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PATIENT BLOOD MANAGEMENT (PBM) STRATEGIES IN BONE MARROW TRANSPLANTATION UNIT - IMPACT ON PRIMARY OUTCOMES: PBM IN BONE MARROW TRANSPLANTATION

Ana Vitória Magalhães Chaves[1]
Yhasmine Delles Oliveira Garcia[2]
Karine Sampaio Nunes Barroso[1]
Hércules Amorim Mota Segundo[1]
Lara Facundo de Alencar Araripe[1]
Paulo Henrique Mariano de Alencar[1]
Luciana Maria de Barros Carlos[3]
Fernando Barroso Duarte[1]

1 Walter Cantidio University Hospital
2 Federal University of Ceará
3 Hematology and Hemotherapy Center of Ceará

Corresponding author: Ana Vitória Magalhães Chaves - email: anavitoriamagalhaesc@gmail.com

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ABSTRACT

Objective: Hematopoietic Stem Cell Transplant (HCT) recipients are among the largest consumers of allogeneic red blood cells and platelets. The impact of Patient Blood Management (PBM) strategies on these recipients is poorly understood. Therefore, we evaluated the PBM strategies and their impact on patients undergoing autologous and allogeneic HCT. **Methodology**: We conducted a retrospective analysis of 333 patients who underwent HCT at the Bone Marrow Transplant Center of the Walter Cantídio University Hospital (HUWC) from 2018 to 2022. Clinical data were collected from medical records. Statistical analysis was performed using Jamovi software version 2.03, with a statistical significance level of p = 0.05. **Results:** The mean age of the patients was 45 years, with 50.5% being male. Of the transplants performed, 62.8% were autologous. The most common diagnosis was plasma cell neoplasia 36.3%. Restrictive strategies were adopted, and the transfusion parameters during HSCT hospitalization were as follows: Hemoglobin <7g/dL, platelets <50,000/µL in case of bleeding or lumbar puncture, <20,000/µL in the presence of fever or central venous access puncture, and

<10,000/µL prophylactically. The transfusion requests consisted of 1 unit of red blood cells and 1 unit of platelet "buffy coat" per administration. During hospitalization, 94.3% of the patients received platelet transfusions, and 50.1% received red blood cells. Patients undergoing allogeneic HCT required more transfusions, experienced more transfusion reactions, and had a higher number of deaths during hospitalization compared to those undergoing autologous HCT ($p<0.0001$). The most frequent transfusion reactions were febrile non-hemolytic (15%). The number of red blood cell and platelet transfusions showed a strong ($p<0.5$) and significant ($p<0.01$) correlation with the collected volume and engraftment time. There was no correlation between the number of transfusions and age or patient survival after hospital discharge. The number of transfusions during this period did not have a significant impact on survival. However, higher mortality was observed among patients who received more transfusions and those who underwent allogeneic HCT. **Conclusion:** The implementation of PBM for HCT recipients was associated with a significant reduction in allogeneic red blood cell and platelet transfusions and a reduction in transfusion-related costs, without any negative impact on clinical outcomes.

Keywords: Blood Transfusion. Erythrocytes. Blood Platelets.

INTRODUCTION

The transfusion of blood components is a widely used therapeutic strategy, often aiming to alleviate symptoms and improve patients' quality of life. However, studies have shown that the adoption of restrictive transfusions is non-inferior and may even improve outcomes in some cases[1].

In Brazil, over 2.95 million transfusions were performed in 2019[2], which has led to increased concern regarding transfusion risks and the promotion of initiatives to rationalize the use of blood components. In this context, in 2021, the World Health Organization issued an alert about the need to adopt Patient Blood Management (PBM) worldwide[2].

This method is patient-centered, preemptive, preventive, and multidisciplinary[3], based on three principles: reducing blood loss, correcting anemia, and treating coagulopathies[2]. PBM is more easily utilized in elective surgical and clinical procedures, where it is possible to diagnose and intervene preemptively in patients with anemia and coagulopathy[4,5]. However, it is a challenging strategy limited to some centers due to lack of knowledge and resources[4].

Implementing PBM is even more challenging in patients with onco-hematological diseases[6] since cytopenias occur routinely, both as a consequence of the underlying disease and chemotherapy treatment[7,8]. Thus, red blood cells and platelets are the main blood components transfused peri-transplant and are fundamental therapies for these patients[4,7]. This study aimed to evaluate restrictive transfusion strategies and their impacts on patients undergoing bone marrow transplantation (BMT)

MATERIALS AND METHODS

This descriptive and retrospective observational study was conducted at the Bone Marrow Transplant Center of Walter Cantídio University Hospital (HUWC-UFC), with the support of the Ceará Blood Center (HEMOCE). The study period covered from January 1, 2018, to December 31, 2022.

Data collection was performed by reviewing medical records and the Blood Bank System (SBS) of HEMOCE. The collected data included clinical, laboratory, and treatment information for patients treated at the transplant center during the study period.

The data were presented as mean and standard deviation for continuous variables, as well as median and interquartile range when not normally distributed. For categorical variables, percentages were used. The variables of interest, including survival, age, and the volume of collected tests, were transformed into tertiles to facilitate analysis.

Continuous variables were tested for normal distribution using the Shapiro-Wilk test. Correlation was assessed using Spearman's rank correlation coefficient. Differences between groups were evaluated using the Kruskal-Wallis test for continuous variables. The association between categorical variables using the Chi-square test, followed by Kendall's Tau-B for ordinal data, or the odds ratio when in 2x2 tables. All statistical tests were performed using Jamovi software version 2.03, with a two-sided approach, and the level of statistical significance was set at $\alpha = 0.05$.

RESULTS

The sample consisted of 333 patients with a mean age of 45 years, of whom 168 (50.5%) were male and 165 (49.5%) were female. Sixty percent of the total patients had some comorbidity, with arterial hypertension being the most frequent (21%). Regarding the type of transplant, 62.8% were autologous and 37.2% were allogeneic. The main diagnoses of patients undergoing BMT were plasma cell neoplasia (36.3%) (Table 1).

Restrictive strategies are adopted in the studied center, and transfusion triggers during BMT hospitalization were: Hemoglobin (Hb) < 7g/dL, platelets <50,000 µL if bleeding or lumbar puncture, <20,000 µL in the presence of fever or central venous access puncture, and <10,000µL prophylactically. The reviewed transfusion requests consisted of 1 unit of red blood cells (RBCs) and 1 unit of platelet "buffy coat" per administration.

Analysis of the transfusion profile during hospitalization for transplantation showed that 167 patients (50.1%) received red blood cell transfusions and 314 (94.3%) received platelet transfusions(Table 1). Allogeneic transplant patients received more transfusions (26.4) and had significantly more transfusion reactions (23.7%) and more deaths during hospitalization when compared to autologous patients (p<.0001) (Table 2). Among the patients who developed transfusion reactions, 15% experienced febrile non-hemolytic reactions, followed by allergic reactions in 8.7% of cases (Table 3). In 3 patients (1%), more than one transfusion reaction was observed.

Analyzing the total population, red blood cell transfusions had a median of 1 unit (0-35 units), while platelet transfusions had a median of 3 units (0-48 doses). The median pre-transfusion hemoglobin (Hb) and platelet count were 6.5g/dL and 9832 µL, respectively. The lost volume in laboratory test collection throughout hospitalization was also analyzed to assess one of the pillars of PBM, which aims to avoid blood loss. In this analysis, the median volume collected was 241.6 ml (Table 3).

In this study, we compared the PBM results of the present study at HUWC with data from Canadian centers.we observed a lower average pre-transfusion hemoglobin level (6.23 g/dL vs. 7.09 g/dL), but with a similar median regarding the number of red blood cell and platelet transfusions. However, in allogeneic transplantation, we observed superior results in the present study regarding red blood cell transfusions and platelet transfusions compared to the Canadian study[11] (Table 4).

In the Spearman correlation matrix, the number of red blood cell and platelet transfusions had a strong (>0.5) and significant (p <0.01) correlation with the collected volume, as well as the engraftment time, meaning that patients who lost more volume in tests or had a longer aplasia time also received more transfusions. There was no evidence of correlation between the number of transfusions, pre-transfusion hemoglobin, and platelet count with age or patient survival after hospital discharge, demonstrating that elderly patients did not require more transfusions and adapted well to the restrictive strategy adopted.

The number of transfusions during this period did not impact survival, which was expected because post-hospital discharge survival is influenced by many other factors. In the analysis of in-hospital mortality, there was higher mortality in patients who received more transfusions and in those undergoing allogeneic transplantation. However, this is a study

bias because some patients, especially those undergoing allogeneic BMT, tend to undergo more tests and transfusions due to their severity, and causality cannot be attributed.

DISCUSSION

A review study comparing restrictive transfusion strategies with liberal ones also did not show an impact on mortality up to 30 days after transplantation and reduced by 43% the risk of a patient receiving a transfusion[9], without affecting the quality of life of these patients[10].

A Canadian study published in 2023 was the first randomized study addressing restrictive strategy in BMT, comparing restrictive transfusion (Hb <7g/dL) with liberal (Hb <9g/dL). The analysis showed that restrictive transfusion was non-inferior to liberal and there was a reduction in transfusion reactions[11], consistent with the present study.

When comparing the restrictive strategy used in this randomized study with that of HUWC, it was identified that HUWC had a lower mean pre-transfusion hemoglobin but a similar median regarding the number of red blood cell and platelet transfusions, except when comparing platelet transfusions only in allogeneic transplant, in which case, HUWC had a higher mean of transfusions[11].

This study suggests that restrictive strategies are effective in reducing blood component transfusions in BMT, as well as reducing patients' exposure to transfusion risks, and reducing costs, without harming patients. Thus, education regarding transfusion medicine is essential so that patients are not exposed to a higher risk of alloimmunization, transfusion graft disease, among others, as there is no evidence that a liberal transfusion strategy improves the quality of life and outcome of these patients[12].

CONCLUSION

Therefore, the existence of clear transfusion triggers associated with a patient-centered approach allows for the rationalization of blood component use efficiently and without harm. Hence, it is necessary to conduct more studies that can confirm these findings so that PBM can be effectively implemented in bone marrow transplantation.

TABLE 1: Patient and transplant characteristics of the study population (N = 333)

Characteristics	
Age at diagnosis, median years (range)	45 (30 - 60)
Patient sex, n (%)	
Male	168 (50.5)
Female	165 (49.5)
Transplant type, n (%)	
Autologous	209 (62.8)
Allogeneic	124 (37.2)
Underlying disease	
Myeloma/ plasmacytic disorder	121 (36.3)
Hodgkin's lymphoma	46 (13.8)
Non-Hodgkin's lymphoma	36 (10.8)
Acute Lymphoblastic Leukemia/lymphoblastic lymphoma	35(10.5)
Acute myeloid leukemia" (AML)	30 (9)
Aplasia	18(5.4)
Myelodysplastic syndrome	12 (3.6)
Chronic Myeloid Leukemia	12 (3.6)
Others*	23 (6.9)
Comorbiditiesn (%)	
hypertension	70 (21)
Smoking	37 (11)
Elitism	16 (5)
Chronic Kidney Disease	14 (4)
lung disease	5 (2)
Congestive Heart Failure	5 (2)
Others	54 (55)
Red blood cell transfusion	167 (50.1)
Platelet transfusion	314 (94.3)

*Others diseases include Chronic Lymphocytic Leukemia (CLL), Chronic Myelomonocytic Leukemia (CMML), Mantle Cell Lymphoma, Follicular Lymphoma, and Marginal Zone Lymphoma.

TABLE 2: Association between type of transplant and transfusions (N = 333).

	Red blood cell transfusion			
Type of Transplant	Yes	No	Total	p value
Autologous	80	129	209	<0.0001
Allogeneic	88	36	124	
	Platelet transfusion			
Type of Transplant	Yes	No	Total	
Autologous	197	12	209	0.970
Allogeneic	117	7	124	
	Transfusion reaction			
Type of Transplant	Yes	No	Total	
Autologous	32	177	209	<0.0001
Allogeneic	49	75	124	
	Death during hospitalization			
Type of Transplant	Yes	No	Total	
Autologous	4	205	209	0.0001
Allogeneic	16	108	124	

Note: P<0,05;

TABLE 3: Analysis of Transfusion Data

Variable	n (%)	Median (IQR)	Mean (SD)
Red blood cell transfusion.	167 (50.1)		
Pre-transfusion HB	155	6.50 (0.60)	6.23 (0.807)
Nº of red blood cell transfusions.	333	1 (3)	2.43 (4.594)
Time to red blood cell independence.	145	9 (5)	12.07 (7.714)
Platelet transfusion	314 (94.3)	-	-
Pre-transfusion platelets.	83	9832.00 (7222.5)	13127.81 (9979.079)
Nº of platelet transfusions.	83	3 (3)	5.29 (7.387)
Pre-transfusion platelets.	333	9 (3)	11.05 (8.552)
Time to platelet independence.	293		
Transfusion reaction occurrence	79(23.7)	-	-
Types of reaction			
Allergic reaction	29(8.7)	-	-
Febrile non-hemolytic reaction	50(15)	-	-
(TACO)	3(1)	-	-
Death during hospitalization	20(6)	-	-
Graft engraftment time	309	11 (5)	12.48 (4.083)
Collected volume	331	241.60 (141.95)	285.10 (190.279)

Note: Hemoglobin (Hb), Interquartile Range (IQR), Standard deviation (SD), Transfusion-Associated Circulatory Overload (TACO).

TABLE 4: Comparative analysis of restrictive transfusion strategy outcomes in autologous and allogeneic hematopoietic stem cell transplantation patients.

Total transplants	HUWC		Canadian center	
Variable	Mean	Median	Mean	Median
Pre-transfusion Hb	6.23	6.5	7.09	6.9
Number of red blood cell transfusions	2.43	1	2.73	2
Number of platelet transfusions	5.29	3	5.97	2
Autologous				
Pre-transfusion Hb	6.5	6.6	7.1	6.9
Number of red blood cell transfusions	0.8	0	1.32	0
Number of platelet transfusions	2.9	2	2.23	2
Allogeneic				
Pre-transfusion Hb	5.9	6.25	7.07	6.9
Number of red blood cell transfusions	5.11	3	4.12	2
Number of platelet transfusions	9.2	6	5.97	2

Note: HUWC=Walter Cantideo University Hospital; HB=hemoglobin

REFERENCES

1. Cable CA, Razavi SA, Roback JD, et al. RBC Transfusion Strategies in the ICU: A Concise Review. Crit Care Med. 2019;47(11):1637-44.

2. Rodrigues RD, Brunetta DM, Costa L, et al. Consensus of the Brazilian association of hematology, hemotherapy and cellular therapy on patient blood management: Anemia tolerance mechanisms. Hematol Transfus Cell Ther. 2024;46(Suppl 1):S77-82.

3. Shander A, Bracey AW Jr, Goodnough LT, et al. Patient Blood Management as Standard of Care. Anesth Analg. 2016;123(4):1051-3.

4. Meybohm P, Richards T, Isbister J, et al. Patient Blood Management Bundles to Facilitate Implementation. Transfus Med Rev. 2017;31(1):62-71.

5. Klein A, Agarwal S, Cholley B, et al. A review of European guidelines for patient blood management with a particular emphasis on antifibrinolytic drug administration for cardiac surgery. J Clin Anesth. 2022;78:110654.

6. Gombotz H, Hofmann A, Norgard A, et al. Supporting Patient Blood Management (PBM) in the EU: a practical implementation guide for hospitals [Internet]. Luxemburgo: European Commission; 2017 [cited 2024 Aug. 25]. Available from: https://op.europa.eu/en/publication-detail/-/publication/93e1bbbf-1a8b-11e7-808e-01aa75ed71a1/language-en

7. Christou G, Iyengar A, Shorr R, et al. Optimal transfusion practices after allogeneic hematopoietic cell transplantation: a systematic scoping review of evidence from randomized controlled trials. 2016;56(10):2607–14.

8. Canadian Blood Services. Patient Blood Management from an Oncology/Hematologist Point of View [Internet]. Ontario; 2023. Available from: https://profedu.blood.ca/en/patient-blood-management-oncologyhematologist-point-view

9. Carson JL, Stanworth SJ, Roubinian N, et al. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Cochrane Database Syst Rev. 2016;10(10):CD002042.

10. Pagano MB, Dennis JA, Idemudia OM, et al. An analysis of quality of life and functional outcomes as reported in randomized trials for red cell transfusions. Transfusion. 2023;63(11):2032–9.

11. Tay J, Allan DS, Chatelain E, et al. Liberal Versus Restrictive Red Blood Cell Transfusion Thresholds in Hematopoietic Cell Transplantation: A Randomized, Open Label, Phase III, Noninferiority Trial. J Clin Oncol. 2020;38(13):1463–73.