RESEARCH ARTICLE

Outcome of plerixafor based stem cell (CD34) mobilisation in autologous stem cell transplant. A Retrospective analysis from a tertiary care centre of Pakistan

Farrukh Ali Khan[1], Fawad Qureshi[2], Urooj Haider Hashmi[3]

Abstract

Objective: To determine the outcome of plerixafor-based stem cell mobilisation in autologous stem cell transplant.

Method: The retrospective study was conducted at the Dow University Hospital, Karachi, and comprised data from February 2019 to December 2024 related to patients who had undergone autologous bone marrow transplant. The outcome of stem cell mobilisation with plerixafor was based on the percentage of patients who achieved the target cell yield of >2×106 cells/kg after plerixafor administration. Adverse effects with plerixafor-based stem cell mobilisation were noted. Data was analysed using SPSS 26.

Results: Of the 35 patients with median age 32 years (interquartile range: 27-46 years), 20(57.1%) were males and 15(42.9%) were females. Median stem cell count after only one dose of plerixafor was 2.9x106 cells/kg (IQR: 2.1-6.0) and 31(88.5%) patients achieved the cut-off value after only 1-2 doses of plerixafor. Median time of neutrophil engraftment after transplant was day 11 (interquartile range: 10-15.5 days), and for platelet engraftment it was day 13 (interquartile range: 11-21 days). Overall, 7(20 %) patients experienced body aches with maximum severity being grade II which was controlled with analgesics.

Conclusion: Plerixafor-based stem cell mobilisation in autologous bone marrow transplantation was found to be effective, having minor side-effects.

Key Words: Plerixafor, CD34 stem cell mobilisation, Autologous stem cell transplantation.

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Introduction

Autologous stem cell / bone marrow transplantation is the treatment of choice in some blood cancers, like relapsed or refractory lymphomas and in multiple myeloma (MM) after achieving optimal response to improve disease-free survival (DFS) and overall survival (OS)[1-4]. The success of autologous bone marrow transplant and post-transplant recovery of patient is based on effective cluster of differentiation-34 (CD34) stem cell mobilisation. Early engraftment with a good stem cell yield pre-transplant significantly impacts morbidity and mortality.

One of the most important steps in autologous bone marrow transplantation is CD34 stem cell mobilisation in the blood from the bone marrow. Different methods are used for CD34 stem cell mobilisation, including granulocyte colony stimulation factor (GCSF), or chemotherapy with GCSF, or plerixafor, which is a C-X-C chemokine receptor type 4 (CXCR4) antagonist that is also used along with GCSF5 in autologous stem cell transplant.

[1-3]Department of Clinical Haematology and Bone Marrow Transplantation, Dow University of Health Sciences, Karachi

Correspondence: Farrukh Ali Khan **Email:** farrukh.ali@duhs.edu.pk

ORCID ID: 0009-0000-6100-1427

Traditional stem cell mobilisation methods, including GCSF alone, or chemotherapy along with GCSF, are commonly employed, but have limited efficacy, especially in the older patients, or the patients treated with multiple lines of chemotherapy, or those with a poor mobilisation potential. Plerixafor has emerged as a promising agent in these scenarios.

The cells in the stroma of bone marrow produce stromal cell-derived factor 1 (SDF-1), which plays a crucial part in CD34 stem cell residing and holding in bone marrow by interacting through CXCR.[4] Plerixafor reversibly inhibits SDF-1 binding on CXCR.[4] Along with plerixafor, GCSF causes microenvironment change in bone marrow that leads to the release of CD34 stem cells into peripheral blood.[6]

CD34 stem cells are extremely low in peripheral blood, but mobilisation with plerixafor and GCSF increases it to 100 times or more without serious side-effects. While chemotherapy along with GCSF for CD34 stem cell mobilisation increases hospitalisation, it also increases the risk of febrile neutropenia and transfusion requirement. Therefore, plerixafor-based stem cell mobilisation seems to be a preferable option to achieve sufficient CD34 stem cell from peripheral blood, which

leads to successful stem cell transplant with minimal adverse effects.[8]

The current study was planned to assess the outcome of plerixafor-based CD34 stem cell mobilisation in autologous stem cell transplant cases in a tertiary care setting.

Materials and Methods

The retrospective study was conducted at the Dow University Hospital, Karachi, and comprised data from February 2019 to December 2024 related to patients who had undergone autologous bone marrow transplant. Data was collected after approval from the institutional ethics review board. Patients with incomplete medical records were excluded.

Other than patients demographics, 'data was collected about primary diagnosis, previous lines of treatment, doses of plerixafor required, number of stem cell collection sessions, total and per-session yield of CD34, as well as neutrophil and platelet engraftment. Adequate or target CD34 stem cell yield was defined as CD34 count 2x106/kg or more. Neutrophil engraftment was defined as the time when absolute neutrophil count was >0.5x10^9/L for three consecutive days after stem cell transplant, and platelet engraftment was defined as 20x10^9/L for seven consecutive days after stem cell transplant without platelet transfusion support. Adverse effects were noted and graded as per common terminology criteria for adverse event version 5.0 (CTCAE v5.0)[9] along with overall patient outcome. Data was analysed using SPSS 26. Categorical data was expressed as frequencies or percentages, while quantitative variables were presented as median with interquartile range (IQR).

Results

Of the 35 patients with median age 32 years (IQR: 27-46 years), 20(57.1%) were males and 15(42.9%) were females. There were 80 stem cell collection sessions. Among the patients, 21(60%) had Hodgkin's lymphoma, 10(28.58%) had MM and 4(11.42%) had non-Hodgkin's lymphoma Further, 18(51.4%) patients received two lines of therapy, followed by 8(22.9%), one line of therapy, 8(22.9%) three lines of therapy, and 1(2.9%) 4 lines of treatment prior to autologous stem cell transplant (Table).

Stem cell mobilisation was done in all patients using GCSF at 10mcg/kg of body weight given subcutaneously once a day for 4 days, and plerixafor at 0.24mg/kg subcutaneously once daily starting from the night of day 4 about eleven hours prior to stem cell collection for a maximum four days (four doses) without routine checking of steady state CD34 count prior to stem cell collection. On day one, the median CD34 stem cell count was 2.9x106/kg (IQR: 2.1-6.0). A total of 24(68.5%) patients achieved CD34 stem cell target yield with a single dose of plerixafor (Figure 1), while 31(88.5%) achieved the target with 1-2 doses of plerixafor. of the 10(28.58%) MM patients, 8(80%) achieved the target yield with a single dose of plerixafor, while 2(20%) needed the second dose (Figure 2). Among the 25(71.42%) lymphoma patients, 17(68%) required a single dose of plerixafor, and 8(32%) needed another dose (Figure 3).

Table: Patient characteristics.

Baseline Characteristics	Median (IQR) or N (Percentages)
Age (Years)	32 (27-46)
Gender	
Male	20 (57.1%)
Female	15 (42.9%)
Diagnosis	
Hodgkin's Lymphoma	21 (60%)
Multiple Myeloma	10 (28.58%)
Non-Hodgkin's Lymphoma	4 (11.42%)
Prior lines of therapy	
One line of therapy	8 (22.9%)
Two lines of therapy	18 (51.4%)
Three or more line of therapy	9 (25.7%)
Plerixafor doses	2 (2-3)
Stem cell collection sessions	2 (2-3)
Total CD34 count (cells x 10^6/L)	5.7 (3.5-9.5)
Neutrophil engraftment duration (days)	11 (10-15.5)
Platelet engraftment duration (days)	13 (11-21)

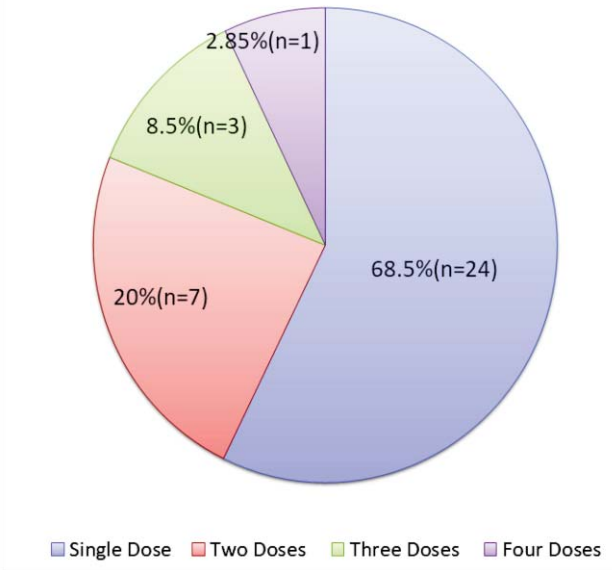
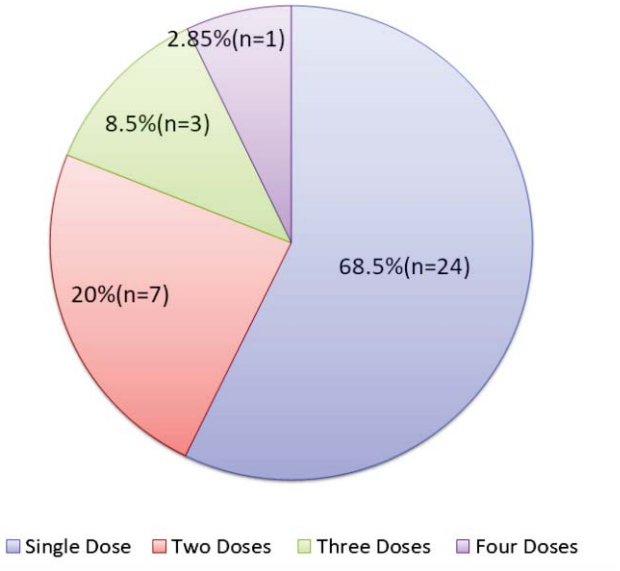


Figure-1: Patients achieving target cluster of differentiation-34 (CD34) stem cell yield.



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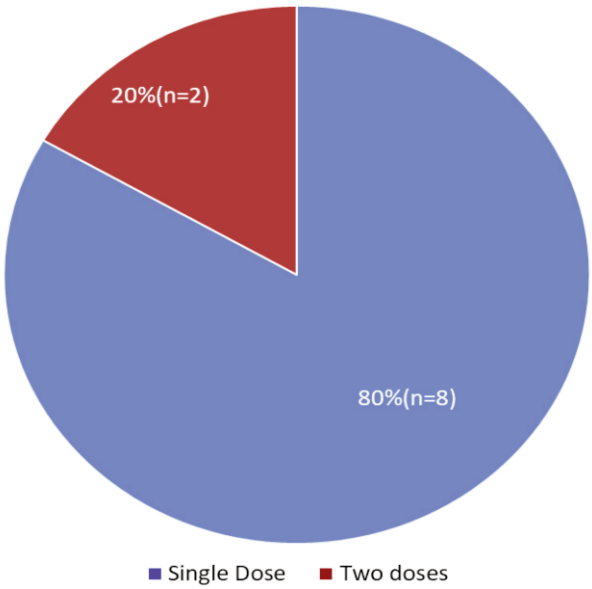

Figure-2: Multiple myeloma cases.

Total median CD34 stem cell count after all the 80 sessions of stem cell collection was 5.7x10^6/kg (IQR: 3.5-9.5106/kg). Median duration of neutrophil engraftment was day 11 (IQR: 10-15.5 days) post-transplant, and that of platelet engraftment was day 13 (IQR: 11-21 days).

The only adverse effect noted in the patients was body aches 7(20%), with maximum severity of grade II9, which was easily managed with analgesics. The overall post-transplant survival was 33(94.2%) on day 30, and 31(88.5%) was on day 100.

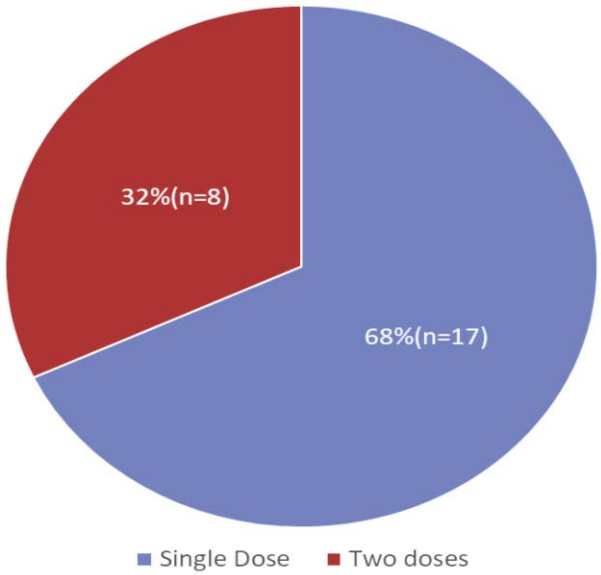

Figure-3: Lymphoma cases.

Discussion

CD34 stem cell collection is an essential step in autologous stem cell / bone marrow transplantation. Over the years, different techniques have emerged to achieve CD34 stem cell count of >2x10^6/kg through peripheral blood stem cell collection.

Tsukada et al. assessed the efficacy and safety of CD34 stem cell mobilisation based on plerixafor with GCSF, and reported that majority of adverse effects were gastrointestinal (12.2%), and the targeted CD34 stem cell count was achieved in 71.1% patients with ≤4 days of treatment[10] compared to 82.5% with up to two doses of plerixafor in the current study. Also, 20% of the current patients had only body ache of grade I or II, which was easily managed with analgesics.

In a meta-analysis of 23 studies using GCSF with plerixafor for CD34 stem cell mobilisation in autologous stem cell transplantation, majority of the patients achieved predetermined CD34 stem cells yield compared to GCSF alone (odds ratio [OR]: 5.33; 95% confidence interval [CI]: 4.34 -6.55). Failure to achieve targeted CD34 stem cell collection ranged 10-50% with GCSF alone or with GCSF in combination with chemotherapy.[11] Patients in the current study received GCSF with plerixafor, and achieved median CD34 stem cell count of 5.7x106/kg.

The current results highlighted the outcome of plerixafor as an alternative to traditional GCSF alone, or GCSF with chemotherapy-based stem cell mobilisation in autologous stem cell transplant. While plerixafor is more effective in terms of stem cell mobilisation[12,] it is relatively

costlier. In view of significant adverse effects, requirement of multiple stem cell collection sessions, delayed engraftment leading to prolonged hospital stays, and increased blood product transfusions required with other stem cell mobilisation protocols, plerixafor-based stem cell mobilisation might actually be more cost-effective.[13]

In a study comprising 398 participants, the median duration of neutrophil engraftment was 11 days, while median duration of platelet engraftment was 17 days in GCSF with plerixafor group.[14] In the current study, the corresponding values were 11 and 13 days.

Zubicaray et al. reported that 55.5% of healthy stem cell donors experienced adverse events with plerixafor-based mobilisation regimen, including bone pain, nausea, low-grade fever, myalgia and abdominal discomfort.15 In contrast, 20% of the current patients only experienced grade I-II body aches.[9]

The upfront use of plerixafor with GCSF, irrespective of clinical risk factors, appeared promising in the current study as 82.8% patients achieved the targeted CD34 stem cell yield with only up to two doses of plerixafor. This was comparable to other studies.[16]

The current study has limitations, including a retrospective design, a relatively small sample size, and the absence of steady state CD34 testing which may have affected the generalisation of the findings. Further prospective studies with larger sample sizes are needed to confirm the current findings.

Conclusion

The use of GCSF with plerixafor for CD34 stem cell mobilisation in autologous bone marrow transplant was positive, with only a few and easily manageable adverse effects.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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