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Stem cell mobilization kinetics in elderly patients with multiple myeloma

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ABSTRACT

In this study, we aimed to investigate whether the procedure and product kinetics differ according to age groups in advanced-age MM patients who underwent autologous HSCT. 59 patients who underwent autologous HSCT were retrospectively analyzed. Then, the patients were divided into two groups as 60–65 years and ≥ 65 years. It was significantly lower in ≥ 65 years group ($p=0.008$) and proportionally, the procedure duration was also significantly shortened in this group ($p=0.013$). Total number of collected CD34 positive stem cells was $6.20 \times 10^6 (\pm 3.83)$ in 60–65 years group while it was $5.51 \times 10^6 (\pm 2.48)$ in ≥ 65 years group with no statistically significant difference ($p=0.825$). In conclusion, there was no significant difference in terms of the number of collected CD34-positive stem cells in this study that investigates the mobilization data, procedure and product kinetics, we think that successful stem cell mobilization can be performed in appropriately selected patients regardless of age.

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1. Introduction

Multiple myeloma (MM), a plasma cell-derived hematological malignancy, manifests itself with monoclonal immunoglobulin production which frequently leads to organ damage such as renal failure, hypercalcemia, anemia and lytic bone lesions [1,2]. Most of MM patients are in advanced age, so the prevalence of MM rises as the average life span of the general population is increasing [3]. The standard treatment approach for young MM patients is autologous hematopoietic stem cell transplantation after induction chemotherapy. This approach can also be applied to the patients who are 65 years or older with satisfactory performance status [4,5].

Autologous hematopoietic stem cell transplantation (HSCT) is a treatment modality with increasing importance in many hematological malignancies including MM. It comprises intravenous infusion of hematopoietic stem cells to the patients who are already treated with high-dose chemotherapy prior to the infusion [6–11]. In recent years, the stem cells are collected from the peripheral

blood of the patients by means of mobilization, which is a method used to increase the content of stem cells in peripheral blood. The medications used for this purpose are called mobilization regimens and an optimal mobilization regimen should support the hematopoietic reconstruction and allow sufficient stem cell collection with minimum number of apheresis. Lately, the role of mobilization regimens and strategies to decrease the mobilization failure has gained importance, because of the growing data about the efficiency and safety of autologous HSCT in patients 65 years or older [12,13].

For stem cell collection, peripheral blood is preferred over bone marrow as the source of hematopoietic stem cells in autologous HSCT [14]. Usually, a central venous line is used during apheresis procedure while a peripheral venous line may be employed only in selected patients. In stem cell mobilization regimens, growth factors may be used solely or combined with chemotherapeutic agents. There are many studies comparing different mobilization regimens [15] including the study by Bozdogan et al. [16]. In addition, the use of CXCR-4 chemokine receptor antagonists has been recently on the rise [17,18].

In this study, we aimed to investigate whether the apheresis procedure and product kinetics differed according to the age groups

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in advanced-age MM patients who underwent autologous HSCT after high-dose chemotherapy.

2. Patients and method

2.1. Patients

This study was performed with patients who were 60 years or older and underwent autologous HSCT with the diagnosis of MM. Demographic and mobilization data of a total of 59 MM patients who underwent autologous stem cell transplantation were retrospectively analyzed. The patients were divided into two groups as 60–65 years and ≥65 years, and then mobilization and stem cell parameters were compared between two groups.

2.2. Mobilization

The stem cell mobilization regimens were granulocyte colony-stimulating factor (G-CSF) alone, G-CSF with chemotherapy, or plerixafor with G-CSF and/or chemotherapy in patients with inadequate stem cell yield. Either a central venous route or a peripheral venous route was chosen for stem cell apheresis procedure according to the availability of a peripheral vein. As for product kinetics acquired with apheresis, the total amount of product was measured in milliliters and CD34+ cells were estimated from the product as number 10⁶/kg. As for procedure kinetics, the volume amount of processed blood, procedure duration, total days of apheresis and total amount of anticoagulant ACD solution used were determined.

2.3. Statistics analysis

Statistical evaluation was made by SPSS 17 program. Data were described as numbers and percentage or mean (±), when appropriate. χ^2 Fisher's exact test was used for evaluating categorical values and Mann Whitney U test for continuous values. All p-values were 2-sided with statistical significance at 0.05 alpha levels.

3. Results

The patient characteristics are presented in Table 1. The median age was 65 (range: 60–75). 34 of the patients were male and 25 were female. Twenty-seven of the 59 patients who underwent peripheral stem cell mobilization were 60 to 65 years while 32

Table 1
 Characteristics of patients.

Age	60–<60 years n (%)	≥65 years n (%)	P value
	27 (45.8%)	32 (54.2%)	NS
Gender			
Female	13 (22.1%)	12 (20.3%)	NS
Male	14 (23.7%)	20 (33.9%)	NS
Height (cm)	165 (155–182) ^b	165 (149–180) ^b	NS
Weight (kg)	77 (49–105) ^b	74.5 (52–95) ^b	NS
Blood Volume (ml)	5217 (±753) ^a	5145 (±649) ^a	NS
Plasma Volume (ml)	3307 (±587) ^a	3165 (±555) ^a	NS
Mobilization Regimen			
G-CSF	11 (18.6%)	10 (16.9%)	NS
Chemotherapy + G-CSF	15 (25.4%)	20 (33.9%)	
Plerixafor	1 (1.7%)	2 (3.4%)	
Venous Access			
Central	20 (33.9%)	24 (40.7%)	NS
Peripheral	7 (11.9%)	8 (13.6%)	

NS (not significant).

^a Mean.
^b Median.

Table 2
 The kinetics of the mobilization.

	60–<60 years n	≥65 years n	P value
Number of days of apheresis (days)	2 (1–4)	2 (1–3)	NS
Total time of apheresis (minute)	426 (241–910) ^b	360 (180–761)	p = .013
TVBP (L)	22.51 (±8.44) ^a	17.87 (±6.57) ^a	p = .008
CD 34 × 10 ⁶ /kg	6.20 (±3.83) ^a	5.51 (±2.48) ^a	NS
TVP (ml)	559 (±413) ^a	359 (±230) ^a	p = .056
ACD Solution (ml)	1500 (±610) ^a	1394 (±490) ^a	NS

TVBP: Total volume of blood processed; TVP: Total volume of product.

^a Mean.
^b Median.

patients were ≥65 years. For mobilization, chemotherapy plus G-CSF was used in 35 (59.3%) patients; G-CSF alone was used in 21 (35.6%) patients and plerixafor plus G-CSF was used in 3 (5.1%) patients. When the patients were compared in two age groups, both groups were found to be similar in terms of age, height, weight and plasma volume of patients ($p > 0.05$). There was no significant difference in mobilization protocols between two groups (Table 1). The median number of days of procedure performed was 2 (1–4) days in patients 60–65 years as it was also 2 (1–3) days in patients ≥65 years ($p = 0.326$). Similar results were observed regarding the preferred venous route in both groups and central venous line was prominently favored (74% v.s. 75%). The volume of processed blood was the only parameter with significant difference between two groups. It was significantly lower in patients ≥65 years ($p = 0.008$) and proportionally, the procedure duration was also significantly shortened in this group ($p = 0.013$). The total number of collected CD34+ stem cells was $6.20 \times 10^6/\text{kg} (\pm 3.83)$ in patients 60–65 years and $5.51 \times 10^6/\text{kg} (\pm 2.48)$ in patients ≥65 years ($p = 0.825$). The total volume of product yielded at the end of mobilization was 559 (±413) milliliters in patients 60–65 years and 359 (±230) milliliters in patients ≥65 years. The product volume was apparently lower in patients ≥65 years, yet the difference did not reach statistical significance ($p = 0.056$) (Table 2).

4. Discussion

Autologous HSCT after high dose chemotherapy is a treatment modality that increases remission rates and survival in various hematological diseases, one of which is MM. Although the bone marrow was the main source of hematopoietic stem cells in the past years in patients undergoing autologous HSCT, currently the peripheral blood is preferred as the main source of stem cells. Preference of the peripheral blood as the stem cell source, provides some benefits such as avoiding hospitalization and general anesthesia, patient comfort during the procedure and post-transplant rapid engraftment kinetics with an acceptable toxicity in patients particularly in advanced-aged ones [19,20]. In this study, stem cell source was peripheral blood in all patients undergoing autologous HSCT.

When the peripheral blood is used as the stem cell source, mobilization procedure, which is defined as moving the stem cells in the bone marrow out to the peripheral circulation, is applied to the patients. Mobilization can be performed by means of using either growth factors alone or in combination with different chemotherapy regimens [21,22]. After mobilization, stem cells are collected from the peripheral blood via apheresis procedure, and stem cell kinetics can be affected from the devices used in apheresis [23,24] and the route of venous access [25,26] as well as the mobilization regimen. While a number of studies recommended the antecubital vein route for apheresis procedure, two recent studies showed that type of the access could alter the total volume of the product and

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