doi:10.4149/neo_2015_094

Outcomes of 167 healthy sibling donors after peripheral blood stem cell mobilization with G-CSF 16μg/kg/day: efficacy and safety

M. KREJCI*, A. JANIKOVA, F. FOLBER, Z. KRAL, J. MAYER

Department of Internal Medicine, Hematology and Oncology, University Hospital Brno and Masaryk University, Jihlavska 20, 625 00 Brno, Czech Republic

**Correspondence: mkrejci@fnbrno.cz*

Received January 23, 2015 / Accepted April 27, 2015

Mobilization of peripheral blood stem cells (PBSC) using the granulocyte colony-stimulating factor (G-CSF) has enabled the collection even from older donors and those with comorbidities. Several clinical parameters have been reported to predict the success of PBSC mobilization.

The aim of our study was to evaluate the safety of PBSC donation in a cohort of 167 sibling donors after mobilization with G-CSF 16 μg/kg/day for 5 days during short- and long term follow-up and to analyse the efficacy, toxicity and factors influencing CD34+ mobilization capacity.

All 167 sibling donors completed the established mobilization protocol. The median yield was $7.9x10^6$ CD34 cells/kg per recipient weight. The optimal target dose of CD34 cells ≥ $4.0x10^6$/kg was achieved in 140 donors (84%). Only in 4 donors (2%) was the CD34+ yield < $2x10^6$/kg. No major toxicities occured.

Factors associated with higher PBSC yields included age < 55 years (p= 0.001), male gender (p= 0.004), preapheresis CD34 cell counts > 51/μL (p < 0.001) and preapheresis leukocyte counts > 45.5 x 10^9/L (p = 0.003). Comorbidity score, performance status and donor weight did not significantly influence PBSC yields. Long-term follow-up was possible in 60% (101/167) of the donors. The median length of follow-up from PBSC donation was 11.9 years. Most of these donors reported good or very good general health (91%), and no hematological malignancies were observed.

The mobilization of PBSC in sibling donors with G-CSF 16 μg/kg/day is an effective and safe procedure with no significant short- and long-term toxicities.

Key words: sibling donor, PBSC mobilization, G-CSF

Allogeneic haematopoietic stem cell transplantation (SCT) plays an important role in the treatment of various haematological diseases [1]. Peripheral blood stem cells (PBSCs) are often used as a source of haematopoietic stem cells [2].

Mobilization of peripheral blood stem cell (PBSC) using the granulocyte colony-stimulating factor (G-CSF) [3-5] has enabled the collection even from older donors and those with comorbidities [6]. The optimal dose of G-CSF for mobilization of PBSCs has been extensively discussed [7] and various doses have been used ranging from 3 to 20 μg/kg/day [7]. Higher PBSC CD34+ yields per recipient weight are linked to faster hematopoietic engraftment and better transplant outcome [8, 9]. On the other hand, there is some evidence that higher G-GSF doses are associated with increased frequency of adverse events in healthy donors [9, 10].

Many clinical parameters with possible impact on the yield of PBSCs including comorbidities, gender, race, donor weight, age, pre-apheresis peripheral blood CD34 cell counts, and others have been evaluated in healthy donors with inconsistent results [2, 6, 7, 12-14]. When PBSC mobilizations in healthy donors started in our centre in 1997, only few clinical data were available. We used G-CSF in the dose of 16 μg/kg/day subcutaneously according to previous publications of Majolino et al. [15, 16]. However, these cohorts of healthy donors had been very small and no follow-up had been carried out. The principal objectives of our effort was to achieve high efficacy of PBSC mobilization with mild or moderate toxicity. In our hands, this protocol mentioned above has been highly successfull for PBSC harvest and is still in use in our centre today.

The long term survival of healthy donors after PBSC mobilization is another important objective. Several observational reports raised concerns regarding an elevated risk of hematological malignancies after G-CSF administration [17, 18], while other authors found no significant association between PBSC mobilization and the incidence of hematological malignancies in age-adjusted analysis [19].

The aim of our study was to evaluate the short-term and long-term safety of PBSC donation in a uniform cohort of 167 related donors after mobilization using G-CSF 16 μg/kg/day and to analyse the efficacy, toxicity, and possible factors influencing the success of CD34+ mobilization.

Materials and methods

Donors. The cohort included 167 consecutive sibling donors (median age 43 years; range 15-73 years). All donors received the mobilization protocol at the Department of Internal Medicine, Hematology and Oncology, University Hospital, Brno, Czech Republic, from January 1997 to December 2007. The study was carried out in accordance with Helsinki Declaration and after approval by the hospital ethics committee. The standard evaluation of donors included medical history, physical examination and laboratory testing. We extracted data on comorbidities, performance status, and weight from medical records of the sibling donors. Comorbidity was tabulated using the Charlson Comorbidity Index (CCI) [20]. Baseline characteristics of the donors are summarized in Table 1.

Mobilization regimen and collection of PBSCs. Donors were mobilized using a uniform regimen of G-CSF (filgrastim) 16 μg/kg/day given twice daily as a subcutaneous injections of 8 μg/kg. Doses were rounded to vial sizes of 300 μg or 480 μg. Preapheresis peripheral blood CD34 counts/μL were measured on day +4 and day +5. Hematopoietic progenitor cells-apheresis (HPC-A) was started on day +4 from the onset of mobilization and proceeded on day +5 and day+6, if the target yield of CD34+ was not reached. The optimal target of CD34+ yield was ≥ 4.0 x 10^6/kg recipient body weight [2, 19], and the minimal target yield of CD34+ cells was 2.0 x 10^6/kg [19]. Mobilization failure was defined as < 20 CD34 cells/μL in the peripheral blood on day 5 as defined in previous publications [12, 13]. However, this did not preclude leukapheresis. All HPC-A procedures were performed using an apheresis system (Cobe Spectra) via bilateral (anterior cubital and forearm) peripheral venous access, whenever possible, or otherwise via a central line in the femoral vein.

Table 1. Baseline characteristics of 167 sibling donors

Donor age in years (median, range)	42 (15-73)
Donor sex	
Male	90 (54%)
Female	77 (46%)
Charlson Comorbidity Index	
0	138 (83%)
≥1	29 (17%)
Karnofsky Performance Status	
100%	148 (89%)
80-90%	19 (11%)
Donor weight (kg), median, range	79 (48-140)

Monitoring of sibling donors and follow-up observations. Complete blood counts were performed before and after each leukapheresis. During and immediately after the apheresis, vital signs and adverse events were documented by the medical staff. Adverse events were graded according to the National Cancer Institute Common Toxicity Criteria for Adverse Events, version 3.

Follow-up of all sibling donors in 6-month intervals, after PBSC harvest included blood counts and viral serology (hepatitis A,B,C, HIV, syphilis). Subsequently, in January 2014, with the median follow-up of 11.9 years (range 7.2-17.0 years) from the PBSC collection, the all sibling donors received a questionnaire regarding their overall health condition and possible development of new health problems after PBSC donation including malignancies. Some informations about the health status of the sibling donors were obtained by phone contact (10%, 17/167).

Statistical analysis. Data were analyzed as of October 31, 2014. To describe the data set, absolute and relative frequencies of values were calculated and quantitative variables were described by mean, standard deviation (SD), median and range. Comparisons between groups were performed using the Mann-Whitney U test. The Spearman's correlation analysis was used to explore possible associations between two quantitative variables. The level of statistical significance was 5% for all tests.

Results

Efficacy of PBSC mobilization. All 167 sibling donors completed the pre-planned mobilization protocol. On day +4 and day +5 of mobilization, preapheresis medians of CD34+ stem cells mobilized into peripheral blood were 51.4/μL and 62.7/μL, respectively. The median of overall PBSC yield was 7.4 x 10^6 CD34 cells/kg per donor weight (range 0.8-28.8) and 7.9 x 10^6 CD34 cells/kg per recipient weight. The median yield of CD34 cells for one apheresis was 3.8 x 10^6/kg per donor weight (range 0.8-14.4). In the majority of sibling donors (140/167, 84%), enough CD34+ cells could be collected in 1 or 2 apheresis procedures. The median number of apheresis was two (range 1-3). The optimal target yield of CD34 cells ≥ 4.0 x 10^6/kg was achieved in 140 donors (84%).

The CD34+ yield was less than 2x10^6/kg recipient body weight in 4 donors (2%) only. Failure of mobilization, defined as CD34 cells < 20/μL on day 5, occured in 4/167 donors (2%). Marrow harvest (2 cases) or second donor mobilization (2 cases) were carried out in these four donors. The optimal amount of PBSC was achieved in all 4 cases and allogeneic transplantation was successfuly performed. No long- term toxicity in these four donors was observed.

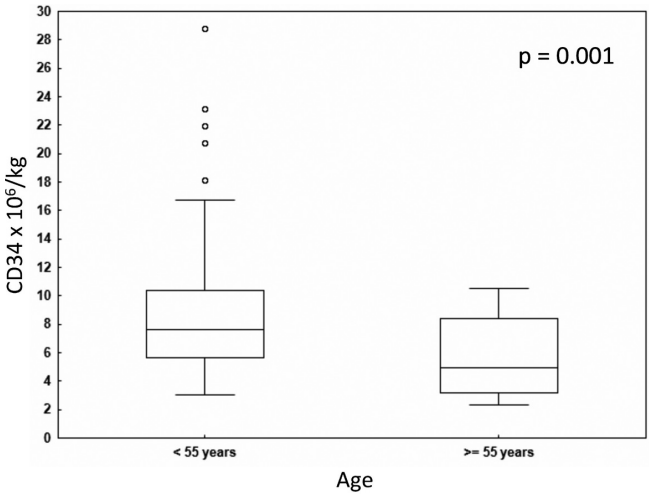

Figure 1. Impact of younger donor age on yield of PBSC mobilization: age < 55 years versus age ≥ 55 years

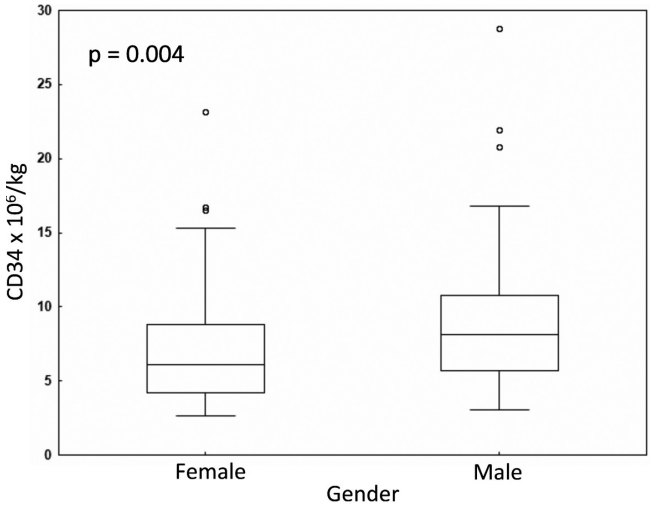

Figure 2. Impact of donor gender on yield of PBSC mobilization: significance of male gender

Finally, allogeneic PBSC transplantation was performed in 98% of recipients (163/167), with 2% of recipients not transplanted because of progression of hematological malignancy (2 patients) or toxicity of conditioning (2 patients). PBSC mobilization parameters are summarised in Table 2.

Predictors of successful mobilization of PBSC. Age heavily influenced the yield of PBSC mobilization. The median yield of CD34 cells in sibling donors aged < 55 years (132/167, 79%) was 7.6 x 10^6/kg compared to 5.0 x 10^6/kg in donors aged ≥ 55 years (35/167, 21%) (p=0.001). Figure 1 depicts CD34 counts by donor age, showing reduced average CD34 cell counts with advancing age. Donor age < 55 years was associated with significantly higher PBSC yield (p= 0.001), comparison of both age groups was performed using the Mann-Whitney U test.

The other important factor for successful PBSC mobilization in our group of donors was gender. Significantly higher yields were achieved in male donors compared to female donors (median CD34 cells 8.1 x 10^6/kg versus 6.1 x 10^6/kg, p =0.004). Impact of donor gender on PBSC mobilization is shown in Figure 2. Male gender of donors was associated with significantly higher PBSC yield (p= 0.004).

The level of peripheral blood CD34 cells before the first apheresis was another predictive factor for overall PBSC yield. The median yield of CD34 cells in sibling donors with preapheresis CD34+ count over 51/μL was 8.6 x 10^6/kg, while it was 5.6 x 10^6/kg in donors with preapheresis CD34+ count under 51/μL (p < 0.001). The correlation of CD34 cell count before the first apheresis and overall yield of CD34 cells after mobilization is shown in Figure 3, preapheresis CD34 cell count > 51/μL was associated with significantly better yield of CD34 cells (correlation according to Spearman's test was 0.571; p < 0.001).

Table 2. Variables related to PBSC mobilization with G-CSF 16μg/kg/day

WBC count (x 10^9/L) before the first apheresis (median, range)	45.5 (19.5-76.0)
PLT count (x 10^9/L) before the first apheresis (median, range)	215 (150-339)
Day 4 preapheresis PB CD34/μL count (median, range)	51 (11-202)
Day 5 preapheresis PB CD34/μL count (median, range)	63 (15-228)
Total CD34 yield x 10^6/kg per recipient weight (median, range)	7.9 (0.5-28.8)
Total CD34 yield x 10^6/kg per donor weight (median, range)	7.4 (0.48-28.4)

Abbreviations: WBC = white blood cells, PLT = platelets, PB – peripheral blood

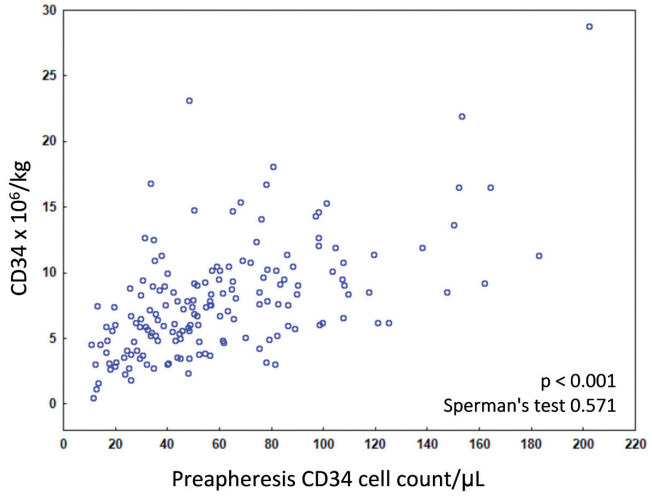

Figure 3. Significant correlation of preapheresis CD34 cell count/μL > 51 and overall yield of CD34+ cells (Spearman's test 0.571; p < 0.001)

The next important factor for optimal PBSC yield in our sibling donors was leukocyte count before the first apheresis. Significantly higher yields of PBSC mobilization were achieved in donors with leukocyte count ≥ 45.5 x 10^9/l compared to leukocyte count < 45.5 x 10^9/l (median CD34 cells 8.4 x 10^6/kg versus 6.4 x 10^6/kg, p =0.003).

The associations between CD34+/kg yields and selected donor parameters are shown in Table 3. The presence of comorbidities, performance status, and donor weight did not have statistically significant impact on CD34 counts or on the incidence of mobilization failures in our cohort of 167 sibling donors. None of the 4 donors who failed PBSC mobilization had comorbidity conditions as defined by the CCI.

The results of univariate analysis and the influence of selected clinical factors on CD34 cell counts are summarised in Table 4.

Safety of G-CSF administration and leukapheresis. The predominant adverse event associated with G-CSF administration was bone pain reported in 83% of the donors. Headache occured in 21% of donors. Flu-like symptoms or other toxicities were reported in 10% of the donor population. All adverse events were grade 1-2 according to CTC criteria. There were no cases of splenic rupture or other major toxicity.

None of the sibling donors discontinued G-CSF administration because of an adverse event.

Administration of G-CSF and leukapheresis both substantially reduced platelet counts [19]. In our group of donors, the median platelet counts after the first and the second leukapheresis were 131 x 10^9/L (range 78-298) and 114 x 10^9/L (range 58-178), respectively. No significant bleeding episode occured.

The most frequent adverse event during leukapheresis was paresthesia associated with hypocalcemia, all cases were grade 1-2 according to CTC criteria and quickly dissappeared after calcium substitution. No thromboembolic complications related to G-CSF administration were observed. Other problems, such as circulatory disturbances, fatigue, or pain at the site of venepuncture occured infrequently, affecting only 2% of donors and were of CTC grade 1-2.

Adverse events during short- and long-term follow-up. No pathological changes in peripheral blood counts were observed at 6 months after PBSC collection and all 167 donors had negative results of viral serology.

Long-term follow-up data were available in 60% (101/167) of the sibling donors.The median length of follow-up from PBSC donation was 11.9 years. Most of these donors reported good or very good general health (91%). Two sibling donors (2/101; 2%) developed clinically significant conditions, including head and neck cancer nine years after PBSC donation and amyotrophic lateral sclerosis eight years after PBSC collection, both these donors died. No cases of hematological malignancies have been reported in our cohort of sibling donors.

Discussion

Mobilization of PBSC with G-CSF and leukapheresis has become a well-established procedure worldwide and is the main technique for the procurement of allogeneic hematopoietic stem cell transplants [7]. HLA-compatible sibling donors have traditionally been considered the optimal hematopoeitic stem cell donor because of their immediate availability and superior outcomes of the transplant compared to unrelated donors [6].

Although G-CSF has a clear dose response relationship, the wide variability in mobilization yields remains a major challenge in the management of the individual donor. A G-CSF dose between 10 μg/kg to 16 μg/kg G-CSF is accepted as a standard and used by most centres worldwide [7, 21].

In this report, we describe the outcomes of 167 sibling donors after PBSC mobilization using the G-CSF dose of 16 μg/kg/day. Our results confirm the high efficacy of this mobilization protocol. The median overall PBSC yield was 7.9 x 10^6 CD34 cells/kg per recipient weight and the yield of mobilization surpassed 4x10^6/kg CD34 cells in the majority of our sibling donors (84%) after one or two apheresis procedures. These results are in concordance with other published studies [2, 6]. The median preapheresis count of CD34 cells on day +5 was 62.7/μL and was similar to previously published reports [6, 13]. Only 2% of our sibling donors (4/167) experienced mobilization failure with CD34+ yield less than 2 x 10^6/kg

Table 3. Association of CD34+/kg recipient yield with selected variables of donor (Spearman´s test)

Variable	Number	Spearman´s test	P-value
Age	167	-0.315	<0.001
Weight	167	0.119	0.059
CD34 cell count (μL) before the first apheresis	167	0.571	<0.001
WBC count (x 10^9/L) before the first apheresis	167	0.228	0.003
PLT count (x 10^9/L) before the first apheresis	164	0.044	0.577

Table 4. Influence of selected clinical factors on the yield of CD34 cells – univariate analysis

Factor	Number	Median CD34 cell count x 10^6/kg	P-value
Age < 55 years versus ≥ 55 years	132/35	7.6/5.0	0.001
Sex (male versus female)	90/77	8.1/6.1	0.004
Karnofsky PS 100% versus 80-90%	148/19	7.8/7.1	0.234
Comorbidities (CCI 0 versus CCI ≥ 1)	138/29	7.9/7.2	0.534
Median of WBC count before the first apheresis (below versus above)	83/84	6.4/8.4	0.004
Median of CD34 cells (μL) before the first apheresis (below versus above)	83/84	5.6/8.6	<0.001

recipient body weight and this proportion is comparable to the rates reported by other groups [2, 22].

Many clinical and laboratory variables have been reported to influence PBSC harvest [2. 6, 7], and a validated predictive model for PBSC mobilization would be very useful in the clinical practice.

In accordance with the literature [2, 7], the mobilization and harvest of CD34+ cells in our donor cohort were significantly more effective in male than in female donors. However, some authors did not confirm the impact of gender on PBSC harvest [6].

The donor age probably significantly influences the PBSC yield. Similar to reports by other authors [6, 13, 23-25] our data show strong association between donor age of 55 years or more and reduced PBSC mobilization.

However, again there are several studies that have not found age to be a significant predictive factor [7, 26].

The preapheresis count of CD34 cells in peripheral blood seems to be another important predictor of successful PBSC harvest [2, 7, 27].Our results confirm a strong correlation between CD34 cell counts before the first apheresis and the overall amount of CD34 cells after mobilization ($p< 0.001$).

The short-term safety of G-CSF application is generally acceptable with grade 1 or 2 toxicities that do not pose serious health risks for the donors. In our cohort of sibling donors, the short-term side effects of G-CSF 16 μg/kg were predominantly bone pain, headache and fatigue with grade 1-2 according to CTC criteria. No serious side effect was observed, it was in concordance with other studies [7, 27]. A transient state of hypercoagulalibity that could give to rise to thrombotic complications especially in older sibling donors could be a potential hazard of PBSC mobilization with G-CSF [7]. However, no thromboembolic complications related to G-CSF administration were observed in our cohort of donors.

Long-term monitoring of sibling PBSC donors is necessary to ensure the safety of PBSC mobilization and collection. The question whether G-CSF exposure of healthy donors increases the risk of developing hematological (especially myeloid) malignancies has been debated since the first allogeneic PBSC mobilizations [7]. The problem remains unanswered and will have to be investigated carefully in future studies. In our study, no cases of hematological malignancies were observed after a median follow-up of 11.9 years.

In conclusion, the mobilization of PBSC in sibling donors with G-CSF at dose of 16 μg/kg/day is an effective and safe procedure with no significant short- and long term toxicities.

References

[1] LJUNGMAN P, BREGNI M, BRUNE M, CORNELISSEN J, DE WITTE T et al. Allogeneic and autologous transplantation for haematological diseases, solid tumours and immune disorders: current practise in Europe 2009. Bone Marrow Transplant 2010; 45: 219–234. http://dx.doi.org/10.1038/bmt.2009.141

[2] RINALDI C, SAVIGNANO C, PASCA S, SPEROTTO A, PATRIARCA F et al. Efficacy and safety of peripheral blood stem cell mobilization and collection: a single-center experience in 190 allogeneic donors. Transfusion 2012; 52: 2387–2394. http://dx.doi.org/10.1111/j.1537-2995.2012.03619.x

[3] STRONCEK DF, CLAY ME, PETZOLDT ML, SMITH J, JASZCZ W et al. Treatment of normal individuals with granulocyte-colony-stimulating factor: donor experiences and the effects on peripheral blood CD34+ cell counts and on the collection of peripheral blood stem cells. Transfusion 1996; 36: 601–610. http://dx.doi.org/10.1046/j.1537-2995.1996.36796323059.x

[4] BOLAN CD, HARTZMAN RJ, PERRY EH, TRAINOR L, MILLER J et al. Donation activities and product integrity in unrelated donor allogeneic hematopoietic transplantation: experience of the National Marrow Donor Program. Biol Blood Marrow Transplant 2008; 14: 23–28. http://dx.doi.org/10.1016/j.bbmt.2008.06.001

[5] PULSIPHER MA, CHITPHAKDITHAI P, LOGAN BR, LEITMAN SF, ANDERLINI P et al. Donor, recipient, and transplant characteristics as risk factors after unrelated donor PBSC transplantation: beneficial effects of higher CD34+ cell dose. Blood 2009; 114: 2606–2616. http://dx.doi.org/10.1182/blood-2009-03-208355

[6] RICHA E, PAPARI M, ALLEN J, MARTINEZ G, WICKREMA A et al. Older age but not donor health impairs allogeneic granulocyte colony-stimulating factor (G-CSF) peripheral blood stem cell mobilization. Biol Blood Marrow Transplant 2009; 15: 1394–1399. http://dx.doi.org/10.1016/j.bbmt.2009.07.005

[7] HOLIG K. G-CSF in healthy allogeneic stem cell donors. Transfus Med Hemother 2013; 40: 225–235. http://dx.doi.org/10.1159/000354196

[8] NAKAMURA R, AUAYPORN N, SMITH DD, PALMER J, SUN JY et al. Impact of graft cell dose on transplant outcomes following unrelated donor allogeneic peripheral blood stem cell transplantation: higher CD34+ cell doses are associated with decreased relapse rates. Biol Blood Marrow Transplant 2008; 14: 449–457. http://dx.doi.org/10.1016/j.bbmt.2008.02.005

[9] BITTENCOURT H, ROCHA V, CHEVRET S, SOCIE G, ESPEROU H et al. Association of CD34 cell dose with hematopoietic recovery, infections, and other outcomes after HLA-identical sibling bone marrow transplantation. Blood 2002; 99: 2726–2733. http://dx.doi.org/10.1182/blood.V99.8.2726

[10] DE LA RUBIA J, MARTINEZ C, SOLANO C, BRUNET S, CASCON P et al. Administration of recombinant human granulocyte colony-stimulating factor to normal donors: results of the Spanish National Donor Registry. Spanish Group of Allo-PBT. Bone Marrow Transplant 1999; 24: 723–738. http://dx.doi.org/10.1038/sj.bmt.1701977

[11] MURATA M, HARADA M, KATO S, TAKAHASHI S, OGAWA H et al. Peripheral blood stem cell mobilization and apheresis: analysis of adverse events in 94 normal donors. Bone Marrow Transplant 1999; 24: 1065–1071. http://dx.doi.org/10.1038/sj.bmt.1702038

[12] SUZUYA H, WATANABE T, NAKAWAGA R, WATANABE H, OKAMOTO Y et al. Factors associated with granulocyte colony-stimulating factor induced peripheral blood stem cell yield in healthy donors. Vox Sang 2005; 89: 229–235. http://dx.doi.org/10.1111/j.1423-0410.2005.00701.x

[13] VASU S, LEITMAN SF, TISDALE JF, HSIEH MM, CHILDS RW et al. Donor demographic and laboratory predictors of allogeneic peripheral blood stem cell mobilization in an ethnically diverse population. Blood 2008; 112: 2092–2010. http://dx.doi.org/10.1182/blood-2008-03-143677

[14] FADILAH SA, MOHD-RAZIF MI, SEERY ZA, NORRAFEAH T, WAN-FARIZA WJ et al. Predictors of the yield of mobilized peripheral blood CD34+ cells in HLA-matched sibling donor. Transfus Apher Sci 2013; 49: 583–589. http://dx.doi.org/10.1016/j.transci.2013.07.032

[15] MAJOLINO I, BUSCEMI F, SCIME R, INDOVINA A, SANTORO A et al. Treatment of normal donors with rhG-CSF 16 micrograms/kg for mobilization of peripherall blood stem cells and their apheretic collection for allogeneic transplantation. Haematologica 1995; 80: 219–226.

[16] MAJOLINO I, SCIME R, VASTA S, CAVALLARO AM, FIANDACA T et al. Mobilization and collection of PBSC in healthy donors: comparison between two schemes of rhG-CSF administration. Eur J Haematol 1996; 57: 214–221. http://dx.doi.org/10.1111/j.1600-0609.1996.tb01366.x

[17] BENNETT CL, EVENS AM, ANDRITSOS LA, BALASUBRAMANIAN L, MAI M et al. Haematological malignancies developing in previously healthy individuals who received haematopoietic growth factors: report from the Research on Adverse Drug Events and Reports (RADAR) project. Br J Haematol 2006; 135: 462–650. http://dx.doi.org/10.1111/j.1365-2141.2006.06312.x

[18] HALTER J, KODERA Y, ISPIZUA AU, GREINIX HT, SCHMITZ N et al. Severe events in donors after allogeneic hematopoietic stem cell donation. Haematologica 2009; 94: 94–101. http://dx.doi.org/10.3324/haematol.13668

[19] HOLIG K, KRAMER M, KROSCHINSKY F, BORNHAUSER M, MENGLING T et al. Safety and efficacy of hematopoietic stem cell collection from mobilized peripheral blood in unrelated volunteers: 12 years of single-center experience in 3928 donors. Blood 2009; 114 : 3757–3763. http://dx.doi.org/10.1182/blood-2009-04-218651

[20] CHARLSON ME, POMPEI P, ALES KL, MACKENZIE CR. A new method of classifying prognostic comorbidity in longinutinal studies: development and validation. J Chron Dis 1987; 401: 373–383. http://dx.doi.org/10.1016/0021-9681-(87)90171-8

[21] KROGER N, RENGES H, SONNENBERG S, KRUGER W, GUTENSOHN K et al. Stem cell mobilisation with 16 microg/kg vs 10 microg/kg of G-CSF for allogeneic transplantation in healthy donors. Bone Marrow Transplant 2002; 29: 727–730. http://dx.doi.org/10.1038/sj.bmt.1703509

[22] ANDERLINI P, DONATO M, CHAN KW, HUH YO, GEE AP et al. Allogeneic blood progenitor cell collection in normal donors after mobilization with filgrastim: the M.D. Anderson Cancer Center experience. Transfusion 1999; 39: 555–560. http://dx.doi.org/10.1046/j.1537-2995.1999.39060555.x

[23] LYSAK D, KORISTEK Z, GASOVA Z, SKOUMALOVA I, JINDRA P. Efficacy and safety of peripheral blood stem cell collection in elderly donors; does age interfere? J Clin Apher 2011; 26: 9–16. http://dx.doi.org/10.1002/jca.20269

[24] AL-ALI HK, BOURGEOIS M, KRAHL R, EDEL E, LEIBLEIN S et al. The impact of the age of HLA-identical siblings on mobilization and collection of PBSCs for allogeneic hematopoietic cell transplantation. Bone Marrow Transplant 2011; 46: 1296–1302. http://dx.doi.org/10.1038/bmt.2010.310

[25] WANG TF, WEN SH, CHEN RL, LU CJ, ZHENG YJ et al. Factors associated with peripheral blood stem cell yield in volunteer donors mobilized with granulocyte colony-stimulating factors: the impact of donor characteristics and procedural settings. Biol Blood Marrow Transplant 2008; 14: 1305–1311. http://dx.doi.org/10.1016/j.bbmt.2008.09.002

[26] DE LAVALLADE H, LADAIQUE P, LEMARIE C, FÜRST S, FAUCHER C et al. Older age does not influence allogeneic peripheral blood stem cell mobilization in donor population of mostly white ethnic origin. Blood 2009; 113: 1868–1869. http://dx.doi.org/10.1182/blood-2008-11-187773

[27] HOSING C, SALIBA RM, HAMERSCHLAK N, KUTNER JM, SAKASHITA AM et al. Peripheral blood stem yield calculated using preapheresis absolute CD34+ cell count, peripheral blood volume processed, and donor body weight accurately predicts actual yield at multiple centers. Transfusion 2014; 54: 1081–1087. http://dx.doi.org/10.1111/trf.12435