e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(5); 1248-1252

Original Research Article

A Study on Factors Influencing the Engraftment of Peripheral Blood Stem Cell Transplantion in Various Hematological Disorders

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Received: 01-02-2026 / Revised: 15-03-2026 / Accepted: 21-04-2026

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Conflict of interest: Nil

Abstract

Aim: The primary aim of this study is to find out the factors that influence the engraftment of haematopoietic stem cells during transplantation in various haematological disorders.

Methods: The study was conducted by collecting the data retrospectively in 14 patients who had undergone PBSCT at Department of Haematology, Tertiary Care Hospital, and Chennai from April-2022 to February- 2024 for a period of 2 years. The speed of engraftment is measured by defined threshold of circulating neutrophils (polymorphonuclear cells or PMNs) PMNs >500/µL or platelets >20,000/µL, for three consecutive days after HSC transplantation.

Results: In the present study on factors influencing peripheral blood stem cell transplantation in 14 patients with hematological disorder, the speed of engraftment was assessed by the first appearance and persistence of neutrophils of >500cells/µL and platelets of >20,000/µL respectively, without transfusion for three consecutive days. The range observed was between 10 and 21 days for neutrophil engraftment. The range observed for platelet engraftment was between 14 and 30.

Conclusion: Autologous PBSCT showed faster PBSC graft engraftment than allogenic PBSCT. Among various hematological malignancies multiple myeloma patients showed relatively rapid PBSC graft engraftment with autologous PBSC as a source. Since early engraftment reduces length of hospital stay, morbidity, mortality and cost of this highly expensive treatment, it is imperative to utilize all available options to enhance the speed of engrafment.

Keywords: Peripheral Blood Stem Cell Transplantation, Haematological disorders, Engraftment.

DOI: 10.25258/ijcpr.18.5.204

Introduction

Haematopoietic stem cell (HSCs) Transplantation remains the only curative option for various haematological disorders. HSCs are present not only in the marrow but also in the peripheral circulation and can be collected by cytapheresis. Normally the numbers of circulating HSCs in the peripheral blood of healthy adults were much less than in the marrow. However, the number of circulating HSCs increases after the suppression of marrow by chemotherapy and even more when mobilising factors are administered. [1]

Peripheral Blood Stem Cells Transplantation (PBSCT) result in more rapid engraftment , give results equivalent to marrow, and may provide faster lymphocyte return, resulting in fewer infections. So, in many transplant centres the PBSCs collection for stem cell transplantation now exceeds marrow collection thus eliminating the risks of anesthesia and the marrow collection process. [2] Thus, considerable interest has developed in the methods to obtain PBSCs from both patients and donors.

PBSCs can be obtained from the peripheral blood by apheresis, but due to the small number of circulating PBSCs, multiple procedures would be necessary to obtain enough cells for transplantation. To further increase the level of circulating PBSCs, donors are given the growth factor G-CSF. In studies of normal individuals, the administration of G-CSF (10 to 20 µg/kg/day)

causes an increase in the percentage of CD34+ cells from 0.05% to 1.5% after 5 days or the use of the agent plerixafor (240µg/kg/day) on the evening of the fourth day of daily G-CSF for stem cell mobilization. The apheresis device uses a centrifuge to separate and collect MNCs, including peripheral blood HSCs, from the blood. In order to achieve a target cell dose of 2 to 5×106 CD34+ cells/kg it is necessary to process 12 to 25 litres of blood or 2.5 to 6.0 times the patient's calculated blood volume. This result in a yield of about 4.5×10^8 CD34+ cells from a single apheresis procedure. [3] The usual dose of CD34+ cells considered suitable for transplantation is about 2.5 to 5×10^6 CD34+ cells/kg or about 2×10^8 CD34+ cells for a 70-kg person. [1] The use of mobilized PBSCs led to significant recovery of neutrophil and platelet levels after transplantation. With PBSCs transplantation, neutrophil recovery occurs within 8-12 days, while platelets recover averages 8-15 days. [4] Apheresis instrument settings such as inlet flow rate, centrifuge speed, collect pump flow rate and anticoagulant: whole blood ratio vary depending on the target cell type to be collected. [5]

The quality of PBSC graft is assessed by its speed of engraftment. The advantage of early engraftment of haematopoietic stem cell transplantation include, reduced incidence of infections associated with post-transplant neutropenia, mortality, morbidity, fewer number of red cell and platelet transfusions may be required and shorten the length of hospital stay. Furthermore this valuable expensive procedure will be available for many numbers of patients who are waiting for their disease to be cured.

Aim: To find out the factors that influence engraftment of haematopoietic stem cell during transplantation in various haematological disorders.

Materials & Methods

The study was conducted in the Department of Transfusion Medicine, The Tamil Nadu Dr.M.G.R Medical University, Guindy, and Chennai by collecting the data retrospectively in 14 patients who had undergone PBSCT at Department of Haematology, Tertiary Care Hospital, and Chennai from April-2022 to February- 2024 for a period of 2 years.

As per AABB criteria, the speed of engraftment is measured by defined threshold of circulating neutrophils (polymorphonuclear cells or PMNs) PMNs >500/µL or platelets >20,000/µL, for three consecutive days after HSC transplantation.[6]

Accordingly, the following factors were analyzed, patient related factors (age, gender, diagnosis), donor related factors (HLA matching for allogenic transplantation, ABO group match), type of PBSCs (Autologous / Allogeneic), CD 34+ cell dose infused per kg recipient body weight.

Results

A total of 14 patients undergoing Peripheral Blood Stem Cells Transplantation procedure were analysed for various factors influencing the stem cell engraftment by retrospective analysis of the available data.

In the present study on factors influencing peripheral blood stem cell transplantation in 14 patients with hematological disorder, the speed of engraftment was assessed by the first appearance and persistence of neutrophils of >500cells/µL and platelets of >20,000/µL respectively, without transfusion for three consecutive days.

In our study, the range observed was between 10 and 21 days for neutrophil engraftment. The range observed for platelet engraftment was between 14 and 30. The data obtained for various factors analyzed for the speed of PBSC engraftment are as follows:

Table 1: Age and Day of Engraftment:

Age in Years	Frequency	Neutrophil Engraftment in Median on day	Platelet Engraftment in Median on day
Below 20	3	15 (12-16)	19(17-20)
20 – 39	8	15(11-21)	18.5(14-30)
40 – 59	3	10(10-12)	14(14-16)

Table 2: Gender and Day of Engraftment:

Gender	Frequency	Neutrophil Engraftment in Median on day	Platelet Engraftment in Median on day
Male	13	14.5 (10-21)	18(14-30)
Female	1	15	20

Table 3: Patient Diagnosis and Day of Engraftment:

Diagnosis	Frequency	Neutrophil Engraftment in Median on day	Platelet Engraftment in Median on day
Acute Lymphoid Leukemia	1	21	30
Acute Myeloid Leukemia	6	15.5(15-17)	19.5(18-23)
Aplastic Anemia	2	13.5(13-14)	16(14-18)
Hodgkin's Lymphoma	1	12	17
Multiple Myeloma	2	10(10)	14.5(14-15)
Non-Hodgkin Lymphoma	2	11.5(11-12)	15.5(15-16)

Table 4: PBSCT Type and Day of Engraftment:

PBSCT Type	Frequency	Neutrophil Engraftment in Median on day	Platelet Engraftment in Median on day
Autologous	5	11(10-12)	15(14-17)
Allogenic	9	15(13-21)	19(14-30)

Table 5: HLA Match and Day of Engraftment:

HLA Match	Frequency	Neutrophil Engraftment in Median on day	Platelet Engraftment in Median on day
12/12	8	15.5(13-21)	19.5(14-30)
6/12	1	15	18

Table 6: Blood Group Match and Day of Engraftment:

ABO Blood Group Match	Frequency	Neutrophil Engraftment in Median on day	Platelet Engraftment in Median on day
ABO compatible	6	16(15-21)	21.5(18-30)
Major Incompatible	1	13	14
Minor Incompatible	1	14	18
Bidirectional	1	15	19

Table 7: Conditioning Regimen and Day of Engraftment:

Regimen Intensity	Frequency	Neutrophil Engraftment in Median on day	Platelet Engraftment in Median on day
Cy + TBI	1	21	30
Cy + Busulfan	6	15.5(15-17)	19.5(18-23)
Cyclophosphamide	2	13.5(13-14)	16(14-18)
BEAM	3	12(11-12)	16(15-17)
Melphalan	2	10(10)	14.5(14-15)

Table 8: CD34+ Cell Dose and Day of Engraftment:

CD 34+cell dose/Kg Recipient Body Weight	Frequency	Neutrophil Engraftment in Median on day	Platelet Engraftment in Median on day
$< 2.5 \times 10^6$	1	21	30
$2.5 – 4.9 \times 10^6$	6	11.5(10-15)	15.5(14-20)
$5.00 – 7.8 \times 10^6$	2	15.5(15-16)	18.5(18-19)
$> 7.8 \times 10^6$	5	15(13-17)	19(14-23)

Discussion

In our study on factors influencing the engraftment of peripheral blood stem cell transplantation on 14 cases of hematological disorder the following features were observed. The relative speed of engraftment was analyzed by median and range values (Neutrophil and platelet engraftment days) obtained from each individual factors.

In the present study patients those who received CD34+ cell dose ranging from 2.5-4.9x10^6cells/kg, achieved rapid neutrophil and platelet engraftment. However, when the CD34+ cell dose was <2.50x10^6cells/kg the neutrophil and platelet engraftment was delayed. Further, in those patient receiving CD34+ cell dose was 5-7.8x10^6cells/kg and >7.80x10^6cells/kg also shown mild delay in engraftment neutrophil and platelet (Table.8). Similarly Attilio Oliveri et al in their study on 80 patients with hematological malignancy undergoing autologous PBSC Transplantation revealed that a CD34+ dose range from 2.5–4.9x10^6cells/kg is safe for complete stable and rapid neutrophil engraftment. In the same study, they also found out

that CD 34+ cell number of 5.0-7.8x10^{6}cells/kg is the optimal number for obtaining rapid platelet recovery. Further, they also found out that infusion of CD 34+ cell number >7.8x10^{6}cells/kg is not advantageous. [7] However, Charles H. Weaver et al suggested that there is a correlation between CD 34+ cell dose of 5.0-7.5x10^6 and rapidity of engraftment of neutrophil and platelets. [8] In present study patients who underwent autologous PBSCT achieved rapid neutrophil and platelet engraftment in median on day 11 and 15 respectively than those who underwent allogeneic PBSCT in median on day15 and 19 (Table 4).

In a similar study by Thissiane et al on 65 haematological disorder patients reported rapid neutrophil and platelet engraftment in median on day 10 and 11 respectively than those who underwent allogeneic PBSCT in median on day19 and 21. [6]

In our study among hematological disorders, Multiple Myeloma patients achieve rapid neutrophil and platelet engraftment than Lymphoma (NHL and HL), Aplastic anaemia and Leukemia (AML and ALL) (Table.3).

Similar to the study by Bensinger W et al on Multiple Myeloma patients on whom autologous haematopoietic stem cell transplant yielded faster engraftment. [9] In our study all Multiple Myeloma patients had received autologous PBSCT. This could be another reason for faster engraftment in these group patients.

In our study, 2 out of 14 patients who received Melphalan conditioning regimen achieved rapid neutrophil and platelet engraftment than others and those who received Cy Bu and Cy TBI achieved delayed engraftment (Table.7).

Similarly study by Thissiane et al found that Melphalan shows faster neutrophil and platelet engraftment engraftment than others and Cy TBI and Cy Bu achieve delayed engraftment than others. [6] In another study by J.Reiffers et al on patients with hematological malignancies found that Bu TBI regimen slows the speed of neutrophil engraftment. [10]

In our study, 9 out of 14 patients received allogenic PBSCs transplantation. One patient with 6/12 HLA matched PBSCs transplantation achieved rapid neutrophil and platelet engraftment and one patient with 12/12 HLA matched PBSCs transplantation achieved delayed neutrophil and platelet engraftment (Table.5).

The probable reason for delayed engraftment in one patient with 12/12 HLA matched PBSCT could be due to the fact that inadequate CD 34+ cell dose of 2.10×10^6 cells/kg was given. The finding of rapid engraftment in 6/12 HLA matched PBSCT could be due to the fact that higher CD 34+ cell dose of 7.6×10^6 cells/kg was given.

This is similar to Pulsipher M A et al study, that is administration of higher doses of CD34+ cells from related or unrelated, fully or partially matched donors that are given to adults or children is consistently associated with more rapid neutrophil and platelet engraftment. [11] In our study, 9 out of 14 patients have been treated with allogeneic PBSCs transplantation and we found out no significant difference in the speed of engraftment between ABO compatible and incompatible PBSCs transplantation. (Table.6)

Similarly G Stussi et al. in their study on 562 patients with allogeneic haematopoietic stem cell transplantation found that ABO incompatibility has no influence on neutrophil and platelet engraftment and that only RBC engraftment was delayed. [12]

The probable reason could be the ABO incompatibility doesn't seem to affect the neutrophil and platelet engraftment in most patients of stem cell Transplant. However, in particular Major ABO incompatibility it may cause delay of RBCs engraftment, or even manifest as Pure Red Cell Aplasia (PRCA).

In our study patients in the age group between 40-59 years had achieved faster neutrophil and platelet engraftment than others (Table.1).The probable reason could be due to autologous PBSCs transplantation in all these three patients in this age group 40-59 years.

Similarly Thissiane et al revealed that PBSC engraftment was more rapid in the 50-59 year age group and they found that the reason could be due to the associated favorable factors like autologous source of PBSC and pretransplant conditioning regimen with melphalan 200 mg and CBV. [6]

Out of total 14 patients in our study, only one female patient who received allogenic transplantation shows no significant difference in neutrophil and platelet engraftment when compared to male (Table.2). However, the study by Thissiane et al found that male gender achieved faster neutrophil and platelet engraftment than female gender. [6]

Conclusion

Autologous PBSCT showed faster PBSC graft engraftment than allogenic PBSCT. Among various hematological malignancies multiple myeloma patients showed relatively rapid PBSC graft engraftment with autologous PBSC as a source. Since early engraftment reduces length of hospital stay, morbidity, mortality and cost of this highly expensive treatment, it is imperative to utilize all available options to enhance the speed of engraftment.

However, analysis of factors influencing successful engraftment from larger number of PBSCT patients would provide some more relevant information in this regard.

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