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Peripheral blood stem cell collection in elderly patients

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Abstract Intensive treatments like autologous blood stem cell transplantations are standard consolidation treatments for lymphoma and myeloma in young people. The upper age limit for these procedures is constantly increasing. Instead of studying the impact of aging on harvesting peripheral blood stem cells (PBSC), we performed a retrospective study to explore the feasibility of collecting stem cells from patients older than 65 years and compared the efficacy to harvest in younger patients. During a period of 7 years, we identified 108 patients with myeloma or lymphoma who were older than 65 years who underwent PBSC collection. Only eight patients failed to produce a successful harvest. The majority of patients only needed one apheresis (71%). There was a median number of 5.3×10^6 CD34+ cells/kg. Our study demonstrated that older patients can also undergo PBSC harvests similar to younger patients.

Keywords Stem cell harvest · Lymphoma · Myeloma

Introduction

Autologous blood stem cell transplantation (ABSCT) is an intensive and standard treatment for lymphoma and myeloma in young people. The upper age limit for these procedures is constantly increasing. Some recent publications demonstrated the feasibility of ABSCT in patients over 60 years. One of the factors directly affecting the feasibility of these procedures is the mobilization of CD34+ cell capacity. However, the available data are contradictory and aging seems to have a negative impact on peripheral blood stem cell (PBSC) harvest. Rather than investigate the impact of aging, we conducted a retrospective study to explore the feasibility of PBSC collection in patients older than 65 years compared with younger people.

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Material and methods

Patient characteristics

During a period of 7 years (2000–2006), we identified 393 patients with lymphoma or myeloma who underwent PBSC harvesting at the Brest Apheresis Service of Blood Transfusion Center. Of these patients, 359 had successful collection attempts; 259 patients were under 65 years, and 100 patients were older than 65 years. The characteristics of all the patients are presented in Table 1.

Prior to harvest, the patients received chemotherapy including various association of drugs. The chemotherapy products used in our patients are presented in Table 2. None of the patients received nucleoside analogs or IMiDs.

Table 1 Characteristics of the patients performing autologous PBSC in Brest Harvest Center

| | | Total | <65years | >65years |
|---------------|----------|--------------|--------------|------------|
| Number | | 359 (375) | 259 (275) | 100 |
| Sex ratio M/F | | 213/146=1.46 | 157/102=1.54 | 56/44=1.27 |
| Age | Mean | 54.3±2.8 | 49±0.75 | 68.9±0.29 |
| | Range | 9–72 | 9–64 | 65–72 |
| Pathology | Lymphoma | 234 (245) | 193 (204) | 41 |
| | Myeloma | 125 (130) | 66 (71) | 59 |

Mean age are expressed with standard error

Mobilization of CD34+ cells and PBSC collection

Following achievement of complete remission or very good partial remission, after the last cycle of chemotherapy, granulocyte colony-stimulating factor was added at day 9, at 10 µg/kg/day to induce CD34+ mobilization. White blood cells and circulating CD34+ cells were monitored beginning day 14 to determine PBSC collection. Apheresis was performed when the circulating CD34+ cells were greater than $10 \times 10^6/\mu\text{L}$ using a Cobe-Spectra cell separator. We aimed to obtain 2×10^6 CD34+/kg of body weight in lymphoma patients. For the myeloma patients, we aimed to obtain 4×10^6 CD34+/kg of body weight; however, it was considered as a success if we obtained 2×10^6 CD34+/kg of body weight. The patients with less than 2×10^6 CD34+/kg of body weight were considered as failure. No supplementary apheresis was performed after obtaining a sufficient collection amount.

Statistical analysis

Appropriate statistical analyses were performed using Epi-table® 6.04 (Epi software). Statistical significance was defined as a *p* value < 0.05. Each value is expressed as ± SD.

Results

Feasibility of PBSC collection in older patients

During a period of 7 years, 359 patients underwent 375 apheresis cycles at the Brest Apheresis Service of Blood

Table 2 Chemotherapy products used for the patients prior to harvest

| Chemotherapy agent | Patients <65years | Patients >65years |
|--------------------------|-------------------|-------------------|
| Velcade | 8 | 1 |
| Antimetabolites | 48 | 13 |
| Alkylating agents | 248 | 49 |
| Topoisomerase inhibitors | 76 | 12 |
| DNA intercalators | 253 | 92 |
| Plant alkaloids | 241 | 94 |

Transfusion Center. Of those, 17 patients had two or more apheresis cycles at different times. Among the 359 patients, 100 patients were more than 65 years. The general results of the apheresis procedures are presented in Table 3.

In our selected population, 34 patients had a CD34+ number that was under the standard (2×10^6 CD34+/kg of body weight); it was considered as a failure. Of these 34 patients, 26 were under 65 years and eight were over 65 years.

Of the selected population, the number of consecutive apheresis to obtain the required amount of cells varied from one to four, but 94% of patients only required one or two aphereses. There was also no significant difference between the two groups. Of the young patients, 75% (207/275) achieved the desired number of CD34+ cells ($>2 \times 10^6$ CD34+/kg of body weight) after only one apheresis. The rate among older patients was 71% (71/100); however, no statistical difference was observed. The median number of CD34+ cells collected from the entire population was 6.3×10^6 CD34+ cells/kg, and there was a significant difference between the young and elderly population (6.67 vs. 5.3×10^6 CD34+ cells/kg, respectively, $p=0.004$). The median number of CD34+ cells collected per apheresis cycle for the entire patient population was 5.2×10^6 CD34+ cells/kg with a significant difference between the two groups (5.54 vs. 4.36×10^6 CD34+ cells/kg, $p=0.02$). The median number of CD34+ cells collected after one apheresis procedure for the entire population was 5×10^6 CD34+ cells/kg, and there was a significant difference between the young and elderly population (5.36 vs. 4.22×10^6 CD34+ cells/kg, $p=0.03$). Furthermore, there was no significant difference regarding the number of CD34+ cells collected during the second and third aphereses.

Results of apheresis in patients with lymphoma

Among the 235 patients with lymphoma, 194 patients were under 65 years, and 41 patients were over 65 years. We performed 204 apheresis cycles on the younger patients (12 patients underwent two aphereses cycles at different times) and 41 apheresis cycles on the elderly patients (none of them required more than one apheresis cycles). All the results are summarized in Table 4. The number of necessary

Table 3 Mobilization results in patients performing apheresis in Brest Apheresis Service of Blood Transfusion Center

| | | Total | < 65years | >65years | <i>P</i> value |
|---------------------|--------------------|-------------|-------------|-------------|----------------|
| Failure | | 34/393=8.7% | 26/285=9.1% | 8/108=0.74% | 0.8 |
| Number of apheresis | Mean | 1.6±0.04 | 1.50±0.05 | 1.59±0.09 | 0.35 |
| | 1 | 375 | 275 | 100 | |
| | 2 | 153 | 113 | 40 | |
| | 3 or more | 54 | 35 | 19 | |
| CD34+ collection | Mean per patient | 6.3±0.21 | 6.67±0.28 | 5.3±0.32 | 0.004 |
| | Mean per apheresis | 5.2±0.23 | 5.54±0.28 | 4.36±0.34 | 0.02 |
| | 1 | 5.0±0.26 | 5.36±0.29 | 4.22±0.34 | 0.03 |
| | 2 | 2.6±0.17 | 2.72±0.21 | 2.27±0.27 | 0.25 |
| | 3 | 1.2±0.11 | 1.30±0.12 | 1.11±0.24 | 0.43 |

Each value is expressed as standard error

apheresis to achieve the target number of cells (2×10^6 CD34+ cells/kg) for the entire patient population was 1.5 apheresis per patient (1.5 in younger patients vs. 1.73 in older patients, $p=0.07$). In our study, 60% of all patients (147/245) achieved the expected rate of apheresis with only one procedure with 62.2% of young patients (127/204) and 53.6% of older patients (22/41). The median number of CD34+ cells per patient from the entire population was 5.9×10^6 CD34+ cells/kg, and there was a significant difference between the two groups (6.2 vs. 4.75×10^6 CD34+ cells/kg, $p=0.04$). The median number of CD34+ cells / apheresis cycle was 5×10^6 CD34+ cells/kg in the entire population with a significant difference between the two groups ($p=0.04$). There were no differences observed in patients who underwent one, two, or three aphereses with regards to the mean CD34+ values.

Results of apheresis in patients with myeloma

Among the 125 total myeloma patients, 66 were under 65 years and 59 were over 65 years. We performed 71 apheresis cycles on the younger patients (five patients underwent two aphereses cycles at different times) and 59 apheresis cycles on the older patients (Table 5). The median

number of apheresis was 1.6 for the entire population with no difference between the younger and the older patients (1.7 vs. 1.49 apheresis per patient, respectively, $p=0.17$). Of the entire population, 79% (103/130) of patients had satisfactory harvests ($>2 \times 10^6$ CD34+ cells/kg) with only one collection without any difference between the two groups (79% vs. 78% for younger and older patients, respectively). The median number of CD34+ cells collected was 7.1×10^6 CD34+ cells/patient with a significant difference between the younger and older patients (8.16 vs. 5.68×10^6 CD34+ cells/patient, $p=0.0005$). The median number of CD34+ cells collected per apheresis cycle was 5.7×10^6 CD34+ cells/procedure with a significant difference between the two populations (6.38 vs. 4.77×10^6 CD34+ cells / apheresis cycle, $p=0.04$). There were no differences observed in patients who underwent one, two, or three aphereses cycles with regards to the mean CD34+ values.

Discussion

Autologous stem cell transplantation is the final standard treatment for lymphoma and myeloma in young people [1,

Table 4 Results of apheresis procedures in patients with lymphoma

| | | Total | <65years | >65years | <i>P</i> value |
|------------------------------------|---|-----------|-----------|-----------|----------------|
| Age | | 50.2±0.92 | 46.6±0.92 | 68±0.43 | 0.0000 |
| Number patients | | 235 | 194 | 41 | |
| Medium number of apheresis/patient | | 1.5±0.05 | 1.5±0.05 | 1.73±0.14 | 0.07 |
| Patients/apheresis procedures | 1 | 245 | 204 | 41 | |
| | 2 | 98 | 77 | 19 | |
| | 3 | 24 | 15 | 9 | |
| Medium nbr of CD34/patient | | 5.9±0.26 | 6.2±0.29 | 4.75±0.47 | 0.04 |
| CD 34/apheresis cycle | | 5.0±0.28 | 5.3±0.32 | 3.77±0.51 | 0.04 |
| CD34/apheresis | 1 | 4.8±0.29 | 5.1±0.33 | 3.60±0.52 | 0.053 |
| | 2 | 2.4±0.18 | 2.5±0.19 | 2.08±0.47 | 0.35 |
| | 3 | 1.0±0.1 | 1.1±0.13 | 0.7±0.14 | 0.052 |

Mean values are expressed with standard error

Table 5 Results of apheresis procedures in patients with myeloma

| | | total | <65 | >65 | <i>P</i> value |
|--|---|-----------|-----------|-----------|----------------|
| Age | | 61.8±0.79 | 55.9±0.75 | 69.6±0.38 | 0.0000 |
| Number patients | | 125 | 66 | 59 | |
| Medium number of apheresis procedure/patient | | 1.6±0.07 | 1.7±0.11 | 1.49±0.1 | 0.17 |
| Patients/ apheresis procedures | 1 | 130 | 71 | 59 | |
| | 2 | 57 | 36 | 21 | |
| | 3 | 19 | 13 | 6 | |
| Medium number of CD34/patient | | 7.1±0.37 | 8.16±0.53 | 5.68±0.43 | 0.0005 |
| CD 34/ apheresis cycles | | 5.7±0.39 | 6.38±0.6 | 4.77±0.46 | 0.04 |
| CD34/ apheresis | 1 | 5.5±0.39 | 6.15±0.6 | 4.64±0.46 | 0.055 |
| | 2 | 2.9±0.35 | 3.15±0.52 | 2.44±0.33 | 0.29 |
| | 3 | 1.6±0.21 | 1.49±0.22 | 1.72±0.54 | 0.62 |

Mean values are expressed with standard error

2]. The upper age limit for this procedure is constantly increasing [3]. ABSCT is the standard approach for several diseases including: non-Hodgkin's lymphoma, early relapsing follicular lymphoma, mantle cell lymphoma, and patients with aggressive B and T cell lymphomas expressing bad features at the time of diagnosis (high IPI). ABSCT helps to improve both overall survival and disease-free survival in younger patients [4–9]. For myeloma patients, ABSCT is often suggested for patients younger than 70 years who are both responders and nonresponders to the first line of treatment. There is also evidence to suggest that double autologous stem cell transplantation is superior to one ABSCT [9]. The procedure is also used in patients who relapse after only one procedure [9–11]. Accordingly to this data, there is increasing interest in performing ABSCT in older patients. In 2008, the EBMT Lymphoma Working Party showed that intensive chemotherapy followed by ABSCT is feasible in patients over 60 years and that age should not be considered as an exclusion factor [3]. This study confirmed previous data [12–14]. One of the factors directly affecting the feasibility of these procedures is the mobilization capacity of CD34+ cells. The available data are contradictory because several studies have demonstrated that mobilization capacity is poorer in elderly patients compared with younger patients [15–19]. Of our 359 patients, the success of the mobilization procedure was similar between younger and older patients: 90.6% versus 92%, respectively. There was a significant difference regarding the number of CD34+ cells collected/patient (Table 2). Even if the quantity of CD34+ was lower in the older population, the quantity obtained was sufficient for performing one or more ABSCT. The number of aphereses necessary to achieve the target was identical in both groups of patients. Of all the patients, 70% achieved the target cell number after only one apheresis. For lymphoma patients, there was no significant difference between the two populations regarding the number of apheresis performed (1.5 vs. 1.73). However, there was a difference between the

younger and older patients regarding the medium number of CD34+ cells/patient (6.2 vs. 4.75, $p=0.04$) and the number of CD34+ cells/ apheresis cycles (5.3 vs. 3.77, $p=0.04$). Even though the quantity of CD34+ cells was lower in the elderly population, it was sufficient for performing an ABSCT. For myeloma patients, there was no difference between the two populations regarding the number of apheresis necessary. However, there was a significant difference between the younger and older patients regarding the median number of CD34+ cells collected per patient (8.16 vs. 5.68, $p=0.0005$) and the median number of CD34+ cells collected per apheresis cycle (6.38 vs. 4.77, $p=0.04$). However, the quantity of CD34+ cells collected in elderly patients was sufficient for performing an ABSCT. It is interesting to note that we only needed one apheresis to have enough cells to perform one ABSCT in elderly patients. Also, it seems to be easier to collect cells from myeloma patients than lymphoma patients (due to aggressivity of chemotherapy?).

In conclusion, the analysis of our data showed that the age of the patients has an impact on mobilization of PBSC in lymphoma and myeloma patients. Even if the quantity of CD34+ cells collected in elderly patients was lower than in younger patients, this quantity reaches the standard requested for performing one or more ABSCTs.

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