Original Article

Transfusion Effect of Single and Random Donor Platelets in Thrombocytopenic Pediatric Patients with Hematological Malignancy at Tertiary Care Hospital

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Abstract

Background

This study was performed to assess differences between Single Donor Platelets (SDP) and Random Donor Platelets (RDP) by evaluating the platelet increment in the form of corrected count increment (CCI), platelet transfusion reaction rates, and the development of refractoriness after multiple platelet transfusions.

Material and Methods

In this two-year prospective study performed at a tertiary care hospital, dose response to platelet transfusions was studied in 68 newly diagnosed pediatric patients with hematological malignancies admitted for induction chemotherapy. The study was divided into three groups based on the type of platelet transfusion received: RDP group: Patients who exclusively received Random Donor Platelets. SDP group: Patients who exclusively received Single Donor Platelets. RDP+SDP group: Patients who received both RDP and SDP. Statistical Analyses Used: Chi-Squared test.

Results

CCI at the end of one hour (1-HR) and 24 hours (24-HR) was significantly greater in the SDP group (p-value 0.0003 and 0.0001, respectively), showing better platelet count increment after SDP transfusion. In the SDP group, the increments after the first and last transfusions were in the same range, whereas in the RDP group, the increments decreased from the first to the last transfusion. Thus, the use of SDPs postponed refractoriness. Maximum cases of the RDP group showed platelet refractoriness (50%), of which 76% were refractory due to an immune cause. The majority of acute platelet transfusion reactions were seen in the RDP group (38.98%), with the most common reaction being febrile non-hemolytic transfusion reaction.

Conclusion

The SDP group showed a better response to platelet transfusion than the other groups (RDP group and RDP+SDP group).

Keywords:

SDP, RDP, Corrected Count Increment, Refractoriness

Introduction

Both single donor platelets (SDP) prepared by apheresis and random donor platelets (RDPs) prepared from whole blood donations are indicated to treat acute hemorrhage secondary to thrombocytopenia or to provide prophylaxis from hemorrhage in leukemia patients. However, there is little information about what is the best platelet product to be transfused—RDPs or SDPs—and whether platelets should be plasma-suspended or additive solution-suspended [1]. Platelets are often transfused without respecting ABO compatibility, but the influence of this practice on platelet transfusion outcomes is not well established. A challenging complication arising from multiple platelet transfusions is platelet transfusion refractoriness [2]. Platelet transfusion refractoriness has several adverse effects, such as increased bleeding risk, longer hospital stays, and increased morbidity and mortality [3].

In this study, we examined the effects of transfusion of RDP and SDP in pediatric leukemic patients, focusing on the platelet count increment in the form of corrected count increment (CCI), platelet transfusion reactions, refractoriness to platelet transfusion after multiple transfusions, and the efficacy and safety of SDP and RDP.

Materials and Methods

This prospective study was conducted from June 2016 to June 2018 at the Blood Bank and Pediatric Department of LTMMC & GH, Mumbai, after obtaining institutional review board approval from the same institute. The study aimed to review, analyze, and determine if there were differences between apheresis platelets or single donor platelets (SDPs) and platelets derived from whole blood or random donor platelets (RDPs) for outcomes in the form of: Corrected count increments (CCI) as an indicator of platelet transfusion response, Platelet refractoriness and Acute reactions to platelet transfusion.

We studied the dose response to platelet transfusions in 68 newly diagnosed pediatric patients with hematological malignancies admitted for induction chemotherapy. Each patient was in almost similar clinical conditions.

Inclusion criteria: All male and female thrombocytopenic patients under 15 years of age scheduled to receive induction chemotherapy for hematological malignancies who had not received transfusions of blood or blood components before entering the study were included.

Exclusion criteria: Patients above 15 years of age, patients who had completed induction chemotherapy, patients who died during induction treatment, and patients receiving heparin or antithrombotic drugs were excluded.

RDP was prepared by platelet concentrates derived from whole blood by the PRP (platelet-rich plasma) method. Single donor platelets were harvested from one random single donor.

After obtaining informed consent from guardians, patients were randomly assigned to receive two types of platelet transfusion (SDP and RDP). SDP transfusion was done based on its availability. After their first platelet transfusion, they were followed up for eight weeks to check for platelet transfusion response, development of platelet refractoriness, and acute reactions following platelet transfusion. The study was divided into three groups based on the type of platelet transfusion received: RDP (random donor platelet) group: exclusively received RDPs, SDP (single donor platelet) group: exclusively received SDPs, RDP+SDP group: received both products (RDPs + SDPs).

Criteria used to check for response to platelet transfusions: After completion of the transfusion of the last platelet unit in each episode, platelet count was checked at 10-60 minutes (1-HR) and 18-24 hours (24-HR) after transfusion. Transfusion responses were expressed as “corrected count increment (CCI)” to evaluate the post-transfusion increment. The corrected count increment

was calculated as the difference between the platelet count within an hour after transfusion and the platelet count before transfusion, multiplied by the body-surface area (in square meters) and divided by the number of platelets.

$$CCI = \frac{Platelet\ increment\ per\ \mu L\ x\ Body\ surface\ area\ (Kg/M^2)}{Total\ number\ of\ Platelet\ transfusions\ x\ 10^{11}}$$

$$Mean\ CCI = \sum \frac{CCI}{N}$$

N= total number of transfusions

Response to platelet transfusion: Each unit of random donor platelets (RDP) contains 5.5 x 10^10 platelets, so 5-packs of random donor platelets contain 2.75 x 10^11 platelets/unit. A single donor platelet pack contains 3 x 10^11 platelets/unit. The expected platelet recovery 10-60 minutes after platelet transfusions should be at least 30% of platelets transfused. The expected platelet recovery at the end of 24-HR should be at least 20% of platelets transfused. A one-hour count less than 30% of expected platelet recovery, or a 24-hour count less than 20% of expected platelet recovery, represents an inadequate response to transfusion. CCI between 10-60 minutes and at the end of 24-HR post transfusion is typically used to determine the adequacy of response to platelet transfusions [3].

In our study, the average body surface area (BSA) calculated was 1.09 kg/m^2. The average platelet transfused was 2.5 x 10^11 platelets/L. The cut-off calculated was 7.5 x 10^9 platelets/L. Platelet refractoriness is defined as a CCI less than expected for at least two sequential platelet transfusions at the end of 1-HR or 24-HR or both [4]. In our study, patients were considered to be platelet refractory if they had 2 serial 1-HR post-transfusion CCIs of less than 3500 or 24-HR post-transfusion CCI of less than 2500. Cell counts of the platelet products were performed by automated cell counter- Sysmex Automated Hematology Analyzer, after all processing was completed. Certain clinical conditions like fever, sepsis, splenomegaly, and DIC that might influence a patient's response to a platelet transfusion [5] were recorded for all study patients from the data available from the patients' files. Causes of platelet refractoriness were grouped into immune and non-immune causes. In our study, a CCI ≤3500 at the end of 1-HR was classified under an immune cause [6]. Whereas a CCI ≤2500 at 24-HR after a normal CCI at 1 hour was classified under a non-immune cause [7].

Occurrence of Acute Platelet Transfusion Reactions: Such as (1) Febrile Non-Hemolytic Transfusion Reaction (FNHTR); (2) Hemolytic Transfusion Reaction (HTR); (3) Allergic reactions were checked and recorded. Trends in the 1-HR as well as the 24-HR CCI for serial RDP and SDP group transfusions were analyzed by comparing the post-transfusion CCI after the first and the last transfusion of each patient in RDP and SDP groups.

Results

Total number of patients in the RDP group was 18, in the SDP group was 12, and in the RDP+SDP group was 38. Of the total 68 patients, 50 (73.52%) were males and 18 (26.48%) were females (Table 1). Forty (59%) were in the age group 10-15 years, 28 (41%) were in the age group 5-10 years, and none were below 5 years.

All platelet transfusions were group-specific. Of the total 745 platelets transfused, 91 were SDP units and 654 were RDP units. Platelets of B+ve and O+ve groups were used in the maximum number (Table 1). Mean CCI at the end of 1-HR in all groups was higher than the mean CCI at the end of 24-HR (Table 1). CCI was higher in the SDP group at the end of 1-HR and 24-HR than in the other two groups (Table 1). The RDP group showed the least response at the end of 1-HR and 24-HR (Table 1).

Table 1: Observations of Gender ,Blood groups, Number of transfusions ,Platelet count increments in RDP,SDP and RDP+SDP group in present study

	RDP	SDP	RDP+SDP	Total
MALE	15	6	29	50
FEMALE	3	6	9	18
BLOOD GROUPS				
A+	147	13		160
A-	13	6		19
B+	196	22		218
B-	14	2		16
0+	145	27		172
0-	57	12		69
AB+	82	9		91
AB-	0	0		0
No of patients	18	12	38	68
No of transfusions	59	38	160	257
Mean CCI				
At end of 1hr	7494.13	9467.43	8828.8	8616.83
At end of 24hr	5489.4	7404.97	7031.23	6732.5

Of the total 257 transfusions, 32 (12.46%) showed inadequate response to platelet transfusion at the end of 1-HR. The number of transfusions showing inadequate response from the RDP group was 12 (20.34%), from the RDP+SDP group was 18 (11.25%), and from the SDP group was 2 (5.3%).

Of the total 257 transfusions, 9% showed inadequate response (less than 20% of expected) at the end of 24 hours. Of these, the maximum transfusions were from the RDP group, 10 (17%), and the minimum were from the SDP group, 2 (5.3%). A lesser number of transfusions with inadequate response at the end of 24 hours were seen in the RDP+SDP group, i.e., 11 (6.8%), than in the RDP group. Thus, the SDP group had the least inadequate responses and a better response to transfusion.

Refractory cases in our study were 21 (30.88%). The maximum number of patients in the RDP group, amounting to 50%, showed refractoriness. The minimum number of refractory cases was seen in the SDP group. 26.31% of cases in the RDP+SDP group were refractory, which is less than in the RDP group (Table 2). Out of 21 refractory cases, 16 were classified under platelet refractoriness due to immune causes, and 5 cases under platelet refractoriness due to non-immune causes (Table 2).

Table 2: Refractoriness to platelet transfusion in different groups and causes

NO.OF PATIENTS	REFRACTORY CASES	PERCENTAGE(%)	Immune cause	Nonimmune cause
RDP[N=18]	9	50%	6	3
SDP[N=12]	2	16.67%	1	1
RDP+SDP[N=38]	10	26.31%	9	1
TOTAL[N=68]	21	30.88%	16	5

Of the 257 transfusions, clinical conditions that might influence transfusion response were present in 138 (53.69%) transfusions, of which 73 (52.89%) showed inadequate response to platelet transfusion in the presence of clinical conditions. Thus, they may be the cause of platelet refractoriness in these cases, whereas 65 (47.11%) showed adequate response to platelet transfusion (Table 3). 25.6% (most common) had fever, 12.06% had splenomegaly, 13.22% had sepsis, and 2.7% had DIC (Table 3).

In the present study, 81 (31.5%) transfusions were associated with acute reactions following platelet transfusion. The maximum number of acute reactions following platelet transfusion were seen in transfusions of the RDP group, accounting for 38.98%, while

the minimum number of platelet transfusion reactions was seen in the SDP group, accounting for 18.42%. The most common acute transfusion reaction observed was Febrile Non-Haemolytic Transfusion Reaction (FNHTR) (Table 4).

Table 3: Effect of clinical factors on platelet transfusion response

	FEVER	SM	SEPSIS	DIC	Total
TRANSFUSION WITH ADEQUATE RESPONSE	30	10	24	1	65
TRANSFUSION WITH INADEQUATE RESPONSE	36	21	10	6	73
	66	31	34	7	138

Table 4: Occurrence of acute reactions following platelet transfusion

TOTAL NO.OF TRANSFUSION [N=257]	FNHTR	HTR	ALLERGIC Reaction	Total	Percent of reactions
RDP group[N=59]	18	0	5	23	38.98%
SDP group[N=38]	3	0	4	7	18.42%
RDP+SDP Group [N=160]	29	0	22	51	31.87%
	50	0	31	81	31.51%
FNHTR=Febrile Non Hemolytic Transfusion Reaction HTR=Hemolytic Transfusion Reaction					

The mean 1-HR as well as 24-HR CCI following the first as well as last transfusion was higher in the SDP group as compared to the RDP group. Patients in the RDP group demonstrated a decrease in the 1-HR and 24-HR mean CCI from the first transfusion to the last transfusion, whereas in the SDP group, they remained in the same range (Table 5).

Table 5: Trends in the l-HR and the 24-HR CCI for serial RDP and SDP group transfusions

		RDP GROUP	SDP GROUP
1-HR INCREMENT	FIRST TRANSFUSION	8756.46	9477.75
	LAST TRANSFUSION	6147.52	9619.09
24- HR INCREMENT	FIRST TRANSFUSION	6205.96	7497.2
	LAST TRANSFUSION	4532.84	7525.53

Discussion

In our study among the refractory cases, a maximum of 90.47% were male and 2% were female. A study done by Slichter et al. [8] on adult leukemic patients also showed similar findings, with male gender showing poor response to platelet transfusion. Thus, gender is likely to affect response to platelet therapy, but the causal mechanism is unclear and not enough scientific literature explaining the reason for this is available. Improved platelet increment at the end of 1-HR and 24-HR associated with increasing patients' age was also noted in our study, similar to Slichter et al. [8]. Corrected count increment at the end of 1-HR was higher in the SDP group (9467.43) compared to the RDP group (7494.13), indicating better response in transfusions with SDPs and better platelet recovery. Slichter et al. [8], the TRAP study [9], and Gmur J et al. [10] have also documented this major advantage of SDP transfusion. Singh et al. [11] concluded that SDP transfusion provides a higher dosage of platelets compared to RDP and Buffy coat Platelet concentrate.

Mean CCI both at the end of 1-HR and 24-HR was significantly higher in the SDP group compared to the RDP group. A similar finding was seen in a study conducted by Gmur J et al. [10]. We also noted that transfusions with both RDP and SDP showed higher CCI compared to transfusions with only RDP, indicating SDP transfusion provides better platelet count increments.

Gmur J et al. [10] reported 33.33% refractory cases, and Slichter et al. (27%) reported a number of refractory cases closer to the present study. However, the TRAP study showed only 10% refractory cases. Further larger population studies are needed to understand and evaluate the burden of this serious problem. Platelet transfusion refractoriness should be accurately diagnosed and evaluated for underlying causes to prevent its adverse outcomes.

In our study, 16 (76.19%) cases showed refractoriness due to immune causes. Among immune causes, the most common is human leukocyte antigen (HLA) class I molecules. Platelet refractoriness due to anti-HLA antibody can be managed by 1) selection of an HLA-cross match-compatible platelet unit, 2) if HLA antibody is identified, selecting the antigen-negative platelet units, and 3) selecting the same HLA-matched platelet unit as the patient.

Patients transfused with the same HLA A, B, C show the best transfusion effect. Preferably, ABO-compatible or ABO-identical fresh platelet transfusion should be done as blood group matched platelets have better outcomes, but the differences in increases in platelet counts are small and are not clinically meaningful in terms of bleeding risk. Leukocyte depletion in platelet components is reported to reduce alloimmunity, or treatment of platelets with ultraviolet beta or gamma irradiation is also effective. Methods of an epitope-based approach for HLA-matched platelets for transfusion have reduced matching difficulty [12].

RDP transfusions can expose recipients to multiple donors and increase patients' alloimmunization. Other measures to manage platelet refractoriness, such as the production of Human leukocyte antigen depleted platelets, slow and continuous infusion of platelets, and the use of monoclonal antibody eculizumab, intravenous infusion of immunoglobulin, are under research. Non-immune causes amounted to five (23.81%) cases. In platelet refractoriness due to non-immunological causes, treating the underlying cause and increasing the frequency of transfusion should be considered. Comont et al. [13] and Daughty et al., in their studies, noted that non-immune causes were more common than immune causes in refractory patients. Further larger studies can provide a better understanding and targeted solutions for platelet refractoriness.

The most common clinical condition observed to affect the post-transfusion platelet response in our study was fever (25.6%), which was comparable to the findings of Slichter et al. Gmur J et al. reported the most common clinical condition to affect post-transfusion platelet response to be DIC. In the present study, 38.98% of platelet transfusion reactions were associated with RDP, and 18.42% of platelet transfusion reactions were associated with SDP. In Heddle N M et al. [14], 28% of the reactions were associated with RDP transfusion and 20% were associated with SDP transfusion.

In our study, acute reactions to platelet transfusions were more common with RDP transfusions, similar to Heddle N M et al. SDP offers lesser donor exposure and thus lesser antigen exposure and bacterial contamination, leading to fewer transfusion reactions [15]. The most common reaction observed in the present study was FNHTR, accounting for 19.45%, which was comparable to Heddle N M et al.'s study.

The mean 1-HR as well as 24-HR CCI observed after the first transfusion were almost similar in both the RDP group and SDP group. The p-value was 0.33 and 0.14 respectively (insignificant). By contrast, mean 1-HR and 24-HR CCI observed after the last transfusion were significantly lower in the RDP group compared to the SDP group. The p-value was 0.05 and 0.001 respectively (significant). Patients in the RDP group demonstrated a decrease in the 1-HR and 24-HR CCI from the first transfusion to the last transfusion, whereas in the SDP group, 1-HR and 24-HR CCI from the first transfusion to the last transfusion were in the same range. The findings of our study were similar to the findings of the Gmur J et al. study.

Conclusion

Cost effectiveness, availability, disease transmission, and alloimmunisation associated with platelet transfusion need to be considered while transfusing platelets. SDP provides better post-transfusion platelet count increments. Also, SDP transfusion can reduce the transfusion frequency needed, risk of transfusion-transmitted infections, occurrence of transfusion reactions, and exposure to multiple donors. Hence, SDP may be preferable to RDP in patients requiring repeated transfusions. Very few studies comparing, in particular, random donor platelets with apheresis platelet concentrates have been done. Therefore, further studies of the same are needed.

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