Uludağ Üniversitesi Tıp Fakültesi Dergisi
Journal of Uludağ University Medical Faculty
50 (3) 367-373, 2024
DOI: https://doi.org/10.32708/uutfd.1518837

ORIGINAL RESEARCH

Effectiveness and Safety of Low-Dose Etoposide Chemomobilization in Patients with Multiple Myeloma and Lymphoma*

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ABSTRACT

Studies have discovered a risk of treatment-related leukemia and myelodysplastic syndromes with high doses of etoposide prompting a closer look, at the effectiveness of lower doses. In this study, we aimed to demonstrate the efficacy of low-dose etoposide in patients with MM and lymphoma. Forty-eight patients with MM and refractory lymphoma who underwent stem cell mobilization with low-dose etoposide (days 1 and 2, 375 mg/m²) and granulocyte colony-stimulating factor (G-CSF, 10-15 µg/kg after the 3rd day) in Bursa Uludağ University Faculty of Medicine Hematology Department Stem Cell Transplantation Unit were analyzed retrospectively. The rate of successful mobilization (> $2x10^6$/kg CD34+ cell collection) was 95% and was performed in a minimum of 1 and a maximum of 3 apheresis. The median collected CD34+ cell count was 9.165 × 10^6/kg (11.7 in good vs 3.98 in poor mobilizers, p<0.001). It was determined that a low number of peripheral CD34+ cells on the first day (Hazard ratio (HR); 0.00, 95% Confidence interval (CI) 0.00-0.660; p=0.040) and prior autologous hematopoietic stem cell transplantation (HR; 1.206, 95% CI 1.009-1.442; p=0.043) were independent risk factors for poor mobilization. Febrile neutropenia occurred in 18.8% (11.4% in good vs 38.5% in poor mobilizers, p=0.048), and 16.7% required erythrocyte transfusions (14.3% in good vs 23.1% in poor mobilizers, p=0.664). In the median follow-up of 35.5 months, no treatment-related secondary malignancy was detected in any patients. Our results show that low-dose etoposide and G-CSF are effective mobilization agents with tolerable toxicity in patients with MM and refractory lymphoma.

Keywords: Low-dose etoposide. Stem cell mobilization. Multiple myeloma. Lymphoma. Autologous hematopoietic stem cell transplantation.

Multipl Miyelom ve Lenfoma Hastalarında Düşük Doz Etoposid Kemomobilizasyonunun Etkinliği ve Güvenilirliği

ÖZET

Çalışmalarda yüksek doz etoposid ile tedaviye bağlı lösemi ve miyelodisplastik sendrom riskinin keşfedilmesi, daha düşük dozların etkinliğine daha yakından bakılmasına neden olmuştur. Bu çalışmada, multiple miyelom (MM) ve lenfoma hastalarında düşük doz etoposidin etkinliğini göstermeyi amaçladık. Bursa Uludağ Üniversitesi Tıp Fakültesi Hematoloji Bölümü Kök Hücre Nakli Ünitesi'nde düşük doz etoposid (1. ve 2. günler, 375 mg/m²) ve granulocyte colony-stimulating factor (G-CSF, 3. günden sonra 10-15 µg/kg) ile kök hücre mobilizasyonu yapılan MM ve refrakter lenfomalı 48 hasta retrospektif olarak analiz edildi. Başarılı mobilizasyon (> $2x10^6$/kg CD34+ hücre toplanması) oranı %95 olup en az 1, en fazla 3 aferezde gerçekleştirildi. Toplanan median CD34+ hücre sayısı 9,165 × 10^6/kg idi (good mobilizerlerde 11,7 vs poor mobilizerde 3,98× 10^6/kg, p<0,001). İlk gün periferik CD34+ hücre sayısının düşük olmasının (Hazard ratio (HR); 0.00, %95 confidence interval (CI) 0.00-0.660; p=0,040) ve önceki otolog hematopoietik kök hücre naklinin (HR; 1.206, %95 CI 1.009-1.442; p=0,043) kötü mobilizasyon için bağımsız risk faktörleri olduğu belirlendi. Hastaların %18,8'inde febril nötropeni saptandı (good mobilizerlerde %11,4 vs poor mobilizerlerde %38,5, p=0,048) ve %16,7'sinde eritrosit transfüzyonu ihtiyacı oldu (good mobilizerlerde %14,3 vs poor mobilizerlerde %23,1, p=0,664). Median 35,5 aylık takip süresinde hastaların hiçbirinde tedaviye bağlı ikincil malignite saptanmadı. Çalışmamızın sonuçları, düşük doz etoposid ve G-CSF'nin MM ve refrakter lenfoma hastalarında tolere edilebilir toksisite ile etkili mobilizasyon ajanları olduğunu ortaya koydu.

Anahtar Kelimeler: Düşük doz etoposid. Kök hücre mobilizasyonu. Multipl miyelom. Lenfoma. Otolog hematopoetik kök hücre transplantasyonu.

Date Received: July 21, 2024
Date Accepted: October 09, 2024

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* Presented as an oral presentation at the "11. Ulusal Kemik İliği Transplantasyonu ve Hücresel Tedaviler Kongresi" (March 2019, Antalya).

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Autologous hematopoietic stem cell transplantation (AHSCT) is a standard treatment approach used in cases under 65 years of age with multiple myeloma (MM) and chemosensitive relapsed high or moderate-grade non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL). In this treatment method, the hematopoietic stem cell support required for high-dose chemotherapy is provided. The optimal strategy for collecting and mobilizing hematopoietic stem cells to the peripheral blood has yet to be defined.[1-3]

The most commonly used agents in peripheral stem cell mobilization are granulocyte colony-stimulating factor (G-CSF) alone, chemotherapy followed by G-CSF, and plerixafor. It is difficult to achieve success in mobilization with G-CSF alone in special patient groups.[4] At the end of a phase 3 study published in 2009, which compared the addition of G-CSF alone with plerixafor and G-CSF, it was possible to collect $5x10^6$/kg cells in five days in 20% of the patients in the G-CSF alone group, while this rate increased to 59% in the arm where plerixafor was added. However, the use of plerixafor is an expensive method and may result in insufficient CD34+ cell count in a small group of patients.[5]

Although G-CSF with cyclophosphamide has been widely used in chemomobilization, the increased risk of febrile neutropenia, potential cardiotoxicity, and increased mobilization failure rates in intensively treated patients have limited the use of cyclophosphamide.[6,7] Few studies examine the addition of low- or high-dose (>1200 mg/m²) etoposide to G-CSF as an alternative agent. (8-10) In addition, there is a concern about secondary malignancy at high doses of etoposide. In our study, low-dose etoposide (days 1 and 2, 375 mg/m²) was selected to reduce potential toxicities such as cytopenia, febrile neutropenia, need for transfusion, and secondary malignancy. It was aimed to reveal the efficacy and toxicity of low-dose etoposide and G-CSF on stem cell mobilization in cases with MM, HL, and NHL.

Material and Method

Patients and treatment

In our center, 48 patients with MM, HL, and NHL over the age of 18 who received low-dose etoposide chemotherapy and G-CSF for AHSCT over 4.5 years were included in the study. Patients mobilized only with G-CSF, DHAP (dexamethasone, high dose cytarabine, cisplatin)+G-CSF, or cyclophosphamide +G-CSF regimen in the mobilization regimen and whose research data were missing were excluded from the study.

A femoral venous catheter was used to give the mobilization regimen. Etoposide (Etoposide Teva) 375 mg/m² was administered intravenously (i.v.) for 4 hours on days 1 and 2, and G-CSF (Neupogen) was administered after the 3rd day in 10-15 µg/kg divided across two doses. Granisetron (Granexa) 2mg orally and dexamethasone (Dekort) 20mg orally were given 30 minutes before each etoposide dose. As antimicrobial prophylaxis, ciprofloxacin (Cipro) 500 mg was given orally once a day after the 5th day.

Leukocyte count was monitored daily after mobilization chemotherapy, and the percentage of CD34+ cells was assessed when leukocytes were 1000/mL. The threshold to start leukapheresis was when >20 CD34+ cells/ mL in the peripheral blood. The policy of a higher CD34+ cells/mL threshold is based on a smaller number of apheresis needed (our goal is to collect target CD34+ numbers in 1 or 2 aphereses) resulting in reduced volumes of apheresate and lower cumulative DMSO dose during AHSCT. All apheresis was performed with the Spectra Optia version 7.2 (TerumaBCT, Lakewood, CO, USA (MNC program)). Apheresis procedures processed at least two times the total blood volumes per day for more than 2 hours to collect at least $2x10^6$/kg CD34+. Apheresis was usually continued until sufficient CD34+ cells for AHSCT had been collected. Citrate-dextrose solution (ACD-A) was used as an anticoagulant. The anticoagulant ratio was 12 to 1. The amounts of CD34+ cells in the peripheral blood and leukapheresis component were determined by flow cytometry using the Navios EX Flow Cytometer (Beckman Coulter). Target CD34+ cell yield was determined as $\geq 4x10^6$/kg cells. Successful mobilization was defined as $\geq 2x10^6$/kg CD34+ cell collection at the end of the mobilization process. The patients were divided into two groups: good mobilizers and poor mobilizers, according to the amount of CD34+ cells collected. Patients with $\geq 5x10^6$/kg CD34+ cells collected in two or fewer cycles of apheresis made up the good mobilizers, and the others made up the poor mobilizers.

The collected product and freezing solution were prepared as a mixture of 10% DMSO (dimethyl sulfoxide) and autologous plasma. A mechanical freezer (–80°C) was used to store frozen samples.

As a systematic approach on the 5th day after transplantation, G-CSF 5 µg/kg/day subcutaneously (s.c.) or i.v. infusion in thrombocytopenic cases was administered. Neutrophil engraftment was recorded on the first day when the absolute neutrophil count without supplementation exceeded ≥ 500/mL for three consecutive days. Platelet engraftment was defined as unsupported platelets exceeding ≥ 20,000/mL for three straight days or not needing a replacement for seven days. Febrile neutropenia was defined as an absolute neutrophil count < 500 cells/µL or expected to fall below < 500 cells/µL within 48 hours in a patient with an orally measured temperature > 38.3°C or >38°C for

1 hour. Red blood cell (RBC) transfusion was performed when hemoglobin (Hb) was < 8 g/dL or if the patient was symptomatic. Platelet concentrate transfusion was administered in patients with a platelet value < 10,000/mL or in the presence of fever or bleeding in patients with a thrombocyte value between 10,000-20,000/mL.

Ethics Statement

This study was carried out with the approval of local ethics committee with reference number 2017-19/40.

Statistical analysis

Fisher's exact test was used to analyze categorized variables, and the Mann-Whitney U test was used to analyze continuous variables. Multivariate logistic regression analysis was used to analyze the influential factors on poorly mobilized patients. Age, gender, diagnosis, prior usage of radiotherapy and lenalidomide, prior AHSCT, disease status, the time between diagnosis and mobilization, number of chemotherapies received, and peripheral CD34+ cell count on the first day were evaluated for this purpose. The results were evaluated at the 95% confidence interval and statistical significance at the p< 0.05 level.

Statistical analysis of data; obtained from The Statistical Package for Social Sciences (SPSS®) for Windows Ver.20.0 (SPSS, Chicago, Illinois, USA) module.

Results

The number of stem cell mobilizations performed in our unit during the 4.5 years covering the data of our study is 148. Of these, 48 were performed with low-dose etoposide chemotherapy and G-CSF. Stem cell mobilization was performed twice on two different dates with the same regimen in only one patient. The age range of 48 patients (34 MM, 8 HL, and 6 NHL) was 25-68 years and the median age was 56.5. Thirty-three (68.75%) of the patients were male and 15 (31.25%) were female. 35.4% of the patients had received at least two chemotherapy regimens and the median chemotherapy regimen was 3 (range; 1-5). Seven of the patients (14.6%) had a history of previous radiotherapy. Nine (18.8%) patients had undergone previous AHSCT, which was more common in the poor mobilizer group (p=0.048). Nine (18.8%) patients had undergone previous AHSCT, which was more common in the poor mobilizer group (p=0.048). Seventeen (35%) patients had a history of unsuccessful mobilization with the G-CSF, G-CSF+plerixafor, or DHAP regimen. Of the patients, 66.7% (32 patients) were in remission at the time of diagnosis, 33.3% had active or residual disease, and 47.9% (23 patients) had received lenalidomide therapy. The median time between diagnosis and mobilization was 14 (4-60) months. The median leukocyte count at the time of mobilization was 9015/mL (1840-83900) and the median platelet count was 48000/mL (15200-137000). The characteristics of the patients are summarized in Table I.

Table I. Patient characteristics

Variable		All (no:48)	Good mobilizer (no:35)	Poor mobilizer (no:13)	*P*-value
Median age, year (range)		56.5 (25-68)	56 (25-68)	61 (44-68)	0.170
Male gender (%)		33 (68.8)	22 (62.9)	11 (84.6)	0.182
Primary diagnosis (%)	MM	34 (70.8)	27 (77.1)	7 (53.8)	0.078
	HL	8 (16.7)	6 (17.1)	2 (15.4)	
	NHL	6 (12.5)	2 (5.7)	4 (30.8)	
Disease status at mobilization (%) Remission		32 (66.7)	19 (54.3)	13 (100)	***0.002****
No. of prior chemotherapy regimens (range)		3 (1-5)	3 (2-5)	3 (1-5)	0.343
Prior radiotherapy (%)		7 (14.6)	3 (8.6)	4 (30.8)	0.075
Prior lenalidomide (%)		23 (47.9)	17 (48.6)	6 (46.2)	0.882
Prior AHSCT (%)		9 (18.8)	4 (11.4)	5 (38.5)	***0.048****
Median time from diagnosis to mobilization, months (range)		14 (4-60)	13 (4-60)	14 (5-43)	0.658

No: number, MM: multiple myeloma, NHL: Non-Hodgkin lymphoma, HL.: Hodgkin lymphoma, AHSCT: Autologous hematopoietic stem cell transplantation

Successful mobilization was performed in 46 patients (95.8%), with a median number of apheresis cycles of 1 (range; 1-3).) The median cell collection day was 12 and ranged from day 8 to day 17. Of the patients, 72.9% (35 patients) were in the good mobilizer group and 27.1% (13 patients) were in the poor mobilizer group. On the first day, the median peripheral CD34+ cell count was 58/µL (14-1180) and the median total peripheral CD34+ cell count was 95.25/µL (14-1180). This number was 130/µL in the good mobilizer group and 35/µL in the poor mobilizer group (p= 0.000). The median amount of CD34+ cells collected was 9.165x106/kg (2.6-49.76), which was 11.7x106/kg in the good mobilizer group and 3.98x106/kg in the poor mobilizer group (p= 0.000). CD34+ cell collection of 10x106/kg and above was performed in 41.7% (20 patients) of the patients. The median number of apheresis cycles was one in both well-mobilized and poorly mobilized patients, and it extended to a maximum of 2 days in the good mobilier group and up

to 3 days in the poor mobilizer group (p=1,000). While the median apheresis initiation day was day 12 in the good mobilizer group, it was day 11 in the poor mobilizer group (p=0.175). The median infused CD34+ cell count was 6.205x106/kg (2.6-33.48x106/kg), and this count was 3.98x106/kg in poor mobilizer and 7.16x106/kg in good mobilizer group (p= 0.000).

Eight patients (16.7%) needed at least one RBC transfusion (14.3% of good mobilizer and 23.1% of poor mobilizer group). Twenty-five patients (52.1%) required platelet suspension at least once (42.9% of good mobilizer and 76.9% of poor mobilizer group). It was observed that the need for platelet suspension replacement was significantly increased in poorly mobilized patients (p= 0.036). Nine patients were complicated with febrile neutropenia (5 patients poor mobilizer and 4 patients good mobilizer), and the risk of complications with febrile neutropenia was significantly increased in the poor mobilizer group (p=0.048).

Of the patients who needed RBC transfusion, 6 had MM, 2 had lymphoma, 17 of the patients who needed platelet transfusion had MM, and 8 had lymphoma. Eight MM and one lymphoma patient were complicated with febrile neutropenia. The median neutrophil engraftment day of the patients was 11 (9-40) and the median platelet engraftment day was 14 (6-54). When good and poor mobilizer groups were compared, no significant difference was found in neutrophil engraftment time (11 vs 12, p= 0.632), while a significant difference was found in platelet engraftment time (12 vs 18.5, p=0.041). The median time from mobilization to transplantation was 34.5 days. No treatment-related myelodysplastic syndrome (t-MDS) or acute myeloid leukemia (AML) was found in any of the patients in the median follow-up of 35.5 months (minimum 2, maximum 96). Efficacy and safety data are presented in Tables II and III, respectively.

In the analyses carried out to examine the factors affecting the success of mobilization, the following was observed: In univariant analysis, poor mobilization was associated with active disease status, prior AHSCT, and low peripheral CD34+ cell count. As a result of the multivariate analysis, low peripheral CD34+ cells on the first day (Hazard ratio (HR);0.00, 95% Confidence interval (CI) 0.00-0.660; p=0.040) and prior AHSCT (HR;1.206, 95% CI 1.009-1.442; p=0.043) were found to be independent risk factors for poor mobilization. Univariate and multivariate analysis results are presented in Table IV.

Table II. Mobilization efficacy

Variable	All	Good mobilizer	Poor mobilizer	*P*-value
No. of patients (%)	48	35 (72.9)	13 (27.1)	
Succesful collection (%)	46 (95.8)	35 (100)	11 (84.6)	0.069
Median days of apheresis (range)	1 (1-3)	1 (1-2)	1 (1-3)	1.000
Median peripheral CD34+ cell count on the first day of apheresis (x10^{6}CD34+/kg)	58 (14-1180)	109 (17-1180)	19 (14-71)	***<0.001****
Median collected CD34+ cell count (x10^{6}CD34+/kg)	9.165 (2.6-49.76)	11.7 (5.4-49.76)	3.98 (2.6-4.75)	***<0.001****
Median infused CD34+ cells count (x10^{6}CD34+/kg)	6.20 (2.6-33.48)	7.16 (4.03-33.48)	3.98 (2.6-4.75)	***<0.001****
Median days from mobilization to apheresis	12 (8-17)	12 (9-15)	11 (8-17)	0.175

No: number

Table III. Mobilization safety

Variable	All	Good mobilizer	Poor mobilizer	*P*-value
No. of patients	48	35	13	
RBC transfusion (%)	8 (%16.7)	5 (%14.3)	3 (%23.1)	0.664
Platelet transfusion (%)	25 (%52.1)	15 (%42.9)	10 (%76.9)	***0.036****
Febril neutropenia (%)	9 (%18.8)	4 (%11.4)	5 (%38.5)	***0.048****
Median days to neutrophil engraftment (>0.5x10^9/L)	11 (9-40)	11 (9-40)	12 (10-15)	0.632
Median days to platelet engraftment (>20x10^9/L)	14 (6-54)	12 (6-54)	18.5 (9-37)	***0.041****

No: number, RBC: Red Blood Cell

Table IV. Univariate and multivariate analysis for good mobilizer and poor mobilizer

Variable	Univariate	Multivariate	H.R. (95% CI)
Age	0.170		
Gender	0.182		
Primary diagnosis	0.078		
Disease status at mobilization	***0.002****		
No. of chemotherapy regimens	0.343		
Prior radiotherapy	0.075		
Prior lenalidomide	0.882		
Prior AHSCT	***0.048****	***0.043****	***<0.001****(0.00-0.660)
Time from diagnosis to mobilization (month)	0.658		
Peripheral CD34+ cell count on the first day of apheresis	***<0.001****	***0.040****	***1.206****(1.009-1.442)

H.R.: Hazard ratio, No: number, AHSCT: autologous hematopoietic stem cell transplantation

Discussion and Conclusion

Determining the appropriate strategy for stem cell mobilization in MM and recurrent lymphoma cases is difficult. Adding low- or high-dose (>1200 mg/m²) etoposide to G-CSF is an approach that has been used successfully, and there are several examples of wide dose ranges ranging from 200 mg/m² to 2.4 g/m² in the literature.[8-12] While successful mobilization was achieved in 83.52% of patients in the study of Güner et al., published in 2016, using 200 mg/m² etoposide, this rate was 82.3% in the study of Özkan et al. in 2014, in which 1.6 g/m² etoposide was used.[9,10] In a study published in 2009 comparing two doses of etoposide (1 g/m² and 1.5 g/m²), no significant difference was found between the two groups in terms of efficacy and toxicity.[13]

In our study, it was demonstrated that low-dose etoposide (375 mg/m²) and G-CSF (10-15 µg/kg divided into two doses) regimen was an effective mobilization agent on patients with MM and refractory lymphoma with a 95.8% success rate and acceptable toxicity. In addition, it has been shown that the number of peripheral CD34+ cells on the first day and prior AHSCT are independent risk factors in poorly mobilized patients. Furthermore, peripheral stem cell mobilization with low-dose etoposide and G-CSF is thought to be effective on other factors (such as age, prior usage of lenalidomide and radiotherapy, and the number of rounds of chemotherapy received) and patient groups with prior mobilization failure.

In the study of Song et al. on patients diagnosed with MM, cyclophosphamide ($3g/m^2$)+G-CSF and etoposide (375 mg/m^2)+G-CSF regimens were compared, and the median CD34+ cell count was found to be significantly higher in the etoposide arm (27.6×10^6 CD34+ /kg vs. 9.6×10^6 CD34+ /kg, $P < 0.001$). Mobilization failure was lower in the etoposide group (1.6% vs. 10.8%, $P = 0.062$), and the frequency of serious infections was higher in the cyclophosphamide group (18.5% vs. 7.9%, $P = 0.117$).[14]

There is a wide range for the targeted CD34+ cell amount. A dose of > $5x10^6$/kg CD34+ cells is considered optimal for rapid and sustained hematopoietic recovery.[15] The median number of CD34+ cells collected in our study was $9.165x10^6$/cell/kg, ranging from 5.6 to $33.73x10^6$/cell/kg in the literature.[9-11,16,17] In our study, it was possible to collect >$10x10^6$/kg cells, sufficient for two transplantations, in 20 of the 46 patients (43.5%).

Although 17 (35.4%) of 48 patients had a history of unsuccessful mobilization with G-CSF, DHAP, or G-CSF+plerixafor, our successful mobilization rate was 95.8%, which suggests that low-dose etoposide+G-CSF may be an effective treatment option in patients with MM and refractory lymphoma with previous mobilization failure. Similarly, in the study of Zuckenka et al., which investigated the efficacy of adding optional plerixafor to the etoposide+G-CSF regimen, this regimen was found to be effective in patients who had previously been unsuccessfully mobilized with plerixafor.[18] Since studies are showing that the use of high-dose etoposide may increase the development of secondary malignancy, the importance of using low-dose etoposide was emphasized by selecting low-dose etoposide in our study. In the study of Krishnan et al., 51 of 62 patients were given 2 g/m², and the remaining nine patients were given 1 g/m² or 1.5 g/m² etoposide, which was shown that high-dose etoposide was associated with a 12.3-fold increased risk of AML.[19] However, in the study of Mahindra et al. comparing etoposide ($2g/m^2$) + G-CSF with G-CSF alone, it was reported that there was no increase in the risk of t-MDS or AML in the etoposide+G-CSF arm.[11] In our study, no treatment-related secondary malignancy developed in any patients at a median follow-up of 35.5 months.

The state of the bone marrow at the time of mobilization is also an important predictive factor for successful mobilization. Bone marrow involvement in lymphoma patients and infiltration of bone marrow with plasma cells in patients with MM have a negative effect on stem cell mobilization.[20,21] In our study, the median plasma cell ratio was 2% in patients with MM and ranged from 0% to 40%, while bone marrow involvement was not observed in patients with lymphoma. While bone marrow involvement was found to be 3% in a study conducted with lymphoma cases in the literature[22], it was found to be 5% in two studies conducted with myeloma cases.[10,23] There was no difference in the percentage of bone marrow involvement between good and poor mobilizer groups. When studies with etoposide were scanned, no other study was found in the literature comparing this parameter between good and poor mobilizer groups.

In our study, similar to the literature, it was found that the rate of febrile neutropenia (11.4% vs. 38.5%), the need for platelet transfusion increased (42.9% vs. 76.9%) in the poorly mobilized group[9,16,24] It is seen that the rate of febrile neutropenia varies between 6-69% in the literature.[8-11,23]

Following infusion of mobilized peripheral progenitor blood cells, neutrophil engraftment is rapid enough to occur in approximately 8 to 10 days, and platelet engraftment in 10 to 12 days. The CD34+cell dose/kg has proven to be useful because patients receiving more than $2x10^6$ CD34+cells/kg usually have a rapid and sustained hematopoietic recovery. Administration of higher doses of CD34+ cells/kg may result in slightly faster platelet engraftment following hematopoietic stem cell transplantation, with a

minimal effect on neutrophil engraftment and possibly a positive effect on overall survival.[25] In our study, the median infused CD34+ cell count was $6.205x10^6$/cell/kg, ranging from 5.58 to $12.13x10^6$/cell/kg in the literature. In our study, the median neutrophil engraftment day was 11, which was reported in the literature to vary between 9 and 11 days. Although the median platelet engraftment day varies between 9 and 17 days in the literature, it was found to be 14 days in our study, and following the literature, the platelet engraftment day was prolonged in the poorly mobilized group.[8-11,16,23] It was observed that the median neutrophil and platelet engraftment days were significantly shortened in patients with highly infused CD34+ cells.

The limitations of this study are that it was designed retrospectively, and this situation caused the loss of some data, the number of patients was small, and the patient groups with MM and lymphoma were heterogeneously distributed; the study was single-center and not comparative.

The results of this study show that low-dose etoposide (375 mg/m²) and G-CSF are suitable mobilization regimens with high efficacy and tolerable toxicity in patients with MM and lymphoma. Another point to be emphasized is that no secondary malignancy was observed in our median follow-up period of nearly three years. In addition, we think this method is effective and safe in patients with previous mobilization failure or who have undergone autologous hematopoietic stem cell transplantation and received intensive treatment regimens. There is a need for more comprehensive studies comparing the long-term side effects and advantages of low-dose etoposide with different mobilization agents.

Ethics Committee Approval Information:
Approving Committee: Bursa Uludag University Faculty of Medicine Clinical Research Ethics Committee
Approval Date: 26.12.2017
Decision No: 2017-19/40
Researcher Contribution Statement:
Idea and design: F.M.S., V.Ö., F.Ö.; Data collection and processing: F.M.S.; Analysis and interpretation of data: F.M.S., V.Ö., F.Ö.; Writing of significant parts of the article: F.M.S.
Support and Acknowledgement Statement:
This study received no financial support. We thank apheresis technician Ali Gül at the Stem Cell Transplantation Unit of Bursa Uludağ University.
Conflict of Interest Statement:
The authors of the article have no conflict of interest declarations.

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