



Original Research



Does platelet/ lymphocyte ratio a predictor of CD34+ peripheral blood stem cell yield in the healthy donors mobilized with GCSF?

Zafer Gokgoz

Department of Hematology, Faculty of Medicine, Yuksek İhtisas University, Turkey

E-mail address: drzafergokgoz@gmail.com

HIGHLIGHTS

Consequently, a high platelet/lymphocyte ratio may be correlated with the number of collected CD34+ stem cells

ARTICLE INFO

Article history

Received Date: March 04th, 2020

Revised Date: June 01st, 2020

Accepted Date: June 04th, 2020

Keywords

Lymphocyte ratio

CD34+

Stem Cells

ABSTRACT

This research aimed to determine whether there is a correlation between platelet/lymphocyte ratio the number of collected CD34+ stem cells. This retrospective study included 94 adult related stem cell donors who were healthy and volunteer by screening their files between the years 2016 and 2018. All donors were mobilized using 2.5 mcg/kg lenograstim or filgrastim and underwent peripheral stem cell apheresis. Complete blood counts were tested at baseline before G-CSF administration (pre-G-CSF), and before PBSC collection after mobilization with G-CSF administration. The patients were divided into two groups as aged below and over 50 years old. From these comparative data, only BMI value of the group aged below 50 years was statistically significantly lower than the other group, whereas no statistically significant difference was found between the groups in terms of other parameters. The numbers of the collected CD34+ stem cells of both age groups were similar, and no significant difference was found. The values of platelet/lymphocyte ratio, early measurement of CD34+ stem cells and the amount of the collected CD34+ stem cells of both groups at the first and second days of the procedure were found similar. This research show that a high platelet count and consequently, a high platelet/lymphocyte ratio may be correlated with the number of collected CD34+ stem cells but our hypotheses revealed insignificant outcomes.

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*Corresponding Author:

Zafer Gokgoz

Department of Hematology, Faculty of Medicine, Yuksek İhtisas University, Turkey

Karakaya Mahallesi, Baglum Bulvari No.1, 06291, Kecioren, Ankara, Turkey

E-mail: drzafergokgoz@gmail.com

Phone:+90 312 3297 425



1. INTRODUCTION

Peripheral blood stem cell collection for allogeneic or autologous stem cell transplantation has become the standard treatment modality thanks to easy-applicability and rapid haematological reconstitution compared with stem cell collection from bone marrow harvest in many malignant and benign cases.^{1,2} Stem cell mobilization is performed with granulocyte-colony stimulating factor (G-CSF) in healthy donors. The donor response to G-CSF influences the number of CD34+ cells and eventually transplantation outcomes. Low level of peripheral blood stem cell increases the risk for graft failure.³ On the other hand, transplantation of high CD34+ stem cell doses increases the risk for acute graft versus host disease (GVHD).⁴ Nevertheless, a high level of stem cell infusion in the patient is considered to be associated with faster immune reconstruction.⁵ As known, G-CSF causes lymphocytosis, however, G-CSF has several effects on T-cell subgroups such as especially mobilization of naive T lymphocytes, reduced adhesion molecules and chemokine receptors, reduced T-helper-1-related cytokines and increased regulatory T (T-reg) cells.⁶ It is also known that G-CSF suppresses pro-inflammatory cytokines and increases secretion of IL-10. All these effects indicate the immunosuppressive nature of G-CSF in healthy humans.⁷ On the other hand, it has been shown that platelet count in the peripheral circulation decreases due to G-CSF administration.⁸ The reduction in platelet count is directly proportional with G-CSF dose.⁹ Baseline platelet counts prior to the onset of G-CSF administration is strongly correlated with the amount of mobilized CD34+ stem cells.^{10,11}

In the light of all these information from the literature, we have retrospectively evaluated whether there is a correlation between the platelet/lymphocyte ratio as a cheap and easy-applicable method and the number of collected CD34+ stem cells.

2. MATERIAL AND METHOD

This retrospective study included 94 adult related stem cell donors who were healthy and volunteer by screening their files in the Bone Marrow Transplant Unit of Medicana Ankara International Hospital between the years 2016 and 2018 (Ethics Committee Approval Dated 08.02.2019, Number:26). All donors were over 18 years old. A haematologist from the bone marrow transplant team approved the donors by evaluating their detailed anamnesis, physical examination, complete blood count, biochemistry and infection markers, blood grouping and Rh typing, and pregnancy testing in the females of childbearing age. The donors with a chronic disease and ongoing medication were excluded from the study. Body mass index (BMI) was calculated according to the formula $BMI = \text{weight (in kilograms)} / \text{height (in meters squared)}$. All donors were mobilized using 2.5 mcg/kg lenograstim or filgrastim and underwent peripheral stem cell apheresis.

The onset of G-CSF administration was accepted as the 1st day, and the donors underwent mobilization procedure with Fresenius (Bad Homburg, Germany) device if the early measurement of CD34+stem cells resulted in $20 \times 10^6 / L$ at the 5th day. The collection of minimum $2 \times 10^6 / \text{kg}$ body weight CD34+ stem cells was targeted. The donors underwent apheresis procedure for 1 or 2 days according to that target cell dose or transplant planning of the patient. The blood volumes were processed for 2-4 times and coagulated with 40-90 mL/minute acid-citrate dextrose as the coagulant in the healthy donors (HD) determined to be performed the procedure at the second day. The healthy donors (HD) were administered 10% Calcium Gluconate. Complete blood counts were tested at baseline before G-CSF administration (pre-G-CSF), and before PBSC collection after mobilization with G-CSF administration.

The parameters were analyzed by SPSS for Windows Version 23.0. The continuous variables were expressed as median (minimum-maximum); numbers while percentages were used to express categorical variables. The differences between continuous variables of two groups were calculated by Mann-Whitney-U test. The repeated measures were compared by Wilcoxon test. Chi-square test was used in the analysis of categorical parameters. Spearman Rho

correlation was used to calculate the correlation of two continuous variables. The $p < 0.05$ value was accepted as the statistical significance level.

3. RESULTS AND DISCUSSION

Totally 94 donors were included in the study. The study group consisted of 38 females and 56 males. The patients were divided into two groups as aged below and over 50 years old. This distribution was based on the consideration that the platelet/lymphocyte ratio may have an impact on the amount of CD34+ stem cells depending on donor age. Median haemoglobin (Hb) value was 15 g/dl in the group aged below 50 years, whereas that value was 14.7 g/dl in the group aged ≥ 50 years. WBC counts of the groups were found $7.08 \times 10^3/\text{mL}$ and $7.24 \times 10^3/\text{mL}$, respectively. Body mass index (BMI) value of the younger group was 24.9, whereas that value was 27.8 in the group aged ≥ 50 years ([Table 1](#)). From these comparative data, only BMI value of the group aged below 50 years was statistically significantly lower than the other group, whereas no statistically significant difference was found between the groups in terms of other parameters. The numbers of the collected CD34+ stem cells of both age groups were similar, and no significant difference was found ([Table 2](#)). In addition, we have analyzed the platelet/lymphocyte counts in two groups as < 100 and > 100 ([Table 3](#)). The values of platelet/lymphocyte ratio, early measurement of CD34+ stem cells and the amount of the collected CD34+ stem cells of both groups at the first and second days of the procedure were found similar.

In the present study, we have analyzed the relationship between baseline platelet/lymphocyte ratio and the amount of CD34+ stem cells collected following mobilization. The previous studies have suggested assumptions on predicting a number of the CD34+ stem cells based on various demographic and laboratory analyses and reported that the most effective factors on CD34+ stem cell apheresis yield are G-CSF dose administered in the donor as well as age, gender and the bodyweight of the donor,¹⁰ however, no study on platelet/lymphocyte ratio has been conducted yet as far as we know. It has been aimed to predict the amount of CD34+ stem cells that can be collected by performing an easy and low-cost method in this study.

The peripheral blood stem cell collection from healthy donors induced with G-CSF is an easy technique with a low incidence of complication. The amount of the collected CD34+ stem cells has various effects on engraftment. The detection of these effects in the early pretransplantation period is important in the regulation and prediction of the posttransplantation period.

It is known that a high level of baseline platelet count before G-CSF administration is proportional to the number of mobilized CD34+ stem cells.^{10,11,12} In the present study, we did not analyze the relationship of platelet count with baseline value before G-CSF administration and number of the CD34+ stem cells before the procedure. In addition, some studies have suggested that the amount of the collected stem cells may decrease with advancing age, whereas some other studies assert the contrary to this conclusion.¹³ Various studies on donor age have presented different outcomes.^{14,15} De La Rubia et al. have reported that a higher number of CD34+ stem cells was collected in the younger donors. From this point of view, we distributed our donors into two groups as ones aged below and over 50 years old. We have determined that the platelet/lymphocyte ratio was not significantly correlated with the amount of CD34+ stem cells in both groups.

Our study has some limitations. As our study is retrospective, we could not obtain lymphocyte subgroups and also it would be better if we could search interleukins, tumour necrosis factors, and interferon-alpha because these mediators are effected by G-CSF also, if we could not use one type of generic for all donors we had to use filgrastim or lenograstim both.

4. CONCLUSION

As an overall conclusion, we have assumed that a high platelet count and consequently a high platelet/lymphocyte ratio may be correlated with the number of collected CD34+ stem cells or contrarily a platelet/lymphocyte ratio encountered below a certain threshold value due to extremely reduced platelet count after G-CSF administration may also be proportional with the collected CD34+ stem cells in developing hypotheses of the study. However, both of our hypotheses revealed insignificant outcomes.

DISCLOSURE STATEMENT

The authors reported no potential conflict of interest.

FUNDING INFORMATION

The authors declared that this case had received no financial support.

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Table 1. The demographic characteristics of the donors

	Age Group		p
	<50 of age (n=54)	≥50 of age (n=40)	
	Median (min-max) / n (%)		
Gender			0.724**
Female	21 (38.9%)	17 (42.5%)	
Male	33 (61.1%)	23 (57.5%)	
Hgb (mg/dL)	15 (9.5-17.3)	14.7 (11.3-16.7)	0.857*
WBC (x10³/μL)	7.08 (4.02-11.7)	7.24 (4.39-11.3)	0.731*
Weight (kg)	73.5 (50-102)	79 (50-107)	0.096*
Height (cm)	170 (153-188)	169 (148-180)	0.016*
BMI (kg/m²)	24.94 (18.94-35.71)	27.8 (20.52-40.27)	0.001*

*Mann Whitney-U test. ** Chi-square test

Table 2. Efficacy and effect of HSC mobilization according to age group of the donors

	Age Group		p*
	<50 of age (n=54)	≥50 of age (n=40)	
	median (min-max) / n(%)		
Apheresis number			0.320***
First	45 (83.3%)	30 (75.0%)	
Second	9 (16.7%)	10 (25.0%)	
Blood volume processed (mL)			
First	350 (200-455)	341.5 (230-407)	0.319
Second	280 (230-377)	323 (220-391)	0.347
Difference between first and second p**	0.038	0.123	
CD34⁺ cell apheresis day 1 and 2 (10⁶/L)			
First	61 (19-284)	60.5 (10-138)	0.731
Second	39 (27-64)	27.5 (5-121)	0.086
Difference between first and second p**	0.859	0.066	
CD34 (yield/kg)			
First	4.56 (1.7-19.01)	4.25 (1.08-10.99)	0.244
Second	2.23 (1.32-3.33)	1.78 (0.83-12.73)	0.221
Total	4.85 (1.71-19.01)	4.49 (1.71-15.75)	0.304
Difference between first and second p**	0.260	0.074	
Lymphocyte			
First	2,42 (1,28-4,39)	2,33 (1,15-4,14)	0,328
Second	3,91 (0-7,8)	3,89 (1,71-5,64)	0,745
Platelets			
First	242 (164-483)	228 (114-354)	0,309
Second	203 (114-339)	180 (79,4-356)	0,152
Platelet/lymphocyte ratio (PLO)			
First	101,76 (54,37-206,77)	98,21 (51,68-184,35)	0,722
Second	49,38 (0-134,72)	48,82 (19,93-82,41)	0,994

*Mann Whitney-U test. ** Wilcoxon test. *** Chi-square test

Table 3. Platelet lymphocyte ratio comparisons

	PLO_1		p	PLO_2		p
	<100	≥100		<100	≥100	
CD34 count (apheresis day 1)	61 (10-215)	60.5 (19-284)	0.967	61 (10-284)	37 (37-37)	0.246
CD34 count (apheresis day 2)	24 (5-55)	38 (16-121)	0.272	38 (5-121)	28 (28-28)	0.584
CD34_kg_1	4.41 (1.08-18.3)	4.32 (1.64-19.01)	0.487	4.4 (1.08-19.01)	2.75 (2.75-2.75)	0.261
CD34_kg_2	1.88 (0.83-3.33)	2.12 (1.32-12.73)	0.353	2 (0.83-12.73)	2.54 (2.54-2.54)	0.465
CD34_kg_T	4.67 (1.98-18.3)	4.65 (1.71-19.01)	0.800	4.66 (1.71-19.01)	5.29 (5.29-5.29)	0.699