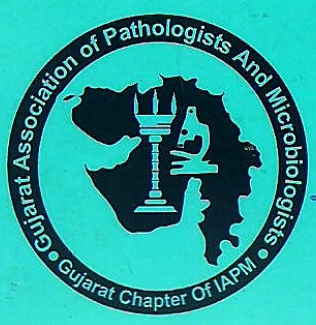
ISSN 0975 - 3109



PATHOLOGY AND LABORATORY MEDICINE

Biennial Journal of GAPM

Volume 1 • Issue 2 • July - December 2009

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PATHOLOGY AND LABORATORY MEDICINE

Biennial Journal of GAPM

ORIGINAL ARTICLE

Single Donor Platelet versus Random Donor Platelet concentrates in patients with thrombocytopenia - Our experience

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Abstract:

Objectives: Platelet transfusions play a key role in therapy for the patients with thrombocytopenia. Superiority of Single donor platelet (SDP) over Random donor platelet (RDP) transfusions is largely assumed, but unproven. This study was performed to find out which method of platelet preparation is better in terms of post transfusion recovery in patients.

Study Design and Methods:

This study included 70 transfusion episodes consisting of 35 SDP and 128 units of RDP. The post transfusion efficacy of transfused platelets was assessed at 1 hour and 24 hours by corrected count increment (CCI) and percentage recovery (PR). Paired 't'-test was used for statistical analysis and a probability of $p<0.05$ was used to reject null hypothesis.

Results:

The mean platelet dose of SDP (n=35) and RDP (n=35) was $3.43 \pm 0.74 \times 10^{11}$ and $2.4 \pm 0.5 \times 10^{11}$ respectively. The mean CCI of SDP at 1 and 24 hrs were $19.2 \pm 12.5 \times 10^3/\mu l$ and $23 \pm 23.4 \times 10^3/\mu l$ respectively. The mean CCI of RDP at 1 and 24 hrs were $15.1 \pm 7.9 \times 10^3/\mu l$ and 15.5

± 12.5 x $10^3/\mu l$ respectively.

Conclusions:

The dosage available from SDP was significantly higher (p value < 0.0001). The post transfusion platelet counts and the increments at 1 hour and 24 hours were significantly higher with SDP transfusion as compared to transfusions with RDP (p values are 0.0009 and 0.003 respectively). However, the CCI and PR in both the groups were comparable (Difference statistically not significant).

Key-words:

Single donor platelet, Random donor platelet, Platelet Apheresis, Corrected count increment, Percentage recovery.

Key Messages:

We can conclude that the platelets prepared by the Apheresis and PRP methods are highly satisfactory after preparation. Although post-transfusion increments were significantly higher in patients who received SDP as compared to RDP, the CCI and PR were comparable in both the groups.

Abbreviations:

RDP	-	Random Donor Platelets
SDP	-	Single Donor Platelets
PRP-PC	-	Platelet Rich Plasma-Platelet Concentrate
BC	-	PC - Buffy Coat PC
PC	-	Platelet Concentrate
CCI	-	Corrected Count Increment
PR	-	Percentage Recovery
HLA	-	Human leukocyte antigen
PPC	-	Pooled platelet concentrates

Introduction:

Platelet transfusions play a key role in therapy for the patients with thrombocytopenia. Now a days, there has been an increasing trend toward using single donor platelets (SDP) by Apheresis as an alternative to pooled random donor platelets (RDP) for platelet transfusion therapy. [1,2] The

use of SDP is preferred over RDP as it represents fewer donor exposures and, as a consequence, lowers risk of virus transmission, alloimmunization, and transfusion-associated septic reactions and "better" platelet quality. Superiority of SDP over RDP transfusions is largely assumed, but unproven. In this study we have analyzed the quality of different platelet concentrates prepared by Platelet Rich Plasma-Platelet concentrate (PRP-PC) and Apheresis methods as per the quality norms recommended and assessed the therapeutic benefits of both of these platelet concentrates in thrombocytopenic patients. This study was also performed to find out which method of platelet preparation is better in terms of post transfusion recovery in patients!

Material and methods

This Platelet Apheresis study was done during time period of August, 2006 to February 2008 at Blood bank, Central Clinical Lab and clinical departments of the hospital after obtaining the ethical committee clearance from the same institute.

During this Period, total number of 110 Single donor Platelet Apheresis Procedure were done on Baxter CS 3000 plus with AMS cell separator, Fenwal division, USA, using closed system apheresis kits and studied with respect to donor's, procedure's and patient's related details. All donors met the donor eligibility criteria as laid down by the Food and Drug Administration (FDA). The platelet apheresis procedures were performed following our standard operating procedure (SOP). All the RDP were prepared from whole blood by PRP method of platelet preparation according to standard guidelines by FDA. Hematological parameters such as platelet count and hemoglobin were measured on an automated analyzer (Sysmex KX-21). This study included 70 transfusion episodes (35 SDP and 35 RDP) consisting of 35 SDP and 128 units of RDP.

The study group:

Patients with different diseases with severe thrombocytopenia (i.e. platelet count <20000/μl) or with active severe bleeding, who required prophylactic or therapeutic platelet transfusion were subjects of the study.

35 patients were evaluated for therapeutic efficacy of RDP prepared by PRP method and 35 patients were evaluated for SDP.

Exclusion criteria:

Patients with Idiopathic thrombocytopenic purpura were excluded from this study.

Sample collection and analysis:

2-3 ml of sample from platelet concentrates was collected aseptically in plain vial prior to the transfusion to the patients. 2-3 ml of patient's blood was collected in EDTA at three different times; one sample prior to the transfusion and the other two samples were collected at 1 hr and 24 hrs post-transfusion respectively. Platelet counting was done by automated cell counter (SYSMEX-KX21).

The main outcomes measured for evaluation of in vivo efficacy of transfused platelets were CCI and PR. These both parameters can be calculated according to following formula,

CCI = (platelet increment/μl) x (body surface area in m^2) / number of platelet transfused (x 10^{11}) = platelets/ μl/ m^2

PPR = [(platelet increment/μl) x (weight in Kg x 75ml)] x 100 / [(platelet count of product/ μl) x (volume of platelets in ml)]

Statistical analysis:

All data were expressed as mean ± SD. We performed statistical comparison by using paired 't'-test for multiple groups. A probability of $p<0.05$ (one sided) was used to consider the difference as significant and to reject null hypothesis. Microsoft Excel 2002 software was used to do all statistical analysis.

Observation and results

This study included 70 patients for transfusion episodes (35 SDP and 35 RDP) consisting of 35 SDP and 128 units of RDP.

SDP prepared by Baxter CS-3000 plus with AMS cell separator at blood bank were transfused to patients with various diseases in need of prophylactic or therapeutic platelet transfusions (**table 1 and Figure 1**) Majority of transfusions were done for Hematological Malignancy(Table 1). Figure 1 and table 1 also show diagnosis of the patients to whom 128

units of RDP were transfused for prophylactic or therapeutic purpose.

Platelet dose:

SDP containing approximately 3×10^{11} platelets is expected to raise platelet count by 30,000 - 60,000/μl. RDP containing approximately 7×10^{10} platelets increases the platelet count by 5,000-10,000/μl. and "standard" platelet dose is 0.5×10^{11} / 1 RDP per 10 kg of body weight and this should increase the count by approximately 40,000/μl. [3] So, adequate Platelet dose is about 1 unit of SDP or 4-6 units of RDP. However due to limited group wise stock and short life time of RDP, we were able to provide approximately 3 to 4 units of RDP per patient.

The mean weight of the patients who received SDP (n=35) and RDP (n=35) was 41.7 ± 21.2 kg and 48.0 ± 8.3 kg (mean±SD) and ranged from 1.2-95 kg, and 34-62 kg respectively. The mean platelet dose of SDP (n=35) and RDP (n=35) was $3.43 \pm 0.74 \times 10^{11}$ and $2.4 \pm 0.5 \times 10^{11}$ (mean±SD) and ranged from $0.9\text{-}4.6 \times 10^{11}$ and $1.2\text{-}3.1 \times 10^{11}$ respectively. All SDP transfusions were ABO identical and RDP transfusions were also ABO identical, when possible, but not as a rule.

On analyzing the parameters in total numbers of patients for each platelet preparation, it was observed that the dosage available from SDP was significantly higher (SDP Vs RDP p value = 0.000000004, significant, table 2).

The overall platelet counts and increments of the both groups are shown in details (Table 2 and Figure 2). The post transfusion platelet counts and the increments at 1 hour and 24 hours were significantly higher with SDP transfusion as compared to transfusions with RDP (p values are 0.0009 and 0.003 for 1 and 24 hrs post transfusion period respectively). However, the CCI and PR in both the groups were comparable (statistically not significant).

Discussion

The in vivo platelet quality can be assessed by using corrected count increment (CCI) and percentage recovery (PR) at 1 hour and 24 hours post transfusion which accesses the functional platelets in circulation after transfusion. [4, 5] If the CCI at 1 hr and 20 hour is <7500 platelets /μL/m2

and < 4500 platelet/μL/m2 and PR at 1 hour and 20 hour <30% and <20% respectively on two consecutive occasions, it indicates platelet transfusion refractoriness. [6]

Platelet transfusion refractoriness is a frequent problem for multi-transfused patients. [7] Contributing causes include alloimmunization, spleenomegaly, fever, frequent infections. [8-11] Several strategies have been added to transfusion practice, in an attempt to minimize the problem: leukoreduction, use of ultraviolet irradiated products, dose dependent platelet transfusion trials, use of ABO identical platelet concentrates, HLA-matched platelet transfusions and use of SDP products. The use of SDP or higher doses of platelets is still controversial and associated with higher costs. Some authors advocate the use of SDP due to less exposure to multiple donors, resulting in smaller risk of contamination with infectious diseases and lower risk of developing alloantibodies. However, it is unclear if using SDP improves outcomes of transfusions, as opposed to using the more easily available pooled platelet concentrates (PPC). [12-20]

In this study, for evaluation of in vivo efficacy of transfused platelets, CCI and PR were calculated at 1 and 24 hrs post-transfusion. The post-transfusion platelet count is affected by the viability of the platelets as well as the number of platelets in the platelet concentrates. It is also affected by the dilution of platelets in the patient's blood volume. CCI and PR have been used to correct the post-transfusion platelet count increment for the patient's blood volume and for the number of platelets in the platelet component.

In the present study, post-transfusion increments at 1 and 24 hrs after platelet transfusion, CCI and PR were analyzed both with respect to the platelet preparation and the underlying disease condition of the patients. In various patients, who received SDP, the post-transfusion platelet counts and increments achieved were significantly higher, as compared to patients who received RDP (p value are 0.0009 and 0.003 for 1 and 24 hrs post transfusion period respectively, highly significant, table 2). However when CCI and PR were calculated, the results with

both preparations were comparable (p values are not statistically significant).

Anderson et al[21] demonstrated that the actual CCI at 1-6 and 18-24 hrs post-transfusion for all three types of PC (SDP, PRP-PC, BC-PC) did not differ significantly. They concluded that transfusion of PRP-PC is associated with a significant increase in non hemolytic febrile transfusion reaction. [21] The results of Anderson et al's study were also comparable to our study and we found that those patients who received RDP had significantly low post-transfusion platelet counts and increments at 1 hour and 24 hours as compared to patients who received SDP. The post transfusion therapeutic efficacy assessed by CCI and PR at 1 hour and 24 hours were comparable in both groups of patients.

Singh R.P. et al[5] had concluded that patients transfused with apheresis-PC had received higher platelet dosage than PRP-PC and Buffy Coat PC (BC-PC) and this difference was statistically significant ($p < 0.001$). The post transfusion platelet counts and increments at 1 hour and 20 hours were significantly higher with apheresis-PC than PRP-PC and BC-PC ($p < 0.001$). However, the CCI and PR in all three groups were comparable. There was significant increase in inter- transfusion interval with apheresis-PC than PRP-PC and BC-PC ($p < 0.05$). [5] This study was also comparable with present study for all of its aspects.

Klumpp et al[17] used a similar methodology to compare low dose platelet (LDPs, mean = 3.1×10^{11} platelets) vs. high dose platelet (HDPs, mean = 5.0×10^{11} platelets). [17] As compared to the administration of HDPs, the administration of LDPs for prophylactic transfusion in hematopoietic progenitor cell transplant patients results in a lower platelet count increment, a lower likelihood of obtaining a posttransfusion platelet increment >20,000/μL, a shorter transfusion-free interval, and a greater relative risk per day of requiring additional transfusions ($p<0.0001$).

In a study performed by Norol et al[22] comparing the platelet doses, increments and PR in AML patients who had undergone allogenic BMT, it was observed that higher the dosage, higher were the platelet count, increments but PR was similar. [22] Three platelet doses [(medium dose

(2-4 × 10^{11} platelets), high dose (4-6 × 10^{11} platelets) and very high dose (>6 × 10^{11} platelets)] were transfused. The author showed that increments in 12 hours post-transfusion platelet count and the time to next transfusion increased with higher platelet doses and this difference was statistically significant ($p<0.01$ to 0.05), but the percentage recovery was similar in all three groups and statistically not significant. The results of Norol's study[22] was also comparable to our study and we found that those patients who received lower doses (i.e. RDP recipients) had significantly low post-transfusion platelet counts and increments at 1 hour and 24 hours as compared to patients who received medium dose (SDP recipient). The post transfusion therapeutic efficacy assessed by CCI and PR at 1 hour and 24 hours were comparable in both groups of patients and statistically not significant.

Gurkan E. et al[20] had performed study to find out superiority of single-donor apheresis platelets (SDP) over pooled platelet concentrates (PPC) transfusions in AML/MDS patients receiving allogeneic hematopoietic stem cell transplantation. The author was unable to detect any clinical relevant difference between SDP and PPC transfusions when used as bleeding prophylaxis after allogeneic hematopoietic stem cell transplantation. SDP provided better post-transfusion platelet counts and CCI (p values are 0.0004 and 0.0001), but this did not translate into clinically important parameters. The author concluded that in the context of allogeneic hematopoietic stem cell transplantation, PPC are as clinically effective as SDP. This study also comparable with present study in all aspects except one matter, CCI was comparable in both the groups (SDP and RDP transfusions) in present study.

Although quality assessment of platelets was done within 24 hours of transfusion in this study, the results of quality testing of RDP and SDP in our department comply within recommended standards up to day 5 of storage. Majority of RDP transfusions were done within 3 days of their preparation. SDP are prepared on demand and hence issued soon after preparation. Our study is limited by its retrospective nature and the lack of a cohort of patients with same diagnosis.

The decision to use any of these products is largely based on cost and availability which are two important factors in a developing country.

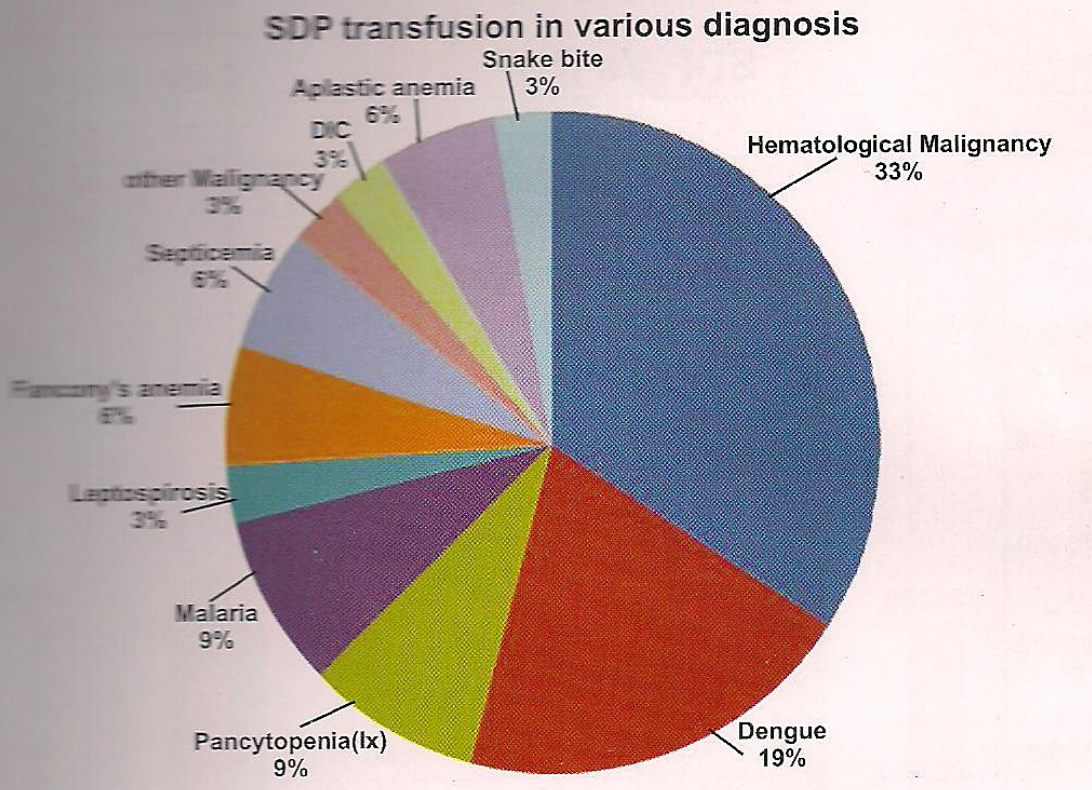
Conclusion:

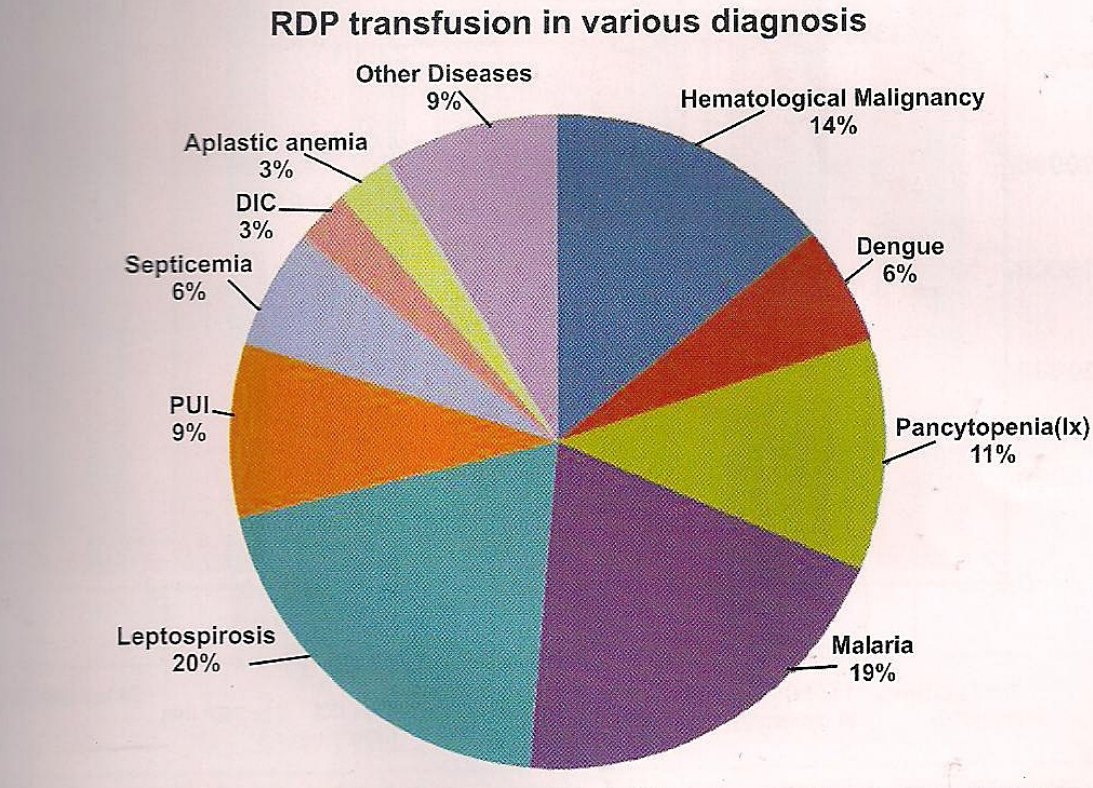
Thus from the present study, we can conclude that the platelets prepared by the both methods are highly satisfactory after preparation. Although post-transfusion increments were significantly higher in patients who received SDP as compared to RDP, but the CCI and PR were comparable in both groups of patients and well above the level to label it as a refractory transfusion.

Currently platelet transfusion therapy is limited by several concerns, including the consequences of alloimmunization in chronically transfused patients and septic reactions caused by bacterial contamination. There is debate about which platelet product should be used; many transfusion services favour the primary use of RDP largely because of the lower cost, whereas others favour SDP.

The following five points should be considered when considering the use of SDP or RDP: (1) the impact on infectious complications, (2) transfusion reaction rate, (3) leuko depletion, (4) reduction of transfusion frequency and, (5) the treatment and prevention of alloimmunization. Ness Paul et al[12] stated that these five areas where SDP have been proposed to have advantages over RDP and SDP offers major advantages over RDP for most of these issues. [12]

Thus, according to logistic terms, SDP are better than RDP, when considering numbers of donors exposure to patient and leuko reduction. However, in developing countries SDP, because of their high cost and more technical expertise required, may be recommended only in selected patients either when RDP in adequate doses are not available, or when HLA-matched platelet transfusions are indicated. RDP transfusions are less demanding in logistic terms and are likely to decrease the economic burden of blood products as far as developing countries are concerned. Our analysis would indicate that, RDP are as clinically effective as SDP.


SDP transfusion in various diagnosis
Snake bite 3%
Aplastic anemia 6%
DIC 3%
other Malignancy 3%
Septicemia 6%
Fanconi's anemia 6%
Leptospirosis 3%
Malaria 9%
Pancytopenia(Ix) 9%
Dengue 19%
Hematological Malignancy 33%


RDP transfusion in various diagnosis
Other Diseases 9%
Hematological Malignancy 14%
Aplastic anemia 3%
DIC 3%
Septicemia 6%
Dengue 6%
PUI 9%
Pancytopenia(Ix) 11%
Leptospirosis 20%
Malaria 19%

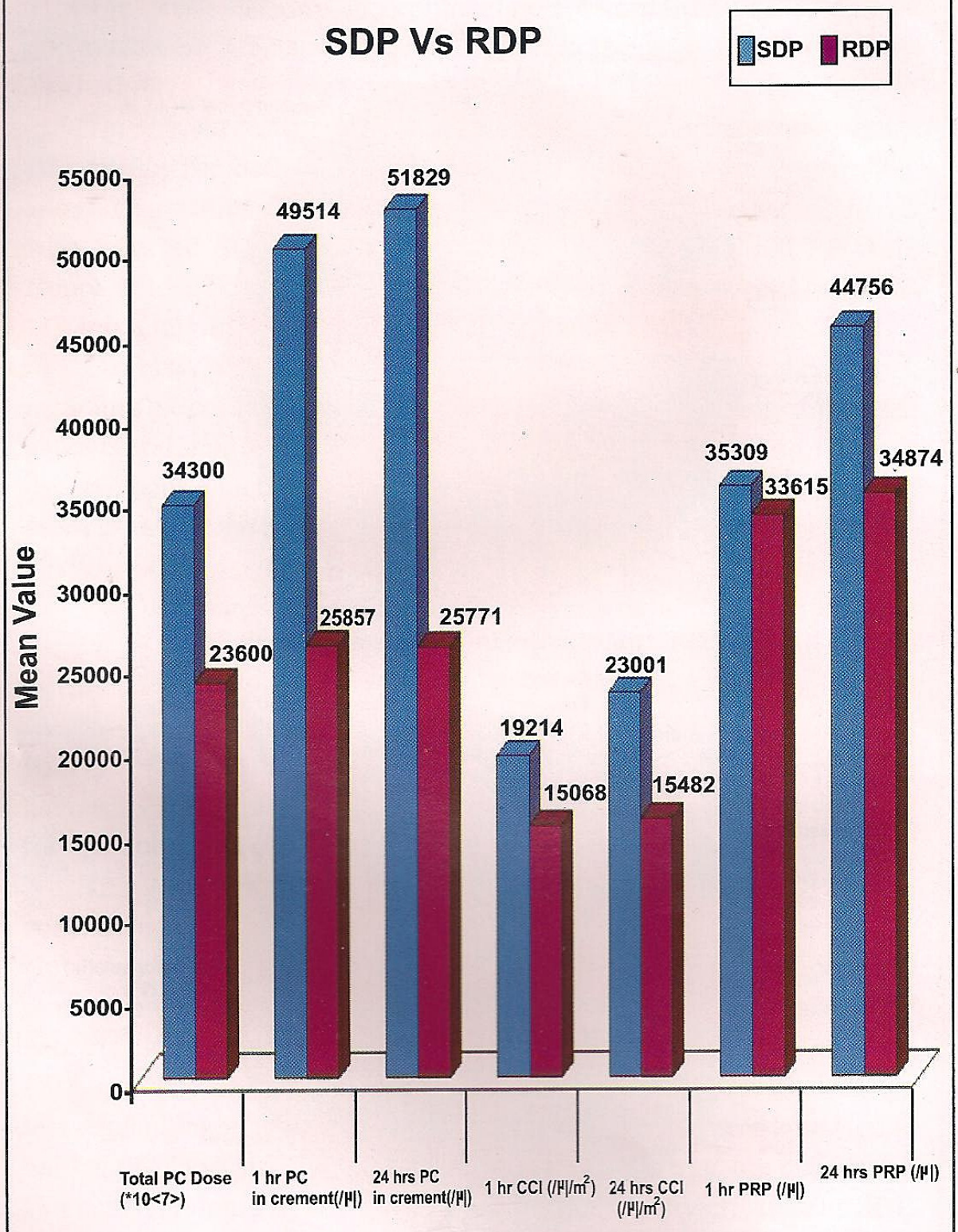

SDP Vs RDP
SDP
RDP
Mean Value
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
34300
23600
49514
25857
51829
25771
19214
15068
23001
15482
35309
33615
44756
34874
Total PC Dose (*10<7>)
1 hr PC in crement(/µl)
24 hrs PC in crement(/µl)
1 hr CCI (/µl/m2)
24 hrs CCI (/µl/m2)
1 hr PRP (/µl)
24 hrs PRP (/µl)

Table 1: SDP & RDP transfusion in various diseases

Type of PC	Diagnosis	n (35)	%
SDP	Hematological Malignancy	12	34
	Dengue	7	20
	Pancytopenia(Ix)	3	9
	Malaria	3	9
	Leptospirosis	1	3
	Fancony's anemia	2	6
	Septicemia	2	6
	Other Malignancy	1	3
	DIC	1	3
	Aplastic anemia	2	6
	Snake bite	1	3
RDP		n (35)	%
	Hematological Malignancy	5	14
	Dengue	2	6
	Pancytopenia(Ix)	4	11
	Malaria	7	20
	Leptospirosis	7	20
	PUI	3	9
	Septicemia	2	6
	DIC	1	3
	Aplastic anemia	1	3
	Other Diseases	3	9

Table 2:

Platelet counts in RDP & SDP transfusions

Sampling time	Platelet counts SDPs transfusion (n = 35)	RDPs transfusion (n = 35)	p value
Total PC dose	$3.43 \pm 0.74 \times 10^{11}$	$2.4 \pm 0.5 \times 10^{11}$	0.0000
	$(0.9\text{-}4.6 \times 10^{11})$	$(1.2\text{-}3.1 \times 10^{11})$	
Pre-transfusion	$23.3 \pm 17.6 \times 10^3/\mu l$	$21.5 \pm 14.9 \times 10^3/\mu$	
	$(2\text{-}63 \times 10^3/\mu l)$	$(1\text{-}70 \times 10^3/\mu l)$	
Post-transfusion	$65.5 \pm 33.4 \times 10^3/\mu l$	$47.4 \pm 26.1 \times 10^3/\mu l$	
(1hr)Count	$(21\text{-}141 \times 10^3/\mu l)$	$(19\text{-}150 \times 10^3/\mu l)$	
Increment	$42.3 \pm 38 \times 10^3/\mu l$	$25.9 \pm 17.9 \times 10^3/\mu l$	0.0009
	$(3\text{-}139 \times 10^3/\mu l)$	$(4\text{-}80 \times 10^3/\mu l)$	
Post-transfusion	$75.1 \pm 45.1 \times 10^3/\mu l$	$47.3 \pm 24.8 \times 10^3/\mu$	
(24hrs) Count	$(26\text{-}200 \times 10^3/\mu l)$	$(16\text{-}123 \times 10^3/\mu l)$	
Increment	$51.8 \pm 43.3 \times 10^3/\mu l$	$25.8 \pm 21.3 \times 10^3/\mu l$	0.003
	$(1\text{-}195 \times 10^3/\mu l)$	$(3\text{-}80 \times 110^3/\mu l)$	
CCI T 1 hr	$19.2 \pm 12.5 \times 10^3/\mu l$	$15.1 \pm 7.9 \times 10^3/\mu l$	NS *
	$(0.94\text{-}62.4 \times 10^3/\mu l)$	$(3.38\text{-}32.1 \times 1\ 10^3/\mu l$	
24 hrs	$23 \pm 23.4 \times 10^3/\mu l$	$15.5 \pm 12.5 \times 10^3/\mu l$	NS *
	$(0.3\text{-}110 \times 10^3/\mu l)$	$(1.9\text{-}57.1 \times 10^3/\mu l)$	
PR I 1 hr	$35.3 \pm 28.8 \times 10^3/\mu l$	$33.7 \pm 17.3 \times 10^3/\mu l$	NS *
	$(2.1\text{-}163 \times 10^3/\mu l)$	$(7.8\text{-}71.8 \times 10^3/\mu l)$	
24 hrs	$44.8 \pm 51.9 \times 10^3/\mu l$	$34.9 \pm 27.9 \times 10^3/\mu l$	NS *
	$(0.5\text{-}223 \times 10^3/\mu l)$	$(4.6\text{-}115 \times 10^3/\mu l)$	

Abbreviation: * NS - Not significant, T CCI - Corrected count increment, I PR - Percentage recovery

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