Transfusion and Apheresis Science 56 (2017) 470–473

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Factors affecting hematopoietic stem cell mobilization and apheresis in allogeneic donors: The role of iron status

Zübeyde Nur Özkurt [a,*], Leyla Batmaz [b], Zeynep Arzu Yeğin [a], Çiğdem İlhan [a]

[a] Gazi University, Faculty of Medicine, Department of Hematology and Stem Cell Transplantation Unit, Turkey
[b] Gazi University, Faculty of Medicine, Department of Internal Medicine, Turkey

ARTICLE INFO

Article history:
Received 14 December 2016
Received in revised form 23 May 2017
Accepted 24 May 2017

Keywords:
Allogeneic stem cell transplantation
Donor
Mobilization
Iron status
Ferritin

ABSTRACT

Infused CD34 cell count has a significant impact on transplant outcome. In this retrospective study, we aimed to analyze the impact of donor iron parameters on peripheral blood stem cell (PBSC) collection. A total of 303 related donors were included in the study. The mobilization regimen, recombinant G-CSF, was given for four consecutive days. A $CD34^+$ cell count below 2×10^6/kg was defined as mobilization failure which was demonstrated in 23 donors (7.6%). Mobilization failure was more frequent in female donors than male donors (13.7% vs 3.4%). Body mass index, mean corpuscular volume, hemoglobin and ferritin levels were found to be lower in donors with mobilization failure. Body mass index was significantly correlated with PBSC count on the 4th day of G-CSF. Body mass index, male gender, mean corpuscular volume and ferritin levels had significant impact on PBSC count. Although PBSC count was found to be similar between female and male donors, female gender was shown to have an adverse impact on PBSC collection, which may be attributed to lower body weight and concurrent iron deficiency.

1. Introduction

Several reports indicate that infused hematopoietic stem cell (HSC) count is closely associated with transplant outcomes. As early neutrophil and platelet engraftment are considered to have favorable impact on survival, identifying risk factors for HSC mobilization in healthy donors as well as optimal donor selection is essential for successful transplantation [1–3].

Peripheral blood is the preferred stem cell source in allogeneic stem cell transplantation [1,4]. Peripheral blood stem cell (PBSC) harvesting is a non-invasive and painless procedure which provides rapid engraftment and fewer complications when compared to bone marrow harvesting [4]. Several factors, including older age [5–9] and female gender [5,7,10,11] were identified as unfavorable factors for PBSC mobilization. There are a few reports about the relationship between iron status and stem cell mobilization in patients with hematological malignancies [12,13]; however, the impact of donor iron parameters on PBSC mobilization has not been investigated. In this retrospective study, we analyzed the impact of the donor iron profile on PBSC collection in 303 healthy donors.

2. Material and methods

2.1. Donor selection

A total of 303 consecutive healthy PBSC donors were enrolled in this retrospective study. All donors were HLA matched and unrelated donors were excluded from the analysis. Donor characteristics including age, gender, weight and height as well as baseline hemoglobin (Hb), mean corpuscular volume (MCV), white blood cell (WBC), platelet (Plt) and ferritin levels were recorded. Body mass index (BMI) was calculated based on the formula, weight/height^2. The study was approved by Gazi University Ethics Committee.

2.2. Mobilization and apheresis

Recombinant G-CSF was used for four consecutive days as mobilization regimen. A total of 214 donors (83.2%) received filgastrim, while 43 donors (16.8%) were mobilized with lenogastrim at a single daily dose of 10 μg/kg. The first apheresis was performed on the fourth day of G-CSF, if the PBSC > 10/μL. G-CSF administration was continued until optimal CD34 count (4×10^6 $CD34^+$ cells/kg) was obtained or mobilization failure (MF) was observed. Mobilization failure (MF) was the primary endpoint which was defined as failure to reach a minimum CD34 count of 2×10^6 $CD34^+$ cells/kg.

* Corresponding author at: Gazi University Medical Faculty, Department of Hematology and Stem Cell Transplantation Unit, Beşevler 06500, Ankara, Turkey.
E-mail address: znozkurt@gazi.edu.tr (Z.N. Özkurt).

http://dx.doi.org/10.1016/j.transci.2017.05.021
1473-0502/

Table 1
Demographic and anthropometric data.

Donor age (years)	33 (12–73)
Donor gender (*n*)	178 male 125 female
Donor relationship *n* (%)	290 (95%) sibling 5 (1.7%) cousin 4 (1.3%) sun 2 (0.7) mother 2 (0.7) father
Height (cm)	
Donor	167.7 ± 9.2
Recipient	166.4 ± 10.5
Weight (kg)	
Donor	72.2 ± 6.4
Recipient	68.6 ± 13.6
BMI (kg/m^2)	
Donor	25.7 ± 5.4
Recipient	25.3 ± 11.8

Height, weight and BMI were expressed as mean ± standard deviation.

Apheresis was performed 2–5 times of the estimated blood volume using standard continuous-flow blood cells separator (Fresenius Com. Tec, Fresenius As. Tec, Fenval Amicus, Fenval CS3000 plus). CD34$^+$ cell counts in the peripheral blood and in the apheresis product were measured by flow cytometry in accordance with the ISHAGE protocol [14].

2.3. Statistical analysis

Categorical variables were compared with chi-square test. Student-*t* and Mann Whitney *U* tests were used to compare continuous parameters. The relationships between HSC count and certain parameters were tested with simple correlation analysis and regression models. PBSC count, total CD34 product and CD34 product/recipient weight were used for analysis of the factors affecting mobilization. Statistical analysis was performed using SPSS 16. All statistical tests were performed two-sided and *p* value 0.05 was considered as statistically significant.

3. Results

A total of 303 donors [median age: 33 (12–73) years; M/F: 178/125] were enrolled in this study. Donor and recipient characteristics are shown in Table 1. The target PBSC count (>10/μL) was obtained in 247 (81.5) and 51 (16.8%) donors, on the fourth and fifth days of G-CSF, respectively. In 4 donors target PBSC count was obtained on the sixth day, however in 1 donor we could not obtain optimum PBSC. Mean PBSC count was found to be 30.2 ± 21.2/μL on the fourth day of G-CSF.

Mobilization failure was determined in 23 donors (7.6%). Target HSC count was obtained after the first apheresis for all 191 donors (63%). Hematopoietic stem cell count in first and total apheresis product was $2.7 \pm 2.3 \times 10^6$/kg and $4.8 \pm 2.3 \times 10^6$/kg based on recipient weight, respectively. Comparison of donor characteristics based on mobilization failure is presented in Table 2. Mobilization failure was more frequent in female donors (13.7% vs 3.4%). Mean PBSCs were not different between male and female (27.4 ± 19.1 vs 31.2 ± 21.3; $p > 0.05$). Mean total CD34 product and CD34 product/weight-recipient were higher in male than female donors (366.5 ± 187.1 vs 279.9 ± 142.2; $p < 0.001$ and 5.2 ± 2.4 vs 4.1 ± 1.9; $p < 0.001$). Mean BMI, Hb, MCV and ferritin levels were lower in donors with mobilization failure. Weight comparison in donors according to recipient was more prominent in donors with mobilization failure (−4.6 ± 25.6 vs +8.6 ± 26.7; $p = 0.02$). Age, WBC and Plt counts were not different between two groups. Mean ferritin level was significantly lower in female donors when compared to male donors (29.9 ± 35.2 vs 80.5 ± 86.7; $p = 0.001$).

Univariate linear regression analysis indicated that BMI (OR: 3.61, $p < 0.001$) had a significant impact on PBSC count which was obtained on the fourth day of G-CSF, however age, WBC, Plt, Hb and ferritin levels had no significant impact on PBSC count ($p > 0.05$). On second linear regression models, BMI (OR: 2.1, $p < 0.001$), gender (OR: 1.56, $p = 0.02$), ferritin (OR: 1.45, $p = 0.03$) and MCV (OR: 1.42, $p = 0.04$) had an impact on HSC count in the total apheresis product. Age, WBC, Plt and Hb levels did not show any significant impact on HSC count of the product ($p > 0.05$). In multivariate analysis, BMI ($p = 0.01$), gender ($p = 0.03$) and ferritin levels ($p = 0.04$) were independent predictive factors for HSC count of total apheresis product.

4. Discussion

In this study, prevalence of MF was 7.6% which was reported to be 2–40% in previous studies. Target HSC count was obtained at the end of the first apheresis in 191 donors (63%) compatible with previous reports (60–80%) [6–8,10,15–17]. This wide range may be attributed to small sample size and lack of standardization including definitions of MF and target HSC count. In a study by Suzuya et al., MF, which was found to be 8.4% in 59 related donors, was defined as PBSC less than 20/μL on the fifth G-CSF day [6]. Rubia et al. described MF as CD34$^+$ cell less than 4×10^6/kg in first apheresis product which was reported to be 40% [16]. Prevalence of MF was 2% in a study by Ings et al. and they collect >4×10^6/kg HSC in first apheresis product in 63% of donors [7]. Our results were compatible with the literature.

Body mass index, Hb, MCV and ferritin levels were lower in donors with MF when compared to cases without MF. Median age was not different between two groups. Mobilization failure was more frequent in female donors, however this difference lost significance when donor body weight was included in the analysis. In addition, median PBSC count was not different in female and male donors. Body mass index had a significant impact on the PBSC count of the fourth G-CSF day. It is well known that donor BMI is an important factor affecting HSC yield [18,19]. Adipose tissue is a source of HSC, and the other explanation of the close relationship between HSCT yield and donor's BMI is that we use actual body weight for G-CSF dose. Donors with higher BMI may be mobilized with overdose G-CSF compared to donors with ideal body weight. Another result of the present study is the donor weight discrepancy according to recipient reported lower among poor mobilizer donors. Donor BMI should be considered especially for the patients with alternative donor option. Furthermore, BMI, gender, and ferritin represented an independent impact on HSC count of the apheresis product in multivariate models.

A number of studies demonstrated a relationship between advanced age [5–11,15–17] and MF in HSC donors. In general, younger age is considered to be a favorable factor for successful collection. Although advanced age may lead to lower HSC counts and increase the risk of apheresis complications, there are some studies that did not confirm the correlation of age and HSC count [11,20,21]. However, the results are conflicting, as pediatric and adult donors were included in the same analysis and cutoff value for age subgroups were different in most of the studies [9,15,16]. In our study, mean age was not found to be different between cases with or without MF.

Female donors were shown to have higher risk of MF compared to males in several studies [5,7,10,11]. This increased risk was attributed to the higher blood volume of male donors due to higher body mass. In our study, PBSC counts on the fourth day of G-CSF were similar between male and female donors; however,