SHORT COMMUNICATION

Adverse Events During Apheresis Procedures: Audit at a Tertiary Hospital

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Received: 12 January 2016 / Accepted: 9 May 2016 / Published online: 19 May 2016
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Abstract Apheretic platelets are better quality blood components which reduce donor exposure and chances of TTIs to transfusion recipients when compared to the whole blood derived components. Though safe, these apheretic donations are associated with donor adverse events. We evaluated the incidence of such adverse events associated with the modern apheresis procedures that would provide an insight as well as help formulating preventive steps to avoid frequent occurrences of such events. This prospective audit-based observational study was conducted over 1 year. Donors for plateletpheresis were selected as per the standard operating procedure of the Apheresis Lab. The apheresis procedures were done on the MCS+ (Haemonetics Corp.), Trima Accel (Terumo BCT) and COM.TEC (Fresenius Kabi AG). 1740 apheresis procedures were performed, out of which 1708 were plateletpheresis and 32 therapeutic plasma exchange (TPE) procedures for 7 patients. A total of 102 adverse events were noted; of which, 80 (78.43 %) events were associated with donors, 15 (14.71 %) were owed to equipment related problems and 7 (6.86 %) were technical aberrations. All the events associated with donors were mild. No adverse events were reported with any of the 32 TPEs. Apheresis procedures are associated with adverse events which can be reduced by meticulous donor-vigilance, superior training modules for the technical personnel and continued supervision of experienced transfusion medicine specialists. Continued efforts towards making the donor's experience with apheresis more pleasant give a forward thrust to the noble vision of preparing a voluntary apheresis donor pool in India.

Keywords Apheresis · Adverse events · Citrate effects · Vaso-vagal reactions

Introduction

Over decades, increased demand of platelet transfusions for patients with various medical and surgical diagnoses led to accelerated usage of technologically advanced “Apheresis” for platelet concentrates which is conducted under the transfusion medicine specialist's supervision in special dedicated areas [1]. In apheresis, whole blood is drawn from healthy donors, processed in specialized equipments viz. the automated cell separators which facilitate in-line separation of cellular from plasma component and then, selective extraction of required component with the ‘depleted blood’ being returned back to the donors. Many authors have reported the apheresis as a safer procedure which is associated with less frequent adverse donor reactions as compared to whole blood donations [2, 3]. A multi-centric study reported the frequency of adverse reactions observed in apheresis donations ranges from 0.32 to 6.81 % [4]. Though these apheresis procedures share a few common adverse events with the whole blood donations (e.g. vaso-vagal reactions, hypovolemia, haematoma formation, etc.), these are associated with few unique adverse events which are not associated with standard phlebotomies and/or whole blood donations [2, 3]. These may be attributed to the usage of anticoagulant ‘Acid-Citrate-Dextrose’ (ACD) causing hypocalcemia and longer donation periods [4].

We evaluated the incidence of the adverse events associated with the modern apheresis equipments and techniques at our centre that would provide an insight as well as help formulating preventive steps to avoid frequent occurrences of such events.

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Materials and Method

This prospective audit-based observational study was conducted from January 2015 through December 2015. Donors for plateletpheresis were selected as per the standard operating procedure (SOP) for the apheresis lab of the department. All the donors were medically fit and of age between 18–60 years weighing ≥ 60 kgs. All the donors had haemoglobin level of ≥ 12.5 gm/dL and platelet count of $\geq 150 \times 10^3/\mu\text{L}$ (LH 750, Beckman-Coulter, Inc., USA). History of non-consumption of non-steroidal anti-inflammatory drugs (NSAIDs) in the last 72 h was taken. All donors were non-reactive for possible TTI markers viz. HIV, HBV, HCV [by Chemiluminescence (Architect i1000 SR, Abbott Diagnostics, USA)], Malaria and Syphilis [by RPR (Span Diagnostics Ltd., India)]. The apheresis procedures were done on 3 cell separators viz. the MCS+ (Haemonetics Corp., Braintree, USA), Trima Accel (Terumo BCT, Lakewood, USA) and COM.TEC (Fresenius Kabi AG, Bad Homburg vor der Höhe, Germany). Adverse events were stratified into donor related, equipment malfunction and technical aberrations [5]. Donor related adverse events occurring during apheresis donations were broadly classified as local and systemic reactions. All adverse events were noted by nursing/technical staff under the supervision of a transfusion medicine specialist, to eliminate observer bias.

Results

A total of 1740 apheresis procedures were performed on the aforementioned equipments, out of which 1708 were plateletpheresis and 32 were therapeutic plasma exchange (TPE) procedures for 7 patients (Table 1). A total of 102 (5.86 %) adverse events were reported. Among these 102 adverse events, 80 (78.43 %) events were associated with donors, 15 (14.71 %) were owed to equipment related problems and 7 (6.86 %) were technical aberrations. All the events associated with donors were mild. No adverse events were reported with any TPEs.

Donor related adverse events included 20 (19.6 %) vascular injuries (hematoma formation), 47 (46.1 %)

anticoagulant associated events due to infused citrate and 13 (12.73 %) vaso-vagal reactions (VVRs). The rate of vascular injury, citrate reaction and VVRs in plateletpheresis (N = 1708) were 1.2 %, 2.7 % and 0.76 %, respectively. *Equipment related problems* comprised 15 (14.71 %) events those included 4 (3.93 %) air purge failures (2 in MCS+ and 1 each in COM.TEC and Trima), 3 (2.94 %) defective kits (leakage from separation chamber in 2 kits for COM.TEC and in 1 kit for MCS+) and 8 (7.84 %) high/low AC ratio (in MCS+ leading to disabling the ACD drip monitor). *Technical aberrations* included 7 (6.86 %) events which included 2 (1.96 %) wrong selections of programme modules (COM.TEC), 3 (2.94 %) events due to ACD being connected early (Trima) and 2 (1.96 %) events due to the donor line clamp, not being opened on time (Trima).

Discussion

Donor related adverse events viz. local reactions often present as haematomas. These are usually the result of faulty phlebotomy techniques leading to extravasation of blood. Present study reported an occurrence of 1.2 % of vascular injuries among all the plateletpheresis procedures which is similar to that reported by Barbosa et al. [1] and Philip et al. [1, 6]. Most of the vascular injuries were committed by the relatively inexperienced newly joined staff nurses or the technical staffs in the apheresis lab. Female apheresis donors suffering a higher incidence rate of adverse events in comparison to the male apheresis donors have been reported by Tomita et al. [7]. However, present study did not report incidence of any adverse events in all 18 female donors who underwent plateletpheresis procedures which may be a chance occurrence only.

Citrate related reactions associated with apheresis are common donor related mild adverse events which are transient and self-limiting [2]. This well-known phenomenon is the result of the chelation of ionised calcium by the citrate present in ACD [8]. We found 2.7 % of the reported citrate reactions that is higher than that reported by Philip et al. [6] but lower than that reported by Barbosa et al. [1] which may be attributed to administration of oral calcium tablets to the donors at the beginning of the procedures, difference in the donor characteristics, duration of the procedures and equipments used. McLeod et al. [4] reported 0.39 % of overall citrate reactions among donors undergoing apheresis procedures in his multi-institutional study. In accordance to Bolan et al., we administered mouth dissolving oral calcium tablets to these donors when they complained of paraesthesia/tingling or numbness sensations around the mouth or cramps in the fingers or

Table 1 Type of apheresis procedures stratified as per the equipments used

	Plateletpheresis	Therapeutic plasma exchange
MCS+	949	–
Trima	475	–
COM.TEC	284	32
Total	1708	32

toes while undergoing the procedures and found to allay the symptoms. However, Das et al. [8] reported insignificant effects of such interventions which may be because of the differences in the individual donor characteristics, the rate and amount of citrate infusion and the equipment used.

Systemic reactions are mainly VVRs, triggered by either the anxiety related to apheresis procedure or the apprehension of needle-prick [6]. Present study reported a higher incidence of systemic reactions in comparison to that reported by other authors, which may be attributed to our apheretic donor pool, consisted of only replacement donors [4, 6].

Equipment related problems can be multiple like air purge failures, variation in the AC ratio, changes in calibration of equipment [6]. Proper training modules for the technical personnel will curtail the incidence of such preventable events. In addition to this, routine maintenance visits by the system engineers will also be helpful. Defective kits can be due to excessive kinks in tubing, any breakage of separation chamber (detected as leakage from kits at the time of priming), or needle cap not in place. These can be avoided by proper inspection of the kits at the site of manufacturing as well as at the apheresis lab before installation.

Technical aberrations are one of the causes of adverse events in apheresis which can again be reduced by continued training of the technical personnel and under the supervision of the experienced transfusion medicine specialists.

We found the frequency of occurrence of adverse events to be 5.86 % while McLeod et al. reported an overall incidence of 2.18 % in their American study [4]. However, Patidar et al. from India reported a much higher incidence of adverse events in their study [5]. These differences may be attributed to the difference in the individual donor characteristics, the procedural differences, time duration for both the procedures and the time interval between two consecutive donations.

To conclude, though apheresis procedures are safe but are associated with adverse events which can be reduced by meticulous donor vigilance, superior training modules for the technical personnel and continued supervision of experienced transfusion medicine specialists. The adverse events may affect the apheretic donor pool; however, proper donor information materials to educate them will definitely help retaining these donors for further donations. Continued efforts towards making the donor's experience

with apheresis more pleasant gives a forward thrust to the noble vision of preparing a voluntary apheresis donor pool in India.

The effects of the demographic details of the individual donors and equipments on the occurrence of adverse events were beyond the scope of this audit-based study. However, further studies with larger sample size can be conducted to evaluate these factors in an Indian scenario which will pave the way for wider implementation of apheresis based platelet donations for providing better patient care.

Acknowledgments The authors thank Mr. Gyanendra Kumar Shukla for assistance in conducting this study.

Funding This study was not funded by any of the Grant or any other Govt./Non-govt. agencies.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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