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Factors Affecting Stem Cell Mobilization in Patients Treated With Hematopoietic Peripheral Stem Cell Transplantation

Periferik Hematopoietik Kök Hücre Nakli Yapılan Hastalarda Kök Hücre Mobilizasyonunu Etkileyen Faktörler

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ABSTRACT

Objectives: To assess the factors affecting stem cell mobilization in patients treated with hematopoietic peripheral stem cell transplantation.

Patients and Methods: Autologous bone marrow transplants in 143 patients with 169 stem cell harvesting procedures were analysed retrospectively.

Results: Stem cell mobilization was done with Filgrastim in 89 patients (52.7 %) and with Lenograstim in 80 patients (47.3%). For stem cell harvesting, Fresenius apheresis device was used in 69 patients (40.8%), while Haemonetics apheresis device was used in 100 patients (59.2%). In univariate analysis, patient's diagnosis (p=0.005), number of treatment lines before the apheresis procedure (p=0.0004), number of leukocytes and CD34+ cell count at the first day of the apheresis procedure (p=0.0001 and p=0.0005, respectively), mobilization with filgrastim (p=0.00004) and mobilization with the Fresenius apheresis device (p=0.007) were statistically significant. In multivariate analysis, diagnosis of the patient (p=0.01), mobilization with filgrastim (p= 0.001), mobilization with Fresenius apheresis device (p=0.03), and leukocyte count at first day of apheresis (p=0.006) were important factors affecting peripheral stem cell mobilization.

Conclusion: Patient's diagnosis, mobilization with filgrastim and Fresenius apheresis device, peripheral blood leukocyte count at the first day of apheresis seem to be important in affecting peripheral stem cell mobilization.

Keywords: Stem cell mobilization, Hematopoietic peripheral stem cell transplantation, Filgrastim, Lenograstim, Apheresis

ÖZET

Amaç: Otolog kök hücre transplantasyonunun başarısı yeterli sayıda kök hücrenin infüzyonuna bağlıdır. Bu nedenle kök hücre mobilizasyonunu etkileyen faktörlerin tanımlanması önem taşımaktadır. Çalışmamızın amacı, otolog kök hücre nakli uygulanan hastalarda kök hücre mobilizasyonunu etkileyen faktörleri belirlemektir.

Hastalar ve Yöntemler: Otolog kök hücre nakli yapılan 143 hasta ve bu hastalara uygulanan 169 kök hücre aferez işlemi retrospektif olarak değerlendirildi.

Bulgular: Kök hücre mobilizasyonu için 89 (%52.7) hastada Filgrastim, 80 (%47.3) hastada Lenograstim kullanıldı. Aferez işleminde 69 (%40.8) hastada Fresenius, 100 (%59.2) hastada Haemonetics cihazı kullanıldı. Tek değişkenli analizlerde tanı (p=0.005), aferez öncesi tedavi sayısı (p:0.0004), tanıdan afereze kadar geçen süre (p:0.02), aferezin 1. günündeki lökosit ve CD34+ hücre sayısı (p:0.0001; p:0.0005), filgrastim kullanımı (p=0.00004) ve fresenius cihazının kullanımı (p:0.007)'nın kök hücre mobilizasyonunu etkileyen faktörler olduğu görüldü. Çok değişkenli analizlerde ise en önemli faktörlerin tanı (p=0.01), filgrastim kullanımı (p=0.001), fresenius cihazının kullanımı (p=0.03) ve aferezin 1. günündeki lökosit sayısı (p=0.006) olduğu saptandı.

Sonuç: Çalışmamızda tanı, filgrastim ile mobilizasyon, fresenius cihazının kullanılması, ve aferezin 1. gününde periferik kandaki WBC sayısının kök hücre mobilizasyonunu etkileyen en önemli değişkenler olduğu saptanmıştır.

Anahtar Kelimeler: Kök hücre mobilizasyonu, Hematopoetik periferal kök hücre nakli, Filgrastim, Lenograstim, Aferez

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INTRODUCTION

High dose chemotherapy, followed by autologous bone marrow transplantation is used widely in the treatment of hematological and some non-hematological solid tumors. New developments in transplantation medicine have broadened its usage. For a successful autologous bone marrow transplantation and a rapid, stable hematological reconstitution, infusion of a sufficent number and adequate quality of stem cells is necessary. In previous clinical trials, it has been postulated that, infusion of $2x10^6$ cells/kg of CD34+ stem cells is minimally sufficient for a safe neutrophil and thrombocyte engraftment at day 14 after the transplantation. The transfer of hematopoietic progenitor cells (HPCs) from bone marrow to the peripheral blood is called mobilization. Nowadays, peripherally mobilized stem cells is the preferred method over direct bone marrow harvesting for autologous bone marrow transplantation. Higher rates of cell collection, faster engraftment, lower rates of procedural complications, easier accesibility, lower rates of tumor contamination and faster hematopoietic and immune reconstitution are the attributed causes of this situation[1-3]. Because successful autologous bone marrow transplantation is strictly related to the infused quality and number of stem cells, various studies have investigated the factors affecting stem cell mobilization and the causes of inadequate mobilization. Many factors affecting stem cell mobilization have been reported, previously. Diagnosis of the patient, chemotherapies applied and number of therapy lines before autologous transplantation, number of relapses, growth factors used for mobilization, type of apheresis devices used, leukocyte and CD34+ cell count at the first day of apheresis can all affect the success of stem cell mobilization. Several studies have reported distinct and controversial results about these factors. The reason for this disparity can be attributed to small sample size, inclusion of different heterogenous mobilization protocols to the analysis or the absence of exact criteria for unsuccessful mobilization. The purpose of this study is to evaluate the factors affecting stem cell mobilization in patients treated with high dose therapy followed by hematopoietic peripheral stem cell rescue.

PATIENTS and METHODS

In this study we retrospectively analysed 154 patients treated with autologous bone marrow transplantation between the years 1993 and 2010, followed at the Bone Marrow Transplantation Unit, Hematology Division, Marmara University Hospital. A total of 180 harvesting procedures were applied. In eleven cases, harvesting was done from bone marrow and these cases were excluded from the study. One hundered and fortythree patients and 169 apheresis procedures for peripheral stem cell harvesting were analysed. Daily apheresis was performed using continuous flow blood cell separators of the companies Fresenius or Haemonetecs. Median age was 48 (range 18-66). Eighty one (56.6%) patients were male, 62 (43.4%) patients were female. For the 143 patients analysed, the diagnoses were: multiple myeloma in 67 patients (46.9%), acute leukemia in 11 patients (7.7%), Hodgkin's Disease in 31 patients (21.7%), non-Hodgkin's lymphoma in 33 patients (23.1%) and a solid tumor in only one patient (0.7%). Before the apheresis procedure, the median number of disease relapse was one (range 0-5), the median number of treatment lines received was two (range 1-6); the median time between the diagnosis to the apheresis procedure was 13 months (range 1-228). Fortythree patients (30.1%) received involved field radiation therapy before the apheresis procedure. For stem cell mobilization, Filgrastim was used in 89 patients (52.7%) while Lenograstim was used in 80 (47.3%) patients. For stem cell harvesting, a Fresenius apheresis device was used in 69 patients (40.8%), while a Haemonetics apheresis device was used in 100 patients (59.2%). The median apheresis cycle for one mobilization period applied to the patients was 3 days (range 1-4). Median WBC count at the first day of apheresis was 35800/μL (range 6900-96500). Median peripheral blood CD34+ cell count at the first day of apheresis was 15/μL (range 0-125). Median harvested total cell/kg was 11.43×10^8 (range 1.94×10^8–26.30×10^8).Median CD34+ cell/kg count in the harvested product was 4.21×10^6 (0.15×10^6–20.10×10^6).

Statistical Analysis

All continuous variables were dichotomized by use of median values as a cut-off value. Comparisons were made by chi square, Yates correction, and Fisher's exact test appropriately, in univariate analysis. Time to apheresis was estimated as the time elapsed between the date of diagnosis and the date of apheresis. Variables with a p value <0.05 in univariate analysis were included into the multivariate analysis. The multivariate analysis was done by logistic regression analysis with a method of backward selection. Statistical significance was accepted as the two-tailed p value as below 0.05. SPPS version 15.0 was used for the statistical analysis.

RESULTS

Gender and diagnosis, number of treatment lines before the apheresis procedure, time between diagnosis and apheresis, radiotherapy before the apheresis procedure, number of disease relapses before the apheresis and peripheral blood CD34+ cell count the first day of the apheresis procedure had no effect on harvested total cell/kg values. When the age of the patient was taken into account, it was observed that patients over the age of 50 have higher total cell/kg values (p=0.01). In patients having >3 apheresis cycles, harvested total cell/kg value was higher (p=0.02). Apheresis device used was also analysed; harvested total cell/kg was found to be significantly higher with the Fresenius apheresis device than with the Haemonetics apheresis device (p:0.03). Peripheral blood WBC count at day 1 was associated with harvested total cell/kg (p=0.0003). When the effect of G-CSF used was analysed, the total harvested cell/kg was significantly higher with Lenograstim over Filgrastim and this difference was statistically significant (p=0.0000005). (Table I).

Table I. Factors affecting Total cell/kg (Univariate Analysis)

Variables—number (%)	Number of Patients	Total cell/kg ≤10^9 Number. (%)	Total cell/kg >10^9 Number. (%)	p
Age (years)	139			
<50	78	41 (52.6)	37 (47.4)	0.01
≥50	61	19 (31.1)	42 (68.9)	
Sex	139			
Male	80	35 (43.8)	45 (56.3)	0.9
Female	59	25 (42.4)	34 (57.6)	
Diagnosis	138			
Multiple Myeloma	65	27 (41.5)	38 (58.5)	0.08
Acute Leukemia	11	8 (72.7)	3 (27.3)	
Hodgkin's Disease	31	15 (48.4)	16 (51.6)	
Non-Hodgkin's Lymphoma	31	9 (29.0)	22 (71.0)	
Number of relapses before apheresis	141			
≤1	128	59 (46.1)	69 (52.9)	0.7
>1	21	8 (38.1)	13 (61.9)	
Number of treatment lines before apheresis	150			
≤1	30	16 (53.3)	14 (46.7)	0.4
>1	120	51 (42.5)	69 (57.5)	
Radiotherapy before apheresis	139			
Radiotherapy not treated	97	42 (43.3)	55 (56.7)	1.0
Radiotherapy treated	42	18 (42.9)	24 (57.1)	
Time to apheresis(months)	162			
≤12	74	40 (54.1)	34 (45.9)	0.2
>12	88	39 (44.3)	49 (55.7)	
G-CSF	162			
Filgrastim	84	57 (67.9)	27 (22.1)	0.0000005
Lenograstim	78	22 (28.2)	56 (71.8)	
Apheresis Device	162			
Fresenius®	65	25 (38.5)	40 (61.5)	0.03
Haemonetics®	97	54 (55.7)	43 (44.3)	
Number of apheresis cycles	162			
≤3	140	74 (52.9)	66 (47.1)	0.02
>3	22	5 (22.7)	17 (77.3)	
WBC (/μL) in 1st day of apheresis	162			
<35000	73	47 (64.4)	26 (35.6)	0.0003
≥35000	89	32 (36.0)	57 (64.0)	
CD34 (/μL) in 1st day of apheresis	158			
≤15	82	38 (46.3)	44 (53.7)	0.4
>15	76	40 (52.6)	36 (47.4)	

Harvested CD34+ cells/kg was not affected by the age or sex of the patient, radiation therapy before stem cell mobilization and the number of disease relapses before the apheresis procedure. When the diagnosis added into the comparison, the harvested CD34+ cell/kg was significantly higher in Hodgkin's Disease, Multiple myeloma and Non-Hodgkin's lymphoma than acute leukemia respectively (p=0.005) In patients who received more than one treatment line before the apheresis procedure, harvested CD34+ cell/kg was prominently lower (p= 0.0004). The harvested CD34+ cells was higher when time to apheresis was equal or less than 12 months and the number of apheresis cycles was equal or less than three (p=0.02 and p=0.000004). The relationship between peripheral blood WBC and CD34+ cell count at the first day of apheresis and the total harvested CD34+ cell/kg was statistically significant (p=0.0001, p:0=0005). A higher CD34+ cell was obtained when Filgrastim was used instead of Lenograstim during the mobilization procedure (p=0.000004). The Fresenius apheresis device harvested significantly more CD34+ cells than the Haemonetics apheresis device (p=0.007) (Table II).

Achieving a total of ≥10^9 cell/kg was investigated using multivariate analysis. The most affecting factors was the number of apheresis cycles (more than three), mobilization with lenograstim, harvesting with the Fresenius apheresis device and WBC count ≥35.000 at 1st day of apheresis respectively.

If the number of the apheresis cycle was more then three, then the total cell/kg value was six times higher than in patients with less than three cycles (p:=0.02). Achieving a total cell/kg value over 109 was 4 times more likely when the mobilization was done with lenograstim (p=0.0004). Achieving a total cell/kg value over 109 was 4 times more likely when harvesting was done with the Fresenius

device (p=0.001). If the WBC count at the first day of apheresis was equal or more than 35.000/µl, harvesting a total cell/kg value over 109 was 3 times more likely (p=0.00002) (Table III).

In multivariate analysis, diagnosis of the patient was the most important factor affecting total CD34+ cell/kg count. In non-Hodgkin's lymphoma, multiple myeloma and Hodgkin's Disease, the probability of harvesting a total CD34+ cell/kg count over $4x10^6$ was 10, 15 and 17 times higher than acute leukemia (p=0.04; 0.01; 0.01), respectively. The probability of harvesting a total CD34+ cell/kg count over $4x10^6$ was 2.5 times higher with Filgrastim mobilization (p=0.001). The probability of harvesting a total CD34+ cell/kg count over $4x10^6$ was 3 times higher when the apheresis was performed with the Fresenius device (p=0.03). If the WBC count at the 1st day of apheresis was ≥35.000/µl, there was a 3 times higher probability for harvesting a total CD34+ cell/kg count over $4x10^6$ (p=0.006) (Table IV).

Table II. Factors affecting CD34/kg (Univariate Analysis)

Variables—Number (%)	Number of Patients	CD34/kg <4 x 10^6 Number. (%)	CD34/kg ≥4 x 10^6 Number. (%)	p
Age (years)	142			
<50	79	31 (39.2)	48 (60.8)	0.4
≥50	63	29 (46.0)	34 (54.0)	
Sex	142			
Male	80	33 (41.3)	47 (58.8)	0.8
Female	62	27 (43.5)	35 (56.5)	
Diagnosis	141			
Multiple myeloma	67	22 (32.8)	45 (67.2)	0.005
Acute Keukemia	11	8 (72.7)	3 (27.3)	
Hodgkin's Disease	30	9 (30.0)	21 (70.0)	
Non-Hodgkin's Lymphoma	33	20 (60.6)	13 (39.4)	
Number of relapses before apheresis	155			
≤1	134	56 (41.8)	78 (58.2)	0.1
>1	21	13 (61.9)	8 (38.1)	
Number of treatment lines before apheresis	156			
≤1	32	5 (15.6)	27 (84.4)	0.0004
>1	124	65 (52.4)	59 (47.6)	
Radiotherapy before apheresis	142			
Radiotherapy treated	100	47 (47.0)	53 (53.0)	0.1
Radiotherapy not treated	42	13 (31.0)	29 (69.0)	
Time to apheresis(months)	168			
≤12	78	28 (35.9)	50 (64.1)	0.02
>12	90	49 (54.4)	41 (45.6)	
G-CSF	168			
Filgrastim	88	27 (30.7)	61 (69.3)	0.00004
Lenograstim	80	50 (62.5)	30 (37.5)	
Apheresis Device	169			
Fresenius®	69	23 (33.3)	46 (66.7)	0.007
Haemonetics®	99	54 (54.5)	45 (44.5)	
Number of apheresis cycles	168			
≤3	147	57 (38.8)	90 (61.2)	0.000004
>3	21	20 (95.2)	1 (4.8)	
WBC (/µL) in 1st day of apheresis	168			
<35000	78	48 (61.5)	30 (38.5)	0.0001
≥35000	90	28 (32.2)	61 (67.8)	
CD34 (/µL) in 1st day of apheresis	164			
≤15	85	50 (58.8)	35 (41.2)	0.0005
>15	79	25 (31.6)	54 (68.4)	

Table III. Backwards selected logistic regression analysis of factors affecting the probability of total cell/kg ≥10^9

Variable	Coefficient(β)	Standard error of β	OR	%95 CI		p
				Lower Border	Upper Border	
Mobilization with Lenograstim	1.513	0.433	4.54	1.94	10.60	0.0004
Harvesting with Fresenius	1.489	0.451	4.44	1.83	10.73	0.001
Apheresis cycles >3	1.800	0.765	6.05	1.35	27.08	0.02
WBC≥35000/μL at 1st day of apheresis	1.227	0.426	3.41	1.48	7.86	0.00002

OR= Odd Ratio CI= Confidential Interval

Table IV. Backwards selected logistic regression analysis of factors affecting the probability of CD34 cell/kg ≥4 x 10^6

Variable	Coefficient (β)	Standard error of β	OR	%95 CI		p
				Lower Border	Upper Border	
Mobilization with Filgrastim	1.704	0.516	2.41	0.91	6.38	0.001
Harvesting with Fresenius	1.194	0.540	3.30	1.15	9.51	0.03
WBC≥35000/μL at 1st day of apheresis	1.372	0.501	3.94	1.48	10.52	0.006
Diagnosis of Non-Hodgkin's lymphoma	2.324	1.112	10.21	1.16	90.31	0.04
Diagnosis of multiple myeloma	2.719	1.064	15.17	1.89	121.97	0.01
Diagnosis og Hodgkin's Disease	2.864	1.133	17.54	1.91	161.48	0.01

OR= Odd Ratio CI= Confidential Interval

DISCUSSION

In this study, we found that important factors affecting total harvested cell/kg are, more than three apheresis cycles for an apheresis period, mobilization with lenograstim, harvesting with Fresenius device and ≥35.000 WBC count on the first day of apheresis. In addition, we found that important factors affecting total harvested CD34+ cell count are the diagnosis, peripheral blood WBC count on the first day of apheresis, harvesting with Fresenius device and mobilization with Filgrastim.

In achieving the highest total CD34+ cell collection, we found that the most important variable is the patient's diagnosis. We found that the rate of successful CD34+ cell collection was highest in Hodgkin's Disease, followed by multiple myeloma. The lowest rate was found in acute leukemias. We observed that in multiple myeloma and Hodgkin's Disease patients, the probability of CD34+ cell count for being ≥ 4x10^6 was 15 and 17 times higher than in acute leukemia patients, respectively. It seems that the impact of high stem cell damage caused by salvage treatments used in acute leukemia adversely affects the CD34+ cell mobilization. This result is consistent with previous studies[4-8].

There are several studies reporting the effect of peripheral blood WBC and CD34+ cell count on the success of mobilization at first day apheresis[9-18]. In our study, we found that there is a significant relationship between peripheral blood WBC and CD34+ cell count and mobilized total CD34+ cells/kg. However, in multivariate analysis the effect of peripheral blood CD34+ cell count at first day of apheresis on collected CD34+ cell/kg was abolished, whereas the effect of the peripheral blood WBC count was maintained.

The effectiveness of the apheresis device seems to have an influence on the harvested CD34+ cell/kg count. Previous studies compared the efficiency of different apheresis devices on stem cell collection. But the number of studies comparing both devices (Fresenius AS 104 and Haemonetics MCS 3P devices) are limited[19]. In one of these studies,[20] it has been suggested that a higher number of CD34+ cells can be harvested with Fresenius AS104 in pediatric populations. Our results are in line with these findings and suggest that a higher number of total cell/kg or total CD34+ cell/kg can be harvested with Fresenius AS104 in comparison to Haemonetics MCS 3P.

Stem cell apheresis is performed using G-CSF (filgrastim and lenograstim) at our institution. The chemical and physicochemical structures of these two molecules differ. Lenograstim is a glycosylated molecule and this property makes it more stable to pH, temperature and proteolysis effects[21]. Previous in-vitro studies suggest that Lenograstim is more potent than filgrastim[22-24]. But these studies evaluated the mobilization capacities of these agents, and the superiority of lenograstim is shown on healthy donors[25,26] not on patient groups with the exception of limited studies[27]. In our study, a total of 169 apheresis procedures were performed and 89 (52.7%) mobilizations were done with filgrastim, and 80 (47.3%) were done with lenograstim. We found that the total harvested

cell/kg was higher with lenograstim and mobilization with lenograstim was 4 times stronger in collection over 10^9 total cell/kg cells. But when CD34+ cell counts were analysed, the achieved CD34+ cell numbers were higher with filgrastim and after mobilization with filgrastim, collections of cells over $4x10^6$ total CD34+ cell/kg were 2.5 times more likely than that with lenograstim. Lenograstim was found to be more efficient in terms of increasing the total cell/kg values but was inferior to filgrastim in the mobilization of CD34+ cells. This finding may point out that filgrastim is more successful in mobilizing progenitor cells than lenograstim which in turn may provide mobilization of more mature cells to the peripheral blood. It is important to consider this finding, during the mobilization procedure especially in patients with poor stem cell reserve.

In addition, our findings suggest that, age, gender, radiation therapy before stem cell mobilization and number of disease relapses before the apheresis procedure do not have any influence on harvested CD34+ cells/kg. The negative effect of radiotherapy on stem cell mobilization has been reported previously in various studies[28,29]. In our study, receiving radiotherapy before the apheresis procedure did not affect harvested total cell/kg or CD34+ cell/kg negatively. Dose, duration, application fields and magnitude of radiotherapy may modify the stem cell damaging effects of radiation. Our finding of a higher yield of collected CD34+ cell count in patients treated with the apheresis procedure up to 12 months after the diagnosis is in line with certain previous studies but when analysed with multivariate analysis methods, the effect of time from diagnosis to apheresis disappeared. İn multivariate analysis, the negative effect of multiple treatment lines before the apheresis procedure on the harvested CD34+ cell/kg cell count disappeared, also.

In conclusion, we report that, diagnosis of the patient, mobilization with filgrastim, mobilization with Fresenius apheresis device and peripheral blood leukocyte count at the first day of apheresis are variables affecting peripheral stem cell mobilization. We suggest that taking these factors into account before stem cell apheresis may lead to a more appropriate decision making in the selection of mobilization agents and apheresis devices, which in turn may improve the success of mobilization.

REFERENCES

1. Cottler-Fox M, Lapidot T, Petit I, et al. Stem cell mobilization. Hematology 2003;419-437.
2. Lee JL, Kim SB, Lee GW, et al. Clinical usefulness of the hematopoietic progenitor cell counts in predicting the optimal timing of peripheral blood stem cell harvest. J Korean Med Sci 2003; 18: 27-35. doi: 10.1111/j.0041-1132.2004.04166.x
3. Rainer Moog. Management strategies for poor peripheral blood stem cell mobilization. Transfus Apher Sci. 2008; 38: 229–236. doi: 10.1016/j.transci.2008.04.002
4. Mendrone A Jr, Arrais CA, Saboya R, Chamone DA, Frederico Luiz Dulley FL. Factors affecting hematopoietic progenitor cell mobilization: An analysis of 307 patients. Transfus Apher Sci. 2008; 39: 187–192. doi: 10.1016/j.transci.2008.09.012
5. Arslan O, Moog R. Mobilization of peripheral blood stem cells. Transfusion and Apheresis Science 2007; 37: 179–185. doi: 10.1016/j.transci.2007.08.002
6. Weaver CH, Schwartzberg LS, Birch R, et al. Collection of peripheral blood progenitor cells after the administration of cyclophosphamide, etoposide, and granulocyte-colony-stimulating factor: an analysis of 497 patients. Transfusion 1997;37:896–903. doi:10.1046/j.1537-2995.1997.37997454014.x
7. Haas R, Möhle R, Frühauf S, et al. Patient characteristics associated with successful mobilizing and autografting of peripheral progenitor cells in malignant lymphoma. Blood 1994;83:3787–3794.
8. Kasparu H, Krieger O, Girschikofsky M, Kolb A, Bettelheim P, Lutz D. Factors influencing the timing of peripheral blood stem cell collection (PBSC). Transfus Apheresis Sci 1996;17:595–600.
9. Ikeda K, Kozuka T, Harada M. Factors for PBPC collection efficiency and collection predictors. Transfus Apher Sci. 2004;31: 245–259. doi: 10.1016/j.transci.2004.09.008
10. Elliott C, Samson DM, Armitage S, et al. When to harvest peripheral-blood stem cells after mobilization therapy: Prediction of CD34-positive cell yield by preceding day CD34-positive concentration in peripheral blood. J Clin Oncol 1996; 14:970-973.
11. Gidron A, Singh V, Egan K, Mehta J. Significance of low peripheral blood CD34ş cell numbers prior to leukapheresis: what should the threshold required for apheresis be? Bone Marrow Transplant 2008; 42: 439–442.
12. Mehta J, Oyama Y, Winter J, et al. CD34+ cell collection efficiency does not correlate with the pre-leukapheresis hematocrit. Bone Marrow Transplant 2001; 28: 597–601.
13. Gidron A, Verma A, Doyle M, et al. Can the stem cell mobilization technique influence CD34+ cell collection efficiency of leukapheresis procedures in patients with hematologic malignancies? Bone Marrow Transplant 2005; 35: 243–246. doi: 10.1038/sj.bmt.1704781
14. Schots R, Van Riet I, Damianos S, et al. The absolute number of circulating CD34+ cells predicts the number of hematopoietic stem cells that can be predicted by apheresis. Bone Marrow Transplant 1996;17:509-15.
15. Schwella N, Beyer J, Schwaner I, et al. Impact of preleukapheresis cell counts on collection results and correlation of progenitor cell dose with engraftment after high-dose chemotherapy in patients with germ-cell cancer. J Clin Oncol 1996;14:1114-1121.
16. Mohle R, Murea S, Pforsich M, Witt B, Haas R. Estimation of the progenitor cell yield in a leukapheresis product by previous measurement of CD34+ cells in the peripheral blood. Vox Sang 1996;71:90-196.

17. Ford C, Chan K, Reilly W, Peterson F. An evaluation of predictive factors for CD34+ cell harvest yields from patients mobilized with chemotherapy and growth factors. Transfusion 2003;43:622-625. doi: 10.1046/j.1537-2995.2003.00376.x

18. Moncada V, Bolan C, Yau Y, Leitman S. Analysis of PBPC yields during large volume leukapheresis of subjects with a poor mobilization response to filgrastim. Transfusion 2003;43:495-501. doi: 10.1046/j.1537-2995.2003.00361.x

19. Ravagnani F, Siena S, De Reys S, et al. Improved collection of mobilized CD34+ hematopoietic progenitor cells by a novel automated leukapheresis system. Transfusion 1999;39:48–55. doi: 10.1046/j.1537-2995.1999.39199116894.x

20. Bambi F, Faulkner LB, Azzari C, et al. Pediatric peripheral blood progenitor cell collection: haemonetics MCS 3P versus COBE Spectra versus Fresenius AS104. Transfusion 1998 Jan;38(1):70-74.

21. Kishita M. Stability of granulocyte colony-stimulating factor (G-CSF) in serum. Clin Rep 1992;26:221–224.

22. Pedrazzoli P, Gibelli N, Pavesi L, et al. Effects of glycosylated and non-glycosylated G-CSFs, alone and in combination with other cytokines, on the growth of human progenitor cells. Anticancer Res 1996;16:1781–1785.

23. Mire-Sluis AR, Das RG, Thorpe R. The international standard for granulocyte colony stimulating factor (G-CSF). Evaluation in an international collaborative study. Participants of the Collaborative Study. J Immunol Methods 1995;179:117–126.

24. Nissen C, dalle Carbonare Y, Moser Y. In vitro comparison of the biological potency of glycosylated versus non-glycosylated rG-CSF. Drug Invest 1994;7:346–352.

25. Höglund M, Smedmyr B, Bengtsson M, et al. Mobilization of CD34+ cells by glycosylated and nonglycosylated G-CSF in healthy donors – comparative study. Eur J Haematol 1997;59:177–183. doi: 10.1111/j.1600-0609.1997.tb00972.x

26. Watts MJ, Addison I, Long SG, et al. Crossover study of the haematological effects and pharmacokinetics of glycosylated and non-glycosylated G-CSF in healthy volunteers. Br J Haematol 1997;98:474–479. doi: 10.1046/j.1365-2141.1997.2393053

27. Schiødt I, Knudsen LM, Jensen L, et al. Flow cytometry comparison of CD341 subsets in bone marrow and peripheral blood after priming with glycosylated or non-glycosylated rhG-CSF. Bone Marrow Transplant 1998; 21:1167–1169.

28. Tomblyn M, Burns LJ, Blazar B, et al. Difficult stem cell mobilization despite adequate CD34+ cell dose predicts shortened progression free and overall survival after autologous HSCT for lymphoma. Bone Marrow Transplant 2007; 40:111–118. doi: 10.1038/sj.bmt.1705708

29. Dreger P, Kloss M, Petersen B, et al. Autologous progenitor cell transplantation: Prior exposure to stem cell-toxic drugs determines yield and engraftment of peripheral blood progenitor cell but not of bone marrow grafts. Blood 1995; 86(10): 3970-3978.