to highlight that further research will be necessary to establish this relation.

Keywords: Graft vs host disease. Autologous transplantation. COVID-19. Hodgkin's disease. Case report.

Funding: This study did not receive external funding.

LOW INCIDENCE OF ACUTE AND CHRONIC GVHD AFTER PEDIATRIC ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

Adriana Mello Rodrigues[1], Juliana Luiza de Mello Bach[1], Polliany Roberta Dorini Pelegrina[1], Cilmara Cristina Kuwahara Dumke[1], Gisele Loth[1], Fernanda Moreira de Lara Benini[1], Carolina Martins de Almeida Peixoto[1], Alberto Cardoso Martins Lima[2], Carmem Bonfim[1]

1 Hospital Pequeno Príncipe
2 Immunogenetics Laboratory, Complexo Hospital de Clínicas, Federal University of Paraná

Introduction: Although advances in pediatric hematopoietic cell transplantation (HCT) have improved survival, the presence of GvHD remains an important cause of morbidity and mortality after allogeneic HCT.

Objective: Analyze the incidence of acute and chronic GVHD in pediatric patients(pts) submitted to an allogeneic HCT between Feb/2013 and Dec/2020, in a single HCT center.

Method: Retrospective, longitudinal, non-randomized, observational study. Database and medical records were analyzed, and statistics performed using the EZR program.

Results: During this period, 213 pts were transplanted with a median age of 6 years, 62% were male. Diagnosis included malignant diseases (54%), bone marrow failures (23%), inborn errors of immunity (17%) and inborn errors of metabolism (6%). Donors were haploidentical (37%), matched related (37%) and unrelated (26%). Bone marrow (BM) was the preferred stem cell source (82%), peripheral blood (PB) was used in 14% and cord blood (CB) in 4%. Myeloablative regimens(MAC) were used in 80% of pts and cyclosporine(CSA) and methotrexate was the most frequent GVHD prophylaxis (53%). All haploidentical transplants were performed with post-transplantation cyclophosphamide (Haplo-PTCY), CSA and MMF. The median neutrophil and platelet engraftment were 20 and 24 days, respectively and the 100-day cumulative incidence(CI) of rejection was 7%. The CI of CMV reactivation was much higher after HAPLO-PTCY when compared to matched related or unrelated donors (61% vs 38%vs 32%, respectively; p=0,0001). At D100 the CI of grade II-IV acute GVHD(aGVHD) was 21%(grades II n=29; and grades III-IV n=19). Patients with malignant diseases had a higher incidence of grade II-IV aGVHD (40%; p=0.001) as well as those receiving HAPLO-PTCY transplants (29%; p=0.002). Csa + MTX prophylaxis was associated with less aGVHD (15%; p=0;01). The CI of chronic GVHD(cGVHD) was only 7.5% at 2 years (mild n=5; moderate n=6 and severe n=4). The incidence of cGVHD was higher for pts receiving MAC regimens (10%; p=0.03) and, when compared to BM, the use of PB grafts were also associated with a higher risk of developing cGVHD (6% vs 17%; p=0.02). The 2-year and 5-year overall survival(OS) were 80% and 77%, respectively. It was significantly better for nonmalignant diseases (89%;p=0.001) and for pts with malignant diseases transplanted in CR1 (90%; p=0.03). Both CMV reactivation (HR:2.38; p=0.01) and cGVHD (HR:11.43; p= 0.0001) as time dependent variables, were independent predictors of inferior OS.

Conclusion: In this pediatric cohort, we observed a low incidence of cGVHD and confirmed the influence of well-known risk factors such as the use of MAC regimens and PB. Although the rates are low, the deleterious influence in survival is dramatic. Based on these results, strategies to prevent or early detect this complication are urgently needed to improve long-term outcomes.

OUTCOME OF PATIENTS WITH SEVERE OR VERY SEVERE SINUSOIDAL OBSTRUCTION SYNDROME: IMPACT OF THE USE OF DEFIBROTIDE AND INTENSIVE CARE SUPPORT

Anderson Felipe da Silva[1], Viviane de Jesus Torres Lima[1], Lucila Nassif Kerbauy[1], Leonardo Javier Arcuri[1], Mariana Nassif Kerbauy[1], Andreza Alice Feitosa Ribeiro[1], Nelson Hamerschlak[1]

1 Hospital Israelita Albert Einstein, São Paulo, Brazil.

Introduction: Sinusoidal obstruction syndrome (SOS) is a potentially fatal complication after hematopoietic cell transplantation (HCT), especially allogeneic HCT[1]. According to the latest review by the European Group for Blood and Marrow Transplantation[2], the diagnosis is based on clinical and laboratory criteria. In terms of severity, the same study classified SOS into mild, moderate, severe, and very severe, directly related to the mortality[3]. Given a high mortality rate, which can reach >80%4, early diagnosis and correct treatment are critical, with defibrotide (DF) being the only proven medication for treating such complication5.

Objective: Describe the patients with severe and very severe SOS treated in a private Brazilian center.

Methods: A retrospective observational study that included all patients who presented with severe or very severe SOS in the service between January 1, 2007, and May 31, 2021. Data were obtained from medical records and chart analysis.

Results: During this period, 489 patients underwent allogeneic HCT and 27 (5,5%) patients presented SOS, 12 children and 15 adults. Of this total, 17 (63%) died from any cause and 7 (26%) died as a direct complication of SOS. Regarding DF, all but one patient used it, 71% of the evaluable patients completed 21 days of treatment and 96% of the patients started within 48 hours of the diagnosis. The main reason for discontinuation for >24 hours was bleeding (45% of the discontinuations). Of the 27 patients, 81% required transfer to the Intensive Care Unit and 63% underwent dialysis with a mortality rate of 32% and 41%, respectively. Of the 7 patients who died, 1 was classified as severe and 6 as very severe (table 1). The only patient who did not use DF was a 12-year-old child diagnosed with SOS who presented with coagulopathy and suspected bleeding in the central nervous system, without clinical stability that would allow imaging exams to rule out bleeding and evolved to death. The overall survival (OS) at 100 and 180 days were 59.3% (43.3-81.0) and 55.6% (39.6-77.8) respectively (figure 1).

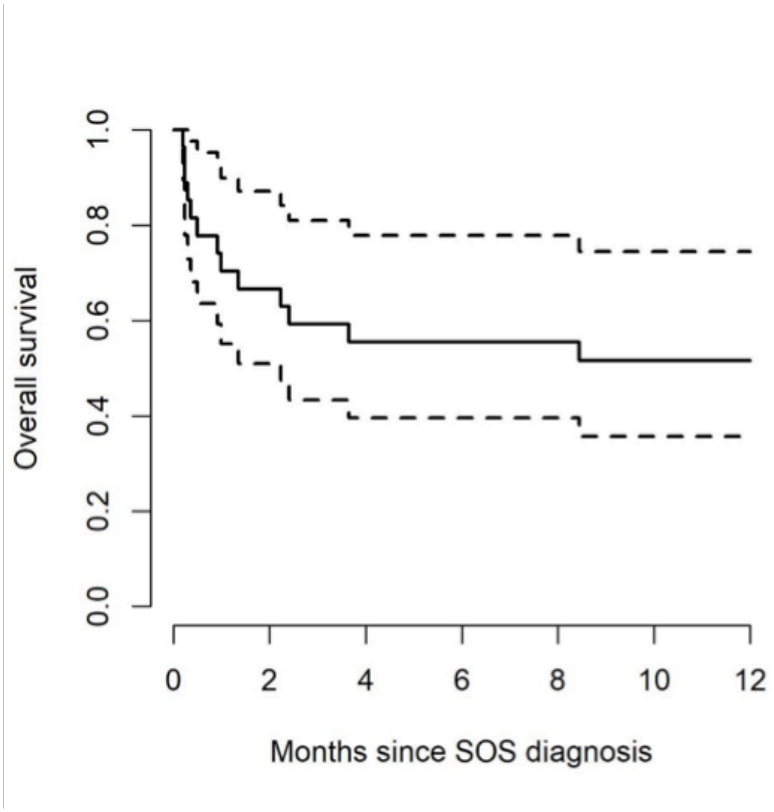
Conclusion: Considering the high severity of this disease, it is of utmost importance the early initiation of the DF, followed by the patients in the study, since early initiation of medication was seen in 96% of patients. The risk of bleeding is cited as a difficulty for the use of DF, with bleeding events occurring between 12-29% of cases6-7, a figure close to the 18% (5/27) of the present study. In terms of mortality using DF, it is progressively worse according to the severity, reaching overall survival of 58% in the group of patients with systemic dysfunction and 32% in cases without dysfunction6, a result comparable to the 60% (6/10) of deaths in patients with very severe condition who used DF in this group. The OS at 100 days of 59.3% is within expectations according to previous prospective studies5,8. In conclusion, our results show that the use of DF in the Brazilian context leads to results that are comparable to the current literature.

Keywords: Complication of hematopoietic stem cells transplantation. Sinusoidal obstruction syndrome. Veno-occlusive disease.

TABLE 1. General description of the SOS population

	Total Children n: 12	Total Adults n: 15	Total n: 27
VOD-associated mortality	3 (25%)	4 (27%)	7 (26%)
Defibrotide Defibrotide ≥ 21 days* Median days used [range] Onset within 48 hours of diagnosis Mortality	11 (92%) 9/10 (90%) 21 [5-51] 11 (100%) 2 (19%)	15 (100%) 6/11 (54%) 21 [3-43] 14 (93%) 4 (27%)	26 (96%) 15/21 (71%) 21 [3-51] 25(96%) 6 (23%)
Dialysis Mortality	9 (75%) 3 (33%)	8 (53%) 4 (50%)	17 (63%) 7 (41%)
Intensive Care Mortality	10 (83%) 3 (30%)	12 (80%) 4 (33%)	22 (81%) 7 (32%)
EBMT – Death/total Severe Very severe	0/7 3/5 (60%)	1/9 (11%) 3/6 (50%)	1/16 (6%) 6/11 (54%)
Discontinuation >24h Bleeding Procedure Clinical instability Unidentifiable	4 2 (50%) 1 (25%) - 1 (25%)	7 3 (44%) 2 (28%) 2 (28%)	11 5 (45%) 1 (9%) 2 (18%) 3 (27%)

FIGURE 1. Probability of overall surival



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PNEUMATOSIS INTESTINALIS FOLLOWING GRAFT VERSUS HOST DISEASE TREATMENT IN HEMATOPOIETIC STEM CELL TRANSPLANTATION: A CASE REPORT

Lucas Oliveira[1], Camila Derminio Donadel[1], Patrícia Oliveira da Cunha Terra[1], Rachel Maria de Souza Soares[1], Marília Adriano Mekdessi[2], Camila Campos Mesquita[1], Patrícia da Silva Laurindo[1], Ana Carolina de Jesus Vieira[1], Isabela Rozatte da Silva[1], Nattália Araujo Alves[1], Thalita Cristina de Mello Costa[1], Juliana Bernardes Elias Dias[1], Fabiano Pieroni[1], Ana Beatriz Pereira Lima Stracieri[1], Juliana Maria Faccioli Sicchieri[1], Márcia Guimarães Villanova[2], Jorge Elias Junior[1], Renato Luiz Guerino-Cunha[1]

1 Department of Medical Images, Hematology and Clinical Oncology, Ribeirão Preto Medical School of University of São Paulo, Ribeirão Preto, SP, Brazil.
2 Internal Medicine Department, Ribeirão Preto Medical School of University of São Paulo, Ribeirão Preto, SP, Brazil.

Introduction: Pneumatosis intestinalis (PI) is a rare condition characterized by the presence of gas within the wall of the small or large intestine, which can be also associated with pneumoperitoneum. In most cases an underlying cause related or not to a gastrointestinal disorder can be identified, such as hematopoietic stem cell transplantation (HSCT), graft versus host disease (GvHD) and high dose steroids. We described a case of a patient who developed extensive pneumatosis intestinalis and pneumoperitoneum during GVHD treatment after HSCT.

Case Report: A 20-year-old male with relapsed B-cell acute lymphoblastic leukemia underwent an haploidentical peripheral blood HSCT. Conditioning regimen consisted of etoposide, TBI 12Gy and post-transplant cyclophosphamide. GvHD prophylaxis consisted of mycophenolate mofetil and cyclosporine. At day 87 post-HSCT, due to gut and liver steroid-refractory GvHD (MAGIC global stage III), ruxolitinib was chosen as a second treatment line and he achieved remission. At day 131, during the infectious screening protocol for a febrile neutropenia, a chest CT-scan showed pneumomediastinum and pneumoperitoneum. At that time, the patient had no abdominal complaints, had no signs of peritonitis and was hemodynamically stable. A further abdominal CT-scan revealed extensive PI (image 1). Laboratory studies showed pH 7.37, bicarbonate 25 mmol/L and lactate 0.89 mmol/L. After being evaluated by the surgical team, a conservative treatment was started with fasting, early parenteral nutritional support, oral metronidazole, inhalation with high flow oxygen and faster immunosuppressors weaning as there were no signs of GVHD activity. The patient evolved clinically well, the CT-scans 2 weeks later showed complete resolution of findings (image 2).

Discussion: PI can be seen as a profound damage of the bowel intramural tissue. However, its etiopathogenesis is unclear. Prolonged and severe immunosuppression, use of antimicrobial agents, fasting, infection and GvHD are the most common causes in the HSCT setting. Despite most patients being asymptomatic, few patients might develop acute abdominal complications leading to a potential life-threatening condition. In this scenario, some variables possibly indicate higher risk, such as signs and symptoms of peritonitis, metabolic acidosis and hyperlactatemia. Post-HSCT, patients with PI should be managed carefully, preferably with a non-surgical approach, in addition to supportive care and treatment of the underlying condition.

Conclusion: Several complications post-HSCT are correlated with the use of steroids, ruxolitinib and the occurrence of GVHD. However, as they are all associated with PI occurrence, this condition is probably underdiagnosed. As a potentially life-threatening condition, physicians should be aware of this complication to promptly intervene in severe cases and carefully judge if invasive procedures are necessary, as conservative management seems to be effective.

Keywords: pneumatosis intestinalis; graft versus host disease; hematopoietic stem cell transplantation.

IMAGE 1: Coronal multiplanar reconstruction

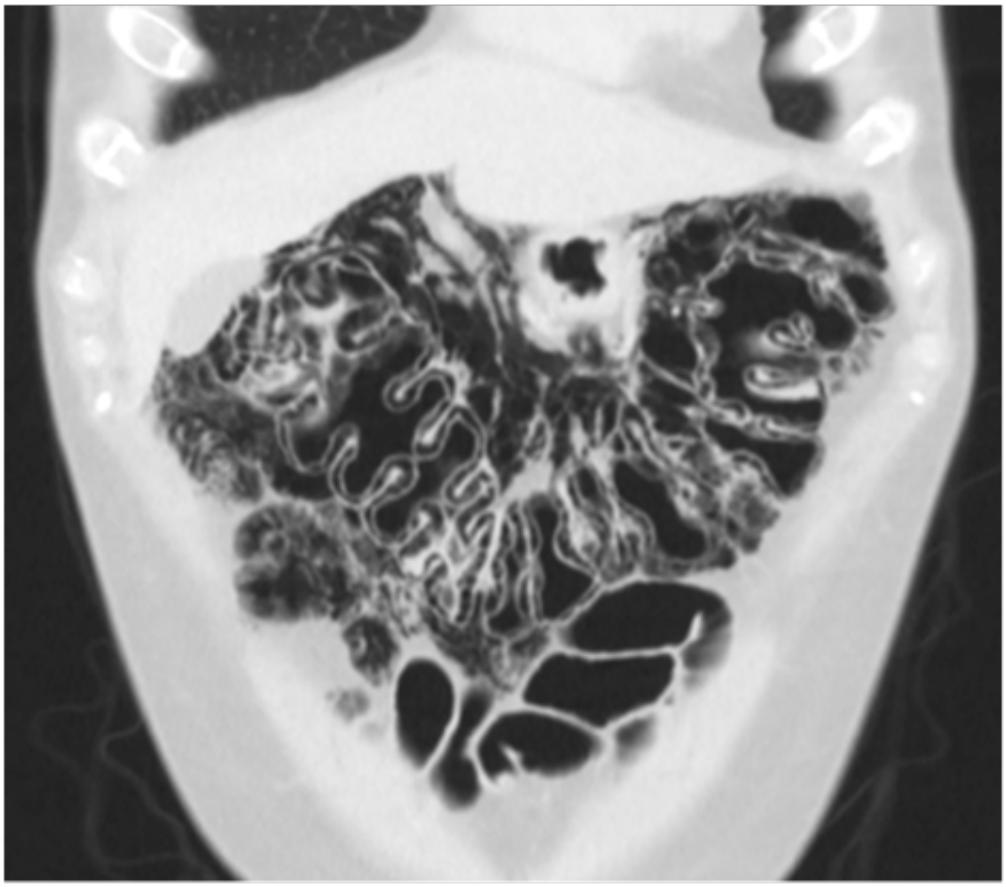
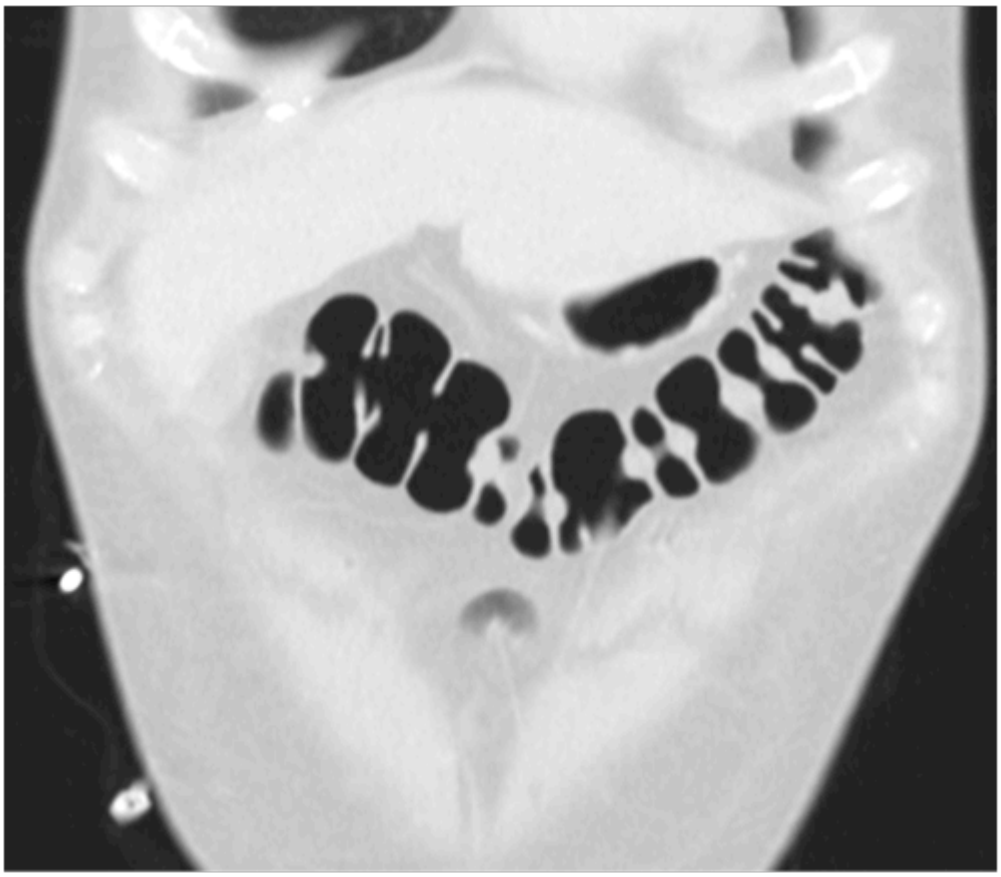


IMAGE 2: Coronal multiplanar reconstruction - 2 week-later CT



SINUSOIDAL OBSTRUCTION SYNDROME, DEFIBROTIDE AND NURSING CARE: AN EXPERIENCE REPORT

Valesca Scalei Cezar1, Janaina da Silva Flôr1, Claudia Cáceres Astigarraga1, Cristhiane de Matos Vieira 1 ,Taiana Kessler Gomes Saraiva1, Gabriela Pereira Flores1.

1Hospital Moinhos de Vento, Porto Alegre, RS, Brasil;

Introduction: Even with advances in the area, the success of hematopoietic stem cell transplantation (HSCT) is largely limited by the toxicity and mortality inherent to the procedure. Among the acute complications observed after HSCT, obstructive sinusoidal syndrome (SOS) has a median incidence of 13.7%, but with wide variations in incidence in individual studies (0 to 62%)1. The diagnosis of SOS is basically clinical and the observation of signs and symptoms is what lead to the diagnosis. The nursing team is essential in observing the clinical signs and symptoms that lead to the diagnosis of SOS, as well as in infusing and observing the para-effects of the only medication available for the treatment of this complication, defibrotide. Case report: Female patient, 40 years old, diagnosed with essential thrombocytosis with evolution to Myelofibrosis and history of multiple previous portal thrombosis, submitted to Allogeneic HSCT, brother was the HLA identical donor, chronically altered bilirubin (BT 2.50; BD:1,47) He received conditioning with Cyclophosphamide and Busulfan (CyBu), SOS prophylaxis with Ursodeoxycholic Acid 300mg every 8 hours started 14 days before admission. Our practice is to establish daily weight before breakfast, diuresis control and fluid balance for allogeneic transplant patients from the beginning of conditioning, in this patient's case, in addition to the usual measures, additional weight measurements were instituted at 17 hours, circumference abdominal and once started with initial weight gain, reduction of all drug infusions in the smallest possible dilution. It started on the fifth day after HSCT (D+5) with a progressive increase in bilirubin (Total Bilirubin (BT) 5.33 mg/dL and Direct Bilirubin (BD) 4.46 mg/dL), on D+6 it reached BT of 11.92 and BD of 10.38 , also demonstrating weight gain, in addition to painful hepatomegaly. On D+6, the patient started with Defibrotide 6.25 mg/kg weight for 6/6 hours. Defibrotide was infused exclusively intravenously, due to drug incompatibilities, it was diluted in 0.9% saline, 50 ml, infused in two hours using a device with filter and infusion pump to control dripping. After 25 hours of the first dose, BT dropped to 9.23 mg/dL and after 21 days of treatment, the patient presented complete resolution of the condition with bilirubin lower than its baseline (BT of 2.32 BD 1.67). Discussion: SOS is characterized by damage to the hepatic sinusoidal endothelium, which results in postsinusoidal portal hypertension leading to weight gain, fluid retention, painful hepatomegaly and multiple organ dysfunction. Defibrotide is the only drug indicated as a treatment for the syndrome and the effectiveness of the treatment depends on the medication being started immediately as soon as the patient shows any sign of liver impairment compatible with the disease, being a high-cost medication2. Conclusion: With signs and symptoms that are often nonspecific and the late onset of severe liver dysfunction, coagulopathy and anasarca, mortality due to SOS reaches 80%, making the nursing care established in these cases extremely relevant.

Keywords: Bone Marrow Transplant; Hepatic Veno-Occlusive Disease;Nursing Care.

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MULTIDISCIPLINARY

NURSING

ACTIONS IMPLEMENTED IN HEMATOPOIETIC STEM CELL TRANSPLANTATION TO COPE WITH THE COVID-19 PANDEMIC

Priscila Mendes Paiva; Juliana Francielle Marques; Adriana Seber; Karina Giadanes; Adriana Aparecida Oliveira.

Hospital Samaritano, São Paulo - SP - Brasil.

Introduction. The onset of the COVID-19 pandemic has aroused great concern among health professionals, especially in oncology and Hematopoietic Stem Cell Transplantation (HSCT) because little is known about the disease and its repercussion in immunodepressed patients. Therefore, numerous discussions were made to implement measures to combat COVID-19.

Objective: To present actions developed to prevent the spread of the virus among employees and hsct-patients of a Private Hospital in São Paulo.

Method: A Crisis Committee was created with hospital managers to discuss the impending needs and scientific and normative updates of health entities in the country and in the world. The adaptations in the routines had oncologists, specialist nurses and other professionals with expertise in the subjects in question, such as Hospital Infection, Intravenous Therapy, among others.

Results: The actions started in March 2020: delivery of mask to patients, companions and collaborators; restriction of companions; differentiated waiting room for the elderly, children and/or neutropenics; telephone screening per nurse on the day before infusion; self parking for patients with prior scheduling; change in the frequency of permeabilization from monthly to quarterly from port-a-cath; expansion of the dressing period of semi-implanted catheter in pediatrics from 7 to 10 days, with teleconsultation of the specialist nurse; training of the patient for home application of medications subcutaneously, with manual, explanatory video and video call for monitoring the application. We also highlight the navigation of patients made by nurses. Among the actions of the specialist nurse, there was an increase in teleconsultation, mainly in the management of side effects related to treatment, avoiding visits to the hospital, monitoring of treatment for oral therapy, management of the schedule of hospitalizations in COVID-free units, with guarantee of RT-PCR collections in drive thru system for patients in HSCT programming, as well as related and accompanying donors (the companions are oriented and sign a science term on the importance of maintaining isolation between rt-pcr collection and hospitalization). From the beginning of the pandemic to July/21, 118 HSCT (69 adults and 49 pediatrics) were performed, 10 of which were non-related donors redome). For employees, there was a change in the work scale, reducing exposure on public transport, strict daily screening at the beginning of duty and decompression actions.

Conclusion: Although many patients expressed the desire to interrupt treatment or fear of going to the hospital, it was noticed that the measures adopted provided confidence and improvement of the patient's experience in the continuity of their treatment. Although he had unrelated allogeneic HSCT because of the safety in redome donor and marrow protocols, medical teams opted for related allogeneic HSCT for some cases.

Keywords: Patient Navigation, COVID-19, Nursing Care, Hematopoietic Stem Cell Transplantation (HSCT).

AUTOLOGOUS BONE MARROW TRANSPLANTATION IN A PARAPLEGIC PATIENT DIAGNOSED WITH ACUTE MYELOCYTIC LEUKEMIA: A CASE REPORT

Lais Leão; Gabriela Rodrigues Rocco de Sá; Viviane Trelesse Vieira; Carolina da Silva Costa; Cristina Vogel; Nelson Hamerschlak.

1 Hospital Israelita Albert Einstein

Introduction: Acute myelocytic leukemia (APL) or AML-M3 is a subtype of acute myeloid leukemia (AML). This type of leukemia has specific morphological changes such as abnormal myelocytes, eccentric nuclei, and abundant granulations in the cytoplasm. The patient diagnosed with ALI presents symptoms and alterations in laboratory tests compatible with coagulation alterations, and may die due to the risk of hemorrhage. However, treatment with trans-retinoic acid (ATRA) associated with chemotherapy has a rapid clinical response in patients, which is why ALI is considered one of the leukemias with the best prognosis. After previous treatment in another service in the patient's home state, he relapsed and had paraplegia after intrathecal chemotherapy. The treatment option at this time was bone marrow transplantation (BMT).

Objectives: To report the experience and difficulties of nurses in the care of a paraplegic patient with ALI in the realization of autologous BMT. METHODS: This is a qualitative, descriptive, case study conducted in the BMT unit of a large hospital in São Paulo during 5 months.

Results: Patient 35 years old, diagnosed with ALI on 07/05/2019 with CNS relapse on 08/2020 presented myelopathy due to chemotherapy toxicity, evolving with progressive lower limb paresthesia with loss of sphincter control. He underwent autologous BMT and had neutrophilic grafting on D+10. During this period, he was transferred to the ICU once due to difficult-to-control neuropathic pain, stabilized in 24 hours, and returned to the unit. His main complications related to BMT were: grade II mucositis, diarrhea, and loss of appetite.

Discussion: During the hospitalization period, the wife was the full time companion. The nursing staff developed the ability to live with and establish a trusting relationship with the couple. The bond with the team during this hospitalization period became increasingly closer due to the length of hospitalization. Throughout the treatment, the communication of the multiprofessional team was essential for the final objective, the reestablishment of the patient's independence and autonomy in the new reality, with learning how to self-surge, care with the skin due to the effect of the chemotherapy, transfers in the use of the wheelchair, with the objective of a safe discharge from hospital. In relation to the work of the nursing team, the team provided planned, unique, humanized care, bringing comfort to patient and family.

Conclusion: Even with the long period of hospitalization, the patient was discharged and scheduled to return as an outpatient for control of laboratory tests and motor rehabilitation. It was a great challenge for the nursing team, a paraplegic patient with prolonged hospitalization; however, with knowledge and safety, it was possible to negotiate more comprehensive care plans involving the care of the whole team involved in rehabilitation and self-care.

CYTOMEGALOVIRUS INFECTION AFTER HAPLOIDENTICAL STEM CELL TRANSPLANT

Fernanda Rackes da Silva Fagundes; Alzira Maria Stelmatchuk; Vaneuza Funke; Natalia Naome Oshiro; Simone Martins Nascimento Piubello.

1Hospital de Clínicas do Paraná, Curitiba, Brasil

Introduction: Among the various challenges in Hematopoietic Stem Cell Transplantation (HSCT) the search for a compatible donor stands out. The chance of a patient finding an HLA-compatible donor in the family can reach 25%, but in many cases it is necessary to look for an unrelated donor in a volunteer donor bank. The probability of finding a donor at the international registries can vary with many factors as number of registered donors, ethnicity and others. The advent of Haploidentical HSCT, however, has added a new possibility of finding a compatible donor, bringing hope to countless patients who are on the waiting list. The main advantage is the immediate availability of the bone marrow, which is clearly an advantage for those who have the time as their main enemy. Some risks, however, can happen in this modality as Graft versus Host Disease (GvHD) and the development of infections as Cytomegalovirus (CMV) reactivation. In post-HSCT patients, the reactivation of this virus typically occurs during hematological recovery until D+120, which can trigger pulmonary and digestive diseases and graft loss. CMV diagnosis can be made by antigenemia or quantitative PCR. In our case, we usually manage the CMV cases with intravenous infusion of Ganciclovir for at least 14 days. If the patient continues with positive antigenemia, he will continue the treatment until two consecutive negative tests.

OBJECTIVE: The main goal is to identify the incidence of CMV reactivation in Haploidentical HSCT and the average time of hospitalization at the Hospital Dia (HD) for treatment. METHOD: Cross-sectional, quantitative study, with data collection through medical records from the System "Sistema Informatizado Hospitalar" (SIH).

RESULTS: In 2020, 30 out of 80 performed HSCT were haploidentical, from which 21 are pediatric (75%) and 7 are adults (25%).Two patients died, one before the infusion of the progenitor cells and the other due to graft failure. Among the diagnoses, the prevalence of Immunodeficiencies and Severe Aplastic Anemia stands out. The CMV reactivation rate was 71.4%, affecting 20 patients. During therapy, the patient remains hospitalized in the HD, monitored and evaluated by a multidisciplinary team, as well through laboratory tests in order to survey the neutropenia. During this period, it was observed an average of 49.2 days of hospitalization, of which 14 days was the minimum length and 157 days the maximum length of hospitalization.

CONCLUSION: High prevalence of CMV in Brazil lead to a high impact of increasing the time of hospitalization, resources use, costs, emotional and physical distress and risks of other associated comorbidities to prolonged hospitalization. Hence, new perspectives of prhrophylaxis, therapy and managemnt of this common viral complication shall be considered for clinical trials.

Keywords: Cytomegalovirus. Haploidentical Transplantation. Cytomegalovirus Infection.

DEMATOUS FUNGUS COLLETOTRICHUM SP. INFECTION IN HEMATOPOIETIC STEM CELL TRANSPLANTATION

Letícia Silva Ribeiro, Gabrielli Mottes Orlandini, Patricia Garcia Guilardi, Andressa Silva Gonçalves, Manoela Rodrigues, Mariana de Oliveira Cardoso, Maryana Schwartzhaupt de Matos

Hospital de Clínicas de Porto Alegre

Introduction: Hematopoietic stem cell transplantation (HSCT) is a complex procedure that causes many adverse effects, mainly related to the conditioning phase. Severe and prolonged neutropenia is one of these complications related to HSCT and can lead the patient to develop invasive fungal infections, responsible for high morbidity and mortality in this profile of patients, especially in the period of aplasia. The classic signs of infectious injury are minimized or suppressed in transplant patients, so the clinical assessment performed by the nurse during the physical examination must be careful in search of phlogistic signs of infection. However, some signs and symptoms not suggestive of infections should be valued, as they may be indicative of the presence of fungi.

Aim: Describe signs and symptoms of Colletotrichum sp. infection post HSCT from the perspective of clinical evaluation and nursing care.

Method: Experience report.

Results: Patient undergoing unrelated allogeneic HSCT, with no known history of contact with contaminated fungi or vegetation. Resident in an urban area. Pancytopenic, post-HSCT, complains of acute and intense pain characterized by burning on the left side of the face, specifically on the side of the nostril and eye epicanthus, rapidly evolving into continuous pain that reduces its intensity through analgesia. After 24 hours, spontaneous and continuous tearing of the left eye. In 48 hours, eyelid ptosis was observed and, in 72 hours, left facial edema. Endoscopic evaluation by the otolaryngologist resulted in detection of spores, hyphae, granulomas and osteonecrosis. Cultures were collected, followed by initiation of lipid-complex amphotericin B, NPO and platelet transfusion for urgent surgical intervention. During the procedure, extensive angioinvasion was identified, making possible the total visual removal of the fungus through the extraction of the middle turbinate and septoplasty. An analysis of the collected specimen identified the demaceous fungus Colletotrichum sp., a pathogen with no known post-HSCT reports. There was no improvement in vital signs, other than pain, from the onset of symptoms to the start of treatment. Amphotericin therapy was terminated and pain, swelling, and tearing ceased. Otorhinolaryngology follow-up was maintained with periodic evaluation. The nursing care that stands out in this report involves those related to pain identification, through the application of a visual analogue scale, to identify the intensity and individual characterization by the patient, administration of prescribed medications according to pain intensity, nasal wash with saline solution pre-surgery, continuous assessment of visual changes in the patient's face, monitoring of postoperative nasal packing, monitoring of bleeding and use of local oxymetazoline and communication of changes to the responsible medical team. The observation of the patient's ventilatory pattern was also a constant concern due to the location of the infectious process and the intense use of opioids for pain management.

Conclusion: The evaluation of the care team must be comprehensive and pain reports may be associated with fungal infectious processes, especially in a period of pancytopenia. The identification of changes, early diagnosis and treatment are crucial in combating fungal infections that affect patients undergoing HSCT.

Descriptors: Invasive Fungal Infections. Nursing care. Bone marrow transplantation.

EXPERIENCE OF SAFETY HUDDLE IMPLEMENTATION IN AN ADULT HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT

Paula Moreira da Silva Sabaini, Maria Fernanda Vasques Esteves, Tamires Fernanda Furlan Paschoa, Carlos Sitta Sabaini, Pablo Hernesto Tarram Via, Neysimelia Costa Villela, George Mauricio Navarro Barros

Barretos Cancer Hospital, Barretos, Brasil

Introduction: Hematopoietic stem cell transplantation (HSCT) is a highly complex procedure, which includes chemotherapies ± radiotherapy, hematopoietic stem cell infusion, frequent transfusion support and invasive devices use. These patients are at high risk for complications following HSCT, such as mucositis, graft-versus-host disease, sinusoidal obstruction syndrome, organ failure, infections, among others, leading to prolonged hospitalizations. In our center during the last 3 years, an average of 85 HSCT per year were performed at the adult department, among autologous and allogeneic. Patient safety is a frequent concern among health professionals, always seeking strategies to reduce damage risks associated with health care. One of the greatest challenges for health managers is to ensure patients care, considering the proper allocation of professionals according to their needs. Incorporating tools that provide efficient care flows management makes it possible to provide better quality care. To guide measures regarding the patients' deterioration risk, we use the MEWS score (Modified Early Warning Scoring), and to evaluate results, we use survival curves and analysis of adverse event reports. In order to improve the multidisciplinary team communication, optimize resources and mitigate risks, the Safety Huddle methodology (safety meeting) was implemented. They are short and regular meetings, designed to engage staff in discussions about existing or emerging security issues. This methodology aims to manage the safety and quality of care, in order to invest in actions to improve the quality of patients' care, those who usually need quick interventions.

Objective: To report the experience of Safety Huddle implementation in an adult HSCT unit, through the use of a tool developed by the multidisciplinary team.

Methods: descriptive study, experience report of the the implementation of the Safety Huddle tool in an adult HSCT unit.

Results: After literature review, the methodology was presented to the multidisciplinary team, with discussions to identify the main safety problems and potential risks to patients. Subsequently, the tool (figure 1) was prepared, validated and implemented.

Conclusions: The literature indicates a fast growth of studies using "huddles" to improve work processes and quality of care. Patients undergoing HSCT has high care demand, due to the complexity of their clinical condition. The tool will optimize the safety culture, communication between the multidisciplinary team, and agility in identifying risk situations to mitigate adverse events.

Keywords: Safety Huddle. Patient safety. Quality. Communication. Hematopoietic stem cell transplantation.

HAPLOIDENTICAL TCTH IN COVID-19 POSITIVE PATIENT: A CASE REPORT

Gabriela Rocco de Sá; Cristina Vogel; Lidiane Soares Sodre; Carolina da Silva Costa; Tania Michele Waisbeck, Mariana Nassif Kerbauy, Nelson Hamerschlak

Hospital Israelita Albert Einstein, São Paulo, Brazil.

Introduction: A 30 year old patient diagnosed with Acute Myeloid Leukemia. Underwent induction with 3+7 protocol and two consolidations with high dose Cytarabine and Midostaurin. He had a COVID-19 infection that delayed the transplantation. He was asthmatic, taking Symbicort, and obese. PCR COVID-19 on 07/04/2020, with positive result. The patient sought emergency care the next day, reporting fever, myalgia, and fatigue. He was discharged after 12 days of hospitalization. Chest tomography with an estimated extension of pulmonary parenchyma involvement between 25 and 50%. The patient maintained the postponement of the transplant until the virus was negative, with observation of the evolution of the disease through bone marrow tests. The patient evolved with mild symptoms of infection, and collected new PCR controls on 07/27, 08/03, 08/20, and 09/14/2020, all positive, quantitative tests showing progressive decrease in viral load. On the other hand, in the bone marrow studies, the evolution of the disease was observed: 08/20 = complete remission and minimal residual disease (MRD negative), 09/16/2020 = MRD positive (0.2%). Because of the severity of the disease and the high risk of relapse, it was decided to follow up with BMT. Patient was asymptomatic.

Objectives: To report the nursing planning with a patient positive for COVID during BMT.

Method: This is a descriptive, case report study.

Results: He underwent haploidentical allogeneic transplantation from his brother. Conditioned with Bussulfan + Fludarabine + Total Medullary Irradiation (TMI) + Cyclophosphamide post. Decisions together with the hospital infection commission: Keep patient on air and contact precaution + negative pressure room with air filtration (HEPA).

Conclusion: Patient was discharged on the 39th day of hospitalization. Neutrophil engraftment on D+14. She had negative PCR tests for COVID-19 (two consecutive), only on 10/23 and 10/24 (three days after grafting), with no subsequent reactivation. We conclude that in order to be able to follow up on the patient's curative therapy, we had to adapt the care of a patient with detected PCR for COVID. Patient performed the BMT outside the unit, in hematology. The specialist nursing performed the care for him in this unit, having no contact with other transplant patients. Meetings were held with the nursing and multi-professional team for reorientation in terms of isolation, negative pressure, dressing, handling of individual protection equipment, and all the psychological support. The patient was discharged with a negative PCR and did not require intensive care support during the entire transplantation period. There was no case of COVID-19 infection in the assisting professionals or in the other patients of the sector during the period. He has now returned to his home town and is stable with respect to his underlying disease. Last bone marrow study on 6/24/2021 with negative MRD and 100% chimerism.

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A PATIENT WITH ERYTHROPOIETIC PORPHYRIA: AN EXPERIENCE REPORT

Letícia Silva Ribeiro, Gabrielli Mottes Orlandini, Patricia Garcia Guilardi, Andressa Silva Gonçalves, Manoela Rodrigues, Mariana de Oliveira Cardoso, Maryana Schwartzhaupt de Matos

Hospital de Clínicas de Porto Alegre

Introduction: Porphyrias are classified as rare diseases, they can be genetic or acquired, resulting from specific enzymatic deficiencies in the heme biosynthesis pathway, which lead to the overproduction and accumulation of metabolic precursors. As heme is synthesized both in the bone marrow, for the production of hemoglobin, and in the liver, mainly as a component of cytochromes, the porphyrias can also be classified, according to the origin of the excess precursors, in erythropoietic porphyrias or hepatic porphyrias. This defect causes an increase in porphyrin, a substance in the red blood cell, which is toxic to the body and leads to symptoms in the nervous system and skin. In extreme cases there is an indication for Liver Transplantation and Hematopoietic Stem Cell Transplantation (HSCT), complex procedures that involve several steps and prolonged hospital stay.

Aim: Describe the care implemented based on the nursing diagnoses for patients with erythropoietic porphyria undergoing HSCT.

Method: Experience report.

Results: To receive the patient in the unit, some routine adaptations were necessary, as the symptoms presented in this type of porphyria are related to direct exposure to light and include pain, redness and itching. Exposure could only occur with yellow light. For this reason, most of the time, she remained with the lights in her room off and away from direct sunlight. During nursing procedures, the yellow bedside light was used. The team was guided to manage the patient without the use of direct light, including at night, which required more attention and preparation, requiring training in the clinical look to carry out an adequate assessment during all stages of the HSCT. The established nursing diagnoses were: ineffective protection related to hematological disorders; acute pain related to the harmful physical agent; risk of allergic reaction related to environmental allergen; risk of infection related to invasive procedure. From this, the main care prescribed were: environmental control (light control for therapeutic benefit); assess pain according to characteristic, location and intensity; perform control of environmental allergens; watch for signs of infection; provide a therapeutic environment.

Conclusion: As this is the first experience with a patient with porphyria, the care required a careful adaptation, which proved to be efficient. With organization, training and preparation, all the necessary conditions for the complete follow-up of the patient, especially in the post-transplant period, were successfully achieved. Adjustments to the environment and routines allowed the clinical condition not to interfere with their care and excellence in overall care. The experience was challenging and resulted in a lot of learning and qualification of the entire team's routines.

Descriptors: Erythropoietic porphyria. Nursing Care. Bone marrow transplantation.

INFECTION PROFILE OF HICKMAN® CATHETERS IN A PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATIONUNIT.

Emanuele Christine dos Santos Pirolli[1], Rebeca Almeida Ferrarese[1], Roberta Nomura[1], Renan Weber da Costa[1], Michele Jankovski Piloni[1], Jaqueline Fátima da Silva[1], Juliana Luiza de Mello Bach[1], Adriana Mello Rodrigues[1], Paula Krys[1], Fabio Araujo Motta[1], Carmem Bonfim[1]

1- Hospital Pequeno Príncipe, Curitiba - Paraná

Introduction: Patients undergoing Hematopoietic Stem Cell Transplantation (HSCT) need a safe and large venous access, for the infusion of cells and transfusion of blood components, as well as for recurrent collect of laboratory tests. The passage of a central venous catheter (CVC) is fundamental for the treatment and, among them, the Hickman® catheter is the most used. Primary Bloodstream Infection (PBI) is one of the most frequent complications associated with the use of CVC and the incidence varies by transplant center.

Objectives This study aims to evaluate the PBI data of Hickman® double-lumen catheters, used in infant-juvenile patients undergoing allogeneic or autologous HSCT, in a pediatric transplant center.

Method: Quantitative retrospective cross-sectional study, from January 2018 to December 2020. Analysis of the medical records of patients with identification of nosocomial central line associated bloodstream infection (CLABSI) by epidemiological criteria, aged between 0 and 17 years, who used a Hickman® catheter and underwent HSCT.

Results: A total of 171 catheters were included, 30 of whom had laboratory PBI. The following microorganisms were isolated: 16 Gram positive cocci (53.33%), 11 Gram negative bacillus (36.67%) and 3 Fungi (10.00%). The main bacterial agents identified were coagulase-negative Staphylococcus (6) - which were mainly Staphylococcus epidermidis (5) - Streptococcus viridans, (4) Escherichia Coli (1 KPC and 2 ESBL), Klebsiella pneumoniae (2) and Streptococcus mitis (2) . The main fungi found were Candida krusei, parapsilosis and tropicalis. Fungal infections, in particular, are a major complication for patients after HSCT, and the presence of an infected CVC is one of the greatest risk factors for candidemia. Finally, 10 different microorganisms were isolated, with 1 case each agent. It was necessary to change 4 catheters, representing 13.33% of all 30 contaminated catheters and 2.34% of 171 catheters inserted during the study period. The others were treated and maintained.

Conclusion: The most frequently isolated microorganisms in cultures are commonly found in usual flora, such as skin, nails, gastrointestinal and genital tract, and were similar to other literature findings. Therefore, it is necessary to standardize care during insertion and handling of Hickman® Catheters in patients undergoing HSCT. Measures being adopted to prevent PBI include the implementation of a Bundle, which is a set of evidence-based practices, which includes maximal barrier precautions at the time of insertion, disinfection of all conections prior to manipulation and drug administration, hand hygiene before every catheter manipulation and catheter protection for bathing. The bundle aims to improve the processes and results of the adopted care, as well as to identify the main flaws.

Keyword: Stem Cell Transplantation, Pediatric, Central Venous Catheter

MAIN NURSING CARE FOR PATIENTS WITH AUTOIMMUNE HAEMOLYTIC ANEMIA

Cristina Oliveira da Costa; Cinthya Cavalcante de Andrade; Natalia Costa Bezerra Freire

Federal University of Ceara1

Introduction: Cold hemolytic anemia is a rare condition that consists of a decrease in red cell survival, due to the presence of cold autoantibodies, IgM antibodies that bind to red cell surfaces, having two mechanisms: through the complement system pathway or of the reticuloendothelial system. Causes can be idiopathic, infections or lymphoproliferative disorders. It can manifest itself acutely or chronically, with symptoms such as: back and leg pain, headache, nausea and vomiting, jaundice, hemoglobinuria, among others.

Objective: To report the experience of resident nurses in Oncohematology regarding the main nursing care provided to patients with cold hemolytic anemia.

Methodology: Descriptive study of the experience report type, experienced by nurses residing in Oncohematology, during the month of June 2021 in a transplant center of a teaching hospital.

Results: During the experience of nursing care to patients with cold hemolytic anemia, nursing care was experienced in the infusion of blood components, the administration of monoclonal antibody, monitoring the entire process from the preparation and administration of pre-infusion medications, time and speed of infusion of anti-CD20 antibody, use of symptomatic medications and thermal blanket, in addition to guidance to the patient on how to keep warm and protect the extremities, these care being effectively implemented to minimize anemia and acute hemolysis in these patients.

Conclusion: The experience of nursing care for patients with hemolytic anemia brought to the practice environment of the residents the knowledge and reflection on the importance of professional training for the provision of safe care that contributes to health promotion and improvement in the quality of life of the patient with this rare condition.

Keywords: Autoimmune hemolytic anemia, Nursing care, Bone marrow transplant.

NURSE NAVIGATOR: DEVELOPMENT OF A PROGRAM IN THE HEMATOPOIETIC STEM CELL TRANSPLANT SERVICE IN THE CONTEXT OF COVID-19

Natalia Naome Oshiro[1]; Fernanda Rackes da Silva Fagundes[2]; Adriana Mendes de Quadros Cavilha[2]; Luciana Puchalski Kalinke[1].

1. UFPR, Curitiba - PR - Brasil;
2. CHC/UFPR, Curitiba - PR - Brasil.

Introduction: The navigation of cancer patients was designed with the purpose of helping the patient throughout their treatment, helping them to overcome socioeconomic, financial, cultural, bureaucratic and psychological barriers that may hinder access to health services and their therapeutic adherence . The developed actions go beyond care management, as the professional supervises the entire treatment process, provides information and support, acts as a link between the patient, family members and caregivers, and the team professionals. In the context of the pandemic, due to changes in health service routines to cope with and control the infection, the role of the Nurse Navigator has been developed as an important strategy to ensure continuity of care for patients in the pre Hematopoietic Stem Cell Transplantation (HSCT) phase, providing the necessary security to prevent SARS-CoV-2 contamination.

Objective: To describe the nursing experience through the Nurse Navigator, in the context of COVID-19, in the care of patients in the pre-HSCT phase.

Method: Experience report.

Results: From the beginning of the pandemic in March 2020 to March 2021, 77 patients were followed, of which 64 underwent allogeneic transplantation (21 related, 18 unrelated, 25 haploidentical) and 13 autologous. Among the containment measures implemented in the service, there was a reduction in the number of admissions, prohibitions on visits and a reduction in outpatient visits. To ensure continuity of care, facilitate access to consultations, screening, clinical services and diagnoses, avoid delays, cancellations and crowding, the figure of the navigator nurse emerged to accompany patients in the pre-HSCT phase, among the actions developed were monitoring of suspected or confirmed cases, clinical screening of patients, monitoring of respiratory signs and symptoms and allocation of specific isolation rooms for suspected disease and testing of symptomatic patients. These actions took place through prior contact via telephone or messaging application, in order to plan together with the patient their access to the health service.

Conclusion: Nurses are responsible for the challenge of planning nursing care to prevent the dissemination of the coronavirus in a high-risk population and to implement measures based on available evidence, periodically updated in order to ensure the continuity of the patient's treatment. Even in the experimental phase, the Nurse Navigator proved to be very important in the adherence and continuity of the patient's treatment in the context of the COVID-19 pandemic.

Keywords: Nurse navigators, Hematopoietic Stem Cell Transplantation; Bone Marrow Transplantation; Coronavirus Infections; SARS Virus; Nursing Care.

NURSING CARE IN POST-TRANSPLANT COMPLICATIONS OF HAPLOIDENTICAL HEMATOPOIETIC STEM CELLS: CASE REPORT OF TRANSPLANTED SISTERS.

Alzira Maria Stelmatchuk, Jéssica Alline Pereira Rodrigues, Adriana Mendes de Quadros Cavilha, Simone Martins Nascimento Piubello, Solange Delazeri, Natália Naome Oshiro1, Fernanda Rackes Fagundes

Universidade Federal do Paraná. Complexo Hospital de Clínicas. Curitiba-PR-Brasil

Introduction: Hematopoietic stem cell transplantation (HSCT) represents an expanding treatment modality, autologous or allogeneic. For allogeneic, because of the impossibility to have 100% compatible related donor, or a non-related compatible, haploidentical transplantation is, sometimes, the only option. However, this type of transplantation is surrounded to a higher risk of complications, which requires adequate management by the nursing team, especially in a context in which sisters experience this situation in the same period.

Objective: To report the nursing care performed in the complications of haploidentical post-HSCT.

Method: Experience report of two patients treated in a Hospital-Day at a University Hospital, which is a national and international reference in HSCT in patients with Fanconi Anemia.

Results: Two sisters with Fanconi Anemia, 31 and 40 years old, from the northeast of the country, were submitted to HSCT in the same period, in a pandemic context, For the youngest one, it was a retransplantation. After hospital discharge, the complications for both were similar, involving pain, nausea, vomiting, lack of appetite, weight loss, high transfusion need, cytomegalovirus (CMV) reactivation, as well as psychological symptoms such as fear and anxiety. It was observed the development of hemorrhagic cystitis in one of them and colonization by multidrug-resistant bacteria in the other, limiting the coexistence between them. Nursing care involved persistence in the guidelines on hygiene and comfort; daily evaluation of oral cavity lesions due to mucositis and CMV infection; guidelines of mouthwashes for symptom relief, working together with the hospital dental service; insistence on offering diets, almost always refused by both, especially because of recurrent nausea, which caused progressive weight loss; administration of medicines and guidance on the schedules of medications used at home, providing optimize rest; in addition to maintaining the family bond, proven beneficial to the treatment of both. Reinforcement to the explanations about the different phases of HSCT as well as nursing support in this moment of uncertainty and discouragement were a constant. Nursing tried to remain available to provide support in view of the complex health needs presented by the patients.

Conclusion: Face to the numerous complications presented and a unique treatment scenario, nursing needs a differentiated appreciation for care, with the objective of providing support, while diagnosing, prescribing and intervening, according to the needs presented by patients.

Keywords: Hematopoietic Stem Cell Transplantation. Bone Marrow Transplant. Nursing care. Outpatient care. Patient Care Planning. Professional Practice.

NURSING CARE PLAN ESTABLISHED UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION CONDITIONING IN CARE RARE SYNDROME - EXPERIENCE REPORT

Letícia Silva Ribeiro, Gabrielli Mottes Orlandini, Patricia Garcia Guilardi, Andressa Silva Gonçalves, Manoela Rodrigues, Mariana de Oliveira Cardoso, Maryana Schwartzhaupt de Matos, Candida Gabriele Andres, Carla Patrícia Michelotti Pereira

Hospital de Clínicas de Porto Alegre

Introduction: Chediak-Higashi Syndrome (CHS) is a rare and potentially fatal autosomal recessive disease characterized by frequent bacterial infections, bleeding tendency, oculocutaneous albinism, photosensitivity and progressive neurological dysfunction and hemophagocytic lymphohistiocytosis is a syndrome of immune hyper-activation that occurs when NK cells and cytotoxic T lymphocytes don't eliminate activated macrophages, leading to excessive production of pro-inflammatory cytokines. Considering the severity of these pathologies, associated with the toxicity of conditioning of Hematopoietic Stem Cell Transplantation (HSCT), the importance of nursing care at this stage becomes evident.

Aims: Describe the nursing care plan based on the nursing diagnoses of a pediatric patient with this rare syndrome undergoing HSCT conditioning.

Method: Experience report. Results: Patient with a history of recurrent oropharyngeal infections. Silver hair color, healthy parents and siblings, age-compatible motor and sensory development. Hospitalized for HSCT as a treatment for CHS. Imaging exams: enlarged spleen and liver. Ferritin, LDH at high levels, leukocytosis - fever, ruling out respiratory infections. Possible acute gastroenteritis. Antibiotic therapy was started, showing improvement in imaging tests. Conditioning with chemotherapy started. The established nursing diagnoses were: Risk of falls related to extremes of age; Risk of allergic response, related to history of allergy and/or multiple procedures; Infection risk, related to an invasive procedure; Ineffective protection related to hematological disorders; Bleeding risk, related to hematological disorders. The prescribed care plan was established taking into account disease severity, age, invasive procedures, clinical and laboratory findings, and drug toxicity. The main prescribed nursing care were: Putting an allergy identification bracelet on the patient; Implement care according to the fall care protocol; Watch for signs of infection; Change central access protect; Disinfect the connections with a 70% alcohol sachet at each handling; Whirl both ways of power picc after use; Use only 10 or 20 ml syringes when handling the picc; Guide the patient/family on unit routines (mask use and hand hygiene); Guide the patient/family on the stages of transplantation (conditioning, cell infusion, medullary aplasia and marrow engraftment); Check vital signs - Pain and oximetry, use CHIPPS pain scale.

Conclusion: The planning and nursing interventions determined in the care plan contributed to the prevention of complications related to the adverse effects of the proposed therapy and to the restoration of the child's health. The nursing guidelines provided to the mother and child showed a positive outcome related to care during the conditioning phase of HSCT.

Keywords: Nursing care plan. Rare disiases. Bone marrow transplantation.

TITLE: NURSING CONSULTATION IN PRE TRANSPLANTATION OF HEMATOPOIETIC STEM CELLS: EXPERIENCE IN HUMANIZATION AND ACCOMMODATION IN A PEDIATRIC CENTER

Jakeline Palmezano Crispim de S. Bufoni; Adriane da Silva Santos Ibanez; Cintia Monteiro Lustosa; Cristiane Menezes Vitoria Alferi; Maria Aparecida Aguiar da Silva; Laís Lima Quintino; Karoline Helena Silva da Silva; Virginio Climaco Araujo Fernandes Junior; Patrícia Shimoda Ikeuti; Olga Margareth Wanderley de Oliveira Félix; Renata Fittipaldi da Costa Guimarães.

Instituto de Oncologia Pediátrica IOP/GRAACC/UNIFESP, São Paulo - SP - Brasil.

Introduction: Services that rely on the activities of specialist clinical nurses (SCN) improve the quality of your health care as these nurses direct their attention to the needs of each patient. The main features of this service are the personalization of care, identification and elimination of possible barriers in the care process, monitoring in all phases of treatment. The process of hematopoietic stem cell transplantation (HSCT) is stressful due to its particularities, which change the lifestyle of the patient and family, interfering with its quality. It is, therefore, important that humanized and quality care is provided. The nurse, in addition to preparing the patient and their family for the transplant, also welcomes them in a humane way through the pre HSCT nursing consultation.

Objective material and method: This is a descriptive study, based on the experience of SCN in HSCT in a pediatric oncology hospital in São Paulo that provide pre-HSCT outpatient care. Results:From January 2019 to December 2020, 200 nursing consultations were carried out. In this consultation that precedes the HSCT, the patient and their family are welcomed by the nurse who assesses their physical and emotional needs. In addition to clarifying doubts and taboos related to the HSCT phases, the nurse seeks to welcome each family by reassuring them, clarifying doubts, and thus reducing their concerns. The SCN in HSCT is the first contact that most of the time the patient and family have in the HSCT service and through the nursing consultation they are able to know the entire history of the patient indicated for the HSCT, in addition to understanding the structure and support of that family. Conveying to this family the need for evaluation by the multidisciplinary team (dentistry, psychology, nutrition, social worker, physiotherapy, among others) to provide the necessary care to the patient during the period of bone marrow transplantation, is also one of the roles of SCN in HSCT.

Conclusion: This humanized way of welcoming the patient and family at the time of the nursing consultation that precedes the HSCT has a positive impact on the expectations of this family regarding hospitalization and the relationship built with the care team. The presence of SCN in a bone marrow transplant center has been shown to be a determining factor in ensuring the success of the proposed treatment, as the possibility of this nurse having a holistic and complete look at the line of care,

Keywords: Hematopoietic Stem Cell Transplantation; Pediatrics, Humanization of Care; Nursing

NURSING DIAGNOSES RELATED TO PEDIATRIC PATIENT CARE WITH CD40 LIGAND DEFICIENCY

Piubello SMN[1,2,] Danski MTR[2], Pontes L[2], Stelmatchuk AM[1], Oshiro NN[1,2], Fagundes FRS[1] Rodrigues JAP[1]

1 Complexo Hospitalar de Clínicas da Universidade Federal do Paraná
2 Universidade Federal do Paraná

Introduction: Deficiency of CD40 ligand (CD40 L) is a primary combined immunodeficiency of T and B lymphocytes characterized by a reduced concentration of immunoglobulins (Ig) such as IgG and IgA and by a high concentration of IgM, therefore, also called Hyper syndrome - IgM. These patients have a greater predisposition to fungal infection, which is more related to the patient's death. Pulmonary involvement such as bronchiectasis may be present over time. This requires the nurse to be aware of the particular needs of this patient, in order to avoid infections that can pose a risk of death.

Objective: to report the experience of nursing at a Hematopoietic Stem Cell Transplantation Center, in the care of patients with CD40 L deficiency, based on nursing diagnoses for care planning.

Method: Experience report.

Results: Nurses at the transplant center of the Hospital de Clinicas Complex, Federal University of Paraná, assist patients with CD40L deficiency based on the diagnoses described by the North American Nursing Diagnosis Association (NANDA), which we discuss below: 1) recreational involvement diminished; 2) ineffective protection; 3) excessive fluid volume; 4) impaired gas exchange; 5) impaired walking; 6) impaired physical mobility; 7) ineffective breathing pattern; 8) activity intolerance; 9) risk of infection. From this, the nurse must guide the family on how to identify signs of infection and hypoxemia, as well as the necessary care, if the child presents these signs. The nurse who assists these patients is always attentive to care for the prevention of infection and, due to the pulmonary impairment characteristic of the disease, it is important for the nurse to guide the family about the risk of hyperhydration. It is also important to highlight that the patient may have difficulty in walking due to dyspnea caused by pulmonary impairment. If the use of inhaled medications is necessary, guidance on the correct use is crucial for greater effectiveness of the treatment.

Conclusion: Since these immunodeficient patients fail to activate antibodies and are susceptible to fungal infections due to pulmonary involvement, nurses should guide caregivers about the need to prevent infections through care for the environment, food and recreational activities developed by the child, paying attention to signs of infection and hypoxemia, in addition to guidance on the use of inhaled medications.

Keywords: Nursing Care, Nursing, Professional Practice

ORGANIZATION OF THE NURSING TEAM TO PERFORM CAR T-CELL THERAPY (CAR T-CELL) IN A BONE MARROW TRANSPLANTATION UNIT (BMT UNIT)

Ana Carolina de Jesus Vieira[1], Camila Campos Mesquita[1], Patrícia da Silva Laurindo[1], Vinícius Augusto dos Reis[1], Roger Eduard Fonseca[1], Sônia Regina Roma de Freitas[1], Bruno Henrique dos Santos[1], Lucas Oliveira[1], Camila Derminio Donadel[1], Patrícia Oliveira da Cunha Terra[1], Warlen Rosa Dutra[1], Vânia Maria Correa[1], Denise Maria Vendramini[1], Leandro Dorigan Macedo[1], Nattália Araujo Alves[1], Thalita Cristina de Mello Costa[1], Juliana Bernardes Elias Dias[1], Fabiano Pieroni[1], Ana Beatriz Pereira Lima Stracieri[1], Renato Luiz Guerino-Cunha[2]

1: Center for Bone Marrow Transplantation and Cell Therapy at Clinical Hospital, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil
2: Department of Medical Images, Hematology and Clinical Oncology, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil

Introduction: CAR T-cell therapy has emerged as a promising and advanced therapeutic approach for the treatment of hematologic malignant diseases. However, life-threatening adverse reactions might occur, such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Challenges to implement CAR T-cell therapy are related to three aspects: 1) selection of patients; 2) human resource training and 3) establishment of a patient-centered care multidisciplinary team. Traditionally, international accreditation in cell therapy is the standard procedure to set up an environment dedicated to CAR T-cell patients. Nevertheless, in addition to high implementation costs, international accreditations are not covered by Brazilian health system (SUS).

Objective: To restructure a BMT unit hosted by SUS to receive patients for CAR T-cell therapy and provide high-quality assistance with cost-effective procedures.

Methodology: In order to provide safe and cost-effective clinical care for recipients of CAR T-cell therapy, we established the BMT Unit as our basis, as recommended by EBMT and ASTCT. Secondly, new nursing protocols were validated emphasizing clinical monitoring, laboratory tests and neurological assessment. Thirdly, a new list of equipment and medications was made in collaboration with the hospital directors. Finally, several educational and training meetings were performed with the correlated areas such as the ICU nurse team, whose assessment scales were made available virtually for the BMT Unit. For adult and children ICU, practices regarding the clinical monitoring of the patient were reviewed. For outpatients, in addition to routine examinations, the COVID-19 test was also performed. For in-hospital patients: monitoring of vital signs and fluid balance, weighing of the patient twice a day, daily application of the ICE score and writing test to evaluate neurotoxicity; detection and management of cell infusion complications. Cell infusion: 10 to 20 mL/minute (less than 30 minutes), using an exclusive central venous catheter line; vital signs were monitored every 15 minutes for the first hour, every 30 minutes for the second hour, and every hour for the following 3 hours.

Results: Nursing care for patients receiving CAR T-cell therapy was carried out with technical quality, based on the systematic monitoring of the patient and early detection of complications that would require rapid intervention. Therefore, three patients were treated in our unit with acceptable management of side effects and clinical complications.

Conclusion: The standardized training of the nursing team and the reorganization of the service, leads to humanized high-quality technical care. Furthermore, a systematic approach with efficient risk analysis and the implementation of well validated nursing care protocols are alternatives to establish a clinical platform to treat patients with advanced cell therapy in low-middle income countries.

PATIENT SAFETY IN BONE MARROW DONATION BY PUNCTURE IN SURGICAL CENTERS: REPORT ON THE EXPERIENCE OF NURSES RESIDENT IN ONCOHEMATOLOGY

Cristina Oliveira da Costa; Cinthya Cavalcante de Andrade; Ítala Barbosa da Silva Monteiro; Larissa Gomes Girão Paiva Soares; Maria Elisa Curado Gomes; Natalia Costa Bezerra Freire

Federal University of Ceara1

Introduction: The collection of hematopoietic stem cells is a complex procedure. The source of cell extraction can be by apheresis, puncture of the iliac crest in an operating room or umbilical cord blood. The donor undergoes an evaluation of the venous network with the sector responsible for collecting cells by apheresis, which may be indicated or contraindicated according to the team's assessment. Among the advantages of collecting hematopoietic stem cells from the bone marrow is that there is no need to place a central catheter, being performed in a single procedure. Disadvantages: use of anesthesia and higher morbidity rates. The Nurse, together with the multidisciplinary team, is responsible for planning and implementing actions aimed at preventing possible adverse events throughout the bone marrow donation process.

Objective: To report the experience of multidisciplinary residency nurses in Oncohematology in the process of collecting bone marrow by puncture of the iliac crest in the operating room.

Methodology: Descriptive study of the experience report type experienced by nurses residing in oncohematology at a teaching hospital. During the months of June and July 2021, two resident nurses experienced the process of collecting bone marrow by puncture of the iliac crest in a hospital operating room, the procedures taking place in the morning shift with a maximum duration of two hours. The bone marrow capture team consisted of two doctors specializing in bone marrow transplantation and two nurses, a specialist in Oncohematology and a clinical nurse.

Results: In all, 03 processes of bone marrow collection by puncture of the iliac crest were carried out in the operating room, which were experienced by the residents. The Systematization of Perioperative Nursing Care (SAEP) was performed in the immediate preoperative period. About the transoperative period: the type of anesthesia used in the three procedures was general. The ventral position was used according to the type of procedure, with care focused on the prevention of injury by surgical positioning, prevention of hypothermia and applied to the surgical safety checklist before anesthetic induction, before surgical incision and before the patient leaves the operating room, in addition to maintaining aseptic technique throughout the procedure for storing the extracted marrow in the closed system collection bag. The time to perform the procedures was an average of 90 minutes.

Conclusion: The safety of bone marrow donors through puncture in the operating room was prioritized, and the actions described were experienced by the residents, contributing this experience to the professional training of the residents.

Keywords: Bone marrow, Surgical Center, Nursing, Oncohematology

PATIENT-CENTERED CARE: DEVELOPING A SPIRITUAL CARE PLAN FOR THE PRACTICE OF NURSING IN BONE MARROW TRANSPLANTATION

Kelly Machado Mensch[1]; Roberta Waterkemper[2]; Rosália Figueiró Borges[3]

1. Hospital Moinhos de Vento, Porto Alegre - RS - Brasil;
2. UFCSPA, Porto Alegre - RS - Brasil;
3. UNISSINOS, Porto Alegre - RS - Brasil.

Introduction: Scientific evidence has shown a positive correlation between spirituality and health, inferring that its development provides physical and emotional well-being and can contribute to the relief of suffering. Objective: To develop a Spiritual Care Plan for patients undergoing Bone Marrow Transplantation (BMT).

Method: This is a qualitative study of the Convergent Care type developed in a BMT inpatient unit of a private hospital in southern Brazil. The study included patients hospitalized in two moments of collection in order to identify spiritual needs: retrospective search of nursing diagnoses and interventions in electronic medical records and questionnaire application in three moments (pre-transplantation, aplasia and discharge. The analysis was performed using simple descriptive statistics. The study was approved by the Research Ethics Committee at UFCSPA. Results: In the first collection stage, 295 admissions were analyzed, totaling 150 patients, men (51%), older than 60 years (47%), whites (97%), married 84% and Catholics (65%). The main clinical diagnosis was Non-Hodgkin's Lymphoma (22%), followed by Acute Myeloid Leukemia (17%). Twenty-four general nursing diagnoses were identified and another 5 linked to spirituality were inferred, through cross-mapping: Hopelessness, Spiritual Suffering, Risk of Impaired Religiosity, Willingness to Improved Spiritual Well-Being and Willingness to Improved Religiosity. As for nursing interventions, seven were inferred: Spiritual Support, Emotional Support, Improving Coping, Facilitating Spiritual Growth, Reducing Anxiety, Assisting Dying and Promoting Hope. In the second stage, 4 patients who underwent allogeneic or autologous transplantation were analyzed. Through the application of the Spiritual Well-being scale, it was observed that the means obtained for the global score remained high in the three assessments. It is noteworthy that the means of the second assessment were the lowest found, when comparing the three moments, both for spiritual well-being and its domains. There was a prevalence of high level for religious well-being in the three moments evaluated and an increase of low/moderate level for high from the second to the third evaluation in relation to existential well-being (p=0.039). Conclusion: the spirituality should be considered as an important strategy for coping with the disease for BMT patients, as it contributes to the process of resignification of meaning and purpose in life. Its implementation can occur through the nursing process that systematizes nurses' actions, allowing for a comprehensive and individualized assessment. Product: A Spiritual Care Plan for BMT patients was developed, in line with their needs, equipping nurses to insert this dimension in their work practice.

PREPARATION AND ADMINISTRATION OF MEDICATIONS: TRAINING AND PERMANENT EDUCATION OF THE NURSING STAFF

Letícia Silva Ribeiro, Katia Kosciuk Lima, Gabrielli Mottes Orlandini, Maryana Schwartzhaupt de Matos, Cleocir Marta Tecchio, Fabiane De Avila Marek

Hospital de Clínicas de Porto Alegre

Introduction: The preparation and administration of medications is one of the most important and complex processes in healthcare institutions, as it is directly related to patient safety. Aiming to prevent the occurrence of adverse events resulting from medication errors, the medication group, composed of nursing technicians, nurses, and pharmacist, developed a training program for the nursing staff of the Protected Environment Unit (PEU) of a public university hospital. The training was carried out by the need to train new collaborators and maintain permanent education of the professionals who already work in this unit, reviewing the institutional standardization of the preparation and administration of the most used medications during the hospitalization of patients in a bone marrow transplant and hematological clinical unit.

Goal: To describe the training and continuing education of the nursing staff regarding the safe preparation and administration of medications in a Protected Environment Unit.

Method: Experience Report.

Results: At the beginning of the year 2021, the medication group met in online meetings via Google Meet and developed the training through a Powerpoint class entitled "General aspects of pharmacodynamics, interaction and administration of medications in the PEU". The class was divided into two blocks: the first theoretical block, lasting approximately two hours, in which the medication process was detailed (medical prescription, validation by the pharmacist, scheduling by the nursing staff, dispensing, preparation and administration), as well as aspects related to patient safety and nursing care. The second block was the practice, lasting approximately one hour, including the handling of infusion pumps, infusion sets, connectors and dose calculations. The theoretical block was carried out through the online platform with prior scheduling. The practical block was carried out in person, during the work shift, also by prior arrangement. The target of participation in this training is 100% of the unit's employees. Up to the present moment the goal reached was 85%.

Conclusion: The procedure of preparing and administering medications is an essential care for the treatment and recovery of health and it's considered a challenge when it comes to the development of a safe practice. Thus, the permanent education of the nursing team is extremely important for patients with onco-hematologic diseases, who remain hospitalized for long periods of time, at risk of any error related to the preparation and administration of medications. The professionals report the importance of it, through the standardization of this priority and constant activity during the work shift, and affirm that this type of training is necessary to maintain the quality and safety of the assistance.

Descriptors: Permanent education. Patient safety. Nursing team.

PREVENTIVE MEASURES FOR CORONAVIRUS 2 SEVERE ACUTE RESPIRATORY SYNDROME (SRAS-COV-2) IN A HEMATOPOIETIC STEM CELL TRANSPLANT UNIT DURING THE COVID-19 PANDEMIC

Liliane Dantas Pinheiro[1]; Livia Mariano[1]; Vanderson Rocha[1]; Thais Guimaraes[1]; Silvia Figueiredo Costa[2]; Hermes Ryoiti Higashino[1]

1. Instituto Central do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo - SP - Brasil;
2. Faculdade de Medicina da Universidade de São Paulo, São Paulo - SP - Brasil.

Introduction: Patients undergoing hematopoietic stem cell transplantation (HSCT) have high risk of complications associated with respiratory infections, and due to the pandemic, changes in clinical practice were needed to prevent transmission following national and international guidelines.

Objective: Report preventive measures at HSCT unit of a tertiary hospital.

Casuistic: Between September 2020 and June 2021, 130 patients admitted at the cell therapy clinical unit (UCTC).

Method: Observational retrospective study.

Results: Adaptation of the unit – The hospital main building, in which UCTC is located, was closed for exclusive treatment of the COVID-19, and UCTC had to be transfer to another institute classified as a clean area. From April to September 2020, 77 patients were hospitalized, and only autologous transplants were performed. After this period, the unit was reopened in the original institute, admitting 130 patients until June 2021. In 2020, there were 26 HSCT (20 autologous and 6 allogeneic) and in 2021, 46 HSCT (33 autologous, 13 allogeneic). Prevention measures used and reinforced with the team/patients - Use of protective masks (surgical mask, previously used when the patient leaved the bed, with the pandemic, started to be used during outpatient clinic visit and inside the room, and N95/PFF2 mask when leaved the inpatient unit) and regular hands hygiene. Use of private uniforms and HSCT evaluation/planning were maintained. Measures implemented - Testing of patients for SARS Cov-2 by RT-PCR before admission; testing and withdrawal of symptomatic workers; prohibition of visits to the patients and maximum unit restriction access; workers vaccination for SARS-cov-2; restriction of circulation in COVID-19 areas by workers, cryopreservation of the donor cells products; use of N95 mask by workers in contact with the patients and individual room. Suspected cases of respiratory infection were tested for SARS CoV-2 and other respiratory viruses and kept outside positive pressure. If suspicion before the conditioning regimen start, patients were discharged and HSCT postponed. UCTC didn't have any confirmed case. One patient was detected in the weekly screening and after investigation, it was considered a false positive. Another patient reported contact with a suspected case during admission and despite a negative test, he was discharged with home isolation and evolving with a positive test and symptoms after one week. A third patient had a positive spouse confirmed 48 hours after admission and because que conditioning had been initiated, isolation measures were intensified, and the patient evolved asymptomatic and with negative tests. Conclusion: Preventive measures, following the recommendations and aligned with the hospital infection commission, associated with continuous orientation of the staff and patients, made it possible to carry out HSCT in a tertiary hospital reference in the treatment of Covid-19.

Descriptors: Hematopoietic Stem Cell Transplantation, SARS-CoV-2, Bone Marrow Transplantation, Coronavirus Infections, Nursing Care

PROPOSAL FOR CONTINUED EDUCATION IN THE REVACCINATION PROGRAM OF PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Paula Moreira da Silva Sabaini[1], Anderson João Simioni[2], Cinthya Corrêa da Silva[3], Maria Fernanda Vasques Esteves[1], Ana Claudia Ferrari dos Santos[2], Vergílio Antônio Rensi Colturato[2], Cristina Vogel[3], Nelson Hamerschlak[3], George Maurício Navarro Barros[1], Clarisse Martins Machado[2,3]

1. Barretos Cancer Hospital, Barretos, Brasil
2. Hospital Amaral Carvalho, Jaú, Brasil
3. Hospital Israelita Albert Einstein, São Paulo, Brasil

Introduction: One of the main barriers on implementation of the revaccination program after hematopoietic stem cell transplantation (HSCT) is the difference between the national and international recommendations and real life. Immunization delay is one of the main difficulties, increasing the patients' susceptibility to infections. Brazil has a special National Immunization Program for immunocompromised patients, broad and free, managed by the Special Immunobiological Reference Centers (CRIEs). However, the post-HSCT revaccination program is complex, with numerous vaccines, multiple doses, to be timely administered. Therefore, the HSCT center, the patient/guardian and the basic health units/CRIEs must be prepared to accomplish the protocol. Health education and its practices have grown progressively in recent decades, especially in the daily activities of health services, such as primary care.

Objective: To develop a post-HSCT immunization training program for Brazilian HSCT centers' physicians, nursing staff and data managers (DM), with tools to improve the referral flow and follow-up of patients during revaccination, allowing the assessment of adherence and completion of the full schedule.

Casuistry: Brazilian HSCT centers' physicians, nursing staff and DMs interested in engaging the training.

Methods: Descriptive, observational, longitudinal study for the implementation of online training, using active methodologies. The teams will be evaluated before and after training, using questionnaires. The training will be based on the following topics: overview of Brazil and worldwide immunization, basic concepts of immunization, vaccine-preventable diseases and post-HSCT patients, and the post-HSCT revaccination schedule. The proposal includes the development of a mobile app for recording immunization by patients, and monitoring by health professionals, also functioning as an educational platform for these professionals. Information about vaccines received will be registered on DMs' databases. The mobile app platform may be adjusted in the future to incorporate each patient's vaccinations information that is available on ConectSUS website.

Results: The implementation of this proposal is expected to favor the timely referral of the patient to start the revaccination program, and to mitigate possible failures that may cause delays, changes in the recommendations or threaten patient safety.

Conclusion: Continuing education in HSCT revaccination program will improve the professional's expertise in this area, favoring appropriate adjustments when necessary, promoting better strategies to ensure patient compliance and improving communication between teams and patients.

Keywords: Health Education. Vaccination. Hematopoietic stem cell transplantation.

USE OF PICC CATHETER IN HEMATOPOIETIC STEM CELL INFUSION: A CASE REPORT.

Diogo Ferreira Ducatti; Patricia Garcia Guilardi; Mariana de Oliveira Cardoso.

Hospital de Clínicas de Porto Alegre, Porto Alegre - RS - Brasil.

Introduction: Bone marrow transplantation (BMT) is one of the most complex treatments in medicine. It consists of replacing a diseased bone marrow with a healthy one, whether from a self-donation or by donating a marrow from a donor. The medulla is composed of hematopoietic progenitor cells that are infused via a wide caliber, deep venous access that allows high flow. Catheters used in stem cell infusion are Hickman-type tunneled catheters for adults and Broviac-type catheters for pediatrics. To Report the experience of using a PICC catheter in BMT.

Methods: This is a case report of a BMT in which a peripherally inserted central catheter (PICC) was used in a 16 years old female patient, 158cm height, 55.3 kg (BSA 1.55 m^2). Allogeneic BMT was performed on 08/03/2021. It was divided into 4 bags that presented a total of 436ml at the end of the infusion.

Results: The catheter used was a 3-way 5 Fr Power PICC and was inserted in the medial region of the left arm (Basilica vein). The infusion of each bag of hematopoietic stem cells should not exceed 15 minutes. This infusion is performed using the drip technique in an equipment with a filter retaining aggregates/clots, but due to the density of the cells, it is sometimes necessary to perform part of the infusion with the aid of a 20 ml syringe and a cannula system, which allows the aspiration of cells and active infusion of them. This technique, in turn, tends to increase the risk of complications due to the speed of the infusion, such as nausea, vomiting, abdominal discomfort and potentialization of other adverse effects of the infusion, such as skin rash. There is also a risk of hardening of the syringe, in some situations the need to replace it, in which case the opening of the system occurs and consequently with increased risk of contamination. In these report, cells did not flow by spontaneous dripping at any time in any of the catheter routes, requiring the use of the syringe system throughout the procedure. Syringe replacement was necessary during the procedure on 3 occasions. The patient had severe nausea, without vomiting, but presented abdominal and lower back pain, and cramps. Skin rash on the face and hands was noted. The discomfort lasted for more than 24 hours even though she was receiving medication.

Final Considerations: In spite of the difficulties that were presented during the infusion, the patient's condition evolved well and she presented bone marrow attachment (transplant success). The drip probably did not occur as expected do to the association of cell density with the reduced caliber of the PICC catheter. The PICC catheter did not show contamination or was associated to infectious process throughout the treatment and proved to be an option for performing BMT when there is a factor that disqualifies the insertion of a thick or tunneled catheter.

PHARMACY

INSERTION OF THE CLINICAL PHARMACIST IN THE ANTIMICROBIAL MANAGEMENT PROGRAM IN A PEDIATRIC CENTER FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION

Laiane de Jesus Oliveira, Juliana Luiza de Mello Bach, Adriana Mello Rodrigues, Polliany Roberta Dorini Pelegrina, Fábio Araújo Motta, Cilmara Cristina Kuwahara Dumke, Fernanda Moreira de Lara Benini, Carolina Martins de Almeida Peixoto, Gisele Loth, Solange Gomes da Silva Ferreira, Nelci Rodrigues Betin, Julliana Bianco Giuriatti Bassani, Carmem Bonfim, Heloisa Arruda Gomm Barreto

Hospital Pequeno Príncipe – Curitiba/PR

Introduction: The antimicrobial management program (PGA) is a strategy to minimize antimicrobial resistance and limit costs, in an hematopoietic stem cell transplant center (HSCT). The role of the clinical pharmacist with the multidisciplinary team in this program contributes to clinical outcomes in the transplant process since they are immunosuppressed patients and have an increased risk of infections by multiresistant organisms. Quantify antimicrobial exposure in days of therapy (DOT) per 1000 patient-days (PD) helps this process.

Objective: Evaluate the use of antimicrobials in days of therapy (DOT) per 1000 patient-days in the period with and without the performance of the pharmacist.

Method: Retrospective study, comparing two periods: March/2019 – March/2020, April/2020 – April/2021. Data were obtained through the institutional business intelligence program weKnow®. The monthly use of antimicrobials was quantified in DOT/1000 (PD).

Results: The total DOT in the period Mar/19 - Mar/20 without the participation of the pharmacist was 4523.6/1000 PD, while in the period of Apr/20 - Apr/21, with the participation of the pharmacist together with an infectious disease specialist, was 4187.1/1000 PD. There is a reduction of 336 (DOT 1000 PD) which represents 1%. Among the primary endpoint, with the most significant impact on antibacterials: vancomycin decreased 4.4% (181 to 173 DOT/1000 PD), linezolid 51.7% (85 to 41 DOT/1000 PD) and levofloxacin, with the most significant reduction 82% (116 to 21 DOT/1000 PD). About meropenem and piperacillin + tazobactam there was an increase of 3.4% and 18% respectively, since piperacillin + tazobactam became the first antibacterial to be used empirically at the time of febrile neutropenia, with the use of prophylactic levofloxacin no longer. The average length of stay was 18 days in both periods and there was no impact on the increase in mortality between the periods.

Conclusion: The follow-up of the clinical pharmacist articulated with the infectologist in the PGA, add to the multidisciplinary team, is an effective strategy that has contributed to greater adherence to clinical protocols, reduction of total DOT without influencing the mortality rate and also contributing to reduced outcomes. exposure to antimicrobials, selection and dissemination of resistant microorganisms.

Keywords: Antimicrobial management, Hematopoietic Stem Cell Transplantation, Clinical Pharmacy

PHARMACEUTICAL INTERVENTIONS IN A PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION CENTER: A RETROSPECTIVE ANALYSIS

Laiane de Jesus Oliveira, Polliany Roberta Dorini Pelegrina, Adriana Mello Rodrigues, Juliana Luiza de Mello Bach, Cilmara Cristina Kuwahara Dumke, Fernanda Moreira de Lara Benini, Carolina Martins de Almeida Peixoto, Gisele Loth, Nelci Rodrigues Betin, Solange Gomes da Silva Ferreira, Julliana Bianco Giuriatti Bassani, Fábio Araújo Motta, Carmem Bonfim, Heloisa Arruda Gomm Barreto

Hospital Pequeno Príncipe – Curitiba, Paraná

Introduction: Pharmaceutical care and assistance are possible through health services, from the promotion of health education, review of pharmacotherapy, as well as the medication management process, including their selection and dispensing. Therefore, it is inherent to the pharmacist to act through pharmaceutical interventions (PI) in identifying, preventing and solving drug-related problems (PRM). Therefore, the inclusion of the clinical pharmacist in the hematopoietic stem cell transplant center (HSCT) team contributes to promoting the rational use of drugs in the optimization of pharmacotherapy, as well as to the pharmacoeconomic impact.

Objective: Describe PI data from follow-up by the clinical pharmacist in a single pediatric HSCT center.

Method: Retrospective, descriptive and cross-sectional study that analyzes pharmaceutical interventions during the pharmacotherapeutic follow-up in patients from SUS and transplanted health insurance in the period from April/2020 to June/2021. The identified PRMs were tabulated according to the parameterization of the PRM codes of the institution's clinical pharmacy service. The acceptance of interventions by the multidisciplinary team, as well as their impact, were evaluated. Pharmaceutical interventions with a pharmacoeconomic impact were also evaluated.

Results: During the study period, 77 patients were followed, 63% of which were allogeneic transplants and 19% were autologous. The number of pharmaceutical interventions totalized 1.872, with an average rate of 95 PI per patient during the hospital stay. Of these interventions, the pharmacological class with the highest percentage was antimicrobials with 45%, followed by chemotherapy and immunosuppressants with 32% and acceptability was 95%. The pharmacoeconomics of the PIs in the period totaled R$634,913.00. The costs avoided through requests for high-cost medications distributed by pharmaceutical assistance programs for SUS patients were representative. During this period, 175 vials of lipid-complex amphotericin B were requested from the Ministry of Health's Systemic Mycoses Program for 4 patients who met the program's criteria, totaling more than R$580,825.00. Also, as an adjuvant to supportive therapy during immunological vulnerability, the request for immunoglobulin for SUS patients via a strategic component totalized 26 vials at an avoided cost of R$49,088.00.

Conclusion: Through the data, the relevance of the inclusion of the clinical pharmacist in the team is verified, enabling the optimization of pharmacotherapy, improvement of health outcomes, significantly contributing to the recovery of patients undergoing transplantation and also cooperating with pharmacoeconomic results.

Keywords: Hematopoietic Stem Cell Transplantation; Clinical Pharmacy, Pharmaceutical Interventions

PHARMACIST'S ACTIVITY IN HOSPITAL DISCHARGE AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION.

Mariana Perez Esteves Silva Motta, Cristina Vogel, Cinthya Corrêa da Silva, Valéria Armentano dos Santos, Daniella Cristina de Oliveira, Nelson Hamerschlak

Hospital Israelita Albert Einstein, Bone Marrow Transplantation Department, São Paulo, Brazil

Introduction: The role of the pharmacist in Hematopoietic Stem Cell Transplantation (HSCT) is referred to in several studies, mainly in Europe and the United States, and has been incorporated as an essential part of the multidisciplinary team involved in the care of the HSCT patient. Some hospital accreditations have been presented critical elements that should be part of the training and performance of pharmacists in this context. Hospital discharge is a critical moment and its planning is also part of the pharmacist's duties, as well as the transition of care. Since 2017, pharmaceutical discharge orientation has been performed at the Institution.

Objective: To present the pharmaceutical orientations at hospital discharge after HSCT in a philanthropic service in the state of São Paulo in 2020.

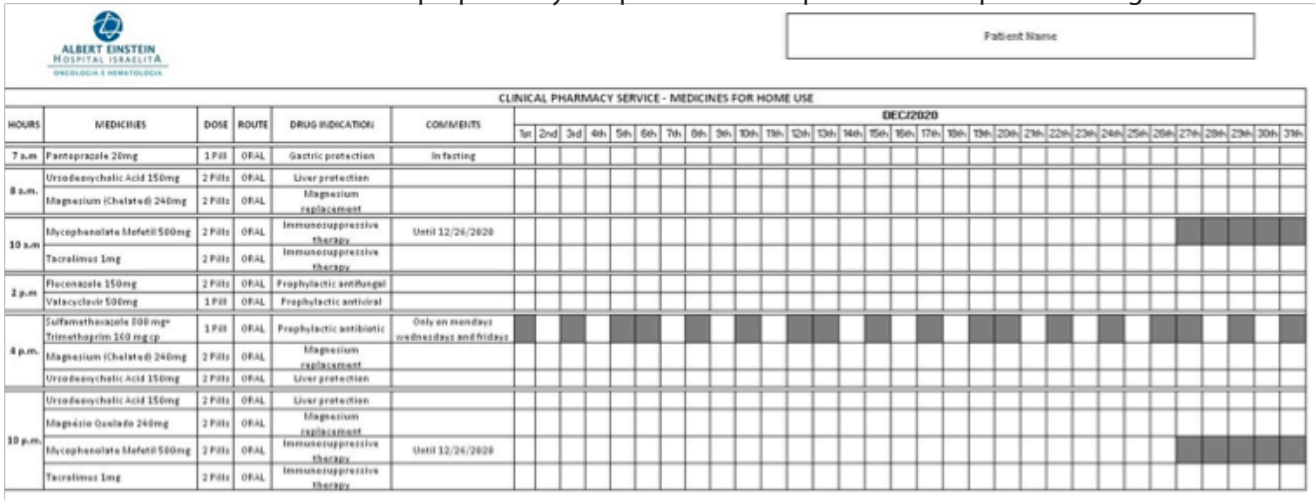
Method: Retrospective analysis of 47 patients undergoing HSCT in 2020. Data were collected by reading the electronic medical record, identifying the evidence of pharmaceutical annotation regarding hospital discharge orientation. The pharmacist provided general information about medications as such the best time to administer the drugs at home, considering drug interactions and particularities of the drugs and treatment duration. Each patient received a personalized medication worksheet with the information provided by the pharmacist, (Figure 1). The pharmaceutical follow-up was continued in the outpatient clinic.

Results: Considering the pandemic context, data of 2020 were chosen, where the indication to HSCT was directed to the most critical patients. Of the 47 patients, 64% (30) underwent allogeneic HSCT and 36% (17) underwent autologous HSCT. The median number of drugs to discharge was 12 drugs per patient in allogeneic HSCT, and 9 drugs per patient in autologous HSCT. The most prescribed drugs were immunosuppressants and prophylactic therapies such as antimicrobials. 91% (43) of patients received pharmacist orientation at discharge, and of the 4 orientations not provided, 3 were for reasons of early death and 1 for an unknown reason.

Conclusions: The pharmacist can develop several activities focused mainly on safety in the use of medications during HSCT. Due to the number of drugs prescribed, the occurrence of adverse events can increase, and pharmaceutical guidance offers greater safety for the patient and the HSCT multidisciplinary team. Assertive discharge orientation by this professional helps to reduce the occurrence of medication-related errors and complications in the treatment. In the context of the pandemic, this can reflect in the reduction of patient exposure to the hospital environment. This study shows opportunities that the pharmaceutical professional has to develop operational procedures in the HSCT area. Data analysis will be continued and outcome indicators such as post HSCT complications and overall and disease-free survival will be evaluated.

Keywords: CLINICAL PHARMACY, HOSPITAL DISCHARGE, HEMATOPOIETIC STEM CELL TRANSPLANTATION.

FIGURE 1: Model of a worksheet prepared by the pharmacist for post HSCT hospital discharge orientation.


ALBERT EINSTEIN
HOSPITAL ISRAELITA
ONCOLOGIA E HEMATOLOGIA

Patient Name

CLINICAL PHARMACY SERVICE - MEDICINES FOR HOME USE

DEC/2020

HOURS	MEDICINES	DOSE	ROUTE	DRUG INDICATION	COMMENTS
7 a.m	Pantoprazole 20mg	1 Pill	ORAL	Gastric protection	In fasting
8 a.m.	Ursodeoxycholic Acid 150mg	2 Pills	ORAL	Liver protection	
	Magnesium (Chelated) 240mg	2 Pills	ORAL	Magnesium replacement	
10 a.m	Mycophenolate Mofetil 500mg	2 Pills	ORAL	Immunosuppressive therapy	Until 12/26/2020
	Tacrolimus 1mg	2 Pills	ORAL	Immunosuppressive therapy	
2 p.m	Fluconazole 150mg	2 Pills	ORAL	Prophylactic antifungal	
	Valacyclovir 500mg	1 Pill	ORAL	Prophylactic antiviral	
4 p.m.	Sulfamethoxazole 100 mg+ Trimethoprim 160 mg cp	1 Pill	ORAL	Prophylactic antibiotic	Only on mondays wednesdays and fridays
	Magnesium (Chelated) 240mg	2 Pills	ORAL	Magnesium replacement	
	Ursodeoxycholic Acid 150mg	2 Pills	ORAL	Liver protection	
10 p.m.	Ursodeoxycholic Acid 150mg	2 Pills	ORAL	Liver protection	
	Magnésio Quelado 240mg	2 Pills	ORAL	Magnesium replacement	
	Mycophenolate Mofetil 500mg	2 Pills	ORAL	Immunosuppressive therapy	Until 12/26/2020
	Tacrolimus 1mg	2 Pills	ORAL	Immunosuppressive therapy	

ROUTINE DEVELOPMENT FOR PERSONALIZED THERAPY WITH BUSULFAN IN THE PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT POPULATION

Joice Zuckermann[1], Gabriel Giron Correa[1], Janaína Aparecida Risczik Arruda Corrrea[1], Bruno Mateus de Castro[2], Thiago Almirante Cunha[2], Alessandra Paz[1], Teresa Dalla Costa [2], Bibiana Verlindo de Araujo[2], Liane Daudt [1], Gabrielli Mottes Orlandini[1], Priscila de Oliveira da Silva[1], Jacqueline Simon[1], Letícia Silva Ribeiro[1], Leila Beltrami Moreira [2]

1 Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, Brasil
2 Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brasil

Introduction: Pharmacy, Laboratory Diagnostics and Hematology services are implementing a personalized busulfan (Bu) therapy routine for the pediatric hematopoietic stem cell transplantation (HSCT) population. Bu is an alkylating agent used in the pre-transplant conditioning to allow the engraftment of new cells and eradication of residual disease. Intravenous (IV) Bu has important pharmacokinetic variability, hepatic and neurological toxicity, and non-linear pharmacokinetics. Low exposure to Bu is associated with transplant failure. Plasma concentration measurements involve a target concentration strategy to achieve and maintain a range for an individual patient.

Objective: to describe the implementation of a routine therapeutic drug monitoring (MTF) for IV Bu in personalized therapy in the pediatric HSCT population.

Methods: The bioanalytical and validation methodology for Bu assay followed Regulamentation RDC 27/2012. High Performance Liquid Chromatography coupled with ultraviolet detection proved to be a precise and accurate method, allowing the use of clinical pharmacokinetics to adjust the administered doses, respecting the effective therapeutic margin for the patient. The routine has been developed since 2017 and it was established that, in the 1st prescription, the dose is defined according to the protocol of the Hematology Service (5mg/Kg). Then, the infusion bag is prepared and administered to the patient from 5 pm, with a total infusion time of 3 hours. Collections for BU determination are performed at times T0: 30 min before starting the busulfan infusion, at 4:30 pm; T4: 9:00 pm; T5: 22:00h; T6: 23:00h; T7: 24:00h in a lytic heparin tube. Collections are carried out by a nurse from the Protected Environment Unit (UAP). Afterwards, the samples are sent to the laboratory to be processed in the first hour of the morning. The results for calculating the area under the curve are released until 2 pm. The clinical pharmacist calculates the new dose, discusses with the team considering the patient's clinical condition, and the doctor prescribes the new dose. Collections are performed for 4 days during the Bu infusion and adjustments are made according to the calculation, patient age and conditioning protocol. Six patients had doses adjusted by custom MTF since the beginning of the drug monitoring.

Conclusion: The implementation of the MTF increases the safety and efficacy of hematopoietic stem cell transplants in a pediatric setting.

PHYSIOTHERAPY

INTENSIVE CARE IN POST HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS

Andrea Cristina Gobus Becker, Carine Lumi, Claudia Caceres Astigarraga, Cristina Ungaretti de Campos Velho, Lisandra Della Costa Rigoni, Marcio Luiz Ferreira de Camillis, Nariane Roberta de França Guimarães, Paola Vicente Timotheo, Priscila Alves Perreira Cidade, Suelen da Silva de Vargas, Renata Hoffmann Longhi

Hospital Moinhos de Vento

Introduction: Hematopoietic stem cell transplantation (HSCT) is the curative treatment option in several onco-hematological diseases. However, it has a high risk of morbidity and mortality due to clinical complicacies and their complications, often requiring intensive care. Severe graft-versus-host disease, respiratory failure, and infectious complications, such as sepsis, are some of the reasons why these patients are referred to the Intensive Care Unit (ICU). In general, a patient transferred to the ICU has a longer hospital stay and a greater chance of death.

Objective: to verify the incidence and clinical reasons for admission to the ICU in patients who underwent HSCT between 2019 and 2021. Describe the incidence and cause of mortality in this group. Methods: A retrospective cohort study, data were collected from medical records of patients who underwent transplantation between 2019 and 2021.

Results: 57 patients who underwent HSCT were analyzed, with a mean age of 50.9 years +/- 14.1. Out of these, 10 patients (17.5%) needed intensive care, with sepsis being the main cause of ICU admission (6 cases, 60%). In terms of length of stay, patients who were sent to the ICU had a median time of 69.5 days, while those who were not had a median time of 31 days. As for the outcome of patients admitted to the ICU, 6 (60%) died, while those who did not need intensive care did not die. The causes that led these patients to death were sepsis, in 4 patients (66.6%), graft-versus-host disease, in 1 patient (16.6%), and Cytomegalovirus in 1 patient (16.6%). Regarding the type of transplant performed on patients admitted to the ICU, 4 patients (40%) underwent autologous transplantation, and 6 patients (60%) underwent allogeneic transplantation. However only 1 autologous patient (10%) died, while 4 patients (40%) in the allogeneic transplant group died. Conclusion: We found that in the studied group the need for intensive care after HSCT is below the 20% described in the literature. In most cases, the reason for admission to the ICU and the cause of death was sepsis. In the group of patients who underwent allogeneic transplantation, mortality was higher when compared to patients who underwent autologous transplantation.

Keywords: hematopoietic stem cell transplantation, intensive care unit, complications, death.

NUTRITION

ANALYSIS OF THE NUTRITIONAL PROFILE OF AMBULATORY HSCT PATIENTS FOLLOWED AT THE NUTRITION DEPARTMENT IN A REFERENCE HOSPITAL IN BRAZIL

Isadora Maria Ferreira, Rita Gonçalves de Souza Simões, Maria Fernanda Vasquez Estevez, Carlos Sitta Sabaini, Pablo Hernesto Tarram Via, Paula Moreira da Silva, George Maurício Navarro Barros

Barretos Cancer Hospital

Introduction: Hematologic neoplasms are relatively common. They represent about 9% of all cancers and are the fourth most diagnosed cancer. Malnutrition is a common problem in cancer patients, having a negative impact over the course of the disease. Patients undergoing Hematopoietic Stem Cell Transplantation (HSCT) are at increased risk of malnutrition both in the pre- and post-transplant phases. In addition to the type of HSCT and conditioning regimens, treatments with immunosuppressants and antibiotics generate a series of side effects, especially metabolic and gastrointestinal. These clinical consequences have been associated with reduced quality of life and reduced response to treatment.

Objective: To assess the nutritional profile of patients seen at the HSCT department's nutrition clinic.

Materials and methods: A survey of the care indicators of the nutrition clinic was made between January 1st, 2020 and December 31st, 2020. The data collected were divided in: 1 – data of first-time consultations (FT) and 2 – data of follow-up consultations (FC). The indicators analyzed were age, sex, weight, height, body mass index, weight variation (WV), symptoms, treatment, diagnoses and dietary route used.

Results and discussion: 45 FT consultations were realized. There was a predominance in male patients (75.6%), with mean age of 43 years old, varying between 18 and 66 years old. The most frequent diagnoses were Multiple Myeloma (31.1%), followed by Hodgkin's Lymphoma (24.4%), Acute Myeloid Leukemia (11.1%), Chronic Myeloid Leukemia (8.9%) and Non-Hodgkin's Lymphoma (8.9%). Regarding the time of HSCT, most (97.8%) were pre-HSCT, 91.1% had completed the chemotherapy and 6.7% were undergoing pre-HSCT chemotherapy. As for general symptoms, 88.9% of the patients didn't present any type of complaint. In the BMI classification, overweight prevailed (40%), followed by eutrophy (28.9%), obesity (20,0%), and the smallest part of the sample (11,1%) was within malnutritional range. About WV, 91.1% didn't present significative weight loss. Most patients (88.9%) maintained oral route as a food route, and 11.1% were using oral nutritional therapy (ONT). Regarding FC, 239 consultations were realized, with the majority consisting of patients evaluated on more than one occasion. There was again predominance of male patients (66.9%), with mean age of 42 years old. The most observed diagnoses were Chronic Myeloid Leukemia (17.2%); other diagnoses (16.7%), which correspond to germ cells tumors (GCT), sickle cell anemia and aplastic anemia; Multiple Myeloma (15.5%); Acute Myeloid Leukemia (13.4%); Hodgkin's Lymphoma (13.0%); Non-Hodgkin's Lymphoma (9.2%) and Acute Lymphoid Leukemia (9.2%). Regarding HSCT moment, most patients (83.7%) were post-HSCT, 12.6% were waiting the procedure and 3.3% were undergoing chemotherapy. It's possible to notice an important change in the profile of symptoms and nutritional status of patients in FC. The percentage of patients without any type of complaint dropped to 66.5%. There were reports of lack of appetite (20.5%), dysgeusia (15.1%), nausea (14.2%), constipation (4.6%) and vomiting (4.2%) There was also a change according to the BMI, most patients were in eutrophic range (41.1%), followed by overweight (25.1%), malnutrition (23.4%) and obesity (10%). As for the type of diet, there was a predominance of oral diet supplemented with ONT (59.8%), followed by patients who maintained exclusive oral route (37.2%), and combined enteral and oral routes (2.9%). Regarding to WV, most (84.9%) didn't present significative weight loss, while only a small portion (12.1%) presented significative weight loss. Conclusion: HSCT is an aggressive treatment that compromises the nutritional status of most patients. Although patients are regularly monitored throughout the treatment by a specialized team, there is a significant increase in malnutrition rates. For this reason, it is necessary to maintain post-BMT nutritional monitoring in outpatient care, taking into account the individual needs of each patient, aiding in the recovery and/or maintenance of nutritional status and functionality.

Keywords: Nutritional Status, Neoplasms, Hematopoietic Stem Cell Transplantation.

NUTRITIONAL PROFILE AND PREVALENCE OF ASSOCIATED COMORBIDITIES IN PATIENTS UNDERGOING HEMATOPOIETIC STEM CELLS TRANSPLANTATION IN A REFERENCE UNIVERSITY HOSPITAL IN FORTALEZA/CE

Kayane Nascimento Da Silva[1]; Priscila Da Silva Mendonça[1]; João Vitor Araujo Duarte[2]; Isabella Araujo Duarte[2]; Karine Sampaio Nunes Barroso[1]; Fernando Barroso Duarte[3].

1. Hospital Universitário Walter Cantídio, Fortaleza - CE - Brasil;
2. Centro Universitário Christus, Fortaleza - CE - Brasil;
3. Hospital Universitário Walter Cantidido, Fortaleza - CE - Brasil

Introduction: Overweight and obesity are currently a serious public health problem with increasing incidence in recent years. They are risk factors for the development of other diseases and contribute to increased morbidity and mortality related to hematopoietic stem cell transplantation (HSCT), influencing the prognosis of patients. The immunosuppressive therapy used triggers metabolic changes such as sodium and fluid retention, hyperglycemia, hypertension and dyslipidemia, and also affects nutritional status.

Objectives: To assess the nutritional status and prevalence of comorbidities associated with HSCT patients.

Methodology: Data from the service indicators such as weight, height and body mass index (BMI) were used to trace the nutritional profile.

Results and discussion: The data include 82 patients, admitted to the HSCT unit from January/2019 to June/2020, adults (67%) and elderly (33%), with almost equal prevalence between the sexes, male (51.9%), mean age 45 years, younger 18 and older 69. In the stratification by disease, most Multiple Myeloma (34.6%) followed by Acute Leukemia and Lymphoma (23.4% each), while by type of autologous transplant (47 .3%) and allogeneic (52.7%). More than half were overweight (64.1%), of which 28.2% were grade I obesity and of the total number of patients only 3.9% were malnourished, according to the BMI for age according to the WHO classification. Among the comorbidities: they were hypertensive (30.9%), diabetic and with cardiac dysfunction (7.4% each), dyslipidemic (4.9%), kidney patients on dialysis and non-dialysis (3.7%) and without comorbidities (54.3%).

Conclusion: Reflecting the current nutritional epidemiological transition, there was a high prevalence of overweight and comorbidities, reinforcing the importance of nutritional monitoring during treatment in view of the adequacy of dietary factors, with a reduction in their negative impact on the development of intra and post complications transplantation and consequently better prognosis and quality of life.

Keywords: Hematopoietic stem cell transplantation. Obesity. Comorbidities. Body mass index.

ODONTOLOGY

EFFECTS OF INCREASING THE DAILY FREQUENCY OF LOW-LEVEL LASER THERAPY IN THE TREATMENT OF ORAL MUCOSITIS: CASE REPORT

Mariana Andrade Costa[1]; Vanessa Tonetto Marques Galves[2]; Thiago de Carvalho Reis[2]; Gabriela Silveira de Araujo[1]; Maria Júlia Pagliarone[1]; Lara Maria Alencar Ramos Innocentini[1]; Karina Alessandra Michelão Grecca Pieroni[1]; Ana Carolina de Jesus Vieira[1]; Camila Campos Mesquita[1]; Thalita Cristina de Mello Costa[1]; Renato Luiz Guerino Cunha[2]; Leandro Dorigan de Macedo[2]

1. Clinical Hospital of Ribeirão Preto Medical School - University of São Paulo, Ribeirão Preto - SP, Brazil
2. Faculty of Medicine of Ribeirão Preto, Clinical Hospital of Ribeirão Preto Medical School - University of São Paulo, Ribeirão Preto - SP, Brazil

Introduction: Oral mucositis (OM) is an inflammatory event that can clinically manifest as erythema and ulcers in patients undergoing chemotherapy and/or radiotherapy. In addition to compromising food and quality of life, OM can increase the susceptibility to infections. Its global incidence can reach 80% in allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT). Among the therapeutic modalities used, the low power laser (LPL) stands out for promoting analgesia, reducing inflammation and stimulating tissue regeneration. Despite the divergences in doses and wavelengths, the daily application of LPL is the most frequent common point between the different protocols.

Objective: The objective of this study is to report the therapeutic success in the treatment of early severe OM, with the performance of LPL twice a day, in a child undergoing allo-HSCT.

Case Report: A 10-year-old male patient was submitted to allo-HSCT for the treatment of recurrent Acute Lymphoblastic Leukemia type B (ALL B), the conditioning protocol started with 4 sessions of total body irradiation, followed by 2 days of Etoposide and 3 days of ATG. From the first day of conditioning, prophylactic LPL sessions (wavelength = 660 nm) were performed daily in the oral cavity to prevent OM. On D-3, the child had grade I OM (World Health Organization Scale - WHO), so an adjustment of topical medications was performed associated with the use of LPL with a wavelength of 780 nm, for therapeutic effect, maintaining daily applications. On D+4, the patient progressed with worsening of the lesions to extensive ulcers in the non-keratinized mucosa associated with severe pain, bleeding and odynophagia, grade IV (WHO). Exfoliative cytology and viral PCR tests were collected from oral lesions to rule out suspected local infection, and the results were all negative. It was decided to adjust the frequency of therapeutic LPL to twice a day. After 4 days of adjustment of the LPL protocol, there was a significant improvement in OM lesions, with a reduction in painful symptoms and bleeding. On D+11 there was complete regression of oral lesions. The biological mechanisms responsible for the clinical effects of LPL are not fully elucidated, but there is consistent evidence that modulation of inflammatory pain occurs through the regulation of levels of biochemical markers.

Conclusion: Therefore, it is believed that increasing the frequency of application of LPL for therapeutic purposes can enhance its clinical effects.

Keywords: Dentistry, Oral Mucositis, Laser

EFFICIENCY OF A PHOTOBIOMODULATION PROTOCOL IN ORAL MUCOSITIS SEVERITY IN PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION AT A NATIONAL REFERRAL HOSPITAL

Jéssika Brito da Costa[1], Ana Cristina Corrêa da Silva[1], Ana Luiza Barboza Vianna[1], Raphaella de Oliveira Pinto Caldas[1], Jorge Ferreira de Araújo[1], Luiz Alberto Valente Soares Júnior[1], Juliana Bertoldi Franco[1], Lívia Mariano[2], Vanderson Rocha[2], Leonardo Jun Otuyama[2], Bruna Del Guerra de Carvalho Moares[2], Maria Paula Siqueira de Melo Peres[1]

1 Dentistry department at Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo – HCFMUSP – São Paulo, Brazil
2 Clinical department of Hematology, Transfusion and cell Therapy at Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo – HCFMUSP - São Paulo, Brazil

Hematopoietic Stem Cell Transplantation (HSCT) is a modality that consists in intravenous infusion of hematopoietic stem cells from the patient himself (autologous) or from a donor of the same species (allogeneic). Oral mucositis (OM) is a debilitating adverse effect of HSCT usually characterized by deep, painful and irregular mouth ulcers, with photobiomodulation as one of the preventive therapeutic measures. According to a 2011 randomized clinical trial, 66.7% of patients were free of ulcers, 33.3% developed grade 2 mucositis when treated with low-level laser therapy, and none showed grade 3 or 4 mucositis. In the control group, in the absence of phtobiomodulation, 95.2% developed mucositis. The aim of the present study is to verify the efficiency of a preventive photobiomodulation protocol for OM during the conditioning and post-transplant period of HSCT. 257 patients were treated with low-level laser preventive therapy from October 2018 to May 2021 at a Clinical Cell Therapy Unit. 58 patients who underwent allogeneic and 199 autologous HSCT have received low-level laser therapy during the conditioning and post-transplant period till engraftment. In the preventive modality (absence of oral lesions and dysphagia) 2J of low-level red and infrared light were applied. After transplantation, patients who presented oral lesions received the therapeutic modality of low-level laser therapy comprising 4J of low-level red and infrared light in regions with established ulceration or erythematous lesions, along with the preventive modality (2J) in free-lesion areas. Also, when dysphagia and presence of pain complaint were identified in the oropharynx region, therapeutic protocol of 4J was applied extraorally in the cervical region. During the analyzed period, among 257 patients who underwent HSCT, 76.26% had mucositis with 38.26% of this total presenting grade 3 and 4 mucositis, and 61.73% presented grade 1 and 2 mucositis. Of all patients, 22.57% were allogeneic and 77.43% were autologous. Of allogeneic patients, 62.07% presented grade 3 and 4 mucositis, while 19.60% of autologous patients presented grade 3 and 4 mucositis. This study concluded that the preventive low-level laser therapy protocol instituted was beneficial while reducing the occurrence as well as OM gravity in HSCT patients.

Keywords: Hematopoietic Stem Cell Transplantation. Dentistry. Photobiomodulation.

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IMPACT OF ORAL MUCOSITIS IN THE OVERALL SURVIVAL OF PATIENTS UNDER HEMATOPOIETIC CELL TRANSPLANTATION: A RETROSPECTIVE STUDY

Introduction: Patients under hematopoietic cell transplantation (HCT) show several changes in the oral cavity, such as oral mucositis (OM), a painful condition that impairs the patient´s nutritional status and quality of life. The OM impact on the overall survival of HCT patients is debatable yet.

Aim: To investigate if the OM frequency and severity impact the overall survival of TCH patients.

Casuistic: Medical records (n=693) from patients enrolled at the bone marrow unit of a private hospital localized in Sao Paulo city were analyzed. The transplants were performed in the period of January 2004 to December 2019.

Methods: The following variables were collected from the medical records: related to the transplantation (type of transplantation, conditioning regimen, and time duration of hospitalization); related to the patient (sex, age, primary disease); and related to the MO (frequency, time duration, and severity degree in accordance with World Health Organization). All the patients had been examined by oral medicine professionals and received oral hygiene guidance; they were also daily examined by the dental professionals and were exposed to photobiomodulation therapy for prevention and treatment of oral mucositis. Overall survival was calculated (Kaplan-Meier curve) and the MO impact was analyzed using the bivariate and multivariate Cox proportional hazards regression.

Results: The majority was male (59.0%), with a predominant age group of 31-60 years (42.5%). The main disease groups were leukemia (28.1%), lymphoma (21.6%), and multiple myeloma (18.2%). Allogeneic TCH (57.3%) was more frequent than autologous (42.7%). Conditioning regimens were composed mainly of melphalan (30.4%), busulfan (30.6%), and total body irradiation (16.2%). From 693 patients, 138 (19.9%) did not show OM, 277 (40.0%) had OM grade 1, 194 (28.0%) grade 2, 59 (8.5%) grade 3, and 24 (3.5%) grade 4. Variables with statistical significance ($p<0.05$) in the overall survival were the type of transplantation (autologous X allogeneic), age, days of hospitalization, and OM degree. In the multivariate analysis, after model adjustments, the patients with allogenic TCH had an overall survival 2.42-fold lower than those with autologous TCH; for each year added to the patient´s age, the overall survival decreased 3%; for each day added to the patient´s hospitalization, the overall survival decreased 1%; independently from the other analyzed variables, the patients with severe OM (grades 3 and 4) had overall survival 74% lower than those without OM or with mild OM (grades 1 and 2).

Conclusion: The severe OM (grades 3 and 4) reduced significantly the overall survival of TCH patients.

Keywords: Hematopoietic cell transplantation. Oral mucositis. Overall survival.

ORAL CARE DURING ACUTE GRAFT VERSUS HOST DISEASE: THE ROLE OF MULTIMODAL DENTAL APPROACHES

Vivian Palata Viola[1], Emilze Mafra de Lima[1], Renata Freitas Varanda[1], George Mauricio Navarro Barros[2], Aline Pereira de Menezes[1], Paulo Sérgio da Silva Santos[3], Victor Tieghi Neto[1], Fábio Luiz Coracin[1]

1 Barretos Cancer Hospital, Dental Service Department
2 Barretos Cancer Hospital, Center for Stem Cell Transplantation and Cellular Therapy
3 Bauru School of Dentistry, University of Sao Paulo

A frequent complication of HSCT is acute graft-versus-host disease (aGVHD), a condition in which donor´s immune cells attack the recipient's healthy tissues and it is a transplant-related mortality condition. The objective is to present a case report of aGVHD involving the oral cavity with a focus on oral care. A 36 year-old white male patient with B-cell lymphoblastic lymphoma underwent to allogeneic hematopoietic stem cell transplantation with a sibling full match HLA and major ABO mismatch (B+ O+) donor. The conditioning regimen comprised fludarabin, melphalan and total body irradiation (200cGy). GVHD prophylaxis was cyclosporine, MMF and ATG. The patient received peripheral blood hematopoietic stem cells (6.43x106/kg). Neutrophil engraftment occured on D+15. The oral mucosa was the first site of aGVHD. Clinical manifestations began on D+27 and were round, well-defined and circumscribed lesions with a redness halo, yellowish and whitish lesions in central region of the buccal mucosa, and ulcers on the lips. Other sites of aGVHD were liver, gut and skin. On D+28 hyperkeratotic lesions of the palate in association with ulcerated lesions on the upper and lower lips caused pain and worsen oral hygiene. Oral care protocols included oral hygiene with topical chlorhexidine 0,12% rinse and topical clobetasol propionate 0,05%, 3 times a day. Photodynamic therapy with low-level laser with 660nm, P=100mW, E=3J was performed for ulcers relief and pain control. In conclusion, oral care protocols improved the quality of life since oral diagnosis of aGVHD, reduced pain morbidity and prevented the worsening of the oral condition.

Keywords: hematopoietic stem cell transplantation, acute oral graft vs host disease, oral care, low-level light therapy.

ORAL LESIONS ASSOCIATED WITH ACUTE GRAFT-VERSUS-HOST DISEASE WITH HISTOPATHOLOGICAL DIAGNOSIS

Gabriela Silveira de Araujo[1], Thiago de Carvalho Reis[2]; Vanessa Tonetto Marques Galves[2]; Mariana Andrade da Costa[2]; Tatiane Cristina Ferrari[3]; Cristina Bueno Brandão[3]; Thalita Cristina de Mello Costa[3]; Renato Luiz Guerino Cunha[1;2]; Maria Julia Pagliarone[2]; Ana Carolina de Jesus Vieira[3]; Camila Campos Mesquita[3]; Leandro Dorigan de Macedo[2;3]

1 Faculty of Medicine of Ribeirão Preto, University of São Paulo, Ribeirão Preto, São Paulo, Brazil
2 Blood Center of the Faculty of Medicine of Ribeirão Preto, University of São Paulo, Ribeirão Preto, São Paulo, Brazil
3 Clinical Hospital of the Faculty of Medicine of Ribeirão Preto, University of São Paulo, Ribeirão Preto, São Paulo, Brazil

Introduction: Acute graft-versus-host disease (GVHDa) is one of the main complications of allogeneic hematopoietic stem cell transplantation (HSCT-alo). Immunopathophysiology is mediated by an inflammatory reaction caused by the activation of donor T cells inserted into the hematopoietic system of a non-fully compatible receiver. The incidence ranges from 30% to 50%, the most important risk factors are incompatibility of the human leukocyte antigen (HLA) system, gender and age difference between donor and receiver, intensity of conditioning regimen, ineffective prophylaxis and peripheral source of stem cells. The most common target organs that make up the classification systems are the skin, liver and intestine. Involvement of the oral cavity is poorly described and often confused with oral mucositis (OM) caused by conditioning.

Objective: The aim of this study was to describe the involvement of the oral mucosa by GVHDa in a patient undergoing HSCT-alo.

Case Report: A 57-year-old male patient with a previous diagnosis of myeloblastic leukemia, intermediate risk, undergoing an alo-HSCT, male akin donor, HLA identical (10/10), ABO isogroup, bone marrow source, FLUMEL 140 and conditioning GVHD prophylaxis with cyclosporine and methotrexate. She presented OM grade IV (WHO) on D+9, resolved on D+15. On D+ 19, patient had neutrophilic grafts and skin lesions, which were biopsied with a diagnosis of grade IV GVHDa. Standard treatment with corticosteroids was started, with partial clinical response. On D+37, he reported burning in the oral mucosa and on D+41 he developed extensive ulcerations in the buccal mucosa, lingual belly and lower lip. Oral lesions were submitted to biopsies that ruled out viral or fungal infection and confirmed a histological pattern compatible with grade III GVHDa. After adjusting the treatment for refractory GVHDa (anti-thymuglobulin and mesenchymal cells), the patient evolved with complete resolution of the oral lesions. However, he died on D+69 after relapse of the underlying disease.

Final Considerations: This case report presents the importance of histological evaluation for GVHDa in the mouth, especially in late inflammatory processes for the development of OM.

Keywords: Hematopoietic Stem Cell Transplantation. Rejection. Neoplasm.

ORAL MUCORMYCOSIS IN PATIENT POST ALLOGEN TRANSPLANTATION

Maria Julia Pagliarone[1]; Thiago de Carvalho Reis[1,2]; Vanessa Tonetto Marques[1,2]; Mariana Andrade Costa[1]; Gabriela Silveira de Araujo[1]; Renato Luiz Guerino Cunha[1,2]; Thalita Cristina de Mello Costa[1]; Ana Carolina de Jesus Vieira[1]; Camila Campos Mesquita[1]; Karina Alessandra Michelão Grecca Pieroni[1]; Cristiane Aparecida Nogueira Bataglion[1]; Leandro Dorigan de Macedo[1,2].

1- University Hospital of the Ribeirão Preto Medical School, Ribeirão Preto, São Paulo, Brazil.
2- Ribeirão Preto Medical School (University of São Paulo), Ribeirão Preto, São Paulo, Brazil.

Introduction: Despite its low incidence (0.6%), mucormycosis is one of the invasive fungal infections with the highest mortality rate in allogeneic hematopoietic stem cell transplantation (HSCT-allo). The main risk factor is chronic immunosuppression and geographic location of risk for the disease. Early diagnosis and treatment are essential for successful treatment. The most common involvement is the rhinocerebral and the manifestation in the oral cavity is uncommon.

Objective: to report a case of mucormycosis with involvement of the tongue and sinuses in a patient after HSCT-allo.

Case report: Patient, 56 years old, male, post HSCT-related allo, HLA identical, source of peripheral blood cells, with indication for HSCT due to Chronic Myeloid Leukemia refractory to the use of TKIs. On day 30 after HSCT, the patient presented macular skin rash, evolving with elevated transaminases, Gamma GT and phosphatase on D+38. One day later, he progressed with inappetence, abdominal pain and diarrhea, and hospitalization was indicated. Skin and bowel biopsies confirmed acute Graft-versus-Host Disease (GVHD) with a MAGIC grade IV (severe) rating. Treatment with methylprednisone 1mg/kg/day was started. Due to the refractoriness to the use of corticosteroids, another 3 lines of treatment were instituted during the hospital stay, including ATG, basiliximab and infusion of mesenchymal cells, without objective response. On D+57, a diffuse white plaque-like lesion was identified in the tongue, with hyperplasia of filiform papillae and depapillary central region. Material was collected for cytology, fungal culture, viral PCRs and incisional biopsy. The patient evolved with paresthesia in the bilateral inframalar region, anosmia and taste alteration. On day 65 after HSCT, necrotic lesions were identified in the nasal region and vallecula. Chest tomography showed pulmonary nodules with a ground-glass halo and opacities. The diagnosis of mucormycosis was made due to positive culture for Rhizopus sp., both in material collected from the tongue and in necrotic lesions of the nasopharynx. Histopathology showed irregular acanthosis, focal parakeratosis, fibrous connective tissue without inflammatory infiltrate. Therapy was started with lipid complex amphotericin and surgical debridement in the nasal cavity on day 67 after HSCT. The patient progressed with clinical worsening, hemodynamic instability, pancytopenia and septic shock, dying on day 70 after HSCT. This case shows the importance of multidisciplinary follow-up and early collection of material for the diagnosis of infectious complications in an atypical location, especially in post-transplant patients undergoing immunosuppressive treatment for GVHD.

Keywords: Graft vs Host Disease. Bone Marrow Transplantation Dentistry. Opportunistic Infections. Mucormycosis.

PHOTOBIOMODULATION WITH LOW POTENCY LASERTHERAPY IN THE PREVENTION OF ORAL MUCOSITIS IN ONCOLOGICAL PATIENTS SUBMITTED TO HEMATOPOIETIC STEM CELL TRANSPLANTATION: PROTOCOLS USED

Flávia Marília Azeredo de Oliveira[1], Fernanda Araújo de Oliveira[1]; Anya Pimentel Gomes Fernandes Vieira Meyer[2]; Cainã Azeredo Fernandes Barreira [2] Talita Vaz de Queiroz[1], Geisa Ferreira Gomes Peixoto[1], Beatriz Stela Gomes de Souza Pitombeira Araújo[1], Karine Sampaio Nunes Barroso[1], Lívia Andrade Gurgel, João Paulo Vasconcelos Leitão[1], Ana Carolina dos Santos Rodrigues[1]

1 Hospital Regional da Unimed
2 Centro Universitário Christus

Introduction: Oral mucositis is one of the complications with the greatest impact on the patient during hematopoietic stem cell transplantation. It can manifest itself in 75-80% of patients if preventive measures are not taken. Although it is already established that low power laser photobiomodulation benefits patients, there is still no standard protocol to be followed by dental teams.

Objective: the purpose of this study is to investigate the effectiveness of a photobiomodulation protocol with low-level laser therapy in the prevention of oral mucositis in transplanted hemato-oncology patients.

Method: A documentary analysis was performed of the care protocols of 136 patients who underwent hematopoietic stem cell transplantation, and also underwent photobiomodulation with low-level laser therapy for the prevention of oral mucositis, evaluating the presence or absence of oral mucositis. The photobiomodulation protocol had the following parameters: red laser diode, wavelength 660 nanometers, 100 mW output power, energy density 35 joules/cm^2, continuous mode, 1 joules of energy per dot, output spot area with a diameter of 0.028cm2, around 78 intraoral points in the deep sulcus regions, buccal mucosa, tongue floor, tongue belly, lateral tongue edges, tongue dorsum, palate, labial commissures, upper and lower lip. Daily sessions, starting on the first day of the patient's chemotherapy conditioning, extending until the second day after the infusion of hematopoietic stem cells (D+2). The data obtained in the research will be organized according to the objective of the study and analyzed with the support of the STATA 14.0 statistical program (Stata® Statistics Package, Stata for Windows).

Results: The total number of transplants in the research was 136 (100%), however, 7 (5.15%) were allogeneic and 129 (94.85%) were autologous. Allogeneic HSCT were excluded for not receiving photobiomodulation until D+2. Of the remaining 129 (100%) patients, 19 (14.72%) were affected by oral mucositis, however, it did not progress beyond grade III (WHO classification).

Conclusion: The protocol used proved to be effective, since the percentage of patients who presented oral mucositis was much lower than that found in the literature. The results showed improvements in patients' well-being, in addition to minimizing the costs of their permanence in hospital care.

Descriptors: Oral Mucositis; Bone marrow cell transplantation; Low-intensity light therapy

PROTOCOL FOR THE PREVENTION AND MANAGEMENT OF HSCT-ASSOCIATED ORAL MUCOSITIS - EXPERIENCE OF THE HOSPITAL DENTISTRY SERVICE IN A QUATERNARY HOSPITAL IN SÃO PAULO

Ana Luiza Barboza Vianna[1], Raphaella de Oliveira Pinto Caldas[1], Ana Cristina Corrêa da Silva[1], Jéssika Brito da Costa[1], Camila Panisello Ferreira[1], Jorge Ferreira de Araújo[1], Juliana Bertoldi Franco[1], Lívia Mariano[2], Vanderson Rocha[2], Luiz Alberto Valente Soares Júnior[1]

1 Divisão de Odontologia, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo – HCFMUSP
2 Unidade clínica de terapia celular Serviço de hematologia, hemoterapia e terapia celular do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo – HCFMUSP

Introduction: Mucositis is one of the most common complications of antineoplastic treatment, being an inflammatory toxic reaction and limiting dose that affects the entire gastrointestinal tract, resulting from exposure to chemotherapy agents and radiotherapy. Oral mucositis (OM) is one of the most frequent changes in the oral cavity in patients undergoing Hematopoietic Stem Cell Transplantation (HSCT), which can reach significant levels of pain and compromise nutrition, in addition to enabling the development of systemic infections. Thus, low-level laser therapy stands out as an effective alternative in the prevention and treatment of OM, reducing its incidence and presenting itself as a non-traumatic, low-cost treatment with good results described in the literature.

Objective: This analysis aims to present the protocol for the prevention and treatment of OM in patients undergoing HSCT in a large hospital in the city of São Paulo.

Methods: In the pre-HSCT phase, dental surgeon (DS) plays an important role in the elimination of active infectious foci of dental origin. During the conditioning and HSCT period, the DS performs daily clinical evaluation and intra and extraoral laser therapy application 5 times a week, at 650nm wavelength, 100mW power and 1-2J/cm^2 energy. In cases of conditioning with Melphalan, there is an indication to perform cryotherapy before, during and after the HSC infusion. OM is classified by the World Health Organization, into different degrees of mucositis (from 0 to 4) according to the appearance of erythema/ulcer in the oral mucosa and changes in diet (solid/pasty/liquid). For patients with OM grade 3 and 4, there is an indication for topical treatment with 0.5% Dexamethasone elixir 3 to 4 times a day. In addition, for lip lubrication, use of 100% HPA Lanolin and salivary substitute for xerostomia/hyposalivation is indicated.

Results: The prevention and treatment of OM must be multi-professional and the DS plays a fundamental role in this context, monitoring the patient in all phases of HSCT (before the beginning of chemotherapy conditioning and during the HSCT procedure).

Conclusion: The predictive assessment of the incidence of OM is important for patient follow-up, as the professional can guide preventive treatment, as well as prevent episodes of bacteremia originating from the oral cavity. Therefore, considering the high incidence of OM and its negative impact on the morbidity and quality of life of patients undergoing HSCT, it is essential to establish a prevention and treatment protocol for OM.

SQUAMOUS CELL CARCINOMA OF THE LIP IN FANCONI ANEMIA: CASE REPORT

Angela Maira Guimarães[1]; Melissa Rodrigues De Araujo[2]; Cassius C Torres-Pereira[2]; Priscila Queiroz Mattos Da Silva[1].

1 Complexo Hospital de Clínicas UFPR, Curitiba, Brasil
2 Universidade Federal do Paraná, Curitiba, Brasil
3 Universidade Federal do Paraná, Curitiba, Brasil
4 Complexo Hospital de Clínicas UFPR, Curitiba, Brasil

a) **Introduction**: Fanconi anemia is a rare autosomal recessive disease, characterized by chromosomal instability and greater predisposition to malignant diseases, especially acute myeloid leukemia and solid tumors of the head and neck. In the present report, this is a male patient, 19 years old, diagnosed with Fanconi Anemia at the age of 8 and submitted to haploidentical hematopoietic stem cell transplantation (HSCT) at age 13, who developed oral lichenoid lesions, erythroplasia and ulcers, compatible with chronic graft-versus-host disease (cGVHD).

b) **Objectives**: we seek to report a case of a patient who has already been followed up with the Hospital's multidisciplinary team for about 9 years, a scenario that allowed for a very accurate care, especially with regard to the evolution of lesions in the mouth. It was only with this constant and diligent care that it was possible to identify a lesion that clashed with those that already presented themselves normally.

c) **Methodology**: The patient's lesions were followed up through clinical and cytological evaluations during a 9-year period.

d) **Result**: In the follow-up period, it was noted that the whitish plaque on the lower lip evolved in size to an exophytic and ulcerated lesion. Therefore, an incisional biopsy was performed, and the histological analysis was compatible with squamous cell carcinoma. Considering this situation, the patient underwent surgery with safety margins and cervical lymphadenectomy.

e) **Conclusions**: The case reported shows that patients with Fanconi anemia, whether or not undergoing HSCT, should be carefully and constantly monitored in relation to the development of oral malignancies, especially when it comes to oral lesions of cGVHD since, as seen in the case under discussion, they can evolve rapidly.

THE ROLE OF THE DENTAL SURGEON IN THE DIAGNOSIS AND EARLY TREATMENT OF ORAL COMPLICATIONS RELATED TO HEMATOPOIETIC STEM CELLS TRANSPLANTATION: A CASE REPORT

Thiago de Carvalho Reis[1 2], Maria Julia Pagliarone[2], Thalita Cristina de Mello Costa[1 2], Mariana Andrade Costa[2], Vanessa Tonetto Marques[1 2], Gabriela Silveira de Araujo[2], Renato Luiz Guerino Cunha[1 2], Adriano Tadeu Dias Marangoni[2], Ana Carolina de Jesus Vieira[2], Camila Campos Mesquita[2], Leandro Dorigan de Macedo[1 2]

1- Faculty of Medicine of Ribeirão Preto (University of São Paulo)
2- Clinics Hospital of Ribeirão Preto (University of São Paulo)

Introduction: The presence of a multidisciplinary team in the care of patients undergoing hematopoietic stem cell transplantation (HSCT) has been identified as fundamental in reducing complications, hospitalization costs and increasing the quality of life of patients, although it does not occur in many Brazilian transplant centers

Objective: To report the role of the dental surgeon in the diagnosis and early treatment of oral complications in a patient with graft-versus-host disease.

Case report: A 25-year-old male patient submitted to HLA-identical allogeneic HSCT for the treatment of severe aplastic anemia, presented on day 66 post-HSCT acneiform skin lesions, and an anatomopathological diagnosis of acute graft-versus-host disease (GVHD) was made. On day 79, post-HSCT patient presented elevated liver enzymes and skin keratosis pilaris, with viral and drug causes being ruled out. Treatment with systemic corticosteroids was started on day 87, the same day that oral lesions were observed. Lesions initially presented with a bilateral punctiform keratotic aspect in the buccal mucosa and palate. After 7 days of evolution, the lesions started to present characteristics of non-scraping white plaques involving more than 50% of the oral mucosa surface (labial mucosa, cheek mucosa, palate, dorsum and belly of the tongue). At the time, a 0.04mg/ml dexamethasone mouthwash was associated with the current systemic immunosuppressive treatment, but without significant improvement of the lesions, which showed a characteristic lichenoid pattern of chronic GVHD only on day 130 (45 days after the initial signs). At this time, the diagnosis of overlap syndrome was made. During the whole period, the patient had no oral complaints. On day 132, during the reduction of systemic immunosuppression, the patient developed an oral ulcer on the hard palate measuring approximately 1.5 cm in its largest diameter. Material from the lesion was collected by scraping and sent to PCR, which identified cytomegalovirus disease. Treatment was performed with valganciclovir 900mg every 12 hours for 3 weeks and topical immunosuppressant was discontinued. The patient progressed with resolution of the oral ulcer and worsening of oral GVHD with progression from score 0 to score 1 (burning in the mucosa, sensation of roughness in the mouth and dysgeusia) and progression of the skin lesions. A 0.05% clobetasol mouthwash was started 3x a day. Additionally, the dose of systemic corticosteroids was increased and associated ruxolitinib. Gradual improvement of symptoms and oral lesions was observed. Currently, the patient has controlled GVHD (without topical oral treatment for more than 30 days, without the use of systemic corticosteroids and in use of ruxolitinib and sirolimus).

Conclusions: The presence of a dentist in the transplant team can improve the quality of life and optimize the use of resources with the early diagnosis of complications in transplant patients.

Keywords: Graft vs Host Disease, Bone Marrow Transplantation, Dentistry, Opportunistic Infections.

Funding: Coordination for the Improvement of Higher Education Personnel (CAPES)

PSYCHOLOGY

ONLINE PSYCHOTHERAPEUTIC GROUPS IN A BONE MARROW TRANSPLANTATION UNIT

Érika Arantes de Oliveira-Cardoso, Denise Maria Vendramini, Ana Luísa Carvalho Guimarães, Juliana Tomé Garcia, Ana Clara Buson de Carvalho, Matheus Issa Melchior, Aline Guerrieri Accoroni, Hellen Cristina Ramos Queiros, Maria Carolina de Oliveira, Renato Luiz Guerino Cunha, Manoel Antônio dos Santos

FFCLRP-USP, RIBEIRÃO PRETO - SP - BRASIL; 2. HCFMRP-USP, RIBEIRÃO PRETO - SP - BRASIL.

Introduction: This study is justified by the need to understand the psychological practice in response to the new coronavirus pandemic (COVID-19), analyzing the implementation of online therapeutic groups offered by the psychology team in a Bone Marrow Transplant Unit of. Objective: To understand the benefits and limits of the implemented interventions, according to the participants' perceptions about the activities.

Method: this is a qualitative, cross-sectional and descriptive-exploratory study. The meetings were transcribed and the material was submitted to a qualitative analysis, through reflective thematic content analysis. For the implementation of the group, patients who were in post-transplant outpatient follow-up were invited, and 17 confirmations of interest were obtained, with five patients in each group. A WhatsApp group was created with these patients, plus three psychologists and two psychology interns. At first, a video and a manual on how to access Google Meets (platform chosen for the meetings) were sent. The meetings took place over an hour and were coordinated by two psychologists and co-coordinated by two interns. In a one-year period, from August 2020 to August 2021, 39 meetings were held, with patients from the Southeast, South, Midwest and Northeast of Brazil.

Results: Five categories were organized: a) Living with the pandemic: fear of being contaminated; anxiety about the bombardment of news; delayed medical procedures; comparison of care needed during the transplant period and those needed to avoid contamination by Covid; b) Changes in their lives after transplantation: physical changes that caused some limitations in the body; c) Hospitalization period: feeling of gratitude for the professionals who were involved in this process and all the care provided; the importance of humanized treatment; changes in family dynamics; the importance of having a good support network; d) The importance of small habits that help in well-being and mental health, from singing to manual activities; e) Importance of the psychology group: space to talk about these aspects, share experiences and listen to different points of view and experiences.

Conclusions: The group that was initially a proposal to talk about the impact of the pandemic proved to be a possibility for broader emotional support. Despite the difficulties reported, the change in routine and concerns about the continuity of treatment due to the suspension of hospital monitoring, the participants had resources to deal with this situation and made use of their previous experience of intensive care and isolation at the time of the transplant. It is concluded that online groups are configured as an effective alternative to offer psychological care and mutual help, favoring resources for comfort, tension relief and maintenance of the support network in times of social distance.

Keywords: psychotherapeutic group, patients, bone marrow transplant

SOCIAL SERVICE

PERFORMANCE OF THE SOCIAL ASSISTANT IN THE BONE MARROW TRANSPLANTATION SERVICE OF THE WALTER CANTÍDIO UNIVERSITY HOSPITAL (HUWC) IN A PANDEMIC PERIOD - AN EXPERIENCE REPORT

Victoria de Padua Moreira; Ana Caroline Freitas do Monte e Silva Forte

Hospital Universitário Walter Cantídio, Fortaleza, Brasil

Introduction: On March 11, 2020 the World Health Organization decreed the coronavirus pandemic, the challenges faced by health with the growing number of cases, the risk of contamination, the lack of supplies and the need to reorganize work protocols, however, when we turn our gaze to the virus, we cannot forget the challenges encountered by those services that have endeavored to maintain the follow-up of patients treated for other illnesses. Objective: This paper discusses the role of the social worker in the bone marrow transplant service, with the aim of answering the following question: How did the social service work with the Bone Marrow Transplant patients at the University Hospital Walter Cantídio, based on the changes caused by the COVID-19 pandemic?

Method: This research is of a qualitative nature, based on the experiences lived in the multidisciplinary transplant residency in the aforementioned hospital. In order to promote our analysis, a bibliographic study was also carried out.

Results: Bone Marrow Transplant is a complex procedure, in which the patient and their support network need to be mobilized due to the procedure. As well as, they must be inserted in a favorable socioeconomic context, within the possibilities of our society. This reality presents challenges in itself, as most patients and their families do not have access to social minimums, and the situation tends to become more acute amidst the COVID-19 pandemic, as this exposes the imminent crisis of public health services and social protection. Given this reality, the work of the multidisciplinary care team has undergone changes in its daily work, in order to preserve and promote the health of its patients. Among some of the changes that impacted the work of the social worker are the decrease in attendance at the BMT outpatient clinic; the need to adapt to forms of access to social protection services, such as public defenders, INSS, CRAS and Non-Governmental Institutions; the interruption of multidisciplinary meetings, among others. However, even with the changes brought about by the new Coronavirus, especially with regard to social distancing, the social service has reinvented itself with the intention and attempt to continue carrying out its activities and the social monitoring of patients. Conclusions: The social worker, as a member of the multidisciplinary team responsible for monitoring pre and post BMT patients, plays a fundamental role in identifying, guiding and forwarding socioeconomic issues that may have an impact on the patient's treatment. Even with the COVID-19 pandemic and changes in the work routine, the professional, based on his theoretical and practical-operational contribution, has the ability to adapt to the new context and keep acting focused on guaranteeing rights.

SOCIOECONOMIC PROFILE OF USERS OF THE BONE MARROW TRANSPLANTATION SERVICE SERVED BY THE WALTER CANTÍDIO UNIVERSITY HOSPITAL (HUWC) SOCIAL SERVICE

Ana Caroline Freitas do Monte e Silva Forte, Naiane Zilma da Silva,Victoria de Pádua Moreira

Hospital Universitário Walter Cantídio

Introduction: BMT is a complex treatment that encompasses several factors and the involvement of a multidisciplinary team to help the user to achieve success in their treatment. The study of the social reality of users of this service is part of the work developed by the social service, in order to identify the social determinants of the health-disease process. Objective: The present work is the partial result of an ongoing research whose objective is to identify the social and economic profile of the population served, in order to answer the following question: what is the socioeconomic profile of the users of the Bone Marrow Transplant service assisted by social service at the Walter Cantídio University Hospital?

Casuistry: The weightings performed derive from the social interview instrument, applied by social workers from the Bone Marrow Transplant Sector to 153 patients treated between January 2019 and April 2021. This study was submitted and approved by the Ethics Committee HUWC to carry out the survey. Method: To answer the questions raised, a social quantitative and qualitative research of documentary type was carried out. For the construction of the socioeconomic profile, six social indicators were evidenced, namely: marital status, race/ethnicity, religion, education, occupation, place of residence and family income. Results: We will list below the most expressive numbers of the survey. As results obtained from 153 users, we can highlight: regarding the criterion, marital status, about 43% reported being married; regarding race/ethnicity, 37% declared themselves brown; with regard to religion, 42.5% call themselves Catholic, following a national trend; regarding education, 31% do not have completed elementary school; with regard to occupation, 23% declared they were farmers, which may express a correlation between this public and exposure to pesticides, establishing an important public health problem; in relation to the place of residence, more than half, 52%, come from the interior of the State of Ceará, which can represent a challenge for the user in carrying out their treatment outside their home; with regard to family income, 47% declared family income up to one minimum wage, which expresses that almost half of these users have minimum subsistence conditions for their maintenance and that of their family.

Conclusions: Based on the above results, it is possible to infer that the indicators reflect the living conditions of users undergoing treatment, the social reality and the challenges they are subjected to. Therefore, we believe that the issue raised can be used as a stimulus for academic discussion and by society in order to think about political strategies for the insertion of transplant recipients in social and citizenship policies, contributing to a practice of comprehensive care, anchored in the principles of SUS.

THE CHALLENGES OF INTERVENTION OF SOCIAL SERVICE IN HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) PROCESSES IN THE SCENARIO OF PANDEMIC CHAOS OF COVID-19: A PROPOSAL FOR METHODOLOGICAL REORGANIZATION

Rafael Terezio Muzi[1]; Margareth Vianna de Souza[2]; Geneviève Lopes Pedebos[2]; Helena Raquel Guedes[1].

1. CHC/UFPR, Curitiba - PR - Brasil;
2. INCA/CEMO, Rio De Janeiro - RJ - Brasil.

Introduction: The health challenge caused by the COVID-19 pandemic has had consequences in all spheres of society, as well as in HSCT processes. In Brazil, under a context of cutting social rights and precariousing public services, the difficulties faced by patients and family members in the process of performing HSCT are accentuated. The increase in unemployment and the impoverishment of the population, the physical and psychological sequelae resulting from the pandemic, the death off family members, the budget reduction in public and social policies and the growing demand for social security and social benefits, as well as phenomena with the loss of coverage of private plans of the public health system and greater demand to the public health system are some of the elements that bring back to the work of social workers inserted inthe multidisciplinary teams of transplant centers. Given the need for the readjustment of the multidisciplinar work in view of the reality presented and assuming the ethical-political position that falls to it, the Social Service teams of three Brazilian reference centers sought to discuss alternatives and initiatives to improve work processes that produce positive impacts on patient care.

Objective: To discuss the reality posed in the Scenario of HSCT in Brazil resulting from the social context of pandemic crisis, from the methodological reorganization of the Social Service teams.

Method: Multicentric articulation in the format of virtual meetings, under the themes "care to families in the pandemic context" and "new challenges in the contexts of HSCT"; documentary analysis for data collection on the number of transplants performed in the period from March 2020 to June 2021, as well as identification of the social demands prevalent in this context and alternative intervention.

Results: The abstract presents the partial results of the proposed articulation, based on the opinion held inthe debates and the data collection inprogress. The systematization of the data and the final presentation will take place in the form of an article. The results will be presented by absolute frequencies and percentages by means of tables or graphs.

Conclusions: The search for articulated solutions among social service professionals in reference centers constitutes an innovative format in the search for better technical-operative interventions within the TCHT in Brazil. The accumulated experiences and exchanges presuppose improving technical intervention in the context of calamities.

Keywords: Social Work. Hematopoietic Stem Cell Transplantation. COVID-19. Technical-operational instruments.

OCCUPATIONAL THERAPY

ADULT HEMATOPOIETIC STEM CELL TRANSPLANTAT AND OCCUPATIONAL THERAPY: USE OF DRAWING AS AN EXPRESSIVE AND SYMBOLIC TOOL

Marina Garrido Souza, Paula Moreira da Silva Sabaini, Carlos Sitta Sabaini, Pablo Hernesto Tarran Via, Maria Fernanda Vasques Esteves, Neysimelia Costa Villela, George Maurício Navarro Barros

1 Barretos Cancer Hospital

Introduction: Hematopoietic stem cell transplantation (HSCT) is a possible treatment for some adult malignant neoplasms and hematologic diseases, marked by clinical complications, long periods of routine break, communication and expression changes. Drawing is a form of language used since childhood, registering moments and allowing reflections through which the unconscious manifests itself, and can be used as a technique, which the person reflects the impression of the "whole" of him/herself.

Objective: To report the drawing experience as a HSCT unit resource, analyzing the impact of hospitalization during the transplantation process.

Methods: Descriptive-analytical and retrospective study; including visits to adult inpatient HSCT unit at an oncology hospital and semi-structured drawings analysis from June 2020 to July 2021.

The drawings used were three trees without leaves, symbolizing three moments of HSCT: 1 – before HSCT; 2 – after hematopoietic stem cell infusion; 3 – at hospital discharge. Data was collected from occupational therapy (OT) register and medical records: age, diagnosis, type of transplant, number of hospitalization days and subsequent analysis of the drawings - colors and color intensity.

Results: The study was carried out with 75 patients, of whom 62 completed the activities. The mean age was 40 years old, and age ranged from 18 to 69 years old; there was an autologous transplant predominance, and Acute Myeloid Leukemia and Hodgkin's Lymphoma were the main diagnoses. During this period, OT performed approximately 2 to 4 visits/week/patient. About the first tree, 100% of the patients reported their expectations regarding the treatment, and their fear and anxiety feelings; the second tree was painted mostly on day 4. Among them, about 92% were hopeful during this period, but 9% reported fear and pain. Thus, the second tree exhibited darker tones and an absence of color diversity, remaining in light and low intensity tones; suggesting the expression of the difficult moment, meeting the expressed fear. In the third tree, 90% of the patients reported their plans, which were expressed in diverse colors and strong tones, suggesting security and the power/control feeling; the other 10% did not paint the third tree due to their own choice, death during treatment or hospital transfer.

Conclusion: Drawing is an expressive resource, but still little used as a form of language expression, little valued since it is pre-judged as a child resource. However, the literature brings drawing to adults as an expressive resource, benefiting from traumatic processes that involve rupture and loss. In this way, TO works to facilitate this expression and language, rescuing moments of pleasure, self-esteem, intrapersonal and interpersonal relationships.

Keywords: Occupational Therapy. Hematopoietic stem cell transplantation. Drawing.

LUDIC APPROACH AS AN OCCUPATIONAL THERAPY STRATEGY IN THE MANAGEMENT OF HOSPITALIZED CHILDREN'S ANXIETY IN FRONT OF PROCEDURES RELATED TO THE HEMATOPOIETIC STEM CELL TRANSPLANTATION PROCESS

Kimberly Camargo de Oliveira[1], Dayane Regina dos Santos[1,2]

1. Departamento de Terapia Ocupacional da Universidade Federal do Paraná, Curitiba, Brasil
2. Complexo Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, Brasil

Introduction: Hematopoietic stem cell transplantation (HSCT) has become an alternative for patients who do not receive a good prognosis from conventional treatment of oncological and hematological diseases. Children undergoing HSCT start to experience several changes and disruptions in their occupations and roles. These changes can negatively impact neuropsychomotor development and the child's player occupational role and generate adverse reactions, resulting in the difficulty in adapting to the hospital environment and routines and in the child's non-collaboration with the team during the procedures. The use of the playful approach and parental guidance on it as a form of behavioral management, as well as the encouragement of the child's player occupational role, promote the favoring of the treatment, as they facilitate the identification of fears, the elaboration of an understanding of the hospitalization process, in addition to making the hospital stay less painful and adverse in order to make it a more humanized space with quality of life.

Objective: To report the playful intervention process performed by Occupational Therapy (OT) in an HSCT service in southern Brazil.

Methodology: Experience report on the playful approach as a OT intervention strategy. A 3-year-old male patient hospitalized for a related HSCT compatible for Sickle Cell Anemia. The hospital stay was 36 days, with hospital discharge on D+26. The child remained most of the time confined to his room, having difficulty in adapting to the hospital routine, demonstrating irritability and agitation that was difficult to control during the procedures with the team and companion. In all, 23 occupational therapy consultations were carried out, aiming to enrich the hospital routine and promote neuropsychomotor development, the performance of the the child's player occupational role and the understanding of the procedures performed to better adapt to the context. During the consultations, a playful approach was used with the child, favoring the understanding of the aspects experienced during hospitalization and parental guidance on the use of this approach in behavioral management during the procedures.

Results: There was a greater identification of the child about their experiences, through activities that stimulate the understanding of the importance of treatment and procedures performed by the health team. Furthermore, it was verified the importance of parental guidance on the use of a playful approach to favor the child's collaboration, also implying a significant gain in the bond with the team and family members and behavioral improvement in the acceptance of routine hospital procedures such as: medication, food, use of mask and room restriction.

Conclusion: The playful approach favors the performance of roles and the main occupation of the child, contributes to reducing stress and enriching the hospital routine and helps in understanding and coping with the child in the face of adverse experiences during hospitalization for HSCT.

Keywords: Occupational therapy. Hospitalized child. Hematopoietic stem cell transplantation. Play and playthings.

OTHERS

AFFECTIVE HEALTH RECORD IN BONE MARROW TRANSPLANTATION: STRATEGY FOR HUMANIZATION AND PERSONALIZATION OF CARE

Dayane Regina dos Santos[1,2], Flávia Yasmin de Oliveira Cardoso[2], Natasha Ramos Palma Domingues[2], Kelly Cristina Emi Shimizu[1], Lara Cássia Silva Sandri[1]

1. Complexo Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, Brasil
2. Departamento de Terapia Ocupacional da Universidade Federal do Paraná, Curitiba, Brasil

Introduction: The hematopoietic stem cell transplantation (HSCT), also known as bone marrow transplantation (BMT), is a high complexity treatment which requires specialized care from professionals from different areas inserted in the same context. The HSCT process demands a long hospitalization period and the experience of countless restrictions, so that the patient sees themselves away from their family, their routine, and their meaningful occupations. In this context, strategies for care that consider the patient beyond their diagnosis and clinical conditions are fundamental in the attempt of promoting humanized attention. The affective health record, different from clinical health records, brings individualized information about patients, covering their personality, preferences, and routine pre-hospitalization.

Objective: To report the experience of implementing the Affective Health Record in a HSCT unit of a public hospital in the South of Brazil, as a strategy for humanization and personalization of care.

Methodology: Report of experience about the implementation and development of affective health records adult and pediatric patients hospitalized for HSCT. The idea arose from interdisciplinary exchange between the Occupational Therapy and Nursing teams, in which the importance of the strategy and the personal information that should be in the Affective Health Record were defined. Then, occupational therapists developed the layout and proposed the confection of the Affective Health Record during their evaluation process that usually takes place up to three days after a patient hospitalization. Personal information such as "Who am I?" "How do I like to be called?" "Favorite food" "What I most like to do" "What kind of music I like" "About me" "Pets" were collected from patients and companions. After the appointment, the information was passed to the computer, in which the personalized record was elaborated, with the patient's color of preference and photo provided by them or their companion (in case they agreed with it). Next, the Affective Health Record was attached to their room door, so all professionals could get to know the patient.

Results: The team recognizes that the action allowed greater bond and communication with the patient and the companion, as well as collaborated to the accomplishment of other humanization actions in the sector. It was possible to observe the patients' satisfaction in performing the activity, as their preferences were validated and considered during the hospitalization process.

Conclusion: The affective health record can contribute to the strengthening of the bond and better communication between team and patient, as it values the life history, considering the singularity of each individual and providing new possibilities for humanized care.

Keywords: Hematopoietic stem cell transplantation. Humanization. Interdisciplinarity. Nursing. Occupational therapy. Affective health record.

COMPARABILITY OF CD34+ CELL ENUMERATION FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION USING TWO DIFFERENT FLOW CYTOMETERS PLATFORMS.

Marcos Paulo Vicari Souza[1]; Camila Marques Bertolucci [2]; Alef Rafael Severino[2]; Rafael Lopes Teotonio[2]; Anderson João Simione[3]; Maura Rosane Valerio Ikoma-Colturato[2,4]; Vergílio Antonio Rensi Colturato[3]; Joana Espricigo Conte Spilari[1]

1. Programa de Residência Multiprofissional - Hospital Amaral Carvalho, Jaú, São Paulo, Brasil
2. Laboratório de Citometria de Fluxo Hospital Amaral Carvalho, Jaú, São Paulo, Brasil
3. Serviço de Transplante de Medula Óssea, Hospital Amaral Carvalho, Jaú, São Paulo, Brasil
4. Sabin Medicina Diagnóstica, Brasília, DF, Brasil

Introduction: correct CD34+ cell enumeration is essential to ensure successful stem cell engraftment for hematopoietic stem cell transplantation (HSCT). ISHAGE single-platform is the gold standard, well validated and widely used flow cytometry protocol for CD34+ cell enumeration in all specimen types used for transplantation. ISHAGE can be implemented in most flow cytometers (CF) available on the market, if they are provided with 3 fluorescence. Commercially available software, which are compatible with each CF model, can be configured according to ISHAGE's recommended acquisition and gating strategies, allowing for protocol reproducibility. As it is a quantitative and highly sensitive test, the pre-analytical and analytical processes must be optimally validated before being implemented in the laboratory's routine. This study demonstrated the validation process of the 10 color FACSLyric (BD)TM, using as comparative data the absolute enumeration of CD34+ cells performed in the 8 color FACSCantoII(BD)TM, a technology already routinely used in our laboratory.

Objetctive: validation of the enumeration process of CD34+ cells obtained in the FACSLyric (BD)TM.

Material and Methods: 269 samples from patients and HSC donors [48 from bone marrow (BM), 152 from pre-apheresis peripheral blood (PB), 69 from apheresis products] as well as 90 commercial control samples were evaluated from April 2019 to March 2020. Single-platform for CD34+ cell enumeration was performed using Stem Cell Kit Enumeration BDTM, following the manufacturer´s recommendations for sample preparation. The kit includes the use of TruCount BDTM tubes containing the reference beads for absolute cell count, anti-CD34PE (8G12) and anti-CD45FITC (2D1) monoclonal markers, and the 7AAD for cell viability assessment, in addition to the erythrocyte's lysis solution. Sample cell count was adjusted to 15 to 40 x 103 cells / µL prior to incubation with monoclonal antibodies. Samples were acquired in parallel on both flow cytometers. The software FACSCanto clinical BDTM and FACSSuite BDTM were used for data analysis respectively in FACSCanto II (BD)TM and FACSLyric10 (BD)TM. Both were configured according to ISHAGE gating strategies. EZR software (version 3.6.3) was used to calculate Pearson correlation coefficients between the results of the two flow cytometers.

Results: correlation coefficients were 97% for PB, 98% for apheresis samples, 99% for BM and commercial controls. Therefore, there were no statistically significant differences in CD34+ cell enumeration between the two flow cytometry platforms ($p<0.001$).

Conclusion: CD34+ cell enumeration can be reproducible across different flow cytometry technologies when pre-analytical and analytical recommendations are strictly followed, ensuring reliability of results for clinical practice.

Keywords: CD34 cell enumeration, HSCT, ISHAGE single-platform, flow cytometry.

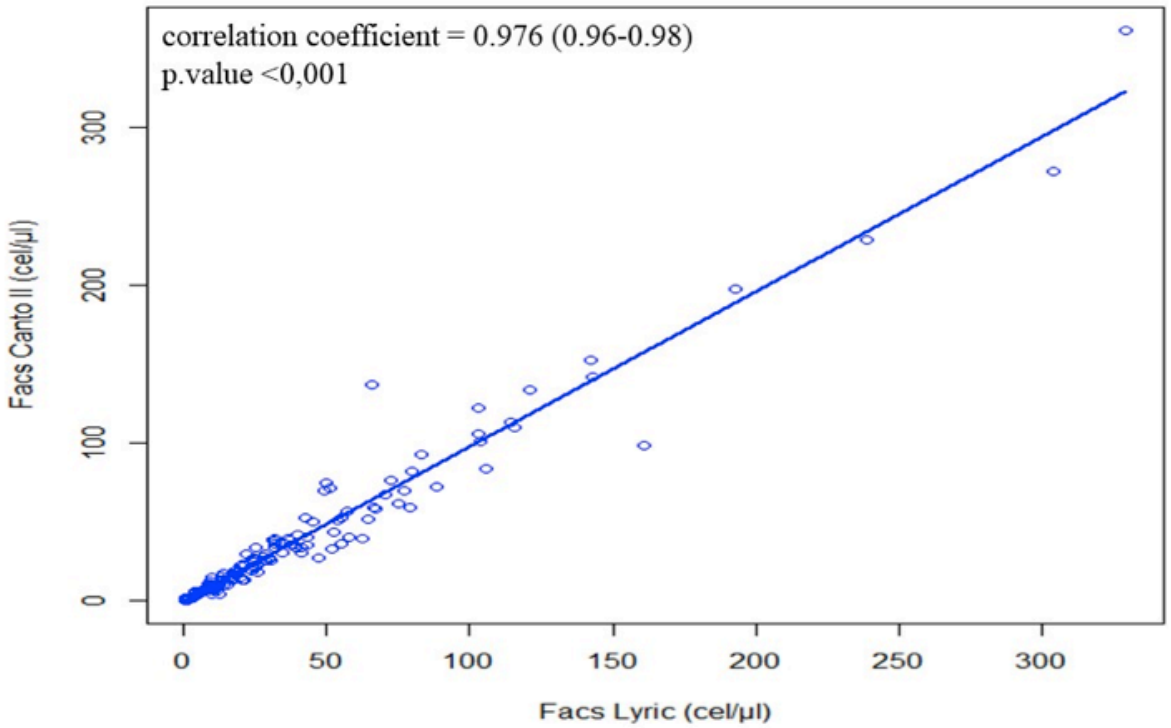


Figure 1: Correlation of CD34+ cell enumeration results between FACSCanto II and FACSLyric flow cytometers in peripheral blood samples.

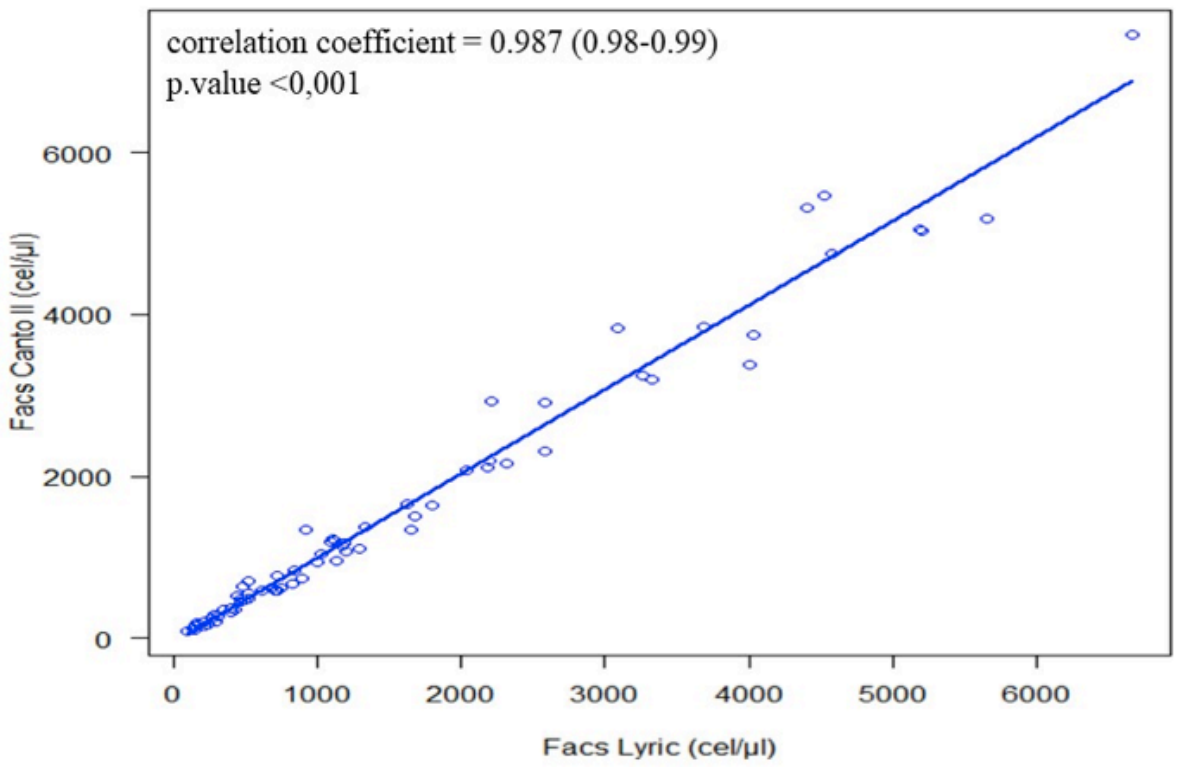


Figure 2: Correlation of CD34+ cell enumeration results between FACSCanto II and FACSLyric flow cytometers in apheresis samples

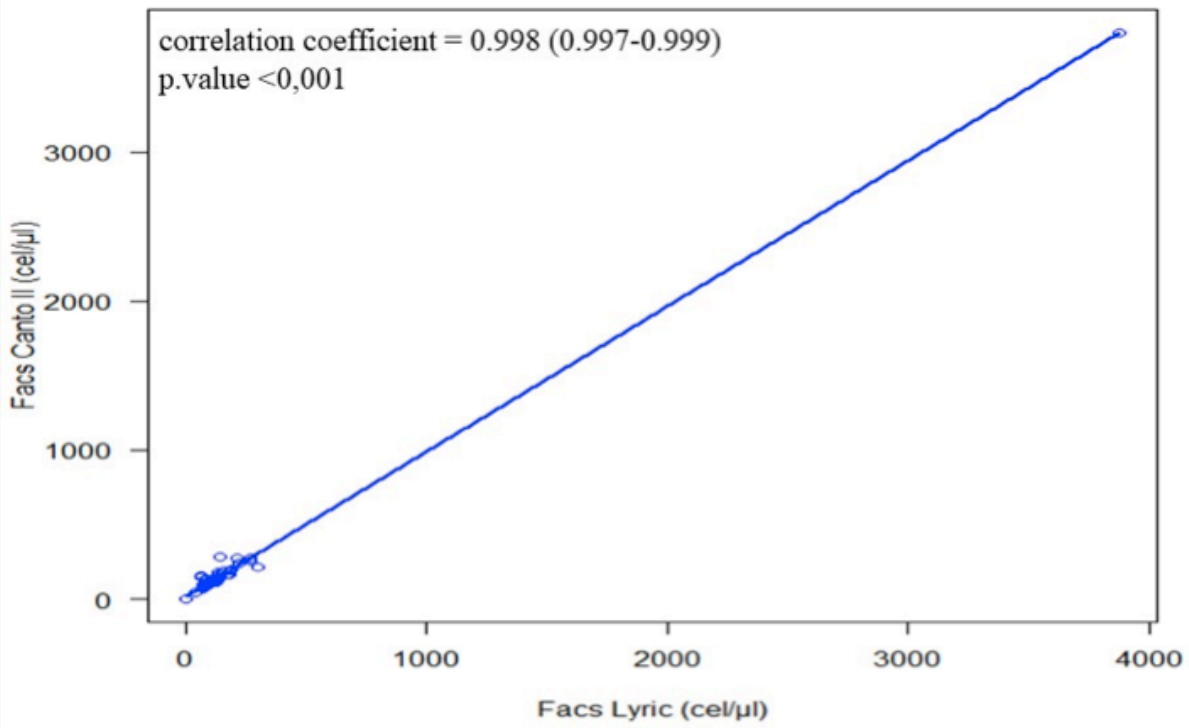


Figure 3: Correlation of CD34+ cell enumeration results between FACSCanto II and FACSLyric flow cytometers in bone marrow samples

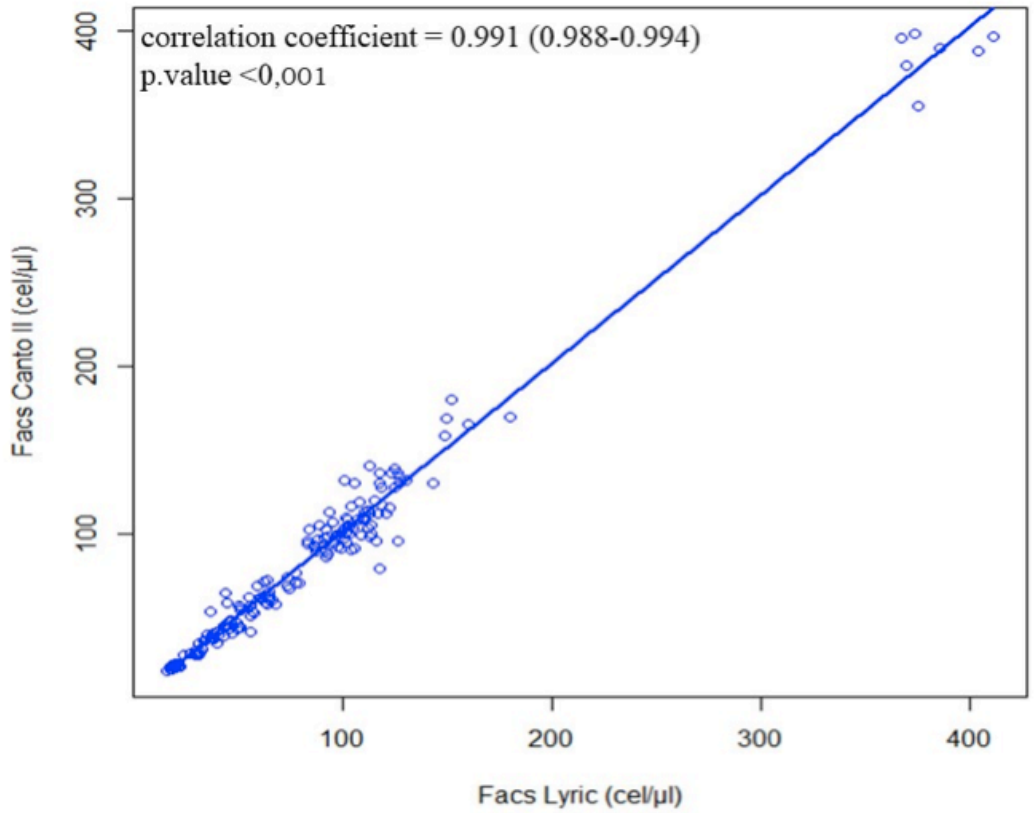


Figure 4: Correlation of CD34+ cell enumeration results between FACSCanto II and FACSLyric flow cytometers in commercial control samples

EDUCATION/HEALTH INTERFACES IN THE HEMATOPOIETIC STEM CELLS TRANSPLANTATION SECTOR DURING THE COVID-19 PANDEMIC

Ana Carolina Lopes Venâncio. V., A.C.L. / PMC – *Hospital Pequeno Príncipe*
Itamara Peters – P., I. / SEED/PR - *Hospital Pequeno Príncipe*
Mariana Saad Weindhart Costa – C., M.S.W. da / *Hospital Pequeno Príncipe*
Cláudio César Teixeira – T. C. C. – *Hospital Pequeno Príncipe*
Head of service: CARMEM BONFIM
Medical team: Juliana Luiza de Mello Bach, Adriana Mello Rodrigues, Cilmara Kuwahara Dumke, Fernanda Moreira de Lara Benini, Gisele Loth, Polliany Roberta Dorini Pelegrina
Nursing team: Emanuelle Christine dos Santos Pirolli
Pharmacy team: Laiane de Jesus Oliveira

Introduction: The continuation of studies during prolonged hospitalizations is a child's right and a duty of the state. Improving practices and on-site training are essential during this period. Studying expands the opportunity to exercise citizenship.

Objective: To show the importance of health/education articulation for the humanization of care and guarantee of rights for children undergoing hematopoietic stem cell transplantation (HSCT) within a high-complexity hospital.

Method: Participatory research-intervention, "pedagogical, social and political practice" that develops reflections to solve a problematic situation for a given community. Work carried out by the Education and Culture Sector that subsidizes educational practices and cultural expansion in a pediatric hospital.

Results: 29 children evaluated during HSCT from April to December/2020 and March to July/2021. Median age of 7 years (3 to 10 years), 69% male. Eight children did not have school enrollment and of the 21 enrolled, 12 had learning gaps, with learning difficulties (n=8) being characterized as requiring an Individualized Teaching Plan. Joining 23 families, 06 exchange difficulties, with partial adherence after intervention. Positive school bond in 06 cases. Of the eight children without registration, we found that the expectation was positive after requesting assistance. Teaching and welcoming strategies were customized with multidisciplinary advice to understand essential actions for treatment and continuity of studies. In the pandemic, remote classes took place via cell phone video calls. Teaching challenges: clinical condition (pain and mood swings), dropping out of school, learning gaps/difficulties, dysfunctional family dynamics, unfavorable bond with learning, negative expectation of treatment, education/socioeconomic level of guardians and internet connection. It was found that socioeconomic and educational level are determining factors in the mediation of treatment and education. Facilitating factors: level of education/socioeconomic, positive bond with learning, family dynamics, level of learning compatible with the year attended, positive expectation of treatment, multidisciplinary work.

Conclusions: In Brazil there is intense inequality that undermines the experience of basic rights. We describe an outline of the educational reality within the pediatric HSCT unit. Despite the difficulties exposed, we see positive points and emphasize the urgency of creating multidisciplinary sectors. In a country lacking social justice, articulating rights is an action of social reparation. The health/education articulation improves and humanizes student-patient care.

Keywords: Health/Education. Multidisciplinary work. Human Rights/Social Justice.

EDUCATIONAL ACTIVITY ABOUT SOCIAL RIGHTS IN AN OUTPATIENT FOLLOW-UP AFTER BONE MARROW TRANSPLANTATION IN A TEACHING HOSPITAL

Cristina Oliveira da Costa; Naiane Zilma da Silva; Maria Nayana Carvalho Tavares1; Natacha Cristina Maciel Paula1; Natalia Costa Bezerra Freire1; Cinthya Cavalcante de Andrade1

Federal University of Ceara

Introduction: Social rights aim to provide individuals with fundamental rights and basic guarantees of equality, described in the constitution, with the aim of guaranteeing a dignified life through rights instituted by the state. The population's lack of knowledge about social rights makes it difficult to access these rights. In the health field, for patients who undergo bone marrow transplantation, there has been an increase in the number of people with socioeconomic vulnerability, and they could benefit from these available devices, but the vast majority of the population is not aware of the existence of these. In view of the above, the action taken promoted access to information related to the Continuous Cash Benefit (BPC) and Sickness Allowance.

Objective: To report the experience of multidisciplinary residents in Transplantation and Oncohematology in an educational activity on social rights in a post bone marrow transplant follow-up clinic in a teaching hospital.

Methodology: Descriptive study of the experience report type. The waiting room type educational activity, developed on July 20, 2021, in a bone marrow transplant follow-up clinic of a teaching hospital. The facilitators were two transplant residents, social workers, a nurse and a psychologist residing in oncohematology. The topics covered were: Sick Pay and Continuous Cash Benefit. Fictional cases and inputs were used as printed illustrative material and a flip-chart, supporting a better understanding of the topic by the public, introducing by reading the fictional cases that listed the subjects: social security, quality of insured, contribution time, profile candidates to claim the benefit and differences between benefits. The activity lasted one hour and thirty minutes. The target audience was patients and caregivers of hematology and bone marrow transplant outpatient clinics.

Results: The intervention had the participation of 31 people from different age groups. During the residents' explanation, the patients actively participated, clarifying doubts that arose, such as: who is entitled to benefits, how to request them, knowledge of the mechanisms for effecting public policies by patients and what are the means of access to implement them.

Conclusion: The educational activity was an efficient experience to promote knowledge about the themes to the participants, being of paramount importance to carry out activities like this, which are instruments for health promotion and contribute to the implementation of social policies.

Keywords: Nursing, Social work, Social rights, Bone Marrow Transplant

LIFE HISTORY: INTERDISCIPLINARY RESOURCE FOR INTERVENTION ON PATIENT IN PROCESS OF HEMATOPOIETIC STEM CELL TRANSPLANTATION

Ilana Leila Barbosa de Lima[1], Flávia Yasmin de Oliveira Cardoso[2], Dayane Regina dos Santos[1,2]

1. Complexo Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, Brasil
2. Departamento de Terapia Ocupacional da Universidade Federal do Paraná, Curitiba, Brasil

Introduction: The hematopoietic stem cell transplantation (HSCT) consists of a high complexity procedure which requires a long hospitalization period and causes restrictions that can implicate in various impacts and ruptures in the life of patients. Such implications can cause physical and psychic suffering, like loneliness, anxiety, distress, and fear. In this context, it is necessary for the interdisciplinary team to employ strategies that go beyond the clinical care, also considering emotional pain, aiming the integrality and multidimensionality of the patient.

Objective: To report the experience of using the technique of Life History as an interdisciplinary strategy for intervention on adult patient in HSCT process.

Method: Report of experience of interdisciplinary intervention on an adult patient hospitalized for her second HSCT. Information collection happened through daily psychology and occupational therapy appointments, at different times. During the Psychology appointments the patient talked about episodes of her life, disease, family members, hospitalization, and treatment. The psychologist transcribed her speech, typed it, and returned it for the patient to read and approve the written content, and, finally passed it on to the Occupational Therapist to put in a book format. In the Occupational Therapy appointments, they researched book formats, illustrations and ways to organize the material, in order to embody the ideas and stories of the patient; photographs chosen by her were also inserted. All the work was personalized according to her preferences, always encouraging her autonomy and active participation. After the appointments, the professionals discussed the case and planned their next steps in the activity.

Results: The engagement of the patient was surprising. She demonstrated pleasure and satisfaction with the activity. Always available and excited, she demonstrated that her self-esteem got more strengthened and higher. Telling her story did her good. She took better care of her appearance, wanted to look better in photos and smiled more. As her enthusiasm grew, it was noticed that the feeling of loneliness diminished, and her autonomy got strengthened. Even during the absence of the professionals referred to, the patient wrote and handed the written material to be typed, chose photos, mobilized the family to send them via cell phone, keeping herself engaged in the whole process. The professional work aims at giving the subject conditions to develop their self-steem, self-knowledge and empowerment to become protagonist in their process. This objective was visibly achieved in this case.

Conclusion: Using the technique of Life History favored the patient higher capacity of hospitalization confrontation and redefinition of her history, valuing subjective and emotional aspects, configurating it as an important resource for intervention on patients that go through the HSCT process.

Keywords: Hematopoietic stem cell transplantation. Interdisciplinarity. Psychology. Occupational Therapy. Life History.

THE EXPERIENCE OF INTEGRATIVE MEDICINE IN AN ONCO-HEMATOLOGIC AND BONE MARROW TRANSPLANT CENTER: ANALYSIS OF THE MULTIDISCIPLINARY TEAM.

Maria Ester Massola, Cinthya Corrêa da Silva, Cristina Voguel, Nelson Hamerschlak

Hospital Israelita Albert Einstein, Bone Marrow Transplantation Department, São Paulo, Brazil.

Introduction: Bone Marrow Transplantation (BMT) is a complex treatment with prolonged hospitalizations. The performance of the multidisciplinary team is fundamental, requiring important interactions between team, patient, and family. Integrative Medicine (IM) offers person-centered care, with non-pharmacological approaches that help in symptom management, relaxation, and well-being. IM is evidence-based and uses integrative therapies, such as yoga, to elicit the Relaxation Response (RR). RR is associated with increased parasympathetic nervous system activity, decreased heart rate, blood pressure and endogenous opioids release. Understanding the value of the IM service to the multidisciplinary team is one way to assess its importance and performance.

Objective: To report the IM experience and analyze its value to the multidisciplinary team in an Onco-Hematology and BMT Center of a private tertiary care hospital.

Methods: Using REDCap, a survey about the IM service was developed, consisting of 18 questions, being five of them demographic. 78 professionals from the onco-hematology multidisciplinary team voluntarily answered the questionnaire.

Results: Between January/2019 and June/2021, 166 transplants have occurred, 69% (115) patients aged 18 years or older; 2,687 IM sessions were performed (3 x/week – for 30 minutes). Specialized integrative therapists taught inpatients and caregivers stress management and self-care tools that elicit RR, sharing yoga techniques, light massage, empathic listening and compassionate care. The survey was answered by 78 professionals: 66% of them were women with a predominance between 34 - 44 years (38%); the majority were physicians and nurses (69%) with 10-20 years of education (49%); 58% were post-graduates. 44 professionals (56%) indicated IM to patients and the feedback was positive (88%). Regarding symptom control, they observed improvements in stress (96%), anxiety (92%), insomnia (80%), and pain (68%). The main benefits noted in patients and caregivers after IM care were relaxation, well-being, and comfort. 67 (86%) responded that IM care helps the team's work and 72 (92%) believed that it positively influences the Patient Experience. It was observed that some professionals are unaware of the service (19%), the techniques used (22%) and how to request the IM team (49%).

Conclusions: It was concluded that for the multidisciplinary team the inclusion of IM is positive: facilitates the team's work, helps patients in the management of symptoms, brings benefits such as relaxation and well-being, and improves the Patient Experience. There are some improvement opportunities for diffusion of IM and the ways its services can be requested. The next step is to conduct a new survey to analyze the value of this service from the patients' point of view.

Keywords: INTEGRATIVE MEDICINE. BONE MARROW TRANSPLANTATION. RELAXATION RESPONSE.

THE IMPORTANCE OF FAMILY SUPPORT IN THE CARE OF PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT).

Luciene do Bu Lourenço[1], Célia Roseli Duarte Redó[2], Yolanda Marques Mazzaro Juhas[3], Lívia Mariano[4], Vanderson Rocha[5]

1. Student of the Psychology Division of the Central Institute of the Hospital das Clínicas FMUSP, São Paulo - SP, Brazil.
2. Social Worker of the Social Service Division of the Central Institute of the Hospital das Clínicas FMUSP, São Paulo – SP, Brazil.
3. Psychologist at the Psychology Division of the Central Institute of the Hospital das Clínicas FMUSP, São Paulo – SP, Brazil.
4. Physician Coordinator of the Clinical Unit of Cell Therapy at the Central Institute of Hospital das Clínicas, FMUSP, São Paulo – SP, Brazil.
5. Technical Director of the Hematology Service, Hemotherapy and Cell Therapy, Division of Internal Medicine I at Hospital das Clínicas, FMUSP, São Paulo – SP, Brazil.

Introduction: When the patient is referred to undergo hematopoietic stem cell transplantation (HSCT), he is weakened, with afraid of the unknown, but with hope of cure. HSCT directly impacts the quality of life, self-esteem and return to social life, causing the patient and their families emotional and socioeconomic suffering, thus requiring multidisciplinary care. During hospitalization, the patient lives a delicate moment, in which their social ties are "interrupted", experiencing a new routine. The presence of family support during treatment is important, as it helps as a defense mechanism and in ways of coping with the disease, minimizing suffering.

Objective: Describe the importance of family support during the therapeutic process of HSCT, in a Social and Psychological perspective.

Method: Description of the perception of care provided to patients and families who are experiencing the HSCT process. In a holistic view, from the speech observation, what are the impacts of distancing family support and how it emotionally affected those involved, understanding and respecting the stories and relationships built before the illness process.

Results: Due to the impairment of the patient's immune system, there are restrictions on family support visits during the HSCT procedure. According to patients and family members, this distancing generates apprehension due to the expectations related to the treatment and because they are weakened due to the diagnosis, restrictions and reactions to the HSCT treatment. In a disease situation, the family structure changes, and it is necessary to adapt to this patient's new lifestyle, to provide support and alleviate the situation of suffering.

Conclusion: The presence of the family member during the patient's treatment helps to establish between them the affections that emerge from the experiences shared throughout the therapeutic process. Patients express that family ties and their welcoming provide a feeling of security and comfort.The role of Social Care and Psychology is to facilitate dialogue, consolidating support service networks, providing a space for welcoming and guidance on the role of caregiver and the importance of psychophysiological self-care for those involved, helping in the process of coping with the patient's disease and minimizing the suffering of this and their families. There are stories of fragile or non-existent, frayed or broken family ties in periods prior to the illness. When we detect the aforementioned situation, we must go beyond everyday actions, evaluating the informal network of which the patient is a part, encouraging adherence to treatment and family support bonds. The family is an important influencing agent in the patient's recovery, because there are lived stories and affection that can expand the possibilities of HSCT effectuation.

Keywords: Hematopoietic Stem Cell Transplants. Psychosocial Assistance. Quality of life. Family Support. Defense mechanism.

TRANSPLANTS X SARS-COV-2, PANDEMIC EXECUTION SCENARIO

Mara Cristina Vianna Barros[1], Caroline Pellicioli Brun [1], Mayara Lindner Brandão[1].

1. Hospital Dom Vicente Scherer do Complexo Hospitalar Santa Casa de Misericórdia de Porto Alegre, Rio Grande do Sul – Brasil

Introduction: The Sars-Cov-2 pandemic caused hematopoietic stem cell transplant centers (TCTH) to need to install care protocols to prevent virus transmission within the units. The implementation of these care that were adopted during the hospitalization of patients and the management with the donors became extremely necessary for the maintenance of the services with quality and safety.

Objective: The aim of this study was to analyze during the Pandemic period, the number of transplants performed, the protocols and changes adopted, and cases of contamination by Sars-Covid-2.

Methods: We describe the approaches adopted during 1 year of the pandemic - from April 1, 2020 to April 30, 2021, in the HSCT unit of the Dom Vicente Scherer Hospital of the Complexo Hospitalar Santa Casa de Porto Alegre. Safety practices were established by the multidisciplinary team during arrival, stay, until the discharge of patients, donors and companions, in addition to the care provided by the care team.

All patients and donors were instructed to remain in isolation at home based on bed availability (preferably for one week). Upon hospital admission, screening was performed for the presence of symptoms and possible infected contacts; as well as the PCR test for Sars-Cov-2 was performed, being released for entry into the unit only after the negative result. For patients who needed a companion, only those with unequivocal dependence, they should undergo CPA at least within 48 hours prior to admission to the hospital. The exchange of companions was not allowed, and they had to remain inside the unit for the entire period of the transplant, including their meals and hygiene. The staff was exclusively for transplant patients, and wore N95 masks and face shield obligatorily throughout the work shift.

Results: From April 1, 2020 to April 30, 2021, a total of 102 Hematopoietic Stem Cell Transplants were performed, 78 of which were Autologous and 24 Allogeneic. Both protocols chosen during the Round were applied as safe for entry into the patients to undergo the transplant, only being released after the result of negative PCR collection, which followed the medical record of each patient.

Donors performed PCR collections, intensifying the safety of the process, and all had negative results.

With the completion of this safety protocol for hospitalization, we obtained negative COVID – 19 results in the BMT in the period.

The restriction of family members in the period proved to be positive, as the released companions were submitted to PCR test collections and after the result, released to stay for follow-up, family members remained in isolation until the patient's hospital discharge.

The nursing team accompanied patients, donors and family members using personal protective equipment, using all the resources for patient safety

Conclusion: The restriction of companions and visits, mass testing for all patients, donors and companions, in addition to the care of the multidisciplinary team with the use of personal protective equipment is extremely important to prevent Sars-Cov-2 outbreaks during a pandemic, allowing the unit active during this restrictive period, with no cases of contamination.

QUALITY AND DATA MANAGEMENT

ANALYSIS OF THE PERFORMANCE OF THE DATA MANAGER (DM) IN THE HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) UNIT BY THE MULTIPROFESSIONAL TEAM.

Cinthya Corrêa da Silva, Cristina Vogel, Leonardo Javier Arcuri, Anderson Felipe da Silva, Mariana Clapis Bello Veloso, Tânia Michele Barreto Waisbeck, Lucila Nassif kerbauy, Gabriela Rocco de Sa, Carolina da Silva Costa, Nelson Hamerschlak

Hospital Israelita Albert Einstein, Bone Marrow Transplantation Department, São Paulo, Brazil.

Introduction: The Hematopoietic stem cell transplantation (HSCT) is a complex treatment, characterized by important multidisciplinary involvement. In this context, the role of a transplantation data manager is to maintain a local database, assist in scientific research, and keep up to date with international registries. In fact, data submission to international registries is one of the prerequisites for some transplant accreditations, such as the Foundation for the Accreditation of Cellular Therapy (FACT). In order to improve the data management of the HSCT unit and receive the 2nd FACT accreditation, in November 2014 the data manager was hired to report the procedure in national and international registries. Understanding the added value of a data manager for the multidisciplinary team is one way to evaluate its performance.

Methods: Development of a survey in RedCap for 86 HSCT professionals, with 20 questions, containing demographic data (5 questions), performance of the multi-professional team with research (location and methods of data collection), and the roles of the data manager (qualifications and added value).

Objective: To evaluate the perception of the HSCT multidisciplinary team of the data manager of a philanthropic transplant center in São Paulo, Brazil.

Results: Seventy-seven of eighty-six (90%) professionals in the HSCT unit responded to the survey. The majority were women (87%), with a median age of 39 (26-67). Physicians and nurses (67%) were the most common professions with most having 10-20 years of undergraduate education (61%); the vast majority were postgraduates (59%) and 21% have a master's and/or doctoral degree (Table 1). 55% (41) of the professionals engage in research in addition to clinical practice. According to the participants, the main DM qualifications required are to manage the HSCT unit data (88%) and understand the bureaucratic procedures for research (77%). In addition, the main value that a DM adds to the team is to facilitate the center's participation in internal and multicenter scientific research, along with availability of standardized data (48%). Most participants declared not only having no direct contact with the DM but also not having access to guidance on data security and bureaucracy of study submission to the Research Ethics Committee (CE). From a scale of 0 to 5, 77% (58) consider very important the inclusion of a data manager in the multidisciplinary team of a transplant unit (=5) and 99% (75) would recommend hiring this type of professional.

Conclusion: It was concluded that the inclusion and interaction of the DM, with the HSCT multidisciplinary team was positive, from the availability of standardized data, to support in the submission of scientific papers. Data sharing and dissemination of the work done with the team may be strategies to improve this result.

Keywords: DATA MANAGER. HEMATOPOIETIC STEM CELL TRANSPLANTATION. MULTIPROFESSIONAL TEAM.

TABLE 1. Demographics and academic background

Sex	N	%
Female	66	87%
Male	10	13%
Age range*	N	%
30 a 40	44	58%
41 a 50	18	24%
51 a 60	11	14%
> 60	2	3%
Professional	N	%
Nurse	24	32%
Doctor	21	28%
Dentist	8	11%
Pharmacist	4	5%
Physiotherapist	4	5%
Other	4	5%
Administrative Technician	3	4%
Nursing Technician	3	4%
Physical Education Professional	2	3%
Biomedical	1	1%
Nutritionist	1	1%
Psychologist	1	1%
Time since graduation	N	%
< 1 year	1	1%
1 a 3 years	2	3%
4 a 6 years	7	9%
7 a 9 years	10	13%
10 a 20 years	41	54%
> 20 years	15	20%
Level of education	N	%
Technical Course	5	7%
Undergraduate	7	9%
Post-graduation	45	59%
Master's Degree	11	14%
Doctorate	5	7%
Post-Doctorate	3	4%

BRAZILIAN DATA MANAGER AND HEMATOPOIETIC STEM CELL TRANSPLANT CENTERS PROFILE ANALYSIS.

Cinthya Corrêa da Silva[1], Paula Moreira da Silva Sabaini[2], Anderson João Simione[3], Bruna Letícia da Silva Santos Geraldo[4],Heliz Regina Alves das Neves[5]

1 Hospital Israelita Albert Einstein, Bone Marrow Transplant, São Paulo, Brazil,
2 Barretos Cancer Hospital, Barretos Bone Marrow Transplant, Barretos, Brazil,
3 Hospital do Câncer Amaral Carvalho - Fundação Amaral Carvalho, Bone Marrow Transplant, Jaú, Brazil,
4 Biosana's Serviços de Saúde, Bone Marrow Transplant, São Paulo, Brazil,
5 Federal University of Paraná, Bone Marrow Transplantation, Curitiba, Brazil,

Introduction: Until recently, neither a consolidated and specific Hematopoietic Stem Cell Transplantation (HSCT) database registry nor infrastructure that would allow outcomes analysis and multicenter studies were available in Brazil. However, there are worldwide databases available on this subject, such as the Center for International Blood and Marrow Transplant Research (CIBMTR). In 2016, change has begun in the national scenario with the Brazilian Society of Bone Marrow Transplantation (SBTMO), CIBMTR and the data managers working group (DMs) partnership. To know the structure of the HSCT centers and the DMs' profile is of great importance for Brazilian registry success.

Objective: To analyze the Brazilian DMs' profile and the infrastructures of the HSCT centers.

Methods: A Google form survey was developed and made available at DMs' WhatsApp group.

Results: Fifty-four DMs from 41 HSCT centers answered the survey. Of these, 83% perform other activities beyond the DMs' function; 52% are paid with HSCT centers resources and most of them are nurses and doctors (66%); 39% are satisfied with that activity and 37% believe in career's progression; 70% are trained through the DM's monthly online meetings (TABLE 1). Among the 41 HSCT centers, 63% are from the Southeast, representing 66% (76/115) of Brazilian centers. Private centers were predominant at the study (46%); 46% of them work with adult and pediatric patients, and 66% of the centers have been active over 10 years; 68% are active at the national and international registries and 63% are certified by SBTMO and the National Transplant System. Of the active centers in CIBMTR, 50% report complete data (CRF) and/or essential data (TED). After the incentive to increase CIBMTR adherence and DMs' training, the main Brazilians HSCT centers are active or in affiliating process to the registries (49) (TABLE 2), allowing the knowledge about some Brazilian HSCT results, based on the latest multicentric works published. The DMs' activities are still not recognized as a profession in Brazil, which makes difficult to find and keep those professionals. The databases maintenance depends on several factors, such as hours of dedication, DMs' experience, number of HSCT performed at the center, and the kind of CIBMTR registry (CRF or TED).

Conclusion: The DMs' presence at the centers is very important to data collection and recording process, indicating the need for national regulation of the profession. SBTMO and partners have enabled the continued education of those professionals, as well as presence in national and international events. The results of these initiatives are positive, but to achieve greater success it is necessary to invest in infrastructure and DMs' maintenance, with multidisciplinary team awareness about the importance of data reporting and government entities support to activate more HSCT centers in national and international registries.

Keywords: DATA MANAGER. BRAZILIAN REGISTRY. HEMATOPOIETIC STEM CELL TRANSPLANTATION.

TABLE1: Data manager profile.

DMs Profile	N	%
Graduation		
No	2	3.70%
Yes	52	96.30%
Professional qualification		
Nurse	25	46.30%
Physician	11	20.37%
Pharmaceutical	4	7.41%
Biomedical	4	7.41%
Biologist	2	3.70%
Information Systems	2	3.70%
Public relations	1	1.85%
Human Resources	1	1.85%
No graduation	1	1.85%
Philosopher	1	1.85%
Chemist	1	1.85%
Nutritionist	1	1.85%
English language mastery		
Basic	12	22.22%
Intermediary	26	48.15%
Advanced	14	25.93%
Fluent	2	3.70%
Activity		
DM exclusive	9	16.67%
Other activities	45	83.33%
Time spent in DM activity		
≥ 6 years	9	16.67%
2 to 5 years	16	29.63%
6 months to 1 year	18	33.33%
< 6 months	11	20.37%
The DM salary comes from		
Paid by the HSCT institution	28	51.85%
Annual reimbursement sent by CIBMTR	5	9.26%
Unknown	10	18.52%
Other	2	3.70%
No salary	9	16.67%
Professional perspective as a DM		
No	17	31.48%
Yes	16	29.63%
Maybe	19	35.19%
Not answered	2	3.70%
Participated in DMs training activities		
Data Manager Training Course offered by AMEO	35	64.81%
National congresses	31	57.41%
International congresses	15	27.78%
DMs' online meetings (monthly)	38	70.37%
Trained at other transplant centers with experienced DMs	14	25.93%
Did not participate	3	5.56%
Level of satisfaction with the managing data role		
Very satisfied	12	22.22%
Satisfied	21	38.89%
Regular	17	31.48%
Unsatisfied	4	7.41%

TABLE 2: HSCT Centers.

HSCT centers	N	%
Region		
Southeast	26	63.41%
South	6	14.63%
Northeast	5	12.20%
Midwest	4	9.76%
Institution type		
Private	19	46.34%
Public	14	34.15%
Private and public	8	19.51%
Active time at performing HSCT		
5 to 10 years	9	21.95%
> 10 years	27	65.85%
< 5 years	5	12.20%
Type of HSCT performed		
Match related	36	87.80%
Mismatch related (Including Haploidentical)	36	87.80%
Unrelated	33	80.49%
Autologous	41	100.00%
Transplanted population		
Adult	18	43.90%
Pediatric	4	9.76%
Adult and Pediatric	19	46.34%
CIBMTR form type reported		
TED forms only	14	34.15%
TED and CRF forms	14	34.15%
Awaiting bureaucratic process	10	24.39%
Does not report data to CIBMTR	3	7.32%
Type of medical record		
Electronic	19	46.34%
Paper	3	7.32%
Electronic + paper (in transition)	19	46.34%
Data storage location		
Excel	31	75.61%
RedCap	8	19.51%
Access	9	21.95%
Other	2	4.88%
None	1	2.44%
Registry that the center participates		
ABTO	36	87.80%
CIBMTR	30	73.17%
WBM/LABMT	29	70.73%
Medical Registration Portal (MDS)	7	17.07%
Participation in multicenter studies		
CIBMTR multicenter study - General	4	9.76%
Haploidentical multicenter study	3	7.32%
None	13	31.71%
Both	21	51.22%
Institution certified by SNT and SBTMO		
No	14	34.15%
Yes	26	63.41%
Unknown	1	2.44%
Active data managers at the institution		
One	26	63.41%
Two	8	19.51%
Three	5	12.20%
≥ Four	1	2.44%
No answer	1	2.44%

DATA FROM BONE MARROW TRANSPLANT CENTER IN A PRIVATE HOSPITAL IN THE NORTHEAST OF BRAZIL

Beatriz Stela Gomes de Souza Pitombeira Araújo, Karine Sampaio Nunes Barroso, Lívia Andrade Gurgel, João Paulo Vasconcelos Leitão, Talita Vaz de Queiroz, Geísa Ferreira Gomes Peixoto, Ana Carolina dos Santos Rodrigues, Fabricia Maria Lopes de Oliveira, Rodrigo Monteiro Ribeiro, Diana Jorge Pires, Flávia Marília Azeredo de Oliveira, Fernanda Araújo de Oliveira

Hospital Regional da Unimed, Fortaleza, Brasil

Introduction: Bone marrow transplantation (BMT) is a highly complex procedure, with proven effectiveness in the treatment of hematological pathologies. Due to the growing need in the private system in Fortaleza, Hospital Regional da Unimed (HRU), a quaternary health institution, a part of the Unimed Fortaleza Cooperative, started perform in 2014 autologous transplants in the Oncohematology Unit. In 2018, BMT center expanded and received an exclusive unit for transplants with 3 bedrooms with a HEPA filter and positive pressure, as well as a specialized multidisciplinary team, being then authorized by the SNT also to perform related and unrelated allogeneic transplants.

Objective: Show data related to bone marrow transplants performed at the Unimed Regional Hospital from 2014 to 2021.

Results: From October 2014 to July 2021, 126 transplants were performed in the unit, 62 (49.2%) in female patients and 64 (50.8%) in male patients, with ages ranging from 15 to 73 years. As for the type of procedure, these are distributed in 114 (90.4%) autologous transplants and 12 (9.6%) allogeneic transplants (07 related, 02 unrelated and 03 haploidentical). The stem cell source used was mostly peripheral blood, in 125 cases; being only 01 collection by puncture of the iliac crest. Multiple Myeloma is the pathology responsible for the largest number of transplants, with 65 patients, followed by Non-Hodgkin's Lymphoma, with 28 patients, and Hodgkin's Lymphoma, with 17 patients. In turn, in allogeneic transplants, the most frequent pathology was AML/MDS with 6 cases, followed by ALL with 5 cases, and Hodgkin's Lymphoma with 1 case, currently being the only private institution to perform allogeneic transplants in the state of Ceará.

Conclusion: The BMT unit at the HRU has been constantly growing, establishing itself as a most complex private transplant center in Ceará. Pediatric transplant's implantation and consolidation is currently our biggest challenge.

Keywords: Bone marrow transplant, hematopoietic

DEVELOPMENT OF A DATA MANAGER TRAINING PROGRAM AT A BRAZILIAN HEMATOPOIETIC STEM CELL TRANSPLANT CENTER

Heliz Regina Alves das Neves; Margareth Kleina Feitosa.

Hospital de Clínicas da Universidade Federal do Paraná.

Introduction: The first hematopoietic stem cell transplantation (HSCT) performed in Brazil was in 1979. There was no HSCT registry in the country. After that, in 1985, a Brazilian HSCT Center become affiliated to the Center for International Marrow Transplant Registry (CIBMTR). In the beginning, there was no data manager (DM). The registry of patients undergoing HSCT was in printed form, by a physician and sent to the CIBMTR by mail or fax. As the number of HSCTs increased, other professionals began recording data. In the 90's, a new professional emerged for the registry, a computer technician (IT) who was trained at the HSCT transplant itself and CIBMTR. In addition to recording HSCTs in printed forms, the IT created a Database in Microsoft Access, where all patients were registered. Later, the HSCT started to be registered in a software designed for BMT practitioners, StemSoft. Data were compressed and sent to CIBMTR by email, using dial-up internet. In 2008, the HSCT registry became electronic, using FormsNet3 (FN3) and, since then, the Brazilian HSCT Center has been training its own DMs and some from other Centers.

Objective: To demonstrate the methodology used for training DMs for the registration of a Brazilian HSCT Center on FN3.

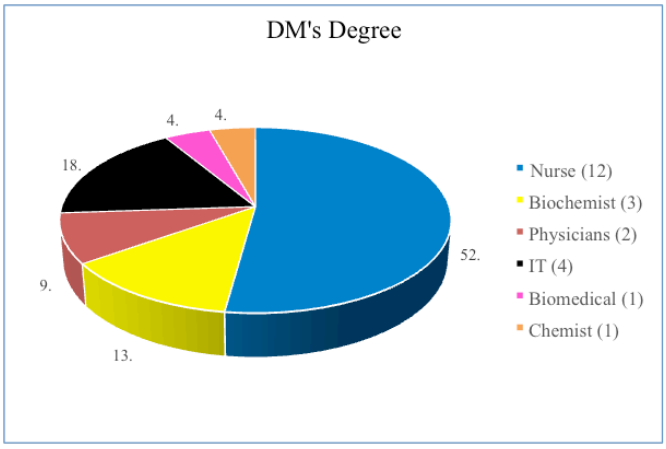
Method: For the DM training, two clinical cases of patients are chosen. At least one clinical case chosen has to have Graft Versus Host Disease (GVHD), as it presents greater complexity in filling. The DM is trained by another more experienced DM, who monitor the completion of the data, from inclusion in the CIBMTR to the 100-day post-HSCT follow-up. After learning, the DM completes a report and the primary DM checks it. The DM also follows the primary DM to understand the management of due forms, how to fix errors and queries in FN3 and also receives guidance on how to maintain a local data record.

Results: Since the beginning of HSCT registration on FN3 in 2008, 23 DMs have been trained. All of DMs have a degree, most of them nurses (12), the others are: biochemists, physicians, IT, biomedical and chemist. Most DM is not exclusively dedicated to the function (93%), the majority works an average of 10 hours a week, supported by resources received from the CIBMTR. For these reasons and the fact that it is not a regulated profession, turnover is very high. Therefore, this training model is still used. The training lasts an average of one week, enough for the DM to understand the process. But there is a need for continuing education, due to the complexity of the information collected, and this requires a special knowledge for quality records.

Conclusion: This training program has formed DMs, who specialize with practice, but it was observed that professionals who work in patient care in a HSCT Service learn faster than others. The maintenance of DMs in HSCT centers is very important to keep records up to date.

Future perspectives: To develop an online training program, in progress.

Key-words: data manager, CIBMTR, Brazilian registry.



PROFILE OF HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS IN A HEMATOLOGY THERAPY CENTER IN SOUTHERN BRAZIL

Valesca Scalei Cezar, Janaina da Silva Flôr, Claudia Cáceres Astigarraga, Cristhiane de Matos Vieira, Taiana Kessler Gomes Saraiva, Gabriela Pereira Flores

Cezar, V.S.1, Flôr, J.S.1, Astigarraga, C.C.1, Vieira, C.M.1, Saraiva, T.K.G.1, Flores, G.P.1.

1Hospital Moinhos de Vento, Porto Alegre, RS, Brasil;

Introduction: Founded in 2015, the Hematological Therapy Center at Hospital Moinhos de Vento (CTHMV) has a multidisciplinary team that is trained and directly involved in the care of patients who need hematopoietic stem cell transplantation (HSCT). Hospital Moinhos de Vento is the only private hospital in the South of the country that performs all types of transplants in both adult and pediatric patients. In 2021, until July, Hospital Moinhos de Vento reached the mark of 158 HSCT performed in patients adults. Objective: To describe the profile of patients undergoing HSCT in an onco-hematological therapy center located in southern Brazil. The variables sex, age, type of transplant, underlying pathology and mortality up to the first 100 days of transplantation were collected.Methods: Descriptive, documentary and retrospective study, developed in a Hematological Therapy Center in southern Brazil, in the period of July from 2015 to July 2021.Results: In these 6 years of HSCT, 158 patients underwent HSCT, 57% male and 43% female. The mean age of patients was 47 years, with a standard deviation of 17 years. Among the HSCT performed, 59% were autologous and 23% were allogeneic HLA identical, 12% HLA mismatch and 6% allogeneic unrelated. Lymphoma diagnosis (Hodgkin or Non-Hodgkin) correspond to 32% of transplants, followed by Multiple Myeloma cases with 29%, Leukemia (lymphoids and myeloid) with 26%, in addition to other non-malignant hematological diseases that correspond to 9% of HSCT.Of the patients transplanted at the HSCT, 10% did not surpass the 100-day post-transplantation mark, corresponding to a mortality rate below that expected in the world literature.Discussion: As in the study by Souza et. al1, 57% of transplants were male individuals. In Latin America, the average age of patients in allogeneic HSCT is 30 years and in autologous 45 years, which corroborates the average age of the center of 47 years. Brazil performs 63% of autologous HSCT and 37% of allogeneic HSCT2, following the national trend, presents 59% of autologous HSCT and the allogeneic ones together represent 51% of the procedures. Diseases with indication of allogeneic HSCT include leukemias, lymphomas and non-malignant diseases, since autologous is the route of choice mainly for lymphoproliferative diseases2, in line with data from CTHMV, where 32% of transplant patients had lymphoma and leukemias represented 26% of transplants performed. CTHMV had a death rate of 10% in the first 100 days after HSCT, a mortality rate similar to those found in the studies by Souza et.al1 and Santos3 with 9.1 and 9.5%, respectively.Conclusion:The therapy center This study has performed a total of 158 transplants since its inauguration in June 2015 and has shown excellent results in terms of patient survival.

Keywords: Bone Marrow Transplant; Hematology; Health Profile.

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THE IMPACT OF DATA MANAGER ADMISSION AND TRAINING ON DATA REPORTING PERFORMANCE TO CENTER FOR INTERNATIONAL BLOOD AND MARROW TRANSPLANT RESEARCH: AN EXPERIENCE REPORT

Jessica Di Chiara Salgado, Luiz Carlos da Costa Junior, Marina Izu, Valéria Gonçalves, Simone Pereira Lermontov, Maria Cláudia Rodrigues Moreira, Décio Lerner

Núcleo de Informação, Ensino e Pesquisa (NIEP), Centro de Transplante de Medula Óssea (CEMO), Instituto Nacional de Câncer José de Alencar Gomes da Silva (INCA), Rio de Janeiro – RJ, Brasil

Introduction: The International Bone Marrow Transplant Registry (IBMTR) was established in 1972 at the Medical College of Wisconsin at the initiative of pioneers in bone marrow transplantation (BMT) in order to better understand the data generated by the centers that were starting to transplant. In 2004, the registry of unrelated transplants from the National Marrow Donor Program (NMDP) merged with the o IBMTR forming the current CIBMTR (Center for International Blood and Marrow Transplant Research), having as a mission to improve access to information and outcomes of transplantation and cell therapy for patients. The CIBMTR is a longitudinal registry that collects data from more than 450 centers in 47 countries around the world. Each patient is registered and followed longitudinally until death or loss to follow-up and aims to help advance BMT to improve patient survival, quality of life, and treatment. In Brazil, the Associação de Medula Óssea do Estado de São Paulo (AMEO) promoted, during the years 2019-2020, training of professional Data Managers (DM) of the Transplant Centers for the systematic data reporting to the CIBMTR.

Objective: report the experience of a BMT center after admission and training carried out in the AMEO and describe the impact on data reporting to the CIBMTR.

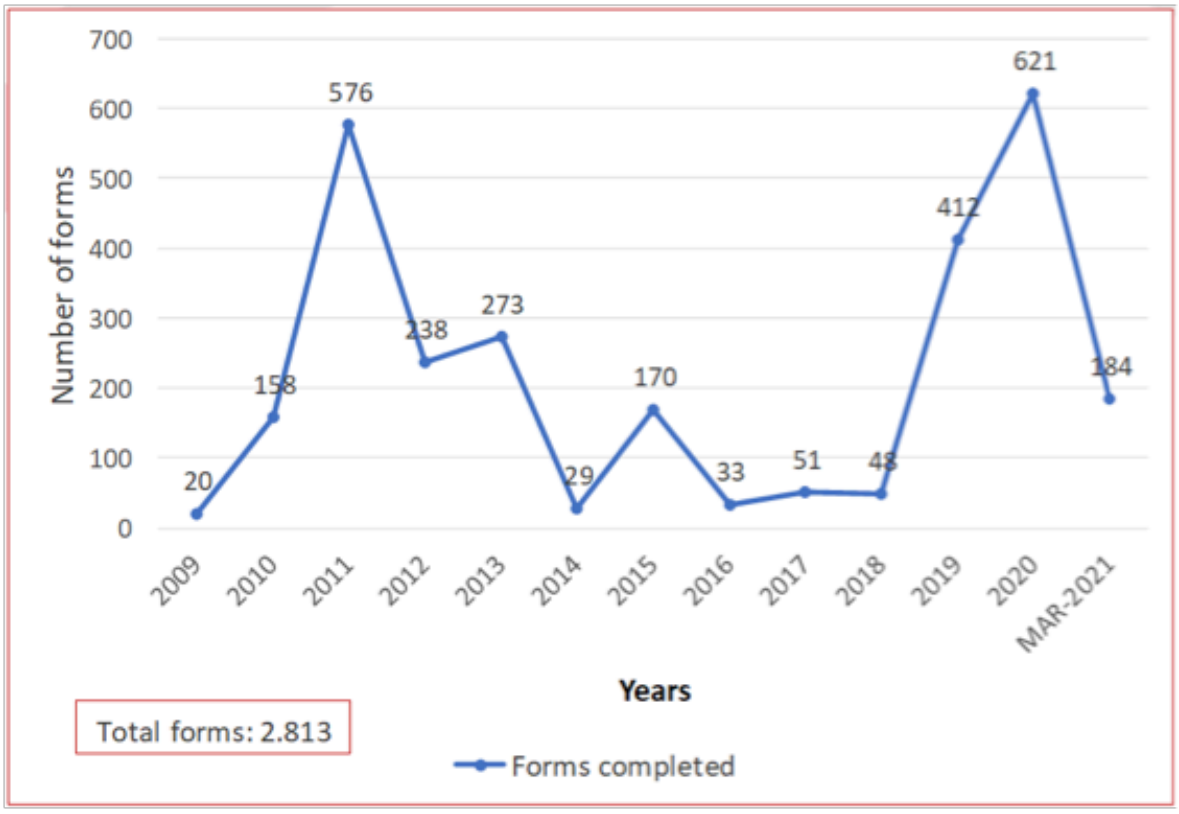
Methods: This is an experience report of a data manager group, in a BMT Center of the federal public network in the state of Rio de Janeiro, in the period from January 2009 to March 2021. To assess performance in this period, the number of completed and submitted forms per year was used as an indicator. These data are available on the CIBMTR Portal.

Result and Discussion: During this period 2,813 forms were reported, being the years 2011 and 2020 with the highest report, with 576 and 621 completed and sent forms, respectively (Graphic 1). In 2020, an increase was evidenced, with a significant improvement in the number of data reported to the CIBMTR. During this same period, the service admitted two new members to make up the data manager group, currently totaling three professionals dedicated to this purpose. In 2009, 20 forms were filled out, with an increase in the years 2010-2011 and a decrease in the following years. In 2019, with the entry of two professionals for data reporting and training at AMEO, there was a clear improvement in reporting, culminating in the year 2021, which achieved the best performance since 2009. These data corroborate that a trained team focused on data management improves the indicators. An even better performance is projected for the year 2022 with the implementation of templates to standardize information during all patient follow-ups.

Conclusions: The admission and training of a team formed and focused on data reporting reflected in the increase in the filling of forms to the CIBMTR as well as improving data reporting performance.

Keywords: Data manager; performance; data reporting; BMT

GRAPHIC 1- Number of forms completed and submitted to CIBMTR from January 2009 to March 2021.



HEMOTHERAPY AND CELL THERAPY

A CASE SERIES OF BONE MARROW CRYOPRESERVATION FOR TRANSPLANTATION

Karen de Lima Prata, Luciana de Almeida Costa, Maurício Colombini Martins, Nathália Gomide Cruz, Paula Renata Machado Passos Pederzoli, Roberta Kelly de Andrade, Marcia Regina Issa Salomão Libânio, André Rolim Belisário

Centro de Tecidos Biológicos de Minas Gerais, Fundação Hemominas, Minas Gerais, Brazil

Introduction: Due to the new Coronavirus pandemic, cryopreservation of hematopoietic progenitor cells (HPC) has been recommended for unrelated allogeneic bone marrow transplantation (BMT). However, bone marrow (HPC-BM) cryopreservation is less used, and few data are available in the literature.

Aim: to describe a center experience with HPC-BM cryopreservation for clinical use.

Methods: This is a retrospective case series study. The HPC-BM units were submitted to red blood cell depletion using hydroxyethyl starch (HES) 450/0.7 and then to centrifugation for volume reduction. The buffy coat volume was adjusted to reach the final nucleated cell (NC) concentration ≤2×108 NC/mL after addition of the cryoprotectant solution (5%HES/5%DMSO). The units were frozen in a mechanical freezer at -80°C and stored in a nitrogen vapor phase tank.

Results: between 10/2020 and 06/2021, eight units of HPC-BM were cryopreserved for use in nine patients (one for two brothers HLA identical). One (11.1%) unit was cryopreserved for autologous and eight (88.9%) for unrelated allogeneic BMT. Five (55.6%) patients were male. The mean age of patients was 14.7 ± 19.1 years (1–42). One (11.1%) patient had neuroblastoma, one (11.1%) CML, one (11.1%) AML, one (11.1%) Griscelli syndrome, two (22.2%) Wiskott-Aldrich syndrome and three (33.3%) ALL. The characteristics of the HPC-BM units were described in table 1. Four (50%) units had a positive microbiological test (Staphylococcus hominis, Staphylococcus epidermidis, Corynebacterium sp and Staphylococcus aureus). The clonogenic assays performed on pre-processing (n=6), post-processing (n=8) and post-thawing (n=7) samples had growth. Six (66.6%) units were released for therapeutic use. We have received engraftment data of four (66.7%) patients. The mean time to neutrophil and platelet engraftment was 17 and 21 days, respectively. Conclusions: HPC-BM cryopreservation showed satisfactory laboratory results, suggesting that the methodology used is safe and efficient. However, more attention is needed due to the high RBC volume to be infused and the bacterial contamination, more frequently observed in HPC-BM units.

Keywords: cryopreservation, bone marrow, bone marrow transplant

Funding: Fundação Hemominas

CHALLENGES IN IMPLEMENTING THE CRYOPRESERVATION LABORATORY OF THE GSH GROUP DURING THE COVID-19 PANDEMIC

Adriana Balthazar Castelhano, Marília Valvasori, Aline Miranda de Souza, Leandro Felipe Figueiredo Dalmazzo, Sérgio Domingos Vieira

Cryopreservation Laboratory - São Paulo Blood Bank - Hemotherapy Services Management Group

Introduction: Working for more than 40 years in the Hemotherapy area, the GSH Group decided to expand their assistance to Bone Marrow Transplantation, and in January 2020, they began the implementation project of the Cryopreservation Laboratory at the São Paulo Blood Bank, for processing, cryopreservation, and storage of hematopoietic progenitor cells. Objective: To present the experience and difficulties encountered during the project in the scenario of the COVID-19 pandemic.

Materials and methods: The implementation of the Cryopreservation Laboratory comprised of the following steps respectively: 1) Preparation and approval of the project; 2) Renovation and adaptation of the physical area, in accordance with RDC 214 of 2018, taking into account the appropriate conditions and flows for receiving, processing, and storing of hematopoietic progenitor cells, totaling 54m2 and consisting of exclusive and dedicated areas: Reception, Antechamber, and Processing Laboratory with controlled environment and HEPA filters, Quality Control Laboratory, Administrative Room and Storage Room; 3) Acquisition of equipment and furniture, highlighting a Flow Cytometer, an ISO 5 Biological Safety Cabin, 3 mechanical freezers at -80°C, and a cryogenic tank that allows its use in the liquid or steam phase; 4) Application for a license from the Health Surveillance Agency of the city of São Paulo; 5) Qualification of equipment, materials, inputs, reagents, and process validation. The main difficulties encountered occurred mainly due to the coronavirus pandemic: a) Due to the increase in the dollar, equipment prices rose from about 2 to 3 times the pre-pandemic quoted figure, and delivery times were also extended; b) The deadlines for performing the services were delayed from 3 to 4 months; c) The technical team joined the adapted `work from home` scheme; d) The inspection visit by the inspection body to obtain a sanitary license took 6 months.

Results: At the end of November 2020, the Cryopreservation Laboratory was ready, and we started the qualification and validation processes. In March 2021, we received the inspection visit from the Sanitary Surveillance Agency regarding our request for a Sanitary License. In the second half of March 2021, the Cryopreservation Laboratory effectively inaugurated its activities, being perfectly harmonized with the requirements and quality standards required by international certifiers. Our accreditation process by FACT and AABB is ongoing. From March to June 2021, we performed 22 procedures, processing, cryopreservation, storage in freezer -80°C and cryogenic tank, in nitrogen vapor at -190°C, quantification of CD34+ and CD3+ cells by Flow Cytometry and release for infusion, CPH-SP products collected by apheresis, and CPH-MO collected in the operating room, from autologous and allogeneic donors, serving REDOME and 5 hospitals in São Paulo and ABC with excellence.

Keywords: Pandemic COVID-19. Laboratory. Processing. Hematopoietic Progenitor Cells. Cryopreservation. Qualification. Validation. Bone marrow.

COMPARATIVE ANALYSIS BETWEEN THE TECHNIQUES FOR DETERMINING CELL VIABILITY - MICROSCOPY WITH VITAL EXCLUSION STAINING TRYPAN BLUE AND FLOW CYTOMETRY WITH 7-AAD

Adriana Balthazar Castelhano, Marília Valvasori, Aline Miranda de Souza, Leandro Felipe Figueiredo Dalmazzo, Sérgio Domingos Vieira

Cryopreservation Laboratory - São Paulo Blood Bank - Hemotherapy Services Management Group

Introduction: The Cell Viability test is an important quality control parameter that should be analyzed throughout the process of collection, manipulation, cryopreservation, and storage of Hematopoietic Progenitor Cells [HPC]. In our service, we standardize the viability study of cryopreserved products, prior to the conditioning of the receptor to receive the cells, a standard not required by Brazilian legislation, but recommended by FACT and AABB standards. Objective: to compare the results of cell viability obtained by microscopy techniques with trypan blue vital exclusion dye, and by flow cytometry with 7-AAD.

Materials and methods: 25 aliquots of 5 units of Cord Blood [HPC(CB)] for validation, and 8 aliquots of Hematopoietic Progenitor Cells obtained from the peripheral blood using an apheresis technology [HPC(A)] for infusion were analyzed between 11/2020 and 06/2021. For the trypan blue technique, a dye was added to the thawed and diluted sample, and a total count of 200 cells between viable (unstained) and non-viable (stained) was performed by a Neubauer chamber and an optical microscope. The sample was labeled 7-AAD in the flow cytometry and incubated, the red cells were lysed, and the sample was read in the flow cytometer.

Results: The thawed HPC-A units had a mean viability per trypan blue of 90% (84-94) and CF with 7-AAD of 94.17% (86.7-98.9) for CD34+ cells and 92.13% (82.8-98.22) for CD45+ cells, with a mean thawing interval of 21 days. From the HPC(CB) units, we obtained the following results: a) mean freezing interval of 7 days: mean viability per trypan blue 84% (81-92) and CF with 7-AAD 94.48% (91.3-98.75) for CD34+ cells and 77.48% (71.68-83.68) for CD45+ cells; b) mean freezing interval of 30 days: mean viability per trypan blue 89% (86-92) and CF with 7-AAD 92.79% (85.98-97.56) for CD34+ cells and 75.81% (71.7 82-83.11) for CD45+ cells; c) mean freezing interval of 60 days: mean viability per trypan blue 90% (88-94) and CF with 7-AAD 94.05 (85.71-98.09) for CD34+ cells and 77.38% (71.32-82.28) for CD45+ cells; d) mean freezing interval of 180 days: mean viability per trypan blue 90% (85-94) and CF with 7-AAD 93.68% (91.55-95.39) for CD34+ cells and 79.28% (75.46-81.75) for CD45+ cells.

Conclusion: The flow cytometry technique with 7-AAD demonstrates greater specificity concerning trypan blue, due to the number of events analyzed (75,000 versus 200 in microscopy). Furthermore, it also detects cells in apoptosis, as well as being able to differentiate viability of total nucleated cells CD45+ and CD34+ cells. All validation samples had adequate CFU growth, and all infused products had a mean grafting time of 10.6 days (9-12). As a differential quality standard, our Cryopreservation Laboratory has standardized the 2 techniques for routine use.

Keywords: Viability. Trypan blue. 7-AAD. Flow cytometry. Validation. Hematopoietic Progenitors Cells. Cryopreserved products.

CRYOPRESERVATION OF BONE MARROW-DERIVED MESENCHYMAL STEM CELLS IN BAGS STORED IN LIQUID NITROGEN

Denise de Oliveira, Juliana A. Preto de Godoy, Kelen Alvarez, Larissa Coa, Andrea T. Kondo, Raquel M. Alves-Paiva, Natalia C. Silva, Zaiane M. Camillo, Jose Mauro Kutner

Cell Therapy Center, Albert Einstein Hospital, São Paulo, SP, Brazil.

Introduction: Mesenchymal stem cells (MSC) are multipotent cells capable of differentiation in various cell types and they are also able to modulate the inflammatory response; these cells could be isolated from diferente sources such as bone marrow (BM-MSC). Recently, some studies proposed the use of MSC in pacients affected by SARS-COV-2 that progressed to severe pneumonia. Cryopreservation with previously validated freezing method and medium is an essential step since these cells should be available at the time of need.

Objectives: This study aims to validate both the cryopreservation method and the medium for MSC cultivated in bioclean rooms.

Casuistry: Fifteen samples evaluated, being 3 viability for validation and 12 pre-infusion viability of BM-MSC.

Method: The standardized freezing medium consisted of a solution of Voluven, Albumin and 10% DMSO; freezing was performed using a programmed freezer and previously validated programmed decay curves.

All cell manipulation was performed in bioclean rooms.

Using the standard method for cryopreservation of cell therapy products in the Cell Therapy Laboratory, cell viability was analyzed after thawing of BM-MSC bags for validation of the method and medium. Cell vaibility was done using the Trypan Blue method.

As long as satisfactory viability was obtained, freezing process of the BM-MSC bags started. Prior to infusion of advanced cell therapy products, feasibility analyzes were carried out using the segment, ensuring the storage of the BM-MSC bags.

Results: For validation, cell viability was evaluated after 7 days of freezing by using 1 segment, resulting in 96.7% of viability. On the eighth day, the BM-MSC bag was thawed with 97.43% of viability; after 35 days of freezing, the result obtained was 96.7% of viability.

After the infusions, analyzing the storage times, using a minimum period of 70 days and maximum of 425 days, we obtained an average of viability 94.67% (99,0-88,9) (n= 12). (Table 1).

Conclusions: a good correlation was observed between the viability of the segments and bags; so the BM-MSC bags that will be used in SARS-COV-2 patients was storage using this method.

An effective freezing method for cryopreservation of BM-MSC was consolidated using sterile manipulation and a safe techniwue capable of maintaining cell viability, which is essential for a ready availability of advanced cell therapy products for infusion.

Keywords: BM-MSC, cryopreservation, advanced cell therapy

TABLE 1

Storage Time	Viability by Trypan Blue
70 days	93,60%
76 days	95,30%
84 days	88,90%
90 days	91,00%
112 days	95,50%
186 days	95,50%
192 days	97,90%
294 days	99,00%%
301 days	96,70%
308 days	97,10%
428 days	92,35
425 days	93,20%

EFFECTS OF CRYOPRESERVATION DURATION ON THE CELL VIABILITY OF CD34+ CELLS AFTER 24 MONTHS

Nicole Raquel Ribeiro Winter[1] Isabel Biasi Yamanaka[1] Miriam Perlingeiro Beltrame[2] Fernanda Fava[2] Luana Bojko[2] Juliane Monteiro Guimarães[2] João Samuel de Holanda Farias[1]

1 Banco de Sangue do Hospital Erasto Gaertner, Curitiba, PR
2 Laboratório de Citometria de Fluxo do Hospital Erasto Gaertner, Curitiba, PR

Introduction: Bone marrow transplant (BMT) is treatment for certain types of cancer, in general blood and immune system diseases, that replace your bone marrow with healthy cells by hematopoietic stem cell transplant. Although cryopreservation is required for prolonged maintenance of CD34+ cells, this process is associated with loss of viability. Dimethyl sulfoxide (DMSO) is one of the most used cryoprotectants. Currently there is no standardized process for this purpose.

Objective: Evaluate the viability of CD34+ cells cryopreserved cells from 2016 to 2019 in a mechanical freezer at -80º C at the Hospital Erasto Gaertner (Curitiba/PR).

Methods: 30 patients underwent a leukapheresis procedure and the material was cryopreserved with a freezing medium containing 11% DMSO in a 1:1 ratio. Cell viability of CD34+ cells was performed by flow cytometry (FACS Canto II-BDBiosciences) after a minimum period of 24 months. The number of leukocytes, the percentage of CD34+ cells (clone 8G2 - BDBiosciences) were evaluated, cell viability of CD34+ cells (7AAD (7-actinomycin D) - BDBiosciences). Flow cytometry was based on the recommendation of the International Society of Hematotherapy and Graft Engineering (ISHAGE).

Results: Descriptive analysis of CD34+ cryopreserved cells (n=30) revealed an average percentage of cell viability of 53,7% for the cryopreserved bags in the period from 2016 to 2019. Three cryopreserved bags from 2016 were analyzed and present a mean viability of 35%. Mean viability of 59% and 56% was verified in the years 2017 (n=6) and 2018 (n=18), respectively. The bags cryopreserved in the year 2019 (n=3) had an average viability of 65%.

Conclusion: Optimal cryopreservation of HSCs requires the consideration of several factors, including composition of the cryoprotectant solution, cell concentration, freezing rate, and storage temperatures. Evaluation of frozen CD34+ cells showed a significant viability loss. These results may suggest that using cells for clinical purposes stored in a mechanical freezer longer than 24 months is not feasible.

Keywords: CD34+ viability; cryopreserved cells; flow cytometry

MICROBIOLOGICAL CONTAMINATION RATE IN HEMATOPOETIC STEM CELLS MANIPULATION: SINGLE CENTER EXPERIENCE

Ana Caroline de Lima Alves; Olga Margareth Wanderley de Oliveira Félix; Mayara Regina Alves Gomes; Adriane da Silva Santos Ibanez; Cintia Monteiro Lustosa; Jakeline Palmezano Crispim de S. Bufoni; Karoline Helena Silva da Silva; Laís Lima Quintino; Patrícia Shimoda Ikeuti; Virginio Climaco Araujo Fernandes Junior; Renata Fittipaldi da Costa Guimarães.

Instituto de Oncologia Pediátrica IOP/GRAACC/Unifesp – São Paulo, Brasil

All phases of hematopoietic stem cell (HSC) manipulation are essential for bone marrow transplantation. As part of quality control, we carry out sterility tests to indicate possible contamination. The most frequent agents are from normal skin flora. If that, HSC can be infused depending on the agent or patient's clinical condition. Objective: To report the contamination rate of a cell processing center (CPC). Method: Retrospective review of manipulated cell data and positive cultures from peripheral blood stem cell (PBSC), bone marrow (BM), donor lymphocytes (DLI), umbilical cord blood (UCB) and mesenchymal cells (MSC), from January 2018 to June of 2021. All procedures were performed in a laminar flow, aseptic technique, and personal protective equipment (hood, disposable apron, and non-sterile gloves). An aliquot of 1 to 3 ml was removed in different phases and inoculated in the Bactec® flask and sent to the referenced microbiology sector. Results: 468 procedures were performed for 335 patients, 45 from an adult transplant center, 276 from a pediatric transplant center and 14 from the REDOM. Table 1 describes the procedures performed, sources, quantity, and phases of aliquot withdrawal. Table 2 describes the contamination rate, agents found and phase. Conclusion: CTHs with positive agents were infused and there were no reports of sepsis. In 2018, the culture was negative in our center, but positive in the transplant center, contamination or growth may have occurred during transport. In 2020, the agent Rothia dentocariosa may have been contamination due to long growth time (greater than 1 day), as all the patient's blood cultures were negative. With the increase in cases between 2018 and 2020, a review of asepsis in collections and in the CPC was carried out by the SCIH, resulting in a decrease in cases. In 2021 all cases were negative.

Keywords: Bone Marrow Transplantation, Contamination rate, Positive Cultures.

TABLE 1

Procedures	Source	Number	Phase
Defrost and dilution	MSC	26	after defrost and dilution
Compatible ABO HSC	BM, PBSC	90	after collection
Cryopreservation	BM, PBSC, DLI	210	final product - supernatant
Defrost and DMSO removal	PBSC, UCB	73	final product - supernatant
Red blood cell depletion	BM	20	after collection and after depletion
Plasma and red blood cell depletion	BM	4	after collection and after depletion
Plasma depletion	BM, PBSC	45	after collection and after depletion

TABLE 2 - S. hominis = Staphylococcus hominis, S. epidermidis = Staphylococcus epidermidis, S. capitis = Staphylococcus capitis

Year	Number of procedures	Positive cultures	Contamination rate (%)	Infectious agent	Phase
2018	130	1	<1	*S. hominis*	after collection
2019	136	3	2	*S. capitis* *S. epidermidis* *S. epidermidis*	after cryopreservation after plasma depletion after collection
2020	130	5	4	*S. epidermidis* *Rothia dentocariosa* *S. epidermidis* *S. epidermidis*	after collection after DMSO removal after collection and RBC depletion after colletion
Until Jun/ 2021	72	N	-	-	-

NON-CONTROLLED RATE FREEZING OF HPC AND MNC WITH DIFFERENT CRYOPROTECTANT SOLUTIONS AND CELL CONCENTRATIONS

Kelen Alvarez, Denise de Oliveira, Natalia C. Silva, Larissa Coa, Zaiane M. Camillo, Andrea T. Kondo, Jose Mauro Kutner,

Cell Therapy Center, Albert Einstein Hospital, São Paulo, SP, Brazil

Introduction: The methodology used for the cryopreservation of Hematopoietic Progenitor Cells (HPC) and Mononuclear Cells (MNC) are considered a critical point for Cell Processing Centers (CPC).

The composition of the solution used to preserve the cells, freezing concentration and period of storage can cause variation in viability and consequently in the final expiration of the product.

Objective: To evaluate and compare the total cell viability in CD34+ cells and CD3 cells from HPC and MNC units cryopreserved with different cryoprotectant solutions and cells concentrations, submitted to non-controlled rate freezing and storage in a mechanical freezer.

Casuistry: 10 cryopreservations were performed with a Voluven, Albumin and DMSO 5% solution with a cell concentration of 150 x 106/mL - group A and 10 cryopreservations were performed with a Voluven, Albumin, Plasmalyte and DMSO 5% solution with a cell concentration of 300 x 106/mL – group B.

Method: For the validation, Cord Blood Units (CBU) and the leukoreduction system chambers, residual from platelets collection kits were used.

Cells viability were analyzed by flow cytometry in total cells from all units, in CD34+ cells from CBU´s, in CD3 cells from products obtained from apheresis pawns, and the Colony Forming Units (CFU) test was performed by sampling.

Results: The average storage time of the units in Group A was 60 days, with an average of 85.18%, 97.02% and 93.78 in total cell, CD34+ and CD3 viability, respectively.

For group B, the average storage was 155 days and 82.87%, 90.10% and 83.59% in total cell, CD34+ and CD3 viability, respectively.

Both groups had CFU growth as expected.

Conclusions: Both methodologies presented results within the expected standards.

Considering reduced supplies, reduced use of DMSO, lower toxicity during HPC transplantation and optimization of storage space, freezing with 300x 106 cells/mL concentration and cryoprotectant Voluven, Albumin, Plasmalyte and DMSO 5% were standardized.

After implementation, patients undergoing transplantation had their granulocytic and platelet grafts monitored, with satisfactory results.

Keywords: Non-controlled rate freezing. DMSO. Cell viability.

PROACTIVE RISK MANAGEMENT IN BAG STORAGE CONTAINING HEMATOPOIETIC STEM CELLS

OLGA MARGARETH WANDERLEY DE OLIVEIRA FÉLIX; SAMIR NICOLA MANSOUR; MARIA APARECIDA AGUIAR DA SILVA; FLAVIO BORGES DA SILVA; ANA CAROLINE DE LIMA ALVES; MAYARA REGINA ALVES GOMES; CARLA CUBERO; RENATA FITTIPALDI DA COSTA GUIMARÃES.

Instituto de Oncologia Pediátrica IOP/GRAACC/Unifesp – São Paulo, Brasil

Cryopreservation and hematopoietic stem cells (HSC) storage are important steps for autologous and some allogeneic transplants. This strategy requires – 80°C mechanical freezer storage or nitrogen tanks, with temperatures ranging from -196°C to –80°C. The temperature must guarantee the viability and safety of the bags. Failures can cause immediate death for patients who are in conditioning for bone marrow transplantation (BMT) or late death for patients undergoing treatment planning. Due to its criticality, our Institution implemented a quality tool to identify vulnerabilities and correct problems before they occur. Objective: Describe Health Failure Mode and Effect Analysis (HFMEA) tool implementation to identify potential failures, consequences, causes and improvement points in bags storage. Method: The Cell Processing Center (CPC) and the Quality Management Group mapped all the process flow from cell collection to defrost and release to BMT. Storage was identified as a critical item and was chosen for HFMEA application. We divided the existing routines into seven steps, 1. In-person temperature monitoring, 2. Remote monitoring system, 3. Existing data records for traceability, 4. Dry ice supply, 5. Nitrogen tanks supply, 6. Contingency plan in case of electrical or mechanical failure and 7. Preventive and corrective maintenance control. All improvement opportunities identified entered the tool's spreadsheet for root cause analysis and a calculation to identify the Risk Priority Number (NPR) before and after the implementation of the improvements. We obtained the NPR by multiplying (severity) x (occurrence) x (detection). The scores ranged from 1 to 10. Severity measures the failure gravity ranging from a minor to a catastrophic event, occurrence measures the number of failure detections, and detection measures the ability to failure detection through existing controls. Conclusion: Implementation of the actions significantly reduced the result of the NPR calculation. We were able to eliminate several risks and increase control in the others. Our Legal signed a contract with a dry ice supplier to guarantee for 24 hours, 7 days a week delivery in case we need to transfer the bags to other freezers. Infrastructure team installed a second audible and visual alarm and a camera in the monitoring room. All stages required training and team engagement and all improvements had very low financial investment

Keywords: Hematopoietic stem cell storage, HFEMEA, Risk Management

HFMEA Tool															
					S x O x D = R							S x O x D = R			
stage	Type of failure	Failure potential effect	Consequences	Current controls	Severity	Ocurence	Detection	Risk	actions	Responsible and term	actions	Severity	Occurrence	Detection	Risk
1	Daily monitoring on and off hours	Heating of the equipment	Loss of bags and samples and death of the patient	POP, FOR, NOR and Distance and Face-to-Face Monitoring System	10	7	1	70	Training of all those involved, reports	Infrastructure Coordinator	immediate	10	4	1	40

POP=standard operating procedure, FOR = Forms, NOR = Standards

PROFILE OF PATIENTS SUBMITTED TO AUTOLOGOUS HEMATOPOIETIC PROGENITOR CELL TRANSPLANTATION: A LABORATORY APPROACH WITH EMPHASIS ON CD34+ CELL QUANTIFICATION

Adriana Balthazar Castelhano, Marília Valvasori, Aline Miranda de Souza, Leandro Felipe Figueiredo Dalmazzo, Sérgio Domingos Vieira

Cryopreservation Laboratory - São Paulo Blood Bank - Hemotherapy Services Management Group

Objective: To trace each patient`s profile submitted to mobilization and quantification of Hematopoietic Progenitor Cells CD34+ (HPC) submitted to autologous bone marrow transplantation assisted by the GSH Group.

Material and methods: Descriptive, observational, and retrospective study. The results of quantification of CD34+ cells in peripheral blood samples (PB) and apheresis (A) were evaluated by flow cytometry at an interval of 4 months.

Results and discussion: The patients that were included in the study were 9 adults and 1 adolescent, who were submitted to CD34+cell mobilization therapy in the Bone Marrow Transplantation units assisted by the GSH Group, from 31 March to 30 June 2021. In total there were 5 males and 5 females and the predominant age group was over 40 years old (60%). Regarding the diagnosis: 4 were diagnosed with multiple myeloma (MM), 1 Non-Hodgkin`s Lymphoma (NHL), 1 Hodgkin's Lymphoma (HL), 1 CNS Lymphoma, 2 germ cell tumors, and 1 adolescent with Ewing's Sarcoma. To initiate the HPC collection by apheresis, quantification of CD34+ cells in peripheral blood was performed, whose mean count was 37 (12-97) CD34+/µL cells. The median CD34+/kg cells collected was 4.56x106 (1.53-12.66). Regarding the number of collections: in 4 mobilizations there was a need for more than one, and 1 of these patients with multiple myeloma needed 3 collections to reach the desired number of cells using GCSF + Plerixafor; and of the total number of patients, 60% of them performed only one collection. We did not observe any case of mobilization failure. There is a considerable interindividual variability in the ability to mobilize CD34+ cells from the bone marrow to the PB (OSAMA et al., 1999).

Conclusion: The experience of our service related to the profile of patients submitted to the HPC collection, and the quantification of CD34+ cells in peripheral blood and the HPC-A product, presented in general, data in agreement with the literature, although we noticed a small number of events. Most patients were over 40 years of age with a prevalent diagnosis of multiple myeloma. However, a significant variation was observed among patients regarding the number of CD34+ cells present in PB, and that obtained in the apheresis collections. Moreover, there were no cases of mobilization failure.

Keywords: Hematopoietic Progenitor Cells. Bone Marrow Transplant. CD34+ cells. Mobilization. HPC collection.

VALIDATION OF PROCESSING AND CRYOPRESERVATION OF HEMATOPOIETIC PROGENITOR CELLS USED FOR AUTOLOGOUS TRANSPLANTATION IN HEMATOLOGY CENTER OF HEMOTHERAPY IN CEARÁ- HEMOCE.

Isabel Aline Fernandes Ferreira[1]; Karine Sampaio Nunes Barroso[1]; Alexsandra Nunes Pinheiro[1]; Kellane Martins De Sousa[1]; Weide Barbosa De Mendonça[1]; Vanessa Fernandes Paiva[1]; Natercia Maria Moura Bruno[1]; Samya Waleska Gomes Nunes[1]; Beatrice Araújo Duarte[2]; Luany Elvira Mesquita Carvalho[1]; Luciana Maria De Barros Carlos[1]; Fernando Barroso Duarte[1]

1. CENTRO DE HEMATOLOGIA E HEMOTERAPIA DO CEARA, FORTALEZA - CE - BRASIL;
2. CENTRO UNIVERSITÁRIO CHRISTUS, FORTALEZA - CE - BRASIL.

Introduction: Due to the critical nature of the processing and cryopreservation of Hematopoietic Progenitor Cells (HPC), aiming the reproducibility of the technique and international quality, we validate the above-mentioned process with the technique applied in the laboratory, described in our Standard Operating Procedure. Acceptance criteria followed national legislation and international literature. Data continues to be collected and discussed on a monthly basis at a reunion of indicators, in the pursuit of management guided by goals.

Objective :To describe the quality of Hematopoietic Progenitor Cell units processed and cryopreserved at HEMOCE, collected by apheresis.

Materials And Methods: All HPC units collected by apheresis and cryopreserved at the Cell Processing Center, from March to May 2021, were analyzed according to the following parameters: evaluation of cell recovery, post-processing cell viability, results of pre and post-processing microbiological tests, time between addition of the cryoprotective solution and start of cryopreservation, total CD34 cells infused in the transplant and neutrophil grafting time.

Results: 100% of the bags processed and cryopreserved in the aforementioned period were analyzed, totaling 21 bags of HPC, collected by the apheresis sector of the Blood Center where the study was carried out. The material was collected from 16 patients from the public and private network of the state, 5 of whom underwent two collections of HPC on different days. After evaluating the described criteria, we obtained the following results: 90.5% of the samples had cell loss in the plasma of less than 5%, 9.5% of the samples did not have this data measured; 100% of the samples have post-processing 7-AAD cell viability greater than 90%; 42 samples of blood cultures were collected: 3 of them were positive and 93% of the samples were negative in the pre- and post-processing, 95% of the samples had less than 30 minutes between the addition of the cryoprotective solution (DMSO) and cryopreservation. All infusions were performed with more than 2x106cel/kg of the recipient, ranging from 2-6x106cel/kg of the recipient and the neutrophilic grafting time was less than 15 days, ranging from D+9 to D+14, being the majority on D+10 in 100% of transplants performed.

Conclusion: By validating the proposed methodology for the processing and cryopreservation of HPC, in a closed system, collected by peripheral blood apheresis, we aim to ensure product quality, and follow the requirements of legislation, as well as standardize the methodology used by the Processing Center Mobile HEMOCE. It was found that all cryopreserved bags analyzed in this period were within the standard and the stipulated goal, completing the first cryopreservation validation process with desired results.

Keywords: Hematopoietic Progenitor Cells (HPC), cryopreservation, Legislation.

VALIDATION OF PROCESSING, CRYOPRESERVATION AND STORAGE OF HEMATOPOIETIC PROGENITOR CELLS

Adriana Balthazar Castelhano, Marília Valvasori, Aline Miranda de Souza, Leandro Felipe Figueiredo Dalmazzo, Sérgio Domingos Vieira

Cryopreservation Laboratory - São Paulo Blood Bank - Hemotherapy Services Management Group

Introduction: RDC 508/2021 states that "The Cellular Processing Center must implement Qualification and Validation actions necessary to show clearly that all processes defined as critical are under control, so as not to make cells and Advanced Therapy Products clinically ineffective, or harmful to the Recipient". In our CPC, we performed the prospective validation of the processing, cryopreservation and storage of hematopoietic progenitor cells, using umbilical cord blood, before the start of our activities in 03/2021. When starting our routine, we monitor the critical parameters of the process and evaluate them with peripheral blood and bone marrow progenitor cells.

Objective: To evaluate whether the defined critical parameters in the validation protocol were achieved and could be used for CPH-SP and CPH-MO, ensuring quality to the product and aiming at the safety of the receiver.

Material and methods: Data analysis of 5 processed CPH-SCUP products was performed, cryopreserved, and stored by our CPC between 11/2020 and 07/2021. The critical parameters were defined according to the literature: 1) nucleated cell recovery after deserytocitation ≥ 70%; 2) nucleated cell recovery after plasma reduction ≥ 80%; 3) nucleated cell recovery after the addition of cryoprotective solution ≥ 90%; 4) negative microbiological test; 5) colony growth in the CFU test; 6) cell viability of CD45+ and CD34+ cells after thawing at 7, 30, 60 and 180 days ≥ 80%.

Results: The results obtained were: 1) recovery of nucleated cells after deserytocitation: mean of 82% and minimum value of 71%; 2) recovery of nucleated cells after plasma reduction: mean of 94% and minimum value of 82%; 3) recovery of nucleated cells after the addition of cryoprotective solution: mean of 102% and minimum value of 90%; 4) negative microbiological test in 100% of pre and post-processing samples, cryoprotective solution and hemosedimentant agent; 5) presence of colony growth in the CFU test in 100% of cryopreserved and thawed units after 15 days of storage; 6) cell viability of CD45+ cells thawed at 7, 30, 60 and 180 days: a median of 90% and a minimum value of 82.5%, cell viability of CD34+ cells thawed at 7, 30, 60 and 180 days: a median of 99% and minimum value of 83.25%.

Discussion: The parameters defined as critical for the processing, cryopreservation, and storage of CPH have been achieved, indicating that the procedures performed in our CPC comply with the law, and with data from other CPCs. The literature on the subject is scarce, and it is important to share results and exchange information between services for standardization. Conclusion: The validation acceptance criteria were achieved and the data presented are consistent, robust and reproducible.

Keywords: Validation. Processing. Hematopoietic Progenitor Cells. Cryopreservation. Viability. Freezing. Bone Marrow Transplant.