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RESEARCH ARTICLE

EVALUATION OF A CELL SEPARATOR FOR EFFECTIVENESS IN THE COLLECTION OF APHAERESIS PLATELETS IN A TERTIARY CARE HOSPITAL

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ABSTRACT: Platelet (PLT) transfusions play a vital role in the management of patients with thrombocytopenia or severely impaired platelet function. Platelet concentrates derived from aphaeresis are preferred in a clinical setting to have lesser alloimmunization rates in patients. There are several aphaeresis machines i.e. cell separators available from different manufacturers that differ in their design, principles, and parameters that ultimately affect the final product. We evaluated an aphaeresis instrument, the Haemonetics MCS + concerning platelet yield, collection efficiency (CE), and collection rate (CR) in a retrospective observational study in 309 donors. The Haemonetics MCS + cell separator efficiently collected apheresis platelets with median PLT yields of 3.63×10^{11}, mean CE of 38.12% ± 11.9% and mean CR of $0.059\pm 0.011 \times 10^{11}$/min. The median blood volume processed was 2654 ml (1293-3940), and the median volume of acid citrate dextrose-A (ACDA) used in collections on the device was 323 (171-455) ml. Also, this device allowed the collection of white blood cell (WBC) reduced platelet-aphaeresis with mean $0.37\pm 0.27x10^6$ WBC content. No serious donor or recipient reactions occurred however minimal adverse reactions encountered during procedures and well managed and tolerated by donors without any hesitations for future donations.

KEYWORD: Haemonetics MCS+, Collection rate, collection efficacy, platelet yield

INTRODUCTION:

The collection of different blood components using cell separators by aphaeresis technique has become common in the field of modern transfusion practices. One such Component is aphaeresis platelets commonly called as Aphaeresis Platelets Concentrate (APC) or Single Donor Platelets (SDP), which has been used in a wide variety of clinical conditions viz. malignancies, supportive therapy for chemotherapy/ radiation, infections like dengue, malaria, and sepsis, indications in neonates, massive transfusion and Disseminated Intravascular Coagulation (DIC).[1]

A wide variety of cell separators are available which differ in their design, features, and working principle. The Hemonetics MCS + cell separator (Manufacturer-Braintree, MA, USA) has been used widely for the collection of leukoreduced platelet mainly (as per manufacturer 3-4 log leuko-reduction). Leukoreduced platelets can be used to reduce platelet alloimmunization, cytomegalovirus (CMV) transmission, and febrile transfusion reactions (FNHTR).[2] However, very few studies have been conducted to evaluate the effectiveness of devices.[3, 4, 5, 6] These studies have reported the relationship for

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platelet (PLT) yield, collection rate (CR), and adverse reactions of different aphaeresis systems for evaluation of efficacy. These studies have done a prospective paired comparison over a period to work out the best aphaeresis protocol for different donors and various aphaeresis types of equipment. However, the above-reported studies were mostly conducted in western countries considering their donor demographics.

However, in India, considering the overall population, the donor parameters differ from the western and so a suitable cell separator selection is in question.

Moreover, blood donation guidelines in India and the standards of platelet aphaeresis donation are comparatively different from the other western countries.[7, 8] There may be certain minor changes too in different institutes as per SOPs to overcome a shortage of donors and high demand for products. Therefore, the effects of certain parameters including PLT yield, weight, body mass index (BMI), and Haematocrit (Hct) on platelet-aphaeresis in India may differ from the others. When procuring a new device for use in the routine production system, it is important to assess its performance with regards to cell collection efficiency, collection rate, and processing time. An additional important aspect is the ability to improve donors' experience in terms of donation time and adverse effects during procedures. Therefore, the reported study was conducted at our Department to evaluate the efficacy and feasibility of the MCS+ Cell Separator. The Aims and objectives of the study were -

I. To assess the efficacy of cell separator for collection of SDP in terms of Collection efficacy (CE), Collection rate (CR), and platelet yield (set yield versus actual yield)

II. To check for the Log reduction of leucocytes in collected products

III. To assess the suitability of cell separator for collection of SDP in a tertiary care center in terms of need of patient care and clinical benefits in terms of quality parameters viz. platelet yield, volume, and leukoreduction in the collected product if satisfactory.

MATERIALS AND METHODS:

Donors:

In this observational retrospective study around 309 platelet-aphaeresis procedures were evaluated. These procedures were performed on Haemonetics MCS + cell separator conducted at Department of Transfusion Medicine, Seth G S Medical College and KEM Hospital, Mumbai over a period of 1 year. The data collection and processing protocol was approved by the IEC (Institutional Ethics Committee) of our institute.

All prospective platelet donors were informed and counseled before the procedure. Those who met the criteria of donation as per DGHS and departmental SOP were screened for Complete Blood Counts (CBC) and Transfusion Transmitted Infections (TTI) status. Donors who were fit for the donation were taken for aphaeresis procedure under medical supervision.

The basic criteria for eligibility for collection of SDP were: Age 18-50 years, Weight >= 55kg, Hb level > 12.5 g/ dL, pre-aphaeresis PLT counts >= 150 x 10^9/L, negative for TTI screening (HIV1, 2, HBsAg, HCV, malaria and syphilis), in good health without any illness, 3 months since last whole blood donation, good venous access and no consumption of NSAIDs/ Aspirin in past 3 days of procedure [9]. Donors having PLT count > 250 x10^9/L with the weight of >= 65 kg were eligible for double volume product collection as per DGHS guidelines and institutional SOP. Senior aphaeresis technicians and resident doctors performed all procedures under the supervision of senior residents or teachers. Antecubital veins were used for venipuncture in all the donors. Vital signs were monitored at the beginning and end of each procedure; donors were

also monitored for adverse events during the procedures.

Device:

Hemonetics MCS + cell separator, a single needle system, was evaluated. It is based on the principle of Intermittent Flow centrifugation (IFC). For Haemonetics MCS plus - Extended storage platelet/ plasma aphaeresis set REF 995 E.A. and a centrifuge bowel of 125mL was used. Different parameters were evaluated for the device like Whole blood flow rate, interface set point, anticoagulant/ whole blood ratio. All the above mentioned parameters were calculated by following reported formulae [10]:

1. Collection efficiency (CE) = Total PLT yield (10^{11}) X 100 / (Pre-aphaeresis PLT count + Post-aphaeresis PLT count /2) X Blood Volume processed

[Where Blood volume processed = TBV processed – ACD (mL)]

2. Collection Rate (CR) = PLT yield/ separation time.

3. Leukoreduction was evaluated by comparing the residual number of leukocytes in APC done on an automated cell counter (Sysmex XT) after it was collected. The number of leucocytes/µL X Total volume of product will give the actual number of residual leucocytes in the SDP.

Statistical analysis

A descriptive analysis was performed to summarize and report the results. Normal distribution of the values was tested using the Kolmogorov–Smirnov test, and homogeneity of variance was tested using Levene's test. Qualitative variables were treated as absolute numbers and frequencies and continuous qualitative variables as median (range) or mean +/- SD. The level of significance was set at $p< 0.05$ to compare pre and post aphaeresis parameters. Statistical analyses were performed using SPSS (the statistical package for social sciences) IBM Corp. Released in 2017.

OBSERVATIONS AND RESULTS:

In our study of 309 procedures, there was only one female donor who met CBC criteria for the donation of SDP. Donors' demographics and laboratory investigations are mentioned in Tables 1 and 2 for pre-procedure and post-procedure viz. CBC counts and procedure-related parameters. There were no significant differences in pre-and post-aphaeresis Hb levels and PLT counts (loss of 15.2% from the pre-procedural count; which is normal as per standard guidelines of DGHS). As per our routine quality control procedure, we test for aphaeresis platelet products as 1% of collections or 4units/ month (NABH guidelines). So the mean residual WBC counts in the product were observed in (N=71units) which was 0.377 X 10^3/ µL, which provided 3 log reduction. The median blood volume processed to reach a PLT yield $\geq 3 \times 10^{11}$ was 2654 (1293- 3940) mL. Also, the median volume of ACD used in collections on the device was 323 (171-455) mL. The median PLT yield was 3.63 (2.5-7.3) $\times 10^{11}$.

Additionally, mean CE was 38.12 ± 11.9 % (08-77%; only one procedure with 8% CE due to hypotension in donor procedure was aborted with a yield of 1.6 and volume of 124 mL collection) and mean CR of 0.0519± 0.011x 10^{11}/ min. Also, the mean WBC content was 0.377± 0.27 x10^6. RBC content in all products was less than set guidelines of less than 0.5mL.

Adverse effects of Plateletpheresis

There were very few complications during and after the procedure. Most of them were mild. The incidence of hematoma was 2% (n=6), signs and symptoms of hypocalcemia in form of peri-oral tingling sensation were 14.56% (n=45) and hypotension 0.67 % (n=2). All ADRs were well

managed by resident doctors, nurse and staff present during the procedure. All reactions responded to decreased flow rates and/or calcium supplementation.

Table 1. Donors' characteristics and laboratory investigations: pre-and post aphaeresis procedure

Sr. No	Variables	Values
1	Gender (Male/ Female)	308/1
2	Age (Years) [a]	32.3 ± 8.03
3	Height (cms) [b]	(Mean 170) (151-181)
4	Weight (kg) [a]	Mean 75.5 ± 10.4
5	Hemoglobin (Hb)pre-procedure (gm/dL) [a]	14.7 ± 0.9
6	Hemoglobin (Hb)post procedure (gm/dL)[a]	14.6 ± 0.92
7	Platelet count pre procedure (X 10^3/ µL)[b]	283 (184-465)
8	Platelet count post procedure (X 10^3/ µL)[b]	240 (158-416)
9	WBC pre procedure(X 10^3/ µL)[b]	7.2 (3.3- 11.5)
10	WBC post procedure(X 10^3/ µL) (n=71)[b]	4.8 (0.1 – 9.6)
11	RBC (X 10^6/ µL) [a] contamination in APC	1.62 ± 0.84
12	Hematocrit (%) [a] of donors	44.53 (44.2- 44.85) ±2.9
13	pH of APC (N=71)[b]	7.3 (6.7-7.7)

a = Mean +/- SD;
b= Median (range);
WBC = white blood cell

Table 2. Plateletpheresis procedure and product data

Sr no	Variable	Median	Range
1	Blood volume processed (mL)	2654	(1293-3940)
2	ACD-A volume (mL)	323	(171-455)
3	Separation time (min)	75	(53-130)
4	Product volume (mL)	257	(124- 447)
5	Platelet yield (×10^{11})	3.63	(2.5-7.3)

DISCUSSION:

There is a continuous improvement in technologies of cell separators in Transfusion Medicine field for efficiently collecting targeted blood components and donor-friendly equipment. Manufacturing companies constantly try to improve their devices to have the best possible outcomes. As it is said "one size does not fit for all", we tried to evaluate the device for our Indian population, as Indian donor demographics are different from those of western countries.

These reported findings were compared with the literature. Our donors needed a little higher time (average 75 minutes). This might be due to the lesser height and weight of Indian donors and a safer approach of keeping a slow flow rate during the procedure to have minimal side effects during or after the procedure. This is different compared to other studies in literature where there is lesser time. [10]

There is little data concerning platelet apheresis with the Haemonetics MCS + device. [3, 6, 10, 17, 18] Ranganathan et al [15] reported that the CE was 50–52% with the Haemonetics device. In that study, blood volume processed was 3200-3400ml. A similar study by Kekik et al [10] revealed processed blood volume of 3290 mL while a median of blood volume processed in our study was i.e. 2654 mL with a range of 1293-3940. This wide range can be explained as, due to the wide range of donors' eligibility parameters viz. weight, height (and so body surface area) and their median platelet count of 283 with a wide range of acceptance of 184-465 that is related with the volume to be processed to achieve final product as per established guidelines (DGHS and NABH) and SOP stated before. This also explains the wide range of time 53-130 min needed for donors to complete the procedure with a median of 75 minutes. Also, for few donors, the medical personnel used a safe strategy approach of keeping the draw and return flow rates slow to take care of adverse effects like hypocalcemia and

hypotension that were tolerated by donors. This was usually observed with apprehensive donors. Salvadori *et al* [16] reported in their study with Haemonetics that CE and CR were comparable with the literature (58.2% and 0.065 × 1011/min. respectively). On the other hand, in that study, the blood volume processed was even lower (2583 mL).

Table 3. Comparative Mean values (with SD or ranges) of different variables in plateletpheresis procedures on Hemonetics MCS plus from different studies:

Study	Sr. No	Study name	Pre-procedure platelet count (platelet count x 10^3/cm)	Platelet yield in the product (SDP) (Platelet yield x 10^{11})	Product volume (mL)	Blood volume processed in procedure (mL)	Collection efficiency (%) Or Collection rate (PLT x 10^{11}/ min)	Time taken for collection (Minutes)
Indian studies	1	Swarup et al [23] **N=40**	244.725	3.33	235.92	2501.97	65.49	71.47
	2	Sheikh et al [24] **N=20**	292 ± 39.7	3.54 ± 0.19	306 ± 19.5	1922 ± 86.7	47.6 ± 13.6	91.15 ± 1.1
	3	Choudhary et al[25] **N=67**	207.8±4 0.7	2.81± 0.72	269.8± 23.7	2917.5± 521.1	59.3± 8.9	126.5± 22.1
	4	Patel et al[2] **N=107**	301 ± 70.6	5.27 ± 1.48	380.46 ± 79.594	3,775.1 ± 432.5	47.38 ± 16.25	-
	5	Ranganathan et al [15] **N=100**	284.91 ± 26.374	-	-	3200–3400	50–52	74.5± 3.12
	6	M Keklik et al [10] **N=60** (Turkey)	269 (160–381)	4.4 ± 0.8	-	3418.20 ± 673.44	59.50 ± 19.44	59.73 ± 8.24
Worldwide studies	7	Bueno et al [26] N=51(Spain)	237 (173-324)	3.64 (0.13)	270 (1)	3072 (1)	CE=64.5 (2.2) CR=0.051 (0.002)	74.3 (2.5)
	8	Noha et al [27] N=40 (Egypt)	262 ±35	5.28± 1.18	410.6± 72.14	-	CE- not calculated CR= 0.06±0.02 PLT x 10^{11}/ min	87.4± 9.7
	9	M Keklik et al, [28] **N= 526** (Turkey)	245 (164–425)	3.7 (3–5.7)	400 (200–450)	3290 (2420–4370)	66.69 ± 13.73%	63 (45–83)
	10	Our study **N=309**	283 (184-465)	3.63 (2.5-7.3)	257 (124-447)	2654 (1293-3940)	38.12	75 (53-130)

Our study on Haemonetics MCS provided comparable PLT yields, CE, and CR (3.63 × 10^{11}, 38.12%, and 0.052 × 10^{11}/min, respectively).[6,14,16] Also, our CR results (0.052 × 1011/min) were similar with the reported averages of 0.052–0.065 × 10^{11}/min.[1, 5, 13, 14]

We evaluated the WBC and RBC content in collected products. White blood cell reduction in PLT components prevents the side effects of WBCs, such as alloimmunization, febrile nonhemolytic transfusion reaction, the transmission of infectious agents, and PLT storage lesion. [17-20] Burgstaler *et al* showed that the WBC content was low (0.33± 0.24 × 10^6) with the Haemonetics MCS. [21] Likewise, Moog and Muller [22] reported that in their study, in-line filtration with Haemonetics resulted in the best WBC reduction (0.08± 0.17 × 10^6) while Keklik [29] showed 0.07± 0.15 × 10^6.

RBC contamination as per established guidelines (NABH) should be traces to less than 0.5mL to prevent adverse transfusion reaction related to RBCs and also sensitization. Our products showed minimal WBC and RBC contents which is still acceptable from the clinical point of view. [11] Table 3 shows comparable results for different variables from different Indigenous and worldwide studies. Our study highlights aspects of large sample size, less donor adverse reaction, comparative concentrated products avoiding more volume to recipients, adequate platelet yield in SDP products as per DGHS guidelines. A comparative less collection efficiency can be explained as the inclusion of few high yield products (n=62) and very few products having inadequate yield (n=3) in analysis. These 03 low yield products were still utilized as half or full dose (yield= 1.7-2.5 x 10^{11}) to patients considering their less yield and volume which is a well-accepted practice.

CONCLUSIONS:

PLT yield and CE have been widely referred to as an important factor for considering the suitability of

a cell separator in both blood banks and donors, and ultimately to transfused recipients for therapy purposes. Our products showed compliances for said factors.

Certain studies were carried out with devices having in-line filtration to get the best results for WBC reduction. However, in developing countries like India procuring such advanced devices and establishing them for use in government hospitals, need large multicentre data for their suitability. We hope that our data will guide in selecting equipment for apheresis units for different blood banks, considering their donor pools and need of the hospital.

Considering our derived results from study and donor demographics, the Haemonetics MCS+ system can be considered as well established and an effective automated platelet collection system for the production of leukoreduced apheresis platelets especially in government setups where the choice for selecting a cell separator is difficult. In future, similar to platelet collection other cell components viz granulocyte, red cells, hematopoietic stem cells harvesting procedures will be evaluated that will help in establishing protocol for Indian population. We intend to compare different cell separators from different manufacturers and to conduct multicenter studies to get best suitable protocols.

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