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Blood group A is a negative risk factor for peripheric blood stem cell mobilization in allogeneic donors

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Abstract

Objective: Many factors, including advanced age and female gender, have been identified as negative factors for peripheric blood hematopoietic stem cell (HSC) mobilization. Similarly, blood group antigens may have an effect on the release of HSCs from the bone marrow niche into the periphery. We aimed to study the effect of ABO and Rh blood groups on peripheral blood HSC mobilization in healthy donors.

Material and Method: The data of 314 healthy donors who underwent peripheric blood HSC mobilization in our center were analyzed retrospectively.

Results: The number of CD34+ cells collected on the first day and in total was the least in donors with blood group A. A statistically significant relation was found between ABO blood groups and the number of CD34+ cells collected on the first day and in total. No relation was found between Rh positivity and the number of CD34+ cells collected.

Conclusion: According to our research in the literature, this is the first study that investigates whether blood groups have an effect on the release of HSCs from the bone marrow niche into the periphery and we observed that blood group A is a negative risk factor for peripheric blood HSC mobilization.

Keywords: blood groups, peripheric, stem cell, mobilization, healthy donors

Introduction

Proteins, glycoproteins, and glycolipids on the surface of erythrocytes define the blood groups' antigens (1). Today, the number of serologically described blood group antigens is more than 600. The majority of blood group antigens are glycoproteins and they are generally described according to their oligosaccharide and amino acid series.

The antigens of ABO blood groups are present on the extracellular membranes of erythrocytes and these antigens are described as complex carbohydrate molecules (2). Besides ABO blood group, Rh blood group is found in the system and at least 45 independent antigens are formed (3).

Progenitor cells constitute only 0.01-0.05% of all nucleated cells in peripheral blood (4,5). Progenitor cells adhere to the micro-environment of the bone marrow with various interactions. The stroma of the bone marrow contains stromal cell-derived factor 1 (SDF-1), vascular cell adhesion molecule (VCAM-1), intercellular adhesion molecule-1(ICAM-1) and P-selectin glycoprotein ligand, all of which are ligands for stem cell adhesion molecules (6-8). Inhibition of these receptor-ligand interactions cause increases in the mobilization of progenitor cells (6,7,9).

It has been shown that selectins have a role in the homing of hematopoietic stem cells (HSCs) in the bone marrow (10, 11). On the other hand, ICAM-1 has a role in leukocyte migration, adhesion, and activation, in addition, it may have a role in the regulation of HSC functions (12-16). In previous studies, a relation was found between ABO blood groups and the expression of ICAM-1 and P- selectin (17-21). In the study conducted by Zhang et al, they revealed that blood group A is related to the lowest expression of ICAM-1 and P- selectin (22).

Studies have shown that the number of HSCs infused is closely related to transplant outcomes. Since early neutrophil and platelet engraftment are thought to have a positive effect on survival, risk factors for HSC mobilization should be identified (23-26).

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As it has been shown that blood group A is associated with lowest expression levels of ICAM-1 and P-selectin, and as selectins play a role in the bone marrow homing of HSCs and ICAM-1 has a role in cell migration; we hypothesized that blood group A may be a negative risk factor for peripheral HSC mobilization. To reveal this, we aimed to study the effect of blood groups on peripheral blood HSC mobilization in healthy donors.

Material and Methods

In this study, the data of healthy allogeneic donors at the age of 18 years and older, who underwent peripheric blood HSC mobilization at our center were analyzed retrospectively. The study was conducted according to the criteria set by the declaration of Helsinki. Each donor signed informed consent before HSC collection. Ethics approval for the study was obtained from the Ethics Committee of the University of Health Sciences, Ankara Dr. Abdurrahman Yurtaslan Oncology Training and Research Center.

Donors were mobilized with a total of 10 µg/kg subcutaneous granulocyte colony-stimulating factor (G-CSF) in 2 divided doses (2×5 µg/kg). On the 4th day, if the peripheric blood CD34+ cells' count is ⩾50/µL, stem cells started to be collected; if not, G-CSF dose was omitted in the donors whose white blood count (WBC) is ⩾ 75.000/mm3 and the G-CSF dose was reduced by half for the donors whose WBC is ⩾50.000/mm3, in other donors, G-CSF continued with the same dose and on the 5th day, peripheric blood-derived stem HSCs were collected with a continuous flow blood separator (Fresenius Kabi, COM.TEC, Germany). A total volume of 150 to 400 mL/kg blood was processed for each apheresis at a flow rate of 50 to 60 mL/min. When the number of CD34+ cells collected could not reach the target, G-CSF was continued and the apheresis procedure was repeated the following day. Filgrastim was used in 204 (87.9%) donors and lenograstim was used in 28 (12.1%) donors. Mobilization failure was defined as a CD34+ cell collection below 2 × 10^6 CD34 + cells / kg.

IBM SPSS Statistics (version 21) was used for statistical analysis. Descriptive statistics were used to summarize the data. The suitability of the variables to normal distribution was examined by visual (histogram and graphs) and analytical methods (Shapiro-Wilk and Kolmogorov-Smirnov test). Categorical data were expressed as a ratio, and numerical data were expressed as median and mean ± standard deviation. Kruskal Wallis tests were used for comparison of non-parametric numerical data between groups. P values <0,05 were treated as statistically significant

Results

A total of 314 healthy donors were included in the study. The median age was 35 years (range 19 to 65 years). 195 (62,1%) donors were female and 119 (37,9%) were male. The target number of CD34 + cells (5 x 10^6 / kg) was reached on day 4 in 221 (70,4.%) donors. In 213 (67,8 %) donors 1 apheresis procedure was performed to achieve the targeted CD34 + cell count (5 x 10^6 / kg), 2 apheresis procedure was performed in 96 (30,6%) donors and 3 apheresis procedure was performed in 5 (1,6%) donors. There was no donor with the number of HSC collected below 2 x 10^6 / kg. The median number of HSCs in the first and total apheresis products were 6,74 x 106 / kg and 7,60 x 10^6 / kg, respectively.

The number of CD34+ cells collected on the first day and in total was the least in donors with blood group A. A statistically significant relation was found between ABO blood groups and the number of CD34+ cells collected on the first day and in total. The median number of the apheresis procedure to achieve target was 1 in all ABO blood groups (Table 1).

277 healthy donors were Rh positive and 37 donors were Rh-negative. No statistically significant relation was found between Rh positivity and the number of CD34+ cells collected on the first day and in total (Table 2).

The number of CD34+ cells collected on the first day and in total was the least in A Rh-positive allogeneic donors (Table 3).

Table 1: Mobilization results of donors according to ABO blood groups

Blood Groups	CD34+ cells collected on the 1st day (median) (10^6/kg)	CD34+ cells collected in total (median) (10^6/kg)	CD34+ cells collected on the first day(median) (/µl)
A (n=113)	5,77 (2-16,6)	6,90 (2,8-20,9)	1073 (200-10207)
B (n=67)	7,93(2,9-26,3)	8 (3-26,3)	1637 (432-5030)
0 (n=114)	6,94 (2 -21)	8 (2,9-21)	1472 (356-4375)
AB (n=20)	7,08 (2,9-16,6)	8,67 (4,7-16,6)	1773 (827-3067)
p-value	0,003**	0,039*	0,001**

Table 2: Mobilization results of donors according to Rh groups

Blood Group	CD34+ cells collected on the first day (median) (10^6/kg)	CD34+ cells collected in total (median) (10^6/kg)	CD34+ cells collected on the first day (median) (/µl)
Rh positive (n=277)	6,83 (2 -26,3)	7,64 (3-26,3)	1317 (200-5030)
Rh negative (n=37)	6,4 (2,5-12,9)	6,9 (2,9-20,9)	1252 (510-10207)
p-value	0,508	0,382	0,547

Table 3: Mobilization results of donors according to ABO and Rh groups

Blood Group	CD34+ cells collected on the first day (median) (10^6/kg)	CD34+ cells collected in total (median) (10^6/kg)	CD34+ cells collected on the first day (median) (/µl)
A Rh (+) (n=95)	5,59 (2-16,6)	6,77 (2,8-16,6)	1065 (200-2708)
A Rh (-) (n=18)	5,71(2,5-11,2)	7(4,5-20,9)	1221 (800-10207)
B Rh (+) (n=62)	7,94 (2-26,3)	8 (2-26,3)	1728 (432-5030)
B Rh (-) (n=5)	7,15(2,9-12,9)	8,5 (3,5-12,9)	1349 (560-1631)
0 Rh (+) (n=102)	6,87 (2-21)	8 (2,2-21)	1494 (356-4375)
0 Rh (-) (n=12)	8,59 (2,8-11,6)	7,40 (2,9-11,6)	1162 (510-2346)
AB Rh (+) (n=18)	6,69 (2,9-16,6)	8,3 (4,7-16,6)	1773 (827-3067)
AB Rh (-) (n=2)	8,67(8,4-8,8)	8,67 (8,5-8,8)	2085 (1297-2874)
p-value	0,042**	0,193	0,000**

Discussion

Allogeneic stem cell transplantation (Allo-SCT) is a potentially curative treatment for a variety of benign and malignant hematological diseases. A successful Allo-SCT depends on the infusion of an adequate quantity of HSCs (27,28). Compared to HSC mobilization in healthy donors, there are more factors affecting the amount of HSCs collected in patients with hematologic malignancy, such as underlying disease, radiotherapy history, type, and number of chemotherapies. As there are more factors affecting the amount of HSCs collected in patients with hematologic malignancy, in this retrospective study, we aimed to analyze the effect of donor blood groups on peripheral blood HSC mobilization in healthy donors.

Mobilization failure rate has been reported as 2-40% in various studies (29-34). The prevalence of mobilization failure was 7.6% in the study conducted by Özkurt et al., where mobilization failure was defined as a collection of less than 2×10^6 CD34+ cell/kg (35). In our study, similarly, mobilization failure was accepted as a cell collection less than 2×10^6 CD34+ cell/kg; and there was no mobilization failure.

To prevent mobilization failure, the factors that have a negative impact on the amount of CD34+ cells collected should be demonstrated. Many factors, including advanced age and female gender, have been identified as negative factors for peripheric blood HSC mobilization (36-38). Similarly, blood group antigens may have an effect on the release of HSCs from the bone marrow niche into the periphery. In a European ancestry population, it was observed that the A1 blood group allele was associated with the lowest expression levels of ICAM-1 and P-selectin (20). In our study, the number of CD34+ cells collected on the first day and in total was the least in donors with blood group A. A statistically significant relation was found between ABO blood groups and number of CD34+ cells collected on the first day and in total.

Human leukocyte antigen (HLA) allele compatibility, young age, and male donor are important factors in allogeneic donor selection. In order to prevent erythrocyte engraftment failure, major and minor ABO blood group incompatibility between patient and donor is avoided.

However, the choice of mobilization method (G-CSF, G-CSF + chemotherapy, or plerixafor) in autologous stem cell collection is made according to the patient's mobilization risk factors. Therefore, identification of all factors affecting HSC mobilization is of great importance.

Conclusion

According to our research in the literature, this is the first study that investigates whether blood groups have an effect on the release of HSCs from the bone marrow niche into the periphery and we observed that blood group A is a negative risk factor for peripheric blood HSC mobilization. Further studies are needed to reveal all the factors affecting mobilization in order to achieve an adequate number of CD34+ cells.

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