DE GRUYTER OPEN

Journal of Interdisciplinary Medicine

ORIGINAL RESEARCH

HEMATOLOGY // INTERNAL MEDICINE

Stem Cell Mobilization and Harvesting Failure in Case of Heavily Pretreated Patients

Eszter Mild[1], Erzsébet Lázár[1,2], Judit-Beáta Köpeczi[1], Enikő Kakucs[1], Marius Găzdac[1], Annamária Pakucs[1,2], Cezara Tudor[1], István Benedek[1,2]

[1] Clinic of Hematology and Bone Marrow Transplantation Unit, Tîrgu Mureș, Romania
[2] University of Medicine and Pharmacy, Tîrgu Mureș, Romania

CORRESPONDENCE

Erzsébet Lázár
Str. Revoluției nr. 35
540042 Tîrgu Mureș, Romania
Tel: +40 265 216 680
E-mail: erzsebetlazarbenedek@gmail.com

ARTICLE HISTORY

Received: October 16, 2017
Accepted: November 20, 2017

Eszter Mild • Str. Revoluției nr. 35, 540042 Tîrgu Mureș, Romania. Tel: +40 265 216 680

Judit-Beáta Köpeczi • Str. Revoluției nr. 35, 540042 Tîrgu Mureș, Romania. Tel: +40 265 216 680

Enikő Kakucs • Str. Revoluției nr. 35, 540042 Tîrgu Mureș, Romania. Tel: +40 265 216 680

Marius Găzdac • Str. Revoluției nr. 35, 540042 Tîrgu Mureș, Romania. Tel: +40 265 216 680

Annamária Pakucs • Str. Revoluției nr. 35, 540042 Tîrgu Mureș, Romania. Tel: +40 265 216 680

Cezara Tudor • Str. Revoluției nr. 35, 540042 Tîrgu Mureș, Romania. Tel: +40 265 216 680

István Benedek • Str. Revoluției nr. 35, 540042 Tîrgu Mureș, Romania. Tel: +40 265 216 680

ABSTRACT

Background: High-dose chemotherapy and autologous stem cell transplantation have become a standard curative treatment in various hematologic malignancies. Many factors can affect the success of mobilization and hematopoietic stem cell harvesting. **Aim:** The aim of this study was to analyze factors that lead to mobilization failure. **Material and Methods:** We conducted a retrospective study on 19 patients with failure of stem cell harvesting. All patients were administered high doses of GCS-F (filgrastim, 15 µg/kg/day) and 0.24 mg/kg of plerixafor on day +5 or +10 of harvesting. **Results:** The median age of the study population was 51 years (range 35–67) and 52.6% (n = 10) were males. The study group included 4 (21%) subjects with multiple myeloma, 6 (31.5%) with Hodgkin lymphoma, 8 cases (42.1%) with non-Hodgkin lymphoma and 1 patient with chronic lymphocytic leukemia. Each patient received 2.78 (range 1–5) lines of chemotherapy, administered in 11.57 (range 2 to over 20) cycles of treatment. **Conclusion:** In hematologic malignancies it is very important to collect stem cells in time, in order to reduce mobilization failure. As we have shown in our studied cases, multiple lines of polychemotherapy with or without radiotherapy lead to mobilization failure.

Keywords: mobilization failure, heavily treated patients, influencing factors

INTRODUCTION

Autologous hematopoietic stem cell treatment is a curative method for subjects suffering from several hematologic malignancies. In these cases, peripheral blood is the preferred source to harvest CD34+ cells.[1] The use of granulocyte-colony stimulating factor (G-CSF) alone or in combination with chemotherapy results in a collection of an adequate number of peripheral blood stem cells (PBSC). The recommended minimally sufficient number of cells is 2×10^6 CD34+ cells/kg, otherwise the procedure is associated with slower blood count recovery, a higher number of transfusion requirements, infections, and longer period of hospitalization.[2–4]

Mobilization failure is the main cause for not being able to perform autologous hematopoietic stem cell (HSC) transplantation.[5] The main factors that influence stem cell mobilization include age, previous therapy, collateral diseases, and genetic polymorphism.[5,6]

An important risk factor for hematopoietic stem cell exhaustion and mobilization failure is represented by successive cycles of chemotherapy. HSCs present changes in their quality throughout development and life, and the greatest proliferation and differentiation potential is present in HSCs obtained from the fetal liver, followed by neonatal and postnatal bone marrow of young and older donors.[7]

AIM OF THE STUDY

The objective of this study was to analyze the factors associated with mobilization failure for autologous PBSC in a group of 19 patients from a single hematology unit.

MATERIAL AND METHODS

We performed a retrospective study in the Bone Marrow Transplantation Unit of Tîrgu Mureș during a 4 year interval from January 1, 2014 to December 31, 2017. During this 4-year period, 212 patients with different hematologic malignancies and 12 donors for allogeneic transplantation underwent stem cell mobilization. From the 224 cases, 19 cases presented failure of mobilization. The present study analyzed the 19 patients with failure of SC harvesting, diagnosed with multiple myeloma, Hodgkin lymphoma, non-Hodgkin lymphoma, and chronic lymphocytic leukemia, in whom a combined mobilization method was used (GCS-F + plerixafor, chemotherapy followed by GCS-F + plerixafor). All subjects were administered high doses of GCS-F (filgrastim, 15 μg/kg/day) and 0.24 mg/kg of plerixafor on day +5 or +10 of mobilization. In all cases, the harvesting was unsuccessful, the PBSC number being under 0.5×10^6 CD34+ cells/kg body weight.

A number of 5 patients were excluded from the study because the mobilization failure was caused by other associated diseases (thrombosis, acute myocardial infarction, respiratory insufficiency, active hepatitis).

RESULTS

The study lot had a mean age of 51 years (ranging between 35–67 years) and included 52.6% (n = 10) males. The study group included 4 (21%) patients with multiple myeloma (one with IgA with previous Hodgkin disease and 3 cases with IgG secretory myeloma), 6 (31.5%) patients with Hodgkin lymphoma (3 with nodular sclerosis, 3 with mixed cellularity lymphoma), 8 cases (42.1%) with non-Hodgkin lymphoma (2 with marginal zone lymphoma, 3 with T-cell lymphoma, 2 with mantle cell lymphoma, and 1 patient with Burkitt lymphoma), and one patient with chronic lymphocytic leukemia.

The mobilization of stem cells was performed with a combination of chemotherapy + GCS-F + plerixafor in 10 cases and GCS-F + plerixafor in 9 cases.

The age distribution is presented in Figure 1, where the highest number of patients had ages between 51 and 60 years.

The mean number of chemotherapeutic lines administered to each patient in the study population was 2.78, with a range between 1 and 5.

The mean number of chemotherapeutic cycles/applications was 11.57, with a range between 2 to over 20 cycles (Figure 2).

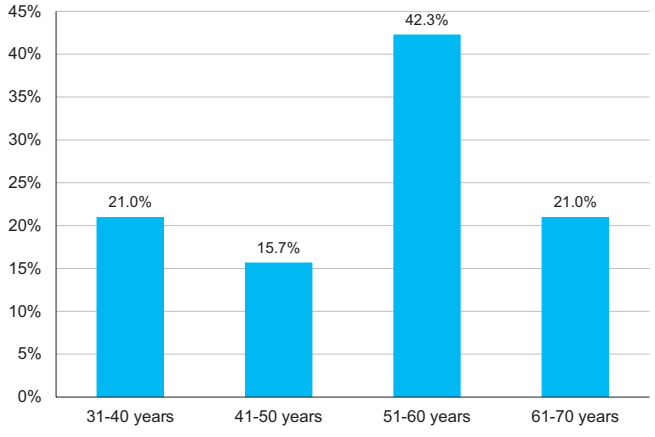

FIGURE 1. Age distribution of the study population

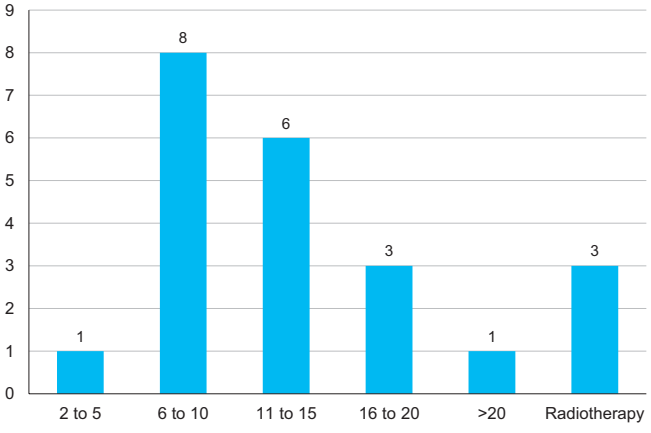

FIGURE 2. The number of chemotherapy applications in the study population

TABLE 1. Hematological parameters in patients with mobilization failure

Parameters	Range of values	Median
WBC, cells/μL	2,980–30,000	9,001
Hemoglobin, g/dL	4.8–14.6	10.83
HTC, %	17.3–42.7	32.85
Platelets, cells/μL	89,000 –723,000	227,000

WBC – white blood cell count; HTC – hematocrit

The median blood cell count prior to stem cell mobilization is illustrated in Table 1.

DISCUSSION

Our study shows that stem cell mobilization failure for autologous HSCT is highly correlated with the type of previous chemotherapy, therapy lines, and diagnosis.

All patients in the study group were heavily pretreated with alkylating agents and purine analogs. Alkylating agents were used in intermittent courses, with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP-like regimen). Other studies have found similar results, indicating that mobilization failure occurs more often when using these agents.[5,8,9]

The highest ratio of mobilization failure occurred in non-Hodgkin lymphoma (8 cases), followed by Hodgkin lymphoma (6 cases) and multiple myeloma (4 cases), similar to the results of a study conducted by Sancho *et al.*[5]

Patients with ages between 51–61 years had the highest ratio of failure.

Previous malignant disease can be mentioned as another important factor causing failure of stem cell mobilization.

A known risk factor in poor mobilization is previous radiotherapy,[5,9] which was present in only 3 cases.

By analyzing the hematological parameters, our results showed that patients with mobilization failure had moderate anemia with serum levels of hemoglobin of 10.83 g/dL and hematocrit of 32.85%, without leukopenia, neutropenia, thrombocytopenia, and serum iron overload. Other studies describe that mobilization failure is more common in patients with thrombocytopenia, neutropenia, anemia, leukopenia.[5,9,10]

CONCLUSION

Many factors can lead to mobilization and stem cell harvesting failure, making it impossible to perform autologous transplantation. We can conclude that in hematologic malignancies it is very important to collect stem cells in time, in order to reduce mobilization failure. As we have shown in our studied cases, multiple lines of polychemotherapy with or without radiotherapy lead to mobilization failure. The use of combined growth factor mobilization by adding plerixafor can increase the number of CD34+ cells, making mobilization possible in selected cases.

CONFLICT OF INTEREST

Nothing to declare.

REFERENCES

1. Korbling M, Anderlini P. Peripheral blood stem cell versus bone marrow allotransplantation: does the source of hematopoietic stem cell matter? *Blood*. 2001;98:2900-2908.
2. To LB, Haylock DN, Simmons PJ, Juttner CA. The biology and clinical uses of blood stem cells. *Blood*. 1997; 89:2233-2258.
3. Jillella AP, Ustun C. What is the optimum number of CD34 peripheral blood stem cells for an autologous transplant? *Stem Cells Dev*. 2004;13:598-606.
4. Vose JM, Ho AD, Coiffier B, et al. Advances in mobilization for the optimization of autologous stem cell transplantation. *Leuk Lymphoma*. 2009;50:1412-1421.
5. Sancho JM, Morgades M, Grifols JR, et al. Predictive factors for poor peripheral blood stem cell mobilization and peak CD34+ cell count to guide pre-emptive or immediate rescue mobilization. *Cytotherapy*. 2012;14:823-829.
6. To LB, Levesque JP, Herbert KE. How I treat patients who mobilize hematopoietic stem cells poorly. *Blood*. 2011;118:4530-4540.
7. Verfaillie CM. Hematopoietic stem cells for transplantation. *Nature Immunology*. 2002;3:314-317.
8. Pozotrigo M, Adel N, Landau L, et al. Factors impacting stem cell mobilization failure rate and efficiency in multiple myeloma in the area of novel therapies: experience at Memorial Sloan Kattering Cancer Center. *Bone Marrow Transplantation*. 2013;48:1033-1039.
9. Worel N, Rosskopf K, Neumeister P, et al. Plerixafor and granulocyte-colony-stimulating factor (G-CSF) in patients with lymphoma and multiple myeloma previously failing mobilization with G-CSF with or without chemotherapy for autologous hematopoietic stem cell mobilization: the Austrian experience on a named patient program. *Transfusion*. 2011;51:968-975.
10. Nur Ozkurt Z, Yegin AZ, Suyan E, et al. Factors Affecting Stem Cell Mobilization for Autologous Hematopoietic Stem Cell Transplantation. *Journal of Clinical Apheresis*. 2010;25:280-286.