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LETTER TO EDITOR

PLERIXAFOR FOR HEALTHY PERIPHERAL BLOOD HEMATOPOIETIC STEM CELL DONORS IN PEDIATRIC ALLOGENEIC HSCT

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INTRODUCTION

Achieving optimum outcomes after allogeneic hematopoietic stem cell transplant (HSCT) is dependent on the stem cell dose administered. It has been documented that for allogeneic HSCT done for malignant indications in pediatrics, a stem cell dose greater than 5 million per kg of recipients body weight was associated with better outcomes , whereas doses less than 5 million per kg could lead to failure[1]. Peripheral blood hematopoietic stem cells (PB-HSC) have become the predominant source of hematopoietic stem cells (HSC) being used worldwide for allogeneic HSCT. Optimum mobilization of these cells into the peripheral blood (PB) from the donor is imperative for a good stem cell yield on apheresis[2]. Granulocyte colony stimulating factor (G-CSF) based mobilisation of the HSC has been the predominant method of mobilizing the stem cells into the PB before apheresis. With G-CSF alone, there may be a failure to mobilize adequate number of stem cells in a significant proportion of healthy donors[3]. Mobilization of PB-HSC into the PB is facilitated with the use of plerixafor. Plerixafor reversibly inhibits the binding of SDF-1 to CXCR4, an interaction that plays an important role in the HSC retention in the bone marrow, thus increasing the number of HSC circulating in the PB. Plerixafor has been approved along with G-CSF for use for autologous HSC harvest in adults. Its use in in pediatric autologous HSCT is also expanding. However, the use of plerixafor for normal donors especially in the pediatric setting has not been studied much.

We present this retrospective review of our experience with the use of plerixafor in healthy donors for our patients undergoing allogeneic HSCT.

METHODS

This study is a retrospective study conducted at a tertiary referral center in north India. Ten patients underwent matched sibling donor or haploidentical HSCT. All of the recipients were children less than 14 y old except for one who was a 20-y old male treated as a child for Philadelphia chromosome positive acute lymphoblastic leukemia and had subsequently relapsed. All donors were children except in two cases where adults were used for haploidentical HSCT. We used plerixafor along with G-CSF in 5 healthy donors for our patients undergoing allogeneic HSCT. Plerixafor was administered to the donor when it was necessary to ensure a good HSC dose e.g for haploidentical HSCT. In case the donor's weight and age were less compared to the recipient, plerixafor was used to ensure a high circulating HSC count for a successful apheresis. It was also used in situations where the amount of plasma was to be kept minimal in the harvest due to incompatibility in the blood groups of the donor and recipient.

Plerixafor was used at a dose of 0.24mg/kg, subcutaneously approximately 11 hrs prior to harvest. All donors were on G-CSF at a dose of 5 mcg/kg twice a day for 4 days before getting plerixafor. We did a CD-34 positive HSC estimation in the PB prior to administering plerixafor, but this was not used to guide the decision regarding plerixafor administration.

In 5 other donors admitted for allogeneic HSCT donation during the same time period, plerixafor was not administered and only G-CSF was used. We compared the outcomes of both the groups.

RESULTS

Ten allogeneic HSCTs were included in the analysis, 5 in which the donor received plerixafor along with G-CSF and in the other five the donor got only G-CSF. In all the HSCT, PB HSC was used. In all cases the recipients were males and the donors were females. In the group in which plerixafor was given the indication for HSCT were as follows: chronic myeloid leukemia (CML) in blast crisis=1, high risk acute lymphoblastic leukemia (ALL)=1, relapsed ALL=1, relapsed acute myeloid leukemia (AML)=1 and X-linked adrenoleukodystrophy (ALD)=1. In the group where the donor did not get plerixafor the indications were: juvenile myelomonocytic leukemia (JMML)=2, High risk ALL=1 and Relapsed AML=2. The age range was 5y-32y for the group that got pre-harvest plerixafor. (Table 1).

TABLE 1: Clinical and hematopoietic mobilization details of both groups

	Plerixafor given	Plerixafor not given	p-value
n	5	5	
Diagnosis	CML in blast crisis=1 High risk ALL=1 Relapsed ALL=1 Relapsed AML=1 X linked ALD=1	JMML=2 High risk ALL=1 Relapsed AML=2	
Sex	Recipient= all males Donor= all females	Recipient=all males Donor=all females	
Type of HSCT	Haploidentical=3 MSD=2	MSD=5	NS
Age of recipient (in years)	10.6+5.7	5.8+3.8	NS
Age of donor (in years)	14.8+13.1	9.4+2.9	NS
Recipient weight (in kg)	28.0+15.5	19.2+11.4	NS
Donor weight (in kg)	31.5+23.3	22.7+7.6	NS
CD 34 pre plerixafor (per cumm)	83.2+77.2	99.0+59.0	NS
CD 34 of harvest product (per cumm)	2789.2+1030.3	1319.0+647.2	0.032**
Stem cell dose (million cells/kg of recipients body weight)	9.7+2.2	7.1+4.7	NS

CML :chronic myeloid leukemia, ALL : acute lymphoblastic leukemia, AML: acute myeloid leukemia, ALD : adrenoleukodystrophy, JMML: juvenile myelomonocytic leukemia, MSD:matched sibling donor, CD: cluster differentiation .
NS: not significant , ** : independent t-test

No significant difference in terms of recipients age and weight; donors age and weight and the CD-34 count in PB pre-plerixafor were there between the two groups. However, the CD-34 HSC count in the harvested product was significantly higher in the group that received plerixafor (p=0.032). The stem cell dose transfused to the patient was also higher when the donor got plerixafor, although the difference was not significant. None of the donors suffered any side effects and underwent the subsequent apheresis uneventfully.

DISCUSSION

In our experience ,the use of plerixafor in healthy donors , for pediatric allogeneic HSCT was safe and associated with a higher HSC count in the harvested product. The use of plerixafor is approved in adults for autologous HSC harvest in lymphomas and multiple myeloma. Recent there has been a recommendation from the EMA for plerixafor use in pediatrics for HSC collection for autologous HSCT in lymphomas and malignant solid tumors[4].

In pediatric patients undergoing allogeneic HSCT, the harvest of adequate PB HSC for a recipient with higher weigh may become difficult. Younger donors and children with smaller body weight are at risk of hemodynamic and metabolic disturbances if subjected to long apheresis procedures for HSC collection. Sevilla et al have reported that the procedure of PBSC collection in children can be associated GCSF related bone pains, thrombosis, risks of catheter insertion , low calcium and hemodynamic instability. In children <20 kg the cardiovascular problems are more frequent during PBSC collection[5]. In up to 5% of donors GCSF based regimens can result in failure of the harvest .In the event of failure of PBSC mobilization a repeat attempt at mobilization or bone marrow collection remains the only salvage option[6].

In our experience the use of plerixafor in pediatric donors (two with age 5 years and one with age of 6 years), was associated with a good rise in the peripheral blood of CD-34 counts and yielded a good HSC count in the harvested product . The two adult donors who received plerixafor also didn't experience any side effects and the drug was effective.

Plerixafor may also be used in situations where one would like to limit the amount of plasma being harvested e.g in case of ABO mismatched allogeneic HSCT . A higher peripheral blood CD-34 count allows for the required amount of stem cells to be harvested in a smaller volume and with lesser number of apheresis cycles for the donor. In case the CD 34 count pre HSCT is not optimal, the use of plerixafor can prevent a second harvest procedure.

In our experience we found that plerixafor was safe and effective in healthy pediatric and adult donors for allogeneic HSCT.

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Declaration: The research was carried out according to the guidelines of Declaration of Helsinki.

REFERENCES

1. Remberger M, Grønvold B, Ali M, et al. The CD34+ Cell Dose Matters in Hematopoietic Stem Cell Transplantation with Peripheral Blood Stem Cells from Sibling Donors. Clin Hematol Int. 2020;2(2):74-81.
2. Chang YJ, Weng CL, Sun LX, et al. Allogeneic bone marrow transplantation compared to peripheral blood stem cell transplantation for the treatment of hematologic malignancies: a meta-analysis based on time-to-event data from randomized controlled trials. Ann Hematol. 2012;91(3):427-37.
3. Hopman RK, DiPersio JF. Advances in stem cell mobilization. Blood Rev. 2014;28(1):31-40.
4. Karres D, Ali S, van Hennik PB, et al. EMA Recommendation for the Pediatric Indications of Plerixafor (Mozobil) to Enhance Mobilization of Hematopoietic Stem Cells for Collection and Subsequent Autologous Transplantation in Children with Lymphoma or Malignant Solid Tumors. Oncologist 2020;25(6):e976-81.
5. Sevilla J, González-Vicent M, Lassaletta A, et al. Peripheral blood progenitor cell collection adverse events for childhood allogeneic donors: variables related to the collection and safety profile. Br J Haematol. 2009;144(6):909-16.
6. Ings SJ, Balsa C, Leverett D, et al. Peripheral blood stem cell yield in 400 normal donors mobilised with granulocyte colony-stimulating factor (G-CSF): impact of age, sex, donor weight and type of G-CSF used. Br J Haemato.l 2006;134(5):517-25.