Joint UKBTS Professional Advisory Committee (1)

Position Statement

Calcium Abnormalities and Apheresis Donation

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Background

There is a concern about pulse and bone density abnormalities in apheresis donors as citrate is used as an anticoagulant during apheresis procedures and it is returned to the donor during the procedure. Citrate is known to be related to arrhythmias. It is also known that citrate may affect calcium metabolism and there is concern that this may lead to bone density changes in donors who have undergone large numbers of apheresis procedures.

Citrate and the heart

Citrate can form a complex with serum calcium resulting in hypocalcaemia. This results in the well-recognized symptoms of citrate toxicity seen in some apheresis donors: tingling around the mouth or in the hands and feet, a metallic taste in the mouth, cramps, carpo-pedal spasm, or nausea and vomiting. It can also cause prolongation of the QTc (corrected QT interval) visible on the ECG. Prolongation of the QT interval can put a person at risk of Torsades de Pointes a form of ventricular tachycardia which is usually self limiting but which can lead to ventricular fibrillation and sudden death.

There is only one study on prolonged QTc intervals in apheresis donors [1]. This purports to show a prolongation of the QTc in these donors, but the heart rate of the donors is not recorded and it is not clear whether this has in part caused the effects encountered. The correction equations used (QT/square root RR) over-correct at heart rates over 60bpm and under-correct at rates <60bpm.

The levels of hypocalcaemia are probably not clinically significant in most normal individuals undergoing apheresis, but arrhythmias particularly Torsades de Pointes may become a risk in some donors especially those who have either/or: [2 & 3]

- pre-existing inherited long QT intervals, Long QT Syndrome (LQTS). Potential donors with this condition may not donate, if the condition is known, as the Blood Safety and Quality Regulations 2005 require permanent deferral of potential donors ‘with active or past serious cardiovascular disease, except congenital abnormalities with complete cure’.

- who are on certain medication known to prolong QT intervals especially if used in combination:

    - non-sedating antihistamines terfenidine & astemizole, fluroquinolone (e.g. levofloxacin) and macrolide (e.g. erythromycin) antibiotics, anti malarials (quinine, halofantrine and melfloquine) and imidazole antifungals (ketonazole)

- tricyclic antidepressants, amitriptyline, doxepin, despramine, imipramine and clomipramine
- maybe haloperidol, chlorpromazine, trifluperazine, pericycline, prochlorperazide, thioridazine and fluperazine
- pimizide
- cisapride

There has been no recorded case of any of these drugs causing any problems in donors undergoing apheresis internationally, despite millions of procedures each year.

There is currently no restriction recommended for donors with a family history of LQTS or using antihistamines or psychoactive drugs undergoing apheresis.

Citrate and Bone

A number of publications have raised the question of the known alteration in calcium metabolism and its long-term affect on apheresis donors bone density [4-6.] In 2003 [7] it was reported that 35% of the donors who had more than 100 plateletpheresis donations had radiological evidence of osteopenia and this was independent of the donors' age and gender. However more recent Dutch studies [8 & 9] and comparing bone density in whole blood and plasmapheresis donors have found that no significant difference in bone mineral density was seen between the 2 groups. A retrospective linkage study in Sweden[10] found that there was no association between total number of apheresis donations and risk of bone fracture. Data on apheresis donations given by Swedish blood donors between 1990 and 2012 were extracted from the Scandinavian Donations and Transfusions database (SCANDAT2). A total of 140 289 apheresis donors were included in the analyses. Although acute changes in calcium metabolism after apheresis donation have previously been reported this study provided evidence that such repeated acute effects among frequent apheresis donors do not cumulatively impact long-term fracture risk.

Therefore there is no recommendation that the total number of apheresis donations given by any one donor be limited. Nor is there any recommendation that the current guidance on frequency of donations be changed. This is currently a minimum interval of two weeks between apheresis platelets and plasma donations, with a maximum of 24 donations per year and a minimum of 48 hours between apheresis leucocytes procedures.

Conclusions

It is not recommended that a restriction be put on apheresis donors with a family history of LQTS or those on antihistamines or psychoactive drugs. There is also no recommended restriction on the total number of donations given by UK apheresis donors or any change in donation frequency. Both these recommendations will be kept under review.

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