To the editor:

Management of anticoagulation-associated toxicity during large-volume leukapheresis of peripheral blood stem cell donors

We write to direct attention to the management of anticoagulation-associated toxicity during large-volume leukapheresis (LVL), a potential source of donor morbidity as described in a recent comprehensive report comparing experiences during marrow and peripheral blood stem cell (PBSC) donation.1

PBSCs are collected from donors during LVL by the process of apheresis.2 During apheresis, anticoagulation is necessary to prevent coagulation and clumping of the collected component. The most frequently utilized apheresis anticoagulant is citrate, which is returned to the donor at a rate that depends on the whole blood processing rate and the ratio of citrate anticoagulant to whole blood.3 The use of citrate-mediated anticoagulation in the apheresis device does not result in systemic anticoagulation due to metabolism and redistribution of citrate in the donor circulation.3,4 Modest but significant elevations in serum citrate levels, however, frequently occur in apheresis donors, who may experience symptoms associated with decreased ionized calcium levels resulting from formation of calcium-citrate complexes.5 The establishment of standard citrate administration rates for plateletpheresis has resulted in procedures that are generally well tolerated.3,5 But during much longer LVL procedures, blood citrate accumulation may eventually outpace metabolism when citrate is administered at rates used during plateletpheresis, resulting in markedly decreased ionized calcium levels and severe donor symptoms.5

There is no single standard method to reduce citrate toxicity during LVL. One approach to this problem is to combine heparin administration with a reduced citrate infusion rate, thus limiting the amount of citrate returned to the donor while providing anticoagulation during apheresis. But heparin administration may also be associated with toxicity,6 and the single serious adverse event that occurred in a donor during PBSC collection in the study by Rowley et al was the development of a large painful hematoma associated with use of a femoral catheter for central venous access and heparin administration.1 Whether this adverse event was caused solely by the use of heparin cannot be established, but administration of 1000 to 2000 units of heparin per hour over several hours of LVL could produce systemic anticoagulation of a degree that might warrant delay in removal of a central venous catheter or require additional monitoring.6

An alternative method to reduce the toxicity associated with administration of large quantities of citrate during LVL is to balance the citrate required for anticoagulation in the apheresis device with a controlled infusion of calcium to the donor.6,8 When dosed according to the citrate administration rate and infused with citrated blood immediately prior to entering the donor circulation, calcium infusions safely and reliably attenuate the decline that normally occurs in donor ionized calcium levels, since the fraction of total calcium present in ionized form exhibits a tight, linear relationship with blood citrate concentration.6,8 The marked elevations in parathyroid hormone and decreases in potassium and phosphate that normally occur due to unopposed citrate administration during LVL are also ameliorated by calcium supplementation.6 When citrate and calcium administration are linked in this fashion, we have noted no significant adverse effects related to calcium prophylaxis in more than 400 leukapheresis procedures of 12 to 25 liters processed, lasting 3 to 5 hours and performed at citrate infusion rates of 2.5 mg/kg/min and higher in children and adults. When utilizing calcium prophylaxis as an antidote to citrate toxicity during LVL, heparin anticoagulation is not required and LVL may be comfortably performed, with or without concomitant laboratory testing.6,8

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References


To the editor:

Thr325Ile polymorphism of the TAFI gene does not influence the risk of myocardial infarction

Plasma TAFI antigen (Ag) levels are almost entirely under the control of the TAFI gene.1,3 Several polymorphisms found to be associated with TAFI Ag levels have been already described,1,4 but a recently performed segregation-linkage analysis indicates that the TAFI-linked quantitative trait loci is unlikely to be one of these already identified polymorphisms.5

Recently, Brouwers et al reported the identification a new polymorphism, 1040C/T, in the coding region of the TAFI gene that...
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