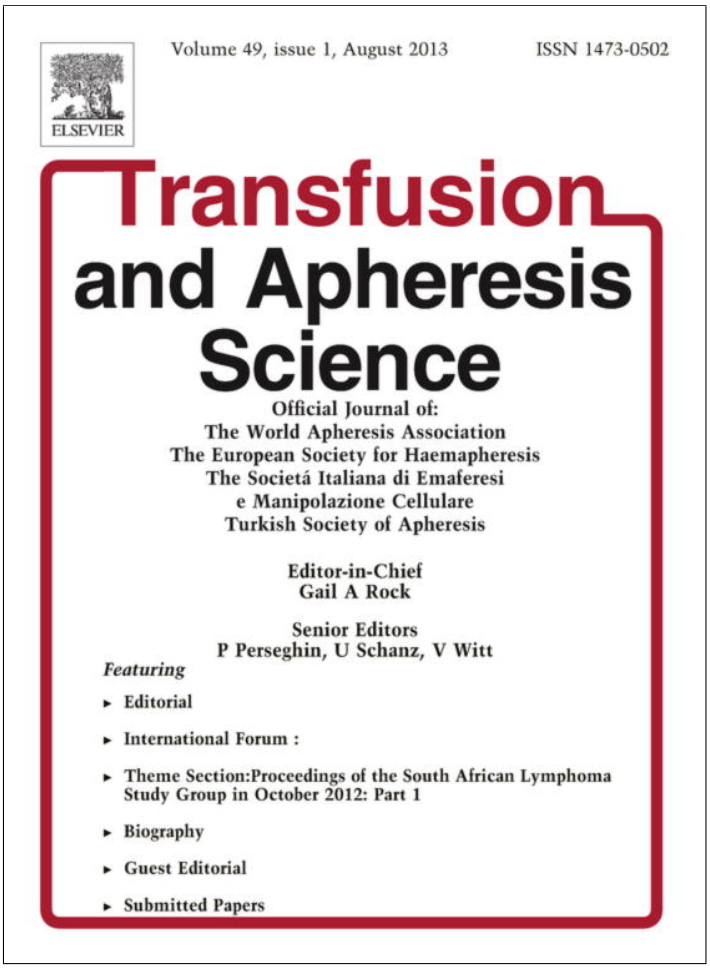

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Letter to the editor

The use of granulocyte colony stimulating factoR (G-CSF) (filgrastim) alone in the mobilization of stem cell in the autologous stem cell transplantation

1. Introduction

Intensive chemotherapy followed by autologous stem cell transplantation (ASCT) in hematological malignancies, particularly in multiple myeloma (MM) and in relapsed or refractory lymphoma is currently the treatment of choice [1–3]. Mobilization of hematopoietic stem cell blood stem cells (HSCs) can be achieved either by the combination of chemotherapy plus growth factors [4,5] or by growth factors alone [6]. However, there is no consensus concerning the dose of growth factor alone that should be administered, with ranges varying from 5 μg to 16 μg/kg body weight [7].

In this context, we report our experience in mobilization of HSCs using growth factor alone at the dose of 15 μg/kg in MM, Hodgkin's lymphoma (HL) and non-Hodgkin lymphoma (NHL).

2. Patients and methods

A total of 122 ASCT performed in our center, from May 2009 to July 31st 2012. This involved concerned 88 patients with MM, 30 with HL and 4 others with NHL. Patients were hospitalized at day 5 on which mobilization started with G-CSF alone (filgrastim) at the dose of 15 μg/kg/daily subcutaneously for 5 days. The white blood cell count was assessed daily. Apheresis was performed at day 2 and day 1 using a Spectra Optia CMN device, and the CD34+ count was assessed by flow cytometry.

A single leukapheresis was performed in MM if the number of CD34+ cells was above 2.106/kg, whereas in HL and NHL the needed number of CD34+ was above 3.106/kg. Failure of mobilization was defined as a level of CD34+ lower than 2.106/kg, after two leukapheresis.

In our study patients were divided into three groups: optimal (>5.0 $\times$ 10^6 $CD34^+$ cells/kg), suboptimal (2.0–5.0 $\times$ 10^6 $CD34^+$ cells/kg) and poor (<2.0 $\times$ 10^6 $CD34^+$ cells/kg) mobilization. Intensification was done using melphalan 200 mg/m^2 on day −1 for MM and using protocols such as CBV (cyclophosphamide, BCNU, Etoposide) or BEAM (BCNU, Etoposide, Aracytine, Melphalan) or EAM (Etoposide, Aracytine, Melphalan) on day 6 to day 1 for HL and NHL.

3. Results

Patients' characteristics are shown in Table 1. The average age was 55 years in MM and 26.5 years in HL and NHL. The average number of apheresis was 1 and that of CD34+ was 3.48 $\times$ 10^6/kg in MM and 3.60 $\times$ 10^6/kg in HL and NHL. Failure of mobilization represented 6 cases (5%) of the 122 ASCT done. In MM, 75% of patients had suboptimal stem cell collection, whereas 20% had optimal stem cell collection and 5% had poor (or failed) collections. In HL and NHL, 74% of patients had suboptimal stem cell collection, whereas 20% had optimal collection and 6% had poor (or failed) collections (Table 2).

Engraftments post-transplant: For leukocyte engraftment, the median number of days was 10 (range; 6–17) and 11 days (range; 7–22) in MM and HL-NHL and for platelet engraftment, the median number of days was 11 (range; 8–23) and 13 (range; 10–37) in MM and HL-NHL respectively (Table 3). No patient required additional G-CSF therapy for the treatment of neutropenia. The most adverse events were, bone pain and headache were reported for 49% and 25% patients, respectively, fever in 25% and asthenia in 18% (Table 4).

4. Discussion

The success of ASCT is, in part, dependent of the level of CD34+ [7], the harvest of which is dependent of the quality of mobilization using either a combination of chemotherapy plus a growth factor [8] or a growth factor alone [9].

The results obtained in our study show an overall success rate of 96% over a total of 163 leukapheresis done. Our results compared to others study using a combination of chemotherapy-growth factor [10] or growth factor alone [11] are identical if not superior.

In the study, the median $CD34^+$Cell yield varied between 2.0–13.3 $\times$ 10^6/kg, the median number of apheresis was 1–2 and the proportion failing to mobilize was 5%-16% and these are the same as our results (3.60 $\times$ 10^6 $CD34^+$; 1 apheresis and 5% failing to mobilize) [12–14].

In a growth factor-alone strategy, filgrastim was associated with faster neutrophil recovery (10–18 days) and

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Table 1
Patients' characteristics.

	MM	HL-NHL
Number of patients	88	34
Mean age (years)	55 (37–67)	26.5 (17–45)
Gender		
Male	53	18
Female	35	16
Mean cytapheresis	1 (1–3)	2 (1–3)
Mean $CD34^+ \times 10^6$/kg	3.48 (2.0–13.22)	3.60 (3–10.12)
Failure of mobilization	4	2

Table 2
Results of mobilization in 122 ASCT (ASCT = autologous stem cell transplantation).

	MM (88)	HL-NHL (34)
Suboptimal stem cell collection $CD34^+$ [2.0–4.99] $\times 10^6$/kg	66 (75%)	25 (74%)
Optimal stem cell collection $CD34^+$ $\geqslant 5.00 \times 10^6$/kg	18 (20%)	7 (20%)
Poor stem cell collection $CD34^+$ $< 2.00 \times 10^6$/kg	4 (5%)	2 (6%)

Table 3
Engraftment parameters after high-dose chemotherapy and ASCT in patients with MM and HL-NHL (ASCT = auto stem cell transplantation).

	MM	HL-NHL
WBC > 500/μl (day of recovery post transplant)	10 (6–17)	11 (7–22)
Platelets > 20,000/μl (day of recovery post transplant)	11 (8–23)	13 (10–37)
RBC transfusion (number per patient)	2 (00–9)	3 (00–10)
Platelet transfusion (number per patient)	1 (00–4)	2 (00–8)

Table 4
Major side effects after mobilizing therapy.

Symptoms	Patients (%)
Bone pain	49
Headache	25
Fever	25
Asthenia	18

with more rapid platelet recovery (12–20 days) [12–14] compared with our study (10 days and 11 days). On the other hand, the rapid onset of neutrophil engraftment after a median of 10–11 days and of transfusion-independent platelet levels of $\geqslant 20 \times 10^9$/l after a median of 11–13 days indicate no alteration of stem cells or diminished proliferation capacity owing to mobilization with G-CSF alone. In terms of toxicity, adverse events are mainly related to bone pain in 49% which was treated with painkillers and fever episodes in 25%.

Mobilization with chemotherapy and G-CSF usually requires hospitalization and up to 30% of them have to be admitted to the hospital owing to neutropenic fever [15–16]. Finally, our study makes the mobilization regimen with G-CSF alone an interesting alternative to chemotherapy and G-CSF in patients with hematologic malignancies such as MM [17], HL or NHL because it can be administered as an outpatient and is not associated with the risk of febrile neutropenia. Similarly, the use of growth factor alone at a dose of 15 μg/kg/day allows a high level of $CD34^+$ cells with suboptimal stem cell collection (75%) and a very low failure rate (5%) without severe adverse events and very acceptable results of engrafment.

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