

Stem cell procurement

Collection of autologous blood for bone marrow donation: how useful is it?

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Summary:

The hospital charts of 495 adult bone marrow (BM) donors to adult patients were reviewed to determine how necessary it is to collect autologous blood for marrow donation. An autologous transfusion was given to 79% of the donors. The median total volume of marrow harvested was 900 ml (range 450–1350 ml). The median number of nucleated cells harvested was 3.2×10^8 /kg patient weight (range 0.9 – 7.4×10^8 /kg patient weight). On the morning following the harvest, the median haemoglobin (Hb) concentrations were 104 g/l (79–135 g/l) in the female and 122 g/l (89–151 g/l) in the male donors autotransfused, and 96 g/l (75–127 g/l) in the female and 119 g/l (88–141 g/l) in the male donors not autotransfused. The post-donation Hb was lower than 85 g/l in four and lower than 90 g/l in 25 donors. Of the 25 donors with post-harvest Hb lower than 90 g/l, 23 were females and 14 had received an autologous transfusion. This study shows that, with a few exceptions, it is not necessary to collect autologous blood from healthy BM donors before the marrow harvest. The post-donation Hb concentrations do not decrease to levels detrimental to healthy persons whether autologous blood is transfused or not.

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the marrow harvest. To study the advantages and disadvantages of storing autologous blood, we reviewed our material obtained from sibling and unrelated BM donors.

Materials and methods

Donors and marrow harvests

In the present study, 574 consecutive BM harvests from 400 sibling and 168 unrelated donors between July 1981 and October 2001 at the Helsinki University Central Hospital were retrospectively evaluated. All unrelated donors were from the Finnish Bone Marrow Donor Registry. In all, 24 BM harvests from sibling donors were excluded from the analysis for the following reasons: 10 donors had been transfused with allogeneic blood before the Hb determination on the morning following the harvest, seven donors were underage, five lacked sufficient information, one donor redonated to the same patient with a short time interval (26 days) between the harvests, and one donor had von Willebrand's disease. In all, 55 marrow harvests from unrelated donors were not included in the study because the recipient was a child and a decision had been made prior to the medical evaluation not to collect an autologous blood unit from the donor. The characteristics of the 495 harvests are presented in Table 1. Two sibling donors donated twice to the same patient. One unrelated donor donated three times to two different patients, and one unrelated donor donated twice to the same patient. The time interval between the marrow harvests from the same donor ranged from 16 weeks to 62 months. Marrow was harvested with small aspirations of approximately 3 ml, and the median total harvested volume was 900 ml. The median number of nucleated cells was 3.2×10^8 /kg patient weight. In eight harvests from sibling donors and in one harvest from an unrelated donor, the nucleated cell dose was below 2×10^8 /kg patient weight. Marrow collection was performed from the posterior iliac crests, and, when necessary, also from the sternum (126 donors). During the years 1981–1983, the BM collections were performed either under epidural anaesthesia or general anaesthesia, thereafter only under general anaesthesia, except one under spinal anaesthesia from a donor with symptoms of respiratory infection.

The median and mean Hb concentrations were calculated separately for donors autotransfused, for donors from whom an autologous blood unit was collected but not reinfused, and for donors from whom an autologous blood

Autologous blood is commonly collected from bone marrow (BM) donors before the harvest and stored to be returned at the time of the marrow donation to reduce the fall of the haemoglobin (Hb) concentration. The potential risks of this policy are infection of the stored blood and errors in the handling and identification of the bags.¹ The postponement of planned transplantation may render the stored units useless. The collection of autologous blood reduces the Hb concentration in the donor already before

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Table 1 Characteristics of the BM harvests

	<i>All donors</i>	<i>Sibling donors</i>	<i>Unrelated donors</i>
Total no. of harvests/donors	495/490	379/377	116/113
Age of donors (years); median (range)	38 (18–68)	39 (18–68)	31 (18–48)
Gender of donors; male/female	292/203	229/150	63/53
<i>Weight of donors (kg); median (range)</i>			
Men	80 (49–134)	80 (49–134)	80 (58–124)
Women	63 (43–126)	64 (43–110)	63 (50–126)
<i>Total volume of marrow harvested (ml)</i>			
Median (range)	900 (450–1350)	900 (450–1350)	930 (600–1200)
Mean	868	848	932
<i>Nucleated BM cells $\times 10^8$/kg patient weight</i>			
Median (range)	3.2 (0.9–7.4)	3.2 (0.9–7.4)	3.4 (1.2–6.2)
Mean	3.3	3.2	3.4

Table 2 Hb concentrations (g/l) prior to and after the BM harvest in adult donors to adult recipients

	<i>Hb concentration (g/l)</i>					
	<i>At donor medical evaluation</i>		<i>Prior to BM harvest</i>		<i>Morning following BM harvest</i>	
	<i>Mean</i>	<i>Median (range)</i>	<i>Mean</i>	<i>Median (range)</i>	<i>Mean</i>	<i>Median (range)</i>
<i>All harvests (N = 495)</i>						
Females (203)	136	136 (117–164)	129	128 (104–152)	103	104 (75–135)
Males (292)	151	151 (121–174)	145	144 (116–172)	121	121 (88–151)
<i>Females</i>						
Auto blood transfused (170)	136	135 (117–164)	128*	127 (104–152)	104**	104 (79–135)
Auto blood not transfused (33)	137	138 (125–152)	135	136 (117–149)	100	96 (75–127)
Collected, not transfused (10)	138	139 (125–144)	136	137 (126–148)	101	101 (88–117)
No collection (23)	136	136 (125–152)	134	136 (117–149)	100	96 (75–127)
<i>Males</i>						
Auto blood transfused (221)	151***	150 (121–174)	143*	143 (116–168)	122*	122 (89–151)
Auto blood not transfused (71)	153	155 (135–171)	151	151 (131–172)	117	119 (88–141)
Collected, not transfused (17)	154	156 (135–168)	149	147 (135–164)	119	120 (102–128)
No collection (54)	153	154 (135–171)	151	152 (131–172)	117	117 (88–141)

Means of Hb concentrations in donors autotransfused and not autotransfused compared with each other.

* $P < 0.001$.

** $P = 0.083$.

*** $P = 0.041$.

unit was not collected (Table 2). The donors from whom an autologous blood unit had been drawn but not reinfused ($N = 27$) and those who had no autologous unit collected ($N = 77$) were included in the group 'not autotransfused'. The Hb concentrations in these two subgroups were very similar at all measurements.

Hb determinations

The Hb concentrations were measured in blood samples drawn from the donors at the time of the medical evaluation before the donation of an autologous blood unit, usually 2–5 weeks prior to the BM harvest, at the time of entering the hospital on the day before the harvest, and on the morning following the harvest. None of the donors was transfused with allogeneic blood between the Hb determinations.

Collection of autologous blood

One unit of blood (450 ml) was routinely collected from the donors at the time of the medical evaluation 2–5 weeks before the harvest. The blood was taken into CPDA-1 whole-blood bags, which can be stored for 35 days. The bags were kept at a temperature of 2–6°C in a blood refrigerator at the hospital blood centre. The autologous blood unit was transfused to the donor after the harvest, usually without Hb checking, on the same day.

Statistics

T-test for two independent samples was used to compare the mean Hb concentrations between the groups of autotransfused and not autotransfused donors.

Table 3 Reasons for not collecting autologous blood at the time of donor medical evaluation

<i>Sibling donors</i>	73
Uncertainty in the proceeding to BMT or the date of transplantation unknown	35
The time interval to BM harvest <14 days	18
The health of the donor uncertain after drawing routine blood samples	9
The type of collection, BM or PBPC, unknown	6
The time interval to BM harvest >35 days	2
Donor's decision	2
Routine blood donation just before medical evaluation	1
<i>Unrelated donors</i>	4
The time interval to BM harvest <14 days	3
The requested cell dose low	1

Results

An autologous blood unit was stored from 418 of the 495 donors (84%; Table 2). Of the 418 donors, 27 (6.5%) with autologous blood stored were not autotransfused. The autologous blood unit was outdated at the time of the marrow harvest because of the postponement of the transplantation in 13 cases, and the transfusion was regarded as unnecessary in 11 cases either because of a relatively high Hb level (>125 g/l) in an extra determination immediately after the harvest or because of the small volume of marrow harvested (<600 ml). Three donors did not receive an autotransfusion for an unknown reason.

A blood unit was never stored from 77 donors (Table 3). The most common reason was that, due to the nature of the disease of the patient, proceeding to the transplantation was not certain or the date of transplantation was unknown. The time interval from the donor's medical evaluation to transplantation was short (<14 days) in 21 cases and long (>35 days) in two cases. In nine cases, the suitability of the donor for general anaesthesia and BM harvest was uncertain at the time of the medical evaluation or the donor felt sick after blood samples had been drawn. In six cases, the donor participated in the EBMT study comparing transplantation with BM or peripheral blood progenitor cells (PBPCs),² and the type of donation was not yet known at the time of the medical evaluation.

At the time of the medical evaluation, the mean Hb concentrations were similar, 136 and 137 g/l, in the female donors autotransfused or not autotransfused later at the time of the BM harvest (Table 2). In the male donors later autotransfused, the Hb concentration was 151 g/l and in those not autotransfused 153 g/l ($P=0.041$). Just before the BM harvest, the Hb concentrations were significantly higher in the donors who were not later autotransfused than in those autotransfused after the marrow harvest (135 vs 128 g/l in the female donors, $P<0.001$, and 151 vs 143 g/l in the male donors, $P<0.001$). On the morning after the harvest, the Hb concentration was 104 g/l in the female donors autotransfused and 100 g/l in those not autotransfused ($P=0.083$). In the male donors autotransfused, the post-harvest Hb level was significantly higher, 122 g/l, than in those not autotransfused, 117 g/l ($P<0.001$). It was not possible to calculate the volumes of crystalloids given to the donors precisely because the volume of fluid infused from

Table 4 Number (%) of donors with a low Hb concentration (g/l) after the harvest

	Hb concentration on the morning following the harvest	
	<90	<85
<i>Sibling donors (N=379)</i>		
Autologous blood transfused (291)	11 (4)	2 (0.7)
Autologous blood not transfused (88)	11 (13)	2 (2)
<i>Unrelated donors (N=116)</i>		
Autologous blood transfused (100)	3 (3)	0
Autologous blood not transfused (16)	0	0

the last crystalloid solution bag was not recorded in every case. The mean registered volumes of crystalloids infused to the donors not autotransfused were significantly higher than those infused to the autotransfused donors (2880 vs 2670 ml, $P=0.01$).

In all, 14 of the 391 donors who were autotransfused (3.6%) and 11 of the 104 donors not autotransfused (10.6%) had an Hb level <90 g/l on the morning following the harvest (Table 4). Of the 14 autotransfused donors with the Hb level <90 g/l, 13 were females. The weight of 10 female donors was <60 kg (median 54 kg; range 50–81 kg). The range of the pre-harvest Hb level in these 13 female donors was 112–130 g/l. The only male donor with a post-donation Hb <90 g/l weighed 49 kg. Of the 11 donors not autotransfused with an Hb concentration <90 g/l after the harvest, 10 were females. Only three donors in this group weighed <60 kg, the median weight being 62 kg (range 55–83 kg). The pre-harvest Hb level ranged from 117 to 136 g/l. Two of the donors had donated an autologous blood unit and nine had not.

Four female donors had an Hb concentration <85 g/l on the morning following the harvest (Table 4). Two of them had been autotransfused. The pre-harvest Hb concentrations in these autotransfused donors were 118 and 126 g/l and the post-harvest Hb concentrations 83 and 79 g/l, respectively. The weights of these donors were 59 and 54 kg and the BM volumes harvested 1000 and 1200 ml. An autologous blood unit had not been collected from two other donors with a post-donation Hb <85 g/l. Their pre-harvest Hb levels were 117 and 128 g/l and the postharvest Hb concentrations 75 and 83 g/l. The donors weighed 83 and 61 kg, and the volumes of marrow harvested were 900 and 1000 ml, respectively.

Discussion

In the present study, the hospital charts of 568 consecutive sibling and unrelated donors were reviewed in order to determine how necessary it is to collect autologous blood before BM harvest to be reinfused at the time of the donation. The guidelines of the World Marrow Donor Association state that the harvest centre should aim at collecting one or more units of autologous blood for transfusion to the donor during or after the harvest procedure.^{3,4} However, the results of the present study

show that only in few donors, if in any, the Hb concentration after the marrow harvest decreases to levels considered detrimental to healthy persons, regardless of whether an autologous transfusion is given or not.

A donation of an autologous blood unit (or several units) before the BM harvest requires the harvest to be performed during the following 2–5 weeks, because the decrease in the Hb level after an autologous blood donation should be compensated before the marrow collection, and, on the other hand, CPDA-1 whole-blood bags can be stored only for 35 days. An autologous blood unit was not drawn from 14.5% of our sibling donors at the time of the medical evaluation, because there was uncertainty of the date of BMT or the time interval was too short or too long. An autologous blood unit was not drawn from only 0.9% of the unrelated donors donating for the first time because of the timing between the medical evaluation and BMT. This reflects the practice of our centre to call an unrelated BM donor to the medical evaluation strictly 2–5 weeks before the fixed BMT date.

In all, 84% of the female and 76% of the male donors were autotransfused. The proportion of autotransfused donors in the present study is slightly lower than it has been in some previous studies among unrelated or family member donors, 90–93%.^{5–7} In the present study, only 23% of the marrow harvests were performed from unrelated donors and 77% from sibling donors. Transfusion of autologous blood may more often be carried out among unrelated than among sibling donors, because the timing between the medical evaluation and operation has to be more fixed in BM harvests from unrelated than from sibling donors.

In the present autotransfused donors, the Hb concentrations were significantly lower on the day before the BM harvest than in the donors not autotransfused. In line with our results, in a randomised study by Billote *et al*,⁸ the patients undergoing unilateral primary total hip replacement, who had donated autologous blood at least 2 weeks prior to surgery, showed lower Hb levels both at the time of admission and in the recovery room than those who had not donated autologous blood. Except one of the hip replacement patients, all the others who were autotransfused received their blood transfusion only postoperatively. None of the 96 total hip replacement patients required an allogeneic transfusion.

On the morning following the harvest, the Hb concentrations in the present BM donors were higher in the donors autotransfused than in those not autotransfused. The higher volumes of crystalloids infused to the donors not autotransfused than those given to the autotransfused donors may at least partly explain the difference seen in the post-donation Hb levels. However, only 0.5 and 2% of the donors autotransfused and not autotransfused, respectively, had an Hb concentration <85 g/l. No donor had an Hb level <75 g/l. Billote *et al*⁸ used an Hb level <70 g/l as the transfusion trigger for healthy total hip replacement patients and <80 g/l for patients with a major comorbid disease if there were no clinical signs of reduced oxygen-carrying capacity. In a multi-institutional, prospective, randomised study by Hebert *et al*,⁹ it was shown that a transfusion threshold as low as 70 g/l was as safe as a higher

threshold of 100 g/l in critically ill patients, with the possible exception of patients with acute myocardial infarction. Healthy humans can tolerate acute normovolemic anaemia to 50 g/l without signs of tissue hypoxia¹⁰ by compensating the decrease in the Hb level with the increase of the cardiac output.^{11,12} In recent years, the trigger for blood transfusion has shifted from a fixed Hb level to the level of Hb necessary to meet the tissue oxygen demands of the patient.¹² All BM donors have undergone a medical evaluation and probably tolerate Hb levels of 70–80 g/l.

Marrow was harvested with small aspirations from the present donors. The mean and maximal total volumes collected from the sibling donors were 850 and 1350 ml. The mean volume of marrow harvested from the unrelated donors was 930 ml and the maximal volume 1200 ml. In the study of Gandini *et al*,⁶ the mean and maximal volumes of marrow collected from 103 unrelated donors were 1110 and 1650 ml, respectively. The median and maximal volumes collected from 493 unrelated donors in the National Marrow Donor Program were 1050 and 2983 ml, respectively.⁵ Small aspirates of BM have been shown to contain abundantly nucleated cells and CFU-GM,¹³ and the harvesting of marrow with approximately 3 ml aspirates from the present donors has contributed to the moderate total volumes harvested. In retrospective studies of blood transfusions to BM donors, it has been shown that the number of transfusions has correlated with the volume of marrow harvested and with the second BM collections.^{14,15} The vast majority (92%) of the donors in the present study with a post-donation Hb <90 g/l were females, many of them weighing <60 kg and with a pre-donation Hb just below the normal range. The small aspiration volumes may benefit especially small female donors who are at the greatest risk for low post-donation Hb levels. A transfusion of an autologous blood unit does not seem to prevent the decrease in the Hb concentration in small female donors after the harvest. It has been calculated that moderate blood losses perioperatively result in lower post-operative haematocrit values in surgical patients who have preoperatively donated autologous blood compared to patients who have not donated autologous blood.^{16,17}

The present study shows that it is not necessary to collect autologous blood from healthy BM donors before the marrow harvest. The post-donation Hb concentrations do not decrease to levels considered detrimental to healthy persons whether autologous blood is transfused or not. Routine collection of autologous blood prior to BM harvest may lead to the wasting of blood. Small aspiration volumes of marrow guarantee that sufficient amounts of nucleated cells can be obtained with moderate total volumes.

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