 DOI: 10.18231/2394-6792.2017.0043

Use of platelete concentrates in thrombocytopenia patients - A Hospital Based study of 138 cases

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Abstract

Background: Platelet transfusion is one of the most crucial therapeutic approaches in Medicine. In addition to their important function in hemostasis, platelet's role in inflammation has become more evident. Also they have severe and fatal adverse reactions also.

Aim: The aim of the study was to determine the number of platelet transfusions that was done during the study period, to study the indications for the transfusions and evaluate its efficacy.

Materials and Method: A total of 138 thrombocytopenic patients who received platelet transfusions were evaluated during a one-year study period from Jan 2015 to Dec 2015 at KIMS Koppal, General hospital with attached blood bank. Conditions associated with the thrombocytopenia were studied and categorized. Pre and post-transfusion platelet counts were done and 24-hour corrected count increment (CCI) was calculated to check the efficacy of transfusion

Results: Majority of the platelet recipients were transfused prophylactically when their platelet counts were >20000/µL. The most common category of diagnosis among these patients was infectious diseases.

Conclusion: Appropriate component therapy should be actively endorsed as it ensures optimum utilization of a scarce resource in a populous country like India. Platelet transfusion must be guided by population of patients under consideration, the clinical conditions of the patients and perhaps even the resources of the transfusing facility and its ability to respond rapidly to patients transfusion needs.

Keywords: Thrombocytopenia, Platelet Transfusion, Platelet Concentrate, Corrected Count.

Introduction

This is the era of component therapy. Therefore there is a need for rational use of platelet concentrate.(1) Platelets, even being one of the smallest cells of the hematopoietic system, have important and well-characterized roles in hemostasis and thrombosis, the maintenance of vascular integrity and the innate immune response.(2) Platelet transfusion indicated to prevent hemorrhage in patients with thrombocytopenia or platelet function defects.(3)

Table 1: Indications of transfusions of platelets in adults(3)

Prophylactic transfusion indications	Platelet count (x 10^3 per µL)
Major surgery or invasive procedure, no active bleeding	≤ 50
Ocular surgery or neurosurgery, no active bleeding	≤ 100
Surgery with active bleeding	< 50 (usually) > 100 (rarely)
Stable, nonbleeding	< 10
Stable, nonbleeding, and body temperature > 100.4°F (38°C) or undergoing invasive procedure	< 20

Table 2: Indications of transfusion of platelets in neonates(3)

Platelet count (x 10^3 per µL)	Indications
< 20	Always transfuse
20 to < 30	Consider transfusion; transfuse for clinical reasons (e.g., active bleeding, lumbar puncture)
30-50	Transfuse if any of the following indications exist: First week of life with birth weight < 1,000 g (2 lb, 4 oz) Intraventricular or intraparenchymal cerebral hemorrhage Coagulation disorder Sepsis or fluctuating arterial venous pressures Invasive procedure Alloimmune neonatal thrombocytopenia

Recently, platelets are also recognized as the main source of circulating soluble CD40 ligand (CD40L, CD154), which plays significant roles in hemostasis, platelet activation, clot stability, interactions with other cells, and upregulation of different mediators.[4]

Reduction in platelet number constitutes an important cause of generalized bleeding. The clinical decision regarding platelet transfusions requires consideration of several variables, including estimation of platelet count and function, cause of thrombocytopenia, the state of coagulation function, the presence or likelihood of bleeding and the hazards of transfusion.[5]

The diverse aspects of platelet physiology make up the clinical efficacy of platelets. Significant progress has been made in platelet transfusion therapy in the last part of 20th century, the use of platelet concentrate increased by 80%. Now two platelet products are available for transfusion, random donor platelets and platelets obtained by apheresis or single donor platelets.[1]

A platelet concentrate containing approximately 0.7 X $10^{(11)}$ platelets should cause a platelet count increase of 5000 to 10,000/ µl in an average sized adult. This should increase the platelet count by approximately 40,000/ µl.[1] It is essential to monitor the efficacy of platelet transfusion in order to guide the use of subsequent transfusions by measuring the platelet counts before and after transfusion[6] or one unit of apheresis platelets should increase the platelet count in adults by 30 to 60 × 103 per µL (30 to 60 × 109 per L).[7]

In neonates, transfusing 5 to 10 mL per kg of platelets should increase the platelet count by 50 to 100 × 103 per µL (50 to 100 × 109 per L).[8] One apheresis platelet collection is equivalent to six pooled random donor platelet concentrates.[9] Spontaneous bleeding through intact endothelium does not occur unless the platelet count is no greater than 5 × 103 per µL (5 × 109 per L).[10]

Though platelet transfusion is crucial in treating life threatening hemorrhage, one must keep in mind the associated hazards, which include a variety of serious or even fatal transfusion reactions, refractoriness, hemolysis from ABO-mismatched transfusions, acute lung injury and sepsis.[4] These risks, along with the difficulty and cost of producing and maintaining adequate supplies of platelets, justify the rationale of using this therapy judiciously.[11] The newer use of platelet concentrate include the repair of bone defects when used with autologous platelets, management of diabetic foot ulcer healing, platelet gel preparation to be used in surgery as glue to manage diffuse oozing in open heart surgery, plastic surgery, eye and ENT and neurosurgery.[1] Current medical literature supports the appropriate use of platelet concentrate. In oncology practice especially, leukoreduced platelet units should be used.[1]

Even though platelet components are widely available, their transfusion still raises a number of challenges and controversies including the threshold or trigger level for platelet transfusion, the appropriate use of prophylactic and therapeutic platelet transfusions, and the dose of platelets necessary.[12]

Contraindications to platelet transfusion include thrombotic thrombocytopenic purpura and heparin-induced thrombocytopenia. Transfusion of platelets in these conditions can result in further thrombosis.[3]

Aims

a. To Study the number of platelet transfusions that was done during the study period.
b. To study the indications for the transfusions and evaluate its efficacy

Materials and Method

The present study included thrombocytopenia patients admitted at KIMS, Koppal general hospital and received platelet transfusion during the study period from 1st January 2015 to 31st December 2015. Patient information was collected from the blood bank component register and medical records of the patients who received platelet transfusion during their course of stay in the hospital. Patient details including age/sex, history, physical examination, investigations including pre and post transfusion platelet counts were noted from their medical records.

The platelet concentrates, which were used for transfusion, were prepared using platelet rich-plasma (PRP) method within 8 hours of collection of whole blood. 24 hour - CCI for each patient was calculated to assess the effectiveness of transfusion using the following formula:

$$CCI = \frac{(\text{Post – pre-transfusion count}) \times BSA}{\text{Number of platelets transfused} \times 10^{-11}}$$

Results

The total number of patients who received transfusion of platelet concentrates in the institute was 138, out of which, 80 were males and 58 were females. The male to female ratio was 1.38. The age of the platelet transfusion recipients ranged from a day old neonate to a 75 year old.

The majority i.e. 82(59.42%) out of the 138-platelet transfusion recipients was from the department of Medicine, followed by 35(25.36%) patients from Pediatrics, 15(10.86%) patients from Obstetrics & Gynecology, 5(3.62%) patients from Surgery and (0.72%) each from ENT and Orthopedics.

Table 3 shows the pre-transfusion platelet counts of the platelet recipients. 81 out of the 138 patients received platelet transfusions when their counts were between 21,000-50,000/µL.

Table 4 shows the number of platelet units utilized by each patient. Single unit transfusions were given to 28 patients out of whom 20 were of pediatric age group. In adults, multiple transfusions at a time were much more common.

Table 3: Pre transfusion platelet counts

Pre transfusion platelet counts(per µL)	No. of platelet recipients	%
<10000	11	7.98
11000-20000	35	25.36
21000-50000	81	58.70
51000-100000	10	7.24
>100000	1	0.72
Total	138	100

Table 4: Number of platelet units utilized

No. of units transfused to an individual patient	No. of platelet recipients	Total no. of platelets utilized
01	28	28
02	44	88
03	26	78
04	20	80
05	06	30
06	10	60
07	01	07
08	01	08
09	01	09
10	01	10
Total	138	398

Broadly classifying the diagnoses given to the patients, the distribution of cases was as given in Table 5. Many patients had more than one diagnosis. The most common category was infectious diseases, which comprised of 82 patients. 25 patients had hematological disorders, 21 had neonatal complications and 15 had obstetric causes. The rest had other miscellaneous disorders.

Table 5: Categories of diagnosis for which platelets were utilized

Diagnosis	No. of platelet recipients	%
Infectious diseases	82	50.30
Hematological disorders	25	15.34
Neonatal complications	21	12.88
Obstetric complications	15	9.20
GI disorders	5	3.06
CNS disorders	1	0.62
Liver disease	4	2.46
LUNG disease	3	1.84
Surgical cases	5	3.06
Pyrexia of unknown origin	2	1.22
Total	163	100

Dengue fever was most common indication for platelet transfusion. A total of 67 cases of dengue fever was diagnosed and confirmed by serological tests. 49 out of 67 patients had pre-transfusion platelet counts between 21,000-50,000/µL, 13 patients had counts between 11,000-20,000/µL and 1 patient had a count below 10,000/µL. Only 4 patients had platelet counts above 50,000/µL.

There were 25 patients having a hematological disorder associated with thrombocytopenia. The commonest were anemia seen in 12 cases and pancytopenia seen in 10 patients. 1 case each of acute lymphoblastic leukemia, immune thrombocytopenia, and thalassemia were present among the cases studied. 21 neonates required transfusion of platelet concentrates. The highest incidence of thrombocytopenia was seen in the 10 cases of preterm births that also had low birth weight. There were 5 cases of birth asphyxia, 1 case of neonatal sepsis and 3 cases of jaundice.

15 patients out of 138 had low platelet counts during pregnancy or after delivery and required transfusion of platelets. The most common associated diagnosis among them was anemia, seen in 9 patients. There were 7 cases of pregnancy-induced hypertension, which included cases of pre-eclampsia, and eclampsia. Other diagnoses included intra-uterine death, pancytopenia, HELLP syndrome, post-partum hemorrhage and acute gastroenteritis. Out of the 138 thrombocytopenic patients who received platelet transfusions, 38(27.54%) cases had a history of bleeding. The most common bleeding manifestation was hematochezia seen in 8 patients. The next frequent manifestations were petechial hemorrhages and epistaxis seen in 5 patients each, followed by malena and vaginal bleeding seen in 4 patients each, and hematemesis and hematuria seen in 4 patients each. 12 out of the 38 patients had bleeding from more than one site.16 patients with bleeding had a platelet count between 21,000-50,000/µL. 10 patients had platelet counts ≤20,000/µL. The rest of the patients had counts above 50,000/µL (Table 6).

Table 6: Pre-transfusion platelet counts in patients with bleeding

Platelet count(per µL) in bleeding patients	No of platelet recipients	%
≤ 5000	2	5.2
6000-10000	3	7.8
11000-2000	10	26.32
21000-50000	16	42.10
51000-100000	6	15.78
>100000	1	2.64
Total	38	100

110 patients out of the 138-platelet transfusion recipients showed an increment in the post-transfusion platelet count. 18 patients showed no increment or further decrease in their platelet counts.40 out of the 110 patients who showed post-transfusion increments in their platelet counts had 24-hour CCI above 10,000/µL. 8 patients showed CCI between 7500-10,000/µL. The rest 62 patients showed CCI below 7500/µL (Table 7).

Table 7: 24-hours corrected count increment after platelet transfusion

24-Hour CCI (per µL)	No. of platelet recipients	%
<5000	40	36.36
5000-7500	22	20
7500-10000	8	7.28
>10000	40	36.36
Total	110	100

Discussion

In a 4-month study conducted in 6 hospitals in Eastern Ontario, Canada by Silver SS et al, a total of 4801 units of platelet concentrates were transfused on 687 occasions to 303 patients. The cardiovascular service utilized the highest number of platelets followed by oncology department.[13] Bayer WL et al, study reveals that the need for platelet concentrates is highest for hematologic malignancies followed by oncology department.[14] Gaur et al. evaluated the utilization of blood and blood components at the blood bank of a tertiary health center and concluded that the most common indication was thrombocytopenia due to leukemia, followed by thrombocytopenia at the time of surgery.[15] Comparing with above studies present study reveals that most common indication for platelet transfusion was thrombocytopenia associated with infectious diseases, priorities for usage of platelet concentrates were different.

Compared to study by P.S. Nair[16] et al spontaneous bleeding in 77.78% was a major manifestation followed by petechiae/purpura accounting for 22.22%.While in a similar study by Dr. Srinivas et al purpura (63%) was the commonest bleeding manifestations followed by spontaneous bleeding (37%).[17] In study done by Patil petechiae was the major manifestation73.9% followed by spontaneous bleeding (26.9%).[18] Similar study by Gandhi AA et al, Petechiae were seen in 47.82% as a major bleeding manifestation followed by 10.14% having gum bleeding, 4.34% had melena and then 2.89% each had hematuria and menorrhagia[19]. Present study reveals most common bleeding manifestation was hematochezia seen in 21.05%. The next frequent manifestations were petechial hemorrhages and epistaxis seen in 13.15% each, followed by melena and vaginal bleeding seen in 10.52% each, and hematemesis and hematuria seen in 10.52% each.

Comparison of causes of thrombocytopenia associated with thrombocytopenia discussed in Table 8. Studies done Prithviraj et al, Srinivasan et al and Amit AG et al malaria was the main cause for trombocytopenia associated with fever, study by Nair et al revealed that septicemia as the main cause for thrombocytopenia associated with fever when compared to present study which showed dengu as predominant cause for thrombocytopenia and who received platelet transfusion.

Table 8: Comparison of causes of thrombocytopenia associated with fever who received platelet transfusions

Diagnosis	Prithviraj p et al	Srinivasan et al	Nair et al	Gandhi AA et al	Present study
Septicemia	4	19	26	5	3
Malaria	54	41	09	46	10
Enteric Fever	6	24	15	5	4
Dengue	15	14	14	30	67
Others	21	2	18	24	3

Compared with Gandhi AA et al most common hematological disorders associated with the thrombocytopenia who received platelet transfusion is megaloblastic anemia (5.34%) followed by hematologic malignancy (1.78%), Goel R et al Platelet transfusions were reported in 10.1% of all hospitalizations for TTP, 7.1% for HIT, and 25.8% for ITP.[20]

Present study shows anemia (48%) and pancytopenia (40%), followed by a single case (4%) of ALL in a 12 year old boy was present in the study whose pre-transfusion platelet count was 5000/µL. One case (4%) of ITP was also seen. In this study, among the 15 patients who utilized platelets during or after pregnancy, 8 had anemia and 5 had PIH which included 1 cases of pre-eclampsia. HELLP syndrome was observed in 1 patient.

Gupta et al. analyzed thrombocytopenia in 146 neonates admitted in neonatal intensive care unit. However, they concluded that factors such as LBW, IUGR and maternal hypertenstion associated with conditions like sepsis, GI problems and hypoxia responsible for thrombocytopenia and necessitate platelet transfusions in these babies. A total of 870 neonates investigated for platelet count, 146 were found thrombocytopenic. 24 neonates were transfused with platelets; out of these, 45.8% (11) neonates received multiple platelet transfusion.[21]

Study done by Bonifacio et al out of 94 cases admitted at NICU 67% had thrombocytopenia due to IVH, Sepsis, NEC and bleeding and platelets were transfused to 85.4% of severe and 64.7% of moderate thrombocytopenia.[22]

9 out of 21 neonates, who received platelet transfusions in the present study, were both preterm and low birth weight, out of which 1 baby had associated meconium aspiration with septicemia and 1 baby had respiratory distress. 2 other neonates were septicemic and 5 had birth asphyxia.

Definitive studies (e.g. well-designed, prospective, randomized clinical trials) are not available either historically or at present to support evidence-based decisions regarding a trigger level of platelet count that indicates prophylactic platelet transfusion. But in one study, these prophylactic platelet transfusions accounted for as many as 74% of all platelet transfusions.[23]

Even though several studies have clearly demonstrated the correlation between thrombocytopenia and the risk of haemorrhage as well as the efficacy of platelet transfusion at reducing that risk, there continues to be controversy regarding the appropriate threshold or "trigger" for prophylactic platelet transfusion -or whether these transfusions are warranted et al.[12]

Reasonable clinical practice, until more definitive data become available, is to transfuse enough platelets per each transfusion to maintain the blood platelet count >10,000/μL in stable non-bleeding patients, >20,000/μL in unstable non-bleeding patients, and >50,000/μL in bleeding patients or in those undergoing invasive procedure.

Jerry E et al studied shows that it was a common practice to use platelet count of 20,000/μLas the trigger level for prophylactic platelet transfusion.[12]

A randomised trial by Heckman et al. considered the impact of reducing the platelet transfusion threshold from 20,000/μL to 10,000/μL in 78 adult patients undergoing induction therapy for acute leukaemia.[24]

In the present study 100 out of 138 patients who received platelet transfusion were transfused prophylactically. No definitive trigger value of platelet count for prophylactic transfusion was observed. Only 39% of those who received prophylactic platelet transfusions had a platelet count less than 20,000/μL. Rest of the prophylactic platelet transfusions were given to patients with platelet count >20,000/μL. No uniform guidelines for prophylactic transfusion therapy were hence found to be followed.

The 24-hour CCI was calculated in each case and a total of 110 patients showed post-transfusion increments in platelet counts. However, in 80 cases, there was either no increment or the increment was not significant. A number of clinical factors such as fever, infection and the administration of certain drugs may reduce the effectiveness of platelet transfusion.

In the present study, 50/80 platelet recipients who had reduced 24-hour CCI had fever associated with the thrombocytopenia. 40/80 patients had an infectious disease.

When prophylactic transfusions are given after a trigger threshold of 10,000 platelets per cubic millimeter or lower is reached, the platelet dose has no significant effect on the incidence of bleeding in patients with hypoproliferative thrombocytopenia, probably because few platelets are needed to maintain hemostasis.

Conclusion

The observations of this study provide information on platelet concentrate usage in our hospital. Thrombocytopenia is a commonly observed hematological entity. Our study of usage of platelet concentrates in thrombocytopenia reveals infectious cause as predominant and common finding because of seasonal and regional variations. Common Bleeding manifestations are petechiae /purpura and gum bleeding. Platelet transfusion has become a progressively more common and important prophylactic and therapeutic procedure in managing thrombocytopenic patients.

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