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Plateletpheresis adverse events in relation to donor and plateletpheresis session profile

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Abstract:

INTRODUCTION: Increasing demand of platelet transfusions for patients has led to a trend in the increased use of automated blood collections. These share many of the same reactions and injuries seen with pooled platelets obtained from whole blood donation but also have unique complications.

AIMS AND OBJECTIVES: To study the adverse events (AEs) of plateletpheresis procedure and their relationship with donor and plateletpheresis procedure session profiles.

MATERIALS AND METHODS: This is a retrospective observational study conducted from January 2016 to December 2016. A two-hundred and thirteen (213) plateletpheresis procedures were performed after taking informed and written consent from the donor. All the donors were male and selected according to the guidelines laid down by Director General of Health Services. The AEs were classified into donor related, kit/equipment related and technique related.

RESULTS: A total of 13 AEs were noted; of which, 8 (61.53 %) events were associated with donors, 3 (23.07 %) were owed to fault in kit/equipment and 2 (15.384 %) were due to technical aberrations. Donor related AEs included vascular injuries [$n = 3$ (1.40%)], vasovagal reactions [$n = 2$ (0.938%)] and perioral tingling sensation [$n = 3$ (1.40%)]. Technique related AEs [$n = 2$ (0.938%)] and kit/equipment related AEs [$n = 3$ (1.40%)] were due to faulty technique and defective kits respectively.

CONCLUSION: Apheresis donations performed on cell separators are safe. Meticulous donor vigilance, superior technical personnel training and experienced transfusion medicine specialist's supervision will make donor's experience more pleasant.

Keywords:

Citrate reactions, donor adverse events, donor profile, plateletpheresis donation, vascular injuries, vasovagal reaction

Introduction

Over decades, increased demand of platelet transfusions for patients with various medical and surgical conditions led to accelerated use of technologically advanced "apheresis" for platelet concentrates.^[1] This has led to a trend in the increased use of single donor platelets obtained by automated blood collections. These collection methods not only share many of the same reactions and injuries seen with pooled platelets obtained from whole blood donation, but also have unique complications due to the collection

method and the frequency at which donation can occur.^[2]

Apheresis procedures are usually well tolerated, but adverse events (AEs) occur in a few cases. They may occur during or after the procedure. The overall rate of AEs with apheresis donation is approximately ten times less than that seen with pooled platelets obtained from whole blood donation, with mild events outnumbering the more severe ones, although the frequency of events requiring hospitalization may be higher in apheresis than with whole blood donation.^[3] Hospitalization is still extremely rare; it occurred in only 0.01% of donations.^[4] AEs

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associated with apheresis donation can be due to delivery of the anticoagulant, vasovagal, allergy, venous access, or machine malfunction. These can be of variable severity.

Aims and objective

To study the AEs of plateletpheresis procedure and their relationship with donor and plateletpheresis procedure session profiles.

Materials and Methods

This is a retrospective observational study which was conducted from January 2016 to December 2016 in the Department of Transfusion Medicine, Government Medical College, Patiala, Punjab, India. A total of 213 plateletpheresis procedures were performed on Trima Accel[®] after obtaining informed written consent from the donors. All the donors were selected according to the guidelines laid down by the Director General of Health Services.^[5] All the donors were of the age between 18 and 60 years, weighing >60 kg and were medically fit. Complete hemogram and ABO and Rh grouping of donors were done. All the donors had hemoglobin level ≥ 12.5 g/dl and platelet count $\geq 150 \times 10^9$ /L. Tests mandatory for transfusion-transmitted infections (HIV-1 and 2, hepatitis B virus, hepatitis C virus, syphilis, and malaria as per guidelines laid down by the Director General of Health Services of India^[5]) of donors were done prior to procedure and nonreactive donors were selected for the procedure. History of nonconsumption of nonsteroidal anti-inflammatory drugs in the past 72 h was taken. The AEs were classified into donor related, kit/equipment related, and technique related.

Donor-related adverse events

They were divided into local reactions and systemic reactions. AEs were classified according to severity into mild, moderate, and severe and according to etiology in a donor into hypotensive reactions, citrate reactions, hematomas, loss of consciousness, seizures, and allergy.

Hypotensive reaction

Hypotension during apheresis donation can result from a number of causes, including intravascular volume depletion, vasovagal reactions, citrate toxicity, and severe allergic reactions. Of these, the most common are vasovagal reactions and citrate toxicity. Symptoms and signs of a vasovagal reaction include lightheadedness, hot flushes, pallor, diaphoresis, nausea, vomiting, decreased heart rate, and decreased blood pressure. Preventive steps include helping the donor feel comfortable and confident throughout the procedure. This is especially important for first-time apheresis donors, as they are more likely to be anxious about the procedure.^[6] Treatment of vasovagal reactions

includes pausing the procedure, lowering the head and raising the feet of the donor (Trendelenburg position), applying cold compresses to the forehead and neck, and reassuring the donor. If moderate or severe symptoms are present, the apheresis procedure should be discontinued.

Citrate reactions

Citrate reactions are the most common adverse effects seen with apheresis procedures. They result from ionized hypocalcemia caused by the infusion of citrate anticoagulant during the procedure. The lowered ionized calcium levels allow spontaneous depolarization of neurons and resulting symptoms include numbness and/or tingling in the lips and nose and sneezing. Moderate symptoms include nausea and/or vomiting; progression of paresthesia to the hands, feet, and/or chest; intense vibrating sensation throughout the body; chills; abdominal cramping; and lightheadedness or hypotension. Severe symptoms include painful muscle cramps, tetany, blurred or double vision, loss of consciousness, cardiac arrhythmia, and seizure.^[3,7] These symptoms are usually progressive in adult donors, so moderate and severe symptoms can usually be avoided through close monitoring and treatment of earlier symptoms.^[3,7] Interventions for mild symptoms include reducing the return rate of the instrument or pausing the procedure to allow the donor to metabolize some citrate and release bound calcium. Additional treatments include administration of oral calcium carbonate or, in severe cases, an intravenous calcium solution.^[3,7]

Hematoma formation

Complications of venous access can occur at any time during an apheresis donation. Hematoma formation and thrombosis are among possible acute complications. Symptoms include pain and/or pressure and bruising and/or swelling at the needle site. If venous access fails during the procedure, the procedure may not be completed and the resulting physical discomfort may influence the donor's decision about donating in the future.^[6] Treatment includes discontinuing the collection, removing the needles, and applying pressure to the site. Since a major risk factor for these reactions is inexperienced phlebotomy staff, prevention strategies include maintaining apheresis personnel competency. Preventive strategies for donors include encouraging donors to be well hydrated before the donation and instructing them to keep the needle sites secure and stable during the donation.^[6]

Loss of consciousness and seizures

Loss of consciousness is uncommon and usually occurs as a result of a vasovagal reaction or severe citrate toxicity. It may be accompanied by tonic-clonic seizures; however, this does not represent true seizure activity.

Allergic reactions

Allergic reactions occur due to reaction to ethylene oxide used to sterilize the disposable set. They occur predominantly in donors who have donated several times. There is intense itching, widespread urticaria, hives or welts, rhinitis, wheezing, tongue or facial edema, shortness of breath, hypotension, diarrhea, laryngeal edema, and cardiopulmonary arrest. This is treated by prescribing antihistaminic and hydrocortisone/epinephrine.

Kit/equipment-related adverse events

These are secondary to improper disposable sets. These are hemolysis, thrombus formation, air embolism, leakage, infection, etc.^[7]

Technique-related adverse events

These are due to improper mounting of the set.

Results

All the 213 donors were male, out of which 136 (63.84%) were voluntary and 77 (36.15%) were replacement donors. Maximum donors (68.07%) were in the age group between 21 and 30 years, minimum age being 19 years and maximum being 60 years. The weight of donors ranged from 60 kg to 115 kg, maximum donors (47.88%) were in the 61–70 kg category; the mean donor height was 170 cm. The prevalent blood type was O positive, which accounted for 35.6% of the donations. The predonation mean hemoglobin and hematocrit values were 13.76 g/dl and 41.2%, respectively. The mean preprocedural platelet count was $281 \times 10^9/L$. In maximum donors (31.92%), preprocedural platelet count was between 201 and $250 \times 10^9/L$, preprocedural platelet count of donors ranged from 170 to $450 \times 10^9/L$.

Plateletpheresis session profile

In maximum donations 114 (53.52%) platelet yield was 3×10^{11} . In 32 (15.02%) donations platelet yield was

6×10^{11} . The mean amount of platelet yield estimated for collection was 3.83×10^{11} . With mean platelet yield of 3.83×10^{11} , mean post procedural platelet count reduction in the donor was $71.09 \times 10^9/L$. The mean volume of blood processed by the equipment was 2362 ml and the mean volume of the product obtained was 310 ml. The mean amount of Acid Citrate Dextrose (ACD) used during the procedures was 258 ml. The mean duration of a plateletpheresis session was 51.04 minutes.

With platelet yield of 6×10^{11} , the mean volume of blood processed by the equipment was 2792 ml, the mean volume of the product obtained was 428 ml and the mean amount of ACD used during the procedures was 310 ml. Donor who had maximum platelet count ($450 \times 10^9/L$) with platelet yield of 6×10^{11} , the volume of blood processed, ACD used during the procedures and duration of the run was less as compared to donor who had minimum platelet count ($260 \times 10^9/L$) with 6×10^{11} platelet yield [Table 1].

Adverse events

A total of 13 AEs were noted; of which 8 (61.53%) events were associated with donors, 3 (23.07%) owed to fault in kit/equipment, and 2 (15.384%) were due to technical aberrations. However, all the AEs associated with donors were mild and none of the donor was hospitalized in the study [Table 2].

Donor-related adverse events

- Vascular injuries were seen in three donors. Bruising was seen in only one donor while hematoma formation was seen in two cases who were first-time donors
- Vasovagal reaction was seen in two donors out of whom one donor was a teenager. Second donor was replacement donor and was reluctant in donating
- Citrate toxicity manifested as perioral tingling sensation was seen in three donors. In these donors, platelet yield was 6×10^{11} , ACD infusion was more. Oral mouth dissolving calcium tablets had been given to all the cases in routine to prevent hypocalcemia.

Table 1: Donor parameters of plateletpheresis session with a platelet yield of 6×10^{11}

Preprocedural platelet count ($n \times 10^9/L$)	Volume of blood processed in ml	Amount of ACD used in ml	Duration of run in min
450 (maximum platelet count)	1966	219	55
260 (minimum platelet count)	3627	390	70

ACD = Acid citrate dextrose

Table 2: Adverse events occurring during plateletpheresis

AEs	Type of AEs	Symptoms	n (%)
Donor related (3.75%)	Vascular injuries	Hematoma	2 (0.938)
		Bruising	1 (0.469)
	Citrate-related reaction	Perioral tingling sensation	3 (1.40)
		Vasovagal reactions	Light headedness, hot flushes, pallor, nausea
Kit/equipment related (1.40%)		Faulty kit	3 (1.40)
Technique related (0.938%)		Faulty technique	2 (0.938)
Total			13 (6.10)

AEs = Adverse events

Technique-related AEs included 2 (0.938%) events; due to low inlet pressure, donor line clamp was not opened on time.

Kit/equipment-related AEs included three defective kits (1.40%).

Discussion

The potential donor should meet several requirements to be accepted as a suitable candidate for blood component donation.^[8] Criteria such as hematocrit or hemoglobin levels, age, weight, and minimum platelet count are important for the safety of the donor.^[9] In this study, all the donors were male. Females did not fulfill the criteria for selection of apheresis donors. Most of the females were anemic, underweight, or had poor veins. Alloimmunization due to repeated pregnancies also make the females unfit for donation.^[10] Several studies show a common profile for donation, in which there are larger number of male donors.^[11-15] Some studies also show that men have lower rates of AEs compared to women in plateletpheresis donation. Another study also pointed out that only women were associated with complications related to the venipuncture.^[16] Weight or body mass is indicated as criterion to maximize plateletpheresis donation because higher platelet yields can be obtained from larger donors with higher blood volume.^[11]

In the present study, technique and equipment-related complications were more as compared to study conducted by Dogra *et al.*^[11] [Table 3]. Technique related complications can be reduced by superior training of technical personnel and strict follow-up of standard operating procedure. Kit/equipment-related complications were due to lot of defective kits. The whole lot of defective kits was replaced by the manufacturer.

The percentage of AEs among healthy donors undergoing plateletpheresis procedures in the present study was 3.7% which was lower as compared to the study by

Dogra *et al.*^[11] and Khajuria *et al.*^[17] and higher than the studies conducted by Philip *et al.*^[2] and McLeod *et al.*^[18] [Table 4]. This low incidence is consistent with the literature, which indicates that the plateletpheresis procedure was well tolerated by donors.^[11]

Vascular injuries

In this study, the frequency of vascular injuries in plateletpheresis was 1.30% which is similar to that reported in literature.^[1,2,17,18] These are usually due to faulty phlebotomy technique by inexperienced technical staff, the number of prior apheresis donations, and the anatomy at the venipuncture. Unlike citrate reactions, which are more likely to occur in repeat donors, the probability of bruising reduces with the number of donations.^[18,19]

Citrate-related adverse events

In this study, the frequency of citrate reactions was 1.4% which is almost equal in comparison to the study done by McLeod *et al.*^[18] and Philip *et al.*^[2] In the study conducted by Dogra *et al.*^[11] and Khajuria *et al.*^[17] citrate reactions were slightly more, i.e. 2.7% and 3.03%, respectively. In the present study, the mean volume of blood processed, the mean amount of ACD used, and the duration of run were more in donors with low platelet count as compared to donors with high platelet count with same platelet yield. This is due to the fact that machine has to process more blood volume with more infusion of ACD to donor to achieve the same platelet yield in donors with low platelet count, thus more AEs. These findings are consistent with the study of Mercan *et al.* who showed that donors who undergo the procedure repeatedly or for prolonged periods are susceptible to an accumulation of citrate as levels exceed the amount that can be metabolized by the body.^[19] Another study revealed that AEs occurred in apheresis procedures which took more time (mean: 77.1 min) and had a higher infusion of ACD (mean: 301.5 ml) compared to those without AEs.^[13]

Citrate can chelate magnesium as well as calcium. Divalent cations (iCa[+], TCa[+], TMg[+]) showed a statistically significant decline after donation ($P < 0.0001$).^[20] However, magnesium supplementation has not been shown to decrease mild citrate-related symptoms. Hence, prophylactic magnesium supplementation is not recommended for plateletpheresis donation. While we

Table 3: Comparison of adverse events in plateletpheresis procedure with other studies

	Donor related (%)	Equipment related (%)	Technique related (%)
Dogra <i>et al.</i> ^[11] (2017)	78.43	14.71	6.86
Present study (2017)	61.53	23.07	15.384

Table 4: Comparison of donor-related adverse events in plateletpheresis in various studies

Name of the study	Vascular injuries (%)	Citrate reactions (%)	Vasovagal reactions (%)	Overall adverse reactions (%)
McLeod <i>et al.</i> (1998) ^[18]	1.15	<1	0.39	2.18
Philip <i>et al.</i> ^[2] (2013)	1.6	0.96	0.09	2.72
Dogra <i>et al.</i> ^[11] (2017)	1.2	2.7	0.76	4.66
Khajuria <i>et al.</i> ^[17] (2017)	1.5	3.03	1.5	6.06
Present study (2017)	1.30	1.4	0.9	3.7

did not determine preprocedural ionized calcium level in the present study, Bolan *et al.*^[21] found an average fall in ionized calcium of 33% from baseline which produces the signs and symptoms of citrate toxicity. In our study, we prescribed mouth-dissolving oral calcium tablets to all the donors during the procedure. In the study conducted by Philip *et al.*,^[2] calcium supplementation was given in the form of 1 g capsules of calcium carbonate orally. The results of administration of oral calcium carbonate and its effects on citrate toxicity by Bolan *et al.*^[21] reported that the administration of 2 g of calcium carbonate was associated with a statistically significant reduction in the severity of paresthesia.^[21,22] The treatment of citrate reactions includes slowing the re-infusion rate, increasing donor blood-to-citrate ratio, oral calcium supplementation, and if required, giving intravenous calcium.^[4,23-25]

Vasovagal reactions

Vasovagal reactions may be attributed to apprehension due to mechanical and psychological factors. In our study, vasovagal reactions were almost similar to that of the study done by Dogra *et al.*^[1] while it was lower in the study conducted by McLeod *et al.*^[18] and Philip *et al.*^[2] and higher in the study done by Khajuria *et al.*^[17] In a study done by Tomita *et al.*^[14] examined that the incidence of vasovagal reactions among male apheresis donors and whole blood donors were 0.83% and 0.99% respectively. They also found that the incidence of vasovagal reactions increased with age among apheresis donors, unlike what has been reported with whole blood donors.

Conclusion

The AEs of plateletpheresis donation are relatively mild and easily treated. Meticulous donor vigilance, superior technical personnel training, and experienced transfusion medicine specialist's supervision will make donors' experience more pleasant, thereby promoting and preparing a voluntary apheresis donor pool in India.

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Conflicts of interest

There are no conflicts of interest.

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