# Safety of Bone Marrow Stem Cell Donation: A Review

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ABSTRACT

Allogeneic hematopoietic stem cell transplantation (HSCT) represents the first choice of treatment or an important therapeutic option for several diseases, but it is still marked by morbidity and mortality. In contrast, the donation of hematopoietic stem cells (HSCs) is considered to be a safe procedure. The invaluable ethical source of donation and its central role in transplantation implies that the greatest attention be due to the donor and to the donation process through a serious monitoring protocol for donor safety. Both the Joint Accreditation Committee and the European Committee pay particular attention to the notification of adverse events and adverse reactions. Bone marrow donation is a well established procedure, that has now been performed for >30 years. Although it does not require drug administration, there is hospital admission for 1–3 days with 7–10 days off work. The main risk is related to the anesthesia. Pain in the aspiration area, together with astenia are considered to be the most frequent side effects, as shown by the USA National Marrow Donor Program experience in 1,193 donations. In the European Group for Blood and Marrow Transplantation analysis performed between 1993 and 2005 on 27,770 first HSCTs from bone marrow, only 1 fatal event (pulmonary embolism) and 12 serious adverse events were observed. The most frequent adverse events were cardiac. The incidence of adverse events was significantly lower ($P < .05$) compared with peripheral blood HSC donors, which confirms the necessity of accurate attention to donor selection and evaluation in bone marrow donation.

Over the past 2 decades, allogeneic hematopoietic stem cell transplantation (HSCT) has become an established therapy with increasing numbers of procedures every year.[1] Several stem cell sources, such as mobilized peripheral blood stem cells (PBSCs), bone marrow (BM), and umbilical cord blood (UCB), are suitable for HSCT in clinical practice. BM harvesting is a well established, effective, and safe method for the collection of HSCs. During the past decade, PBSCs have almost replaced BM as a stem cell source in autologous transplantations. Although PBSCs are used in the majority of cases in allogeneic settings, BM still remains a valuable stem cell source. In Italy in 2008, 1,467 allogeneic transplants were performed, of which 616 (42%) were from a sibling donor (205 from BM and 395 from PB) and 636 (43.4%) from an unrelated donor (188 from BM and 323 from PB).[2]

Today, >11 million bone marrow donors and cord blood units from 58 registries and 36 cord blood banks are available to provide life-saving stem cells to patients in need of them. They can easily be contacted via the internet.[3] These donors are an invaluable ethical source for all humanity, with the mission of providing life-saving help to those in need. It is the responsibility of health institutions and organizations to ensure that the donation process is safe for donors. Fortunately, the great majority of donations occur without complications, but serious side effects from BM or PB donations may occur. Serious adverse events are uncommon, and death is exceedingly rare. Nevertheless, all subjects must be carefully evaluated and fully informed before donation, and the procedure must be performed by experts in the process.[4] Both the Joint Accreditation Committee and the European Union have emphasized the importance of reporting adverse events and reactions.[5,6]

## BONE MARROW DONATION

Hemopoietic stem cells are directly aspirated from both hips (posterior superior iliac crests) under general or regional anesthesia, with the donor hospitalized for at least

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0041-1345/10/$–see front matter
doi:10.1016/j.transproceed.2010.05.029

1 night.[7,8] One or 2 red blood cell autodonations are also necessary before the procedure. The main consequences for the donor are pain and bruising at the site of aspiration, anemia, and the risks of general anesthesia.[9] The donor may require pain killers for a short time after the procedure and some time off work. The fatal and serious adverse events reported are fortunately rare. In. 2001, The World Marrow Donor Association (WMDA) created a serious events/adverse effects registry (SEAR) reporting system, in which >80% of the donor registries worldwide participate. The SEAR database gives good insight into the occurrence of serious events and adverse effects regarding stem cell donation by unrelated donors. Any event concerning the donor that results in death or is life threatening, requires inpatient hospitalization, considerably prolongs existing hospitalization, or results in persistent or significant disability/incapacity must be reported. During 2008, WMDA reported 9 serious adverse events and reactions in bone marrow donors: 1 subject hospitalized for severe chest pain, anxiety related, 1 transfused with ABO-compatible red blood cells from another donor, 1 with non/cardiac chest pain, with abdominal thrombosis and urinary tract infection, 1 with wound infection of staphylococcus epidermidis bacteremia, 1 with a vasovagal reaction or second-degree atrioventricular block and asystole secondary to ondansetron, 1 with deep venous thrombosis, 1 with cauda equina hematoma, 1 with commotio cerebri after collapse. The Italian Bone Marrow Donor Registry reported 4 serious adverse events occurring from 3 hours to 10 years after bone marrow harvest.

### BM Versus PB as Stem Cell Source: Side Effects and Adverse Events

In the Cochrane Central Register of Controlled Trials,[10] 6 relevant randomized controlled trials[8,11–15] were identified comparing allogeneic BM and PB SC donations to address the issue of safety. The 6 trials with 765 related donors (388 BM, 377 PB) provided a range of data on the adverse effects associated with HSC donation as well as comparative findings on the tolerability and safety of the 2 donation methods. Both physical and psychologic side effects were reported. Both BM and PB donors experienced similar psychologic morbidity, and both had fatigue and reduced energy after the procedure. BM donors experienced more pain at the donation site, greater incidence of hemorrhage, anemia, and hypotension, and tendency to have more days of restricted activity, and were more likely to require hospitalization after donation. Even if these data showed a greater number of adverse events in the BM group (56%) compared with the PB group (44%), there is no clear evidence of which collection method is safer for the donor. The main limits of this review were due to limited reports of donors' experiences, short follow-up, and inappropriate and inhomogeneous psychologic morbidity assessment among the trials.[16]

Other information is available from the study of donor registries, including those of unrelated donors. The European Group for Blood and Marrow Transplantation analysis,[17] which was performed between 1993 and 2005 and included 51,024 first HSCT (27,770 BM and 23,254 PB), contained 5 fatal events, only 1 of which was in a BM donor (pulmonary embolism) and 37 serious adverse events (12 BM vs 24 PB; $P < .05$). The most frequent adverse events in BM donation were cardiac and related to the anesthesia.

In a National Marrow Donor Program survey,[18] BM donors most often reported pain at the collection site (82% back or hip pain) and anesthesia-related pain sites: 33% throat pain and 17% postanesthesia headache. In contrast, PBSC donors most often reported bone pain (97%) at various sites during filgrastim administration. Fatigue was the second most reported symptom by both BM and PB SC donors (59% and 70%, respectively). PBSC donors reported a median time to recovery of 1 week compared with a median time to recovery of 3 weeks for BMSC donors. Both BM and PB donors experienced transient changes in their white blood cell, platelet, and hemoglobin counts during the donation process, with most counts returning to baseline values by 1 month after donation and beyond. Serious adverse events were uncommon, but these events occurred more often among BM donors than PB donors: 1.34% in BM donors versus 0.6% in PBSC donors.

### Type of Anesthesia

Bone marrow harvest may be performed under general or regional anesthesia (GA or RA). Although both methods are generally considered to be safe and are commonly used, there are only a few reports that compare their safety and efficacy among SC donors.[19–21] Local anesthesia has reduced risk of trauma, because the patient is awake and vigilant, whereas general anesthesia may produce a minor respiratory risk, because the donor has a secured airway. In a recent retrospective study of 281 BM donations (207 GA, 74 RA), no significant difference was noted regarding numbers of adverse events during and after the procedure, neither in the extent of anesthesia and harvest, nor in the volume and cell harvest. This observation strongly suggests that there is no an "anesthesia of choice," and that the choice depends on the donor or the anesthetist's preference (22).

## CONCLUSIONS

The invaluable ethical source of donation and its central role in transplantation implies that the highest attention should be paid to the donor and to the donation process through a series of safety procedures. Bone marrow donation seems to be less related to serious adverse events, but there is still the need for more randomized trials and of a more accurate reporting system to evaluate the safer type of donation and to perform a longer donor follow-up. Moreover, particular attention has to be paid to donor evaluation with the intent to protect the volunteer from the risk of damaging his or her health and to offer the recipient the best quality of treatment.

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