Original Research Article

Adverse Events Encountered In Platelet Aphaeresis Procedure and Their Management: A Retrospective Study

SHORT TITLE OF PAPER

Adverse Events in Platelet Aphaeresis

Abstract

Background: Platelet aphaeresis is an essential procedure, which meets the demand of single donor platelets (SDP) effectively. The procedure is well tolerated by donors with fewer side effects. Adverse events in Platelet aphaeresis have been reported from as low as 0.32 to 6.81 %.

Aims and objectives: The aim of present study is to ascertain adverse events observed in a large cohort of platelet aphaeresis procedures and determining management strategies to resolve them.

Material and methods: This is a retrospective cross-sectional study, from January 2012 to May 2019 in Blood Bank, Department of Pathology, in a tertiary care centre in Central India. Donors for Platelet aphaeresis were selected based upon the standard criteria of National Aids Control Organization (NACO) guidelines 2017 and Platelet aphaeresis protocol. Leukoreduced SDP were collected by Haemonetics® MCS +, having Leukoreduction bag system. Adverse events encountered were noted and categorized.

Results A total number of 1600 Plateletpheresis procedures were conducted to prepare SDP and transfused to 1054 patients. In total, 24 out of 1600 plateletaphaeresis procedures reported adverse events (1.5%). Donor related adverse events were 16 (66.6%), Kit related 4 (16.66%) procedure related were 4 (16.66%). Three out of 24 procedures were terminated prematurely, 1 due to severe hypocalcaemia (ACD effect) in donor and 2 due to bowl leakage.

Conclusion: Platelet aphaeresis is a safe procedure for donors if done expertly while exercising caution. Adverse events reported are minimal and manageable.

Key words: Platelet aphaeresis, Adverse events, Donor

INTRODUCTION

Platelet aphaeresis has revolutionized the field of transfusion medicine since its introduction in 1970s. Platelet aphaeresis effectively meets the increasing demand of single donor platelet (SDP) units for medical and surgical indications. Platelet units are increasingly being transfused prophylactically to reduce the risk for spontaneous bleeding in patients post chemotherapy or bone marrow transplant [1, 2].

In the procedure of Platelet aphaeresis, platelets are collected from whole blood of donor in repeated cycles (Intermittent Flow system) by an automated system. The process is generally well tolerated by the donors; however, few adverse events have been reported when compared to whole blood donation [3, 4]. Adverse events in Platelet aphaeresis have been reported from as low as 0.32 to 6.81 % [5]. Adverse events can be attributed to effects of procedure on donors (venipuncture, citrate toxicity, vasovagal attacks), faulty aphaeresis kits (punctures and kinked tubing) or aberrancies in equipment functioning. Hospitalization of donor in as a result of Platelet aphaeresis is extremely rare and has been reported to be less than 0.01% [3].

The aim of present study is to ascertain adverse events observed in a large cohort of platelet aphaeresis procedures and determining management strategies to resolve them.

MATERIAL AND METHOD

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This is a retrospective cross-sectional study, carried out from January 2012 to May 2019 in Blood Bank, Department of Pathology, in a tertiary care centre in Central India. Donors for Platelet aphaeresis were selected based upon the standard criteria of National AIDS Control Organization (NACO guidelines 2017) [6] and Platelet aphaeresis protocol. Leukoreduced SDP were collected by Haemonetics® MCS +, which is an intermittent flow device along with leukoreduction bag system.

Adverse events encountered were categorized as follows:

1. ***Donor related adverse events*** –

a) *Vasovagal reactions*: nausea, vomiting, syncope, sweating, pallor, dizziness, weakness, and hypotension.

b) *Vascular injuries*: hematoma formation or bruising at venipuncture site.

c) *Citrate toxicity*:

- Mild: -Tingling sensation starting from perioral area.
- Severe - Loss of consciousness, convulsion, tetany and incontinence.

2. ***Kit related adverse events*** - Faulty or defective kit, comprising punctured or kinked tubing, leaking bowl etc.
3. ***Equipment related events*** – Due to improper mounting of the set or technical fault in machine.

Adverse events were noted by nursing/technical staff and reported to transfusion medicine specialist for proper management. Platelet aphaeresis procedure was completed successfully in most of the cases and only those cases in which donors were in danger or leakage in bowl was observed, were terminated prematurely.

In vitro platelet quality was assessed by manual swirling, volume, Ph (Ph meter) and estimation of hemoglobin, platelet count and white blood cells count by automated hematology cell counter. Minimum platelet count in a unit was not less than 3×10^{11}. Donors were screened for Transfusion Transmitted Infections

(TTIs) i.e. Human Immunodeficiency Virus (HIV) 1 & 2, Hepatitis B Surface Antigen (HbsAg), Hepatitis C Virus (HCV), malaria and VDRL, prior to procedure.

Patient demographic, indication for platelet transfusion and post transfusion platelet rise were also noted.

Donor's data; age, sex, height, weight, hematocrit, pre & post donation platelet count were recorded. All data was compared statistically using Epicalc version 2000 software.

RESULTS

A total number of 1600 Plateletpheresis procedures were conducted to prepare SDP and transfused to 1054 patients, minimum 01 and maximum 09 with an average of 1.52 transfusions/ patient. In the study, age of the donors varied from 18 to 60 years and average age of donors was 35.10± SD 5.04 years. Male: female ratio of donors was 19:1. Pre donation platelets of donors varied from 150 x 10^3 to 400 x 10^3 / cumm. The average pre and post donation platelets/ cumm of donors was 256.96 x 10^3 ± SD 10.9 X 10^3 and 210.08 x10^3 ± SD 11.7 X10^3 respectively with an average fall of platelets /cumm was 55.10X 10^3 ± SD 10.11x10^3. Platelet yield of SDP was observed 3.0 x 10^{11} to 3.6 x 10^{11}/ unit, in 5-6 cycles of aphaeresis procedure (Table 1). Directed donors bought in for specific patient by patient's relatives comprised 80% (1280/1600) and 20% were prelisted voluntary donors.

In the study, age of the patients varied from 3 to 81 years. Average age of the patients was 30.09 ± SD 13.14 years while male: female ratio of the patients was 2:1. Pre transfusion platelets of the patients varied from 2.3 x10^3 to 75 x10^3 /cumm. Average pre and post transfusion platelets/cumm of patients was 22.01 x10^3 ± SD 14.08x10^3 and 60.02x10^3± SD 12.6x10^3 respectively, with an average increment of 34.04 x10^3 ± SD 8.85x10^3/ cumm (Table 1).

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With these general data, could be justified the emerging disorders by the donors.

A total number of 1600 SDP transfusions given in the study, clinically belonged to; dengue- 1136 (71%), malaria- 96 (6%), malignancy- 176 (11%), aplastic anemia- 64 (4%), immune thrombocytopenic purpura -16 (1.0%), liver disorders- 32 (2%), neurosurgical – 16 (1%), active bleeding- 32 (2%) and miscellaneous- 32 (2 %) (Figure 1).

Table 1. Donor and patient demographics

VARIABLE	DONOR	PATIENT
Mean age	35.10± SD 5.04 years	30.09 ± SD 13.14 years
Male : Female ratio	19:1	2:1
Mean pre - donation platelet count / cu mm	256.96 x 10^3 ± SD 10.9 X 10^3	22.01x10^3± SD 14.08x10^3
Mean post- donation platelet count/ cu mm	210.08 x10^3 ± SD 11.7 X10^3	60.02x10^3± SD 12.6x10^3
Average change in platelet count/ cu mm (Fall/Rise)	Fall - 55.10X 10^3 ± SD 10.11x10^3	Rise - 34.04x10^3 ± SD 8.85x10^3

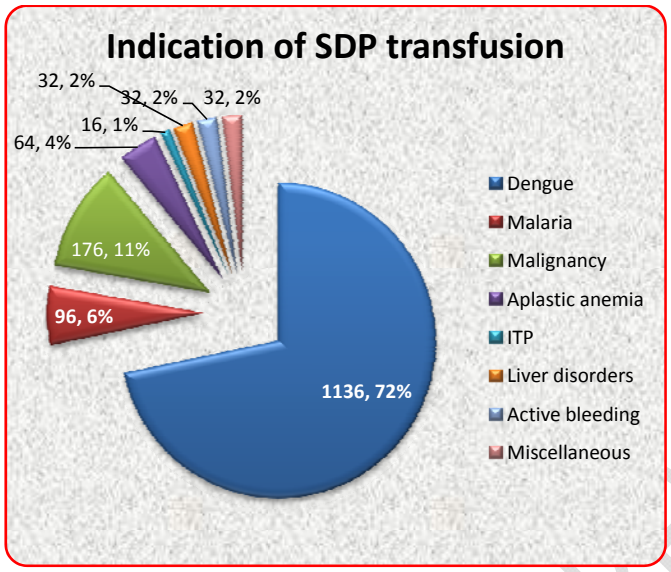

Figure1. Distribution of indications of Single donor platelets by platelet aphaeresis in patients.

In our procedure, donors selected were 86% identical and 14% were compatible for ABO RhD blood group of the patient.

In total, 24 out of 1600 platelet aphaeresis procedures reported adverse events (1.5%). Adverse events are categorized and summarized in Table 2.

Table 2 . Adverse events encountered in platelet aphaeresis procedures.

Adverse events	Type of complication		Number / %	Outcome of Procedure
Donor related 16 (66.6%)	Venipuncture injury		4 (16.66%)	**C**
	Side effects of ACD	Mild	8 (33.33%)	**C**
		Severe	1 (4.16%)	**T**
	Vasovagal complication		3 (12.5%)	**C**
Kit related 4 (16.66%)	Bowl leakage		2 (8.33%)	**T**
	Tube leakage		2 (8.33%)	**C**
Procedure related 4 (16.66%)	ACD drip monitor disabled		1 (4.16%)	**C**
	Air detected		1 (4.16%)	**C**
	RBC spillage		1 (4.16%)	**C**
	Low/high SPM/ DPM		1 (4.16%)	**C**

C- Procedure completed, T- procedure terminated, ACD – Acid citrate dextrose, SPM – system pressure monitor, DPM- donor pressure monitor.

DISCUSSION

Advent of newer advanced techniques is marred with emergence of adverse events and complications; Plateletpheresis is no exception to it. Platelet aphaeresis is although a safe and well tolerated procedure for donors, however, now and then undesirable events emerge as a challenge. We reported an incidence of 1.5 % adverse events in plateletaphaeresis procedure. This falls within the acceptable range reported in other studies [5] while higher incidence (6.06%) was reported by Khajuria K *et al* 2017 [7]. These complications vary according to the donor profile

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and machine system. Proper attention and careful monitoring can, to some extent, prevent such occurrences and lead to 100% success in platelet aphaeresis procedure, especially in technique and machine related faults. However, donor related adverse events are unavoidable and constitute majority of total adverse events encountered in platelet aphaeresis [8, 9].

- Deeply situated, thin veins and irregular vein course in donors can be assessed during donor selection prior to initiation of procedure and expertise in phlebotomy can prevent bruising and hematoma at venipuncture site. We encountered 4 (16.66%) such cases with difficult phlebotomy within the range of results of other studies in which vascular injuries varied from 1.51% to 19.6 %. (9, 10). All such 4 donors in our study were managed by changing the site of venipuncture mid procedure, preferably in opposite arm, and local treatment of injury.

- Citrate related reactions in donor are attributed to chelation of calcium in donor blood by acid citrate dextrose (ACD) solution. The reaction can be mild leading to perioral tingling, to severe, resulting in muscle cramps, tetany, blurred or double vision, loss of consciousness, cardiac arrhythmia, and seizure [4, 10]. Mild symptoms are usually observed in return phase of an aphaeresis cycle, when extracorporeal blood mixed with ACD is transfused back to patient. In accordance with other studies by Philip et al [11] and Bolan et al [12], it is a protocol in our blood bank to supplement donor by 500 mg elemental calcium per cycle of platelet aphaeresis procedure to prevent hypocalcaemia. Despite this practice we reported mild perioral tingling in 8 donors who were managed by slowing the rate of reinfusion of blood in return phase of cycle and careful observation. The symptoms resolved spontaneously during the draw phase of aphaeresis cycle. One donor showed Trousseau sign of latent tetany (eliciting carpal spasm by inflating the blood pressure cuff and

maintaining the cuff pressure above systolic) and Chvostek's sign (tapping of the inferior portion of the cheekbone producing facial spasms) in 4th cycle during return phase. Loss of consciousness and generalized muscle spasm followed. The procedure was terminated prematurely and donor was managed with intravenous calcium and saline administration. Theses citrate related complications are well documented and incidence in our study coincide with result of other studies [8].

- Vasovagal response in donors encountered in aphaeresis procedure is mainly attributed to anxiety, fear and apprehension to needle prick and prolonged procedure. We reported a high incidence (12.5%) of anxiety and fainting of donors during the procedure mainly because of more inexperienced directed donors as compared to voluntary donors which were well acquainted with the aphaeresis procedure. Similar results (12.73 % incidence of vasovagal reactions) were reported by Dogra et al [8], however , lower incidences have been reported in other studies [11]. The 3 donors in our study who experienced vasovagal symptoms like sweating and fainting, were managed conservatively and the procedure was completed after due encouragement and reassurance. We did not report any case of frank hypotension in donor leading to discontinuation of aphaeresis in our study.
- Although single use disposable kits for platelet aphaeresis procedure undergo strict quality control and are assumed to be devoid of any manufacturing defects, we encountered four such kits with two having punctures in tubing and two with leakage in bowl/separation chamber . Similar manufacturing defect in separation chamber, leading to a complication in the procedure, was also reported in other study [8]. In our donors, the leakage in separation chamber/ bowl was caught early in the procedures and was terminated without much blood loss of donors. In 2 cases in which the tubing was punctured, the entire

kit was replaced, retaining the venipuncture (detachable needle), and aphaeresis procedures were completed successfully.

- Minor complications arising during procedure because of improper installation of kit and kinking and knotting of tubing were avoided in our study because of specialist's supervision. Other procedure related adverse events like air detected in system, low or high SPM/DPM or disabled monitors were managed as instructed in equipment manual.
- RBC spillage in platelet collection bag was carefully monitored in all the procedures and was avoided by careful vigilance, except for in one case.

CONCLUSION

In our study, adverse events during platelet aphaeresis were reported to be 1.5%, so we can say that platelet aphaeresis is a safe procedure for donors, if done expertly while exercising caution. Adverse events reported are minimal and manageable. Hemonitics MCS + was found to be patient as well doctor friendly.

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Comment [U5]: Verify: The data of the publications must be unified:

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