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Platelet Transfusion; What and When to Transfuse, a Dilemma of Clinical Practice

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Abstract

Objective: To evaluate the effectiveness of guidelines driven platelet transfusion as well as to compare effectiveness of low verses high dose of the platelets transfusion.

Study design: Observational chart analysis study.

Place and duration of study: Jinnah Post Graduate Medical Center, Medical unit II, for 2 years in 2011 (Study-A) and 2012 (Study-B).

Material and method: Study A included 130 and Study B included 111 patients. In Study-A, retrospective chart analysis was done for all the patients who were either bleeding or had low platelet counts. Platelet transfusions given to these patients were evaluated. Based on these results and WHO bleeding stages; guidelines were structured for futures platelet transfusion. In Study B platelet transfusion were driven by these guidelines. Outcomes in form of discharge and death of patients given low, medium and high dose platelets were compared.

Results: In Study A; 98 patients were transfused platelets, out of which only 76 were actively bleeding; while in Study B platelets were transfused in 65 patients of whom 62 patients were having active bleeding. The outcome in term of patient discharged and expired was seen to be comparable in different dosage groups with a significant P value <0.005.

Conclusion: After following guidelines, 1% inappropriate platelet transfusions were administered as compared to 20% inappropriate transfusions in previous year. Low dose platelets were as effective as high dose platelets.

Keywords: Platelets, Mega units (single donor platelets/ SDP), Manual units (random donor platelets/ RDP)

Introduction

Haemostasis is the termination of bleeding by a complex coagulation process involving vasoconstriction, platelet aggregation and coagulation cascade [1,2]. Platelet disorders can adversely affect this process, either due to deficiency of platelets (thrombocytopenia) or abnormal platelets (thrombocytopathy) [3]. Patients may remain asymptomatic or present with mucosal or cutaneous bleeding, petechiae, purpura, ecchymoses or spontaneous bleeding which can occur when platelet count is <10,000 ul/dl [4]. In thrombocytopathic patients bleeding can occur at any platelet count. There are two types of platelet transfusions i.e. Single Donor Platelets (SDP,mega unit) and Random Donor Platelets (RDP, manual unit). The optimal dose for platelet infusion for prophylaxsis and therapeutic use is a subject of debate. Three trials in this respect are being done of which TOPPS (Trial of Prophylactic Platelets Study) is still underway; StOP (Strategies for the Transfusion of Platelets study) has been halted because of the significant bleeding episodes. The PLADO trial results have been published recently [5]. The aim of this study was to evaluate the overall need of the platelet transfusion and to determine the type and quantum of disease requiring platelet transfusion in a Medical Unit. Additionally it was designed to determine if platelet transfusions were done judiciously before and after implementation of the guidelines, as well as to evaluate the effectiveness of guidelines driven for platelet transfusion strategy.

Methods

This study was conducted in Medical Unit II of Jinnah Postgraduate Medical Center. It was completed over a time period of 2 years i.e. 2010 and 2011. All patients who were bleeding or had low platelet counts and had normal clotting profiles were included. The study had two components. Study-A; chart analysis of 130 patients admitted in 2010 who fulfilled the inclusion criteria were analyzed for clinical and laboratory parameters was done. The type of platelets (RDP or SDP) transfused were also analyzed. Study-B: conducted in 2011, was a prospective chart analyses of 111 patients, after implementing platelet transfusion guidelines was done again. Pre tested Proformas were filled and requirement of platelets were established on the basis of the WHO bleeding stages and guidelines modified by referring to other sources [6-9] (Tables 1 and 2). There was a deliberate policy to transfuse RDP rather than SDP, because of the ease of availability and less expenditure involved.

Patients were divided into five groups on the basis of the platelet counts. Group A had <5000/dl platelets; group B 5000-10,000; group C 10,000-20,000; group D 20,000-50,000; group E>50,000. These groups

were than analyzed for active bleeding and the amount and type of platelet transfusions given. The end points were discharge or death. The data was analyzed by using SPSS version 12. Information has been presented in frequency and percentages. Chi square test was used to calculate the p value.

Grade 0	No bleeding
Grade 1	Petechial bleeding
Grade 2	Mild blood loss (clinically significant)
Grade 3	Gross blood loss, requires transfusion (severe)
Grade 4	Debilitating blood loss, retinal or cerebral associated with fatality

Table 1: Who criteria of bleeding [8]

Prophylactic transfusion				
Platelet count <5000	Always transfuse irrespective of bleeding			
Platelet count 5000-10,000	minor hemorrhage (Grade 1 bleeding)	fever (>38oc)		
Platelet count 10,000- 20,000	coagulation disorder	heparin therapy	bone marrow biopsy planned	lumber puncture planned
Platelet count > 20,000	Grade 2 bleeding	Minor surgical procedures example		
		Biopsy		
		Central venous line		
Therapeutic platelet transfusion				
Platelet count > 50,000	Bleeding patient (all grades)		Non bleeding patient	
	continuous bleeding because of thrombocytopenia i.e. clotting profile normal	qualitative platelet defect (bleeding time > 1.5 the upper limit of normal or positive history	extensive surgery (neurosurgical procedure >100,000 counts)	
Platelet count 10,000-50,000	Grade 3 bleeding	Fall in Hb of 2 gm or HCT of 6%	Trauma patient	In perioperative period (3 days post op or ICU)

Table 2: Platelet transfusion [10,11].

Results

Study A

Out of 130 patients there were 84(64.6%) males and 46 (35.4%) females with a mean age of 30.2 years ± 13.7. The commonest disease was Dengue 78 patients (60%); of them 48 patients (61%) had active bleeding but platelet transfusion was given to 63 patients (80%). Of the transfused Dengue patients, 9 patients (14.2%) had a platelet count of <10,000/dl and 54 patients (85.7%) patients had platelet counts between 10,000 to 50,000 dl. The second most common cause of the bleeding was Aplastic anemia in 18 patients (13.9%) (Table 3).Overall leading presentation was with fever and bleeding from a single or multiple sites in 107 patients (82.3%). Thrombocytopenia (<50,000/dl) was present in 91 patients (70%) and active bleeding from any site was present in 76 patients (58.5%). A total of 91 patients (70%) were transfused platelets, of which 89 patients (64.8%) were given SDP, 5(5.49%) were given RDP and 3(3.29 %) were transfused both. Patients were divided into five groups on the basis of platelet count. In group A there were 3 patients; all were bleeding and all 3 were transfused platelets. In group B there were 13 patients; 10 were actively bleeding and all 13 were transfused platelets. There were 27 patients in group C 19 were actively bleeding and 26 were transfused platelets. Group D had 42 patients; 29 were actively bleeding and 38 were transfused platelets. Group E had 43 patients; 15 were bleeding and 11 were transfused platelets.

Study B

Out of 111 patients there were 69 (62.2%) males and 42 females (37%) with mean age of 34.96+13.9. The leading diagnosis was Malaria this year 37 patients (33.3%). Second most common diagnosis was hematological disorders in 21 patients followed by dengue and viral fever in 16 patients (Table 3). The main presentation of these patients was fever in 82% patients with active bleeding in 59.5% patients from single site in 36.9% patients. In group A, there was 1 patient; he was

actively bleeding and was transfused platelets. In group B, there were 4 patients; all 4 were actively bleeding and all were transfused platelets. There were 12 patients in group C; 11 were actively bleeding and 12 were transfused platelets. Group D; had 53 patients; 49 were actively bleeding and 48 were transfused platelets. Group E; had 41 patients; 40 were bleeding and none were transfused.

DISEASE	STUDY 1 (N130)	STUDY 2 (N 111)
Dengue	78 (60%)	16 (14.4%)
Aplastic Anemia	18 (13%)	7 (6.3%)
Viral fever	12 (9.2%)	16 (14.4%)
Idiopathic thrombocytopenia	7 (5.3%)	3 (2.7%)
Chronic myeloid leukemia	6 (4.6%)	2 (1.8%)
B12 deficiency	3 (2.3%)	4 (3.6%)
Malaria + Dengue	2 (1.5%)	7 (6.3%)
Myelofibrosis	1 (0.7%)	
Myelodysplastic syndrome	1 (0.7%)	
Glanzman thrombocytopenia	1 (0.7%)	
Malaria		37 (33.3%)
Acute myloid leukemia		4 (3.6%)
Malarial hepatitis		4 (3.6%)
Thalasemia		3 (2.7%)
Lymphoma		2 (1.8%)
Chronic lymphocytic leukemia		1 (0.9%)
Acute lymphocytic leukemia		1 (0.9%)
Chronic liver disease		1 (0.9%)
Pyrexia of unknown origin		1 (0.9%)
Sickle Cell anemia		1 (0.9%)
Viral Hemorrhagic fever		1 (0.9%)

Table 3: Frequency of diseases in two studies

Outcomes were also compared for patients transfused with low dose of platelets (RDP), medium dose (SDP) and high dose (both RDP +SDP).Low dose platelets (RDP) were given to 74 patients; 7 patients had medium dose (SDP) and 30 patients were given high dose platelets (RDP+SDP).

Outcomes	Low dose (SDP) (n= 74)	Medium (RDP) (n= 7)	High dose (SDP +RDP) (n=30)
Discharge	45	0	13
Expired	26	5	13
LAMA	3	2	4
P value <0.005			

Table 4: Outcome in three doses of platelet transfusion

Patients who were transfused the high dose were the ones with very low platelet counts <20,000(23 patients) and/or had grade 3, 4 bleeding (16 patients). Patients who were transfused low dose platelets had either counts >20,000 (58 patients) and/or had grade 1, 2 bleeding (63 patients). Medium doses were transfused to patients with platelet count between10,000-20,000 (7 patients) and/or bleeding grade 2 to 3 (5 patients). Comparison of outcomes; discharge, death or Leave Against Medical Advice (LAMA) was found to be similar in all the three groups of platelet doses with a p value of <0.005 (Table 4).

Discussion

Platelet transfusions are given for a variety of indication including those undergoing chemotherapy for leukemia, multiple myeloma, aplastic anemia, AIDS, sepsis, dengue fever, complicated malaria, bone marrow transplant, radiation treatment, organ transplant or surgeries as well as major surgical procedure such as cardio-pulmonary by pass. It has always been presumed that SDP is superior and more efficacious as one unit is equivalent to 6-7 RDP. As SDP is drawn from individual,

the risk of alloimunization is believed to be reduced however according to Trap there is no benefit to using leukoreduced single-donor platelet versus leukoreduced pooled random-donor platelets [6].

This study was undertaken to evaluate the overall need for the platelet transfusion in a medicine department and to determine the type and quantum of diseases requiring platelet transfusions and whether or not such transfusion were done judiciously. The prospective limb of the study examined the effects of implementation of guidelines derived from several sources in reducing injudicious platelet transfusion and reducing cost [7-9].

In this study when comparison of the spectrum of diseases requiring platelet transfusions. We saw that in Study A the main diagnosis was dengue as there was epidemic of dengue in Pakistan from August to November 2010 and more than 21,204 people were reportedly infected [12], While in Study B, the main diagnosis was malaria, which is endemic in Pakistan [13]. Patients had presented not only with usual symptoms of fever but also with complications like cerebral malaria and malarial hepatitis [14].

When stored for 5 days, SDP infusion losses its high potency of platelet [15]. The major advantage of RDP is it is cost effective. For SDP there is need of specialized and costly equipment, high recurring cost and the need of trained personnel. In an epidemic, there is often a shortage of SDP bags as well as other sources, thus creating unnecessary panic in the affected communities.

Our department has a stringent policy for transfusion of blood and blood products. Hence, even in Study A, when no guidelines were being implemented, the rate of inappropriate platelet transfusion was 20% as opposed to 35% documented by ND Kumar et al in their study conducted in India [16]. In Study B after guidelines driven treatment injudicious platelet transfusion were tremendously reduced to 1%, thus reducing the cost of treatment, as well as all the risks associated with transfusion of blood products.

Moreover, it is considered that above a threshold of 10,000 platelets, the platelet dose has no significant effect on the incidence of bleeding, probably because few platelets are needed to maintain homeostasis [17,18]. Some reports also suggest that endothelial integrity can be maintained with platelet counts of as low as 5000 per cubic millimeter [19,20]. The PLADO study concluded that low dose platelet transfusion, according to body surface area, is equivalent prophylactically to the high dose, and the corrected count increment did not differ significantly in patients transfused low, medium or high dose platelets15. Two randomized trials with limited enrollment-one of 111 patients [21] and the other of 119 patients [22]-have compared a low dose of platelets to the standard dose. In both trials, the two doses prevented bleeding to a similar degree. In Study B the number of expiries in the three groups (low dose, medium dose and high dose platelets) were 44 (39.6% .The higher mortality in our study compared to PLADO study may be attributable to the large number of complicated falciparum malaria cases. However, there were no significant differences among the three groups in the occurrence of any specific category of serious adverse events or in the percentage of patients who had one or more serious adverse events; even the number of deaths did not differ significantly among them (Table 4).

This study documents the safety, effectiveness and economy of RDP versus SDP. RDP is easily available in all hospitals where blood-banking services are available.

Conclusion

Cost effectiveness, availability, disease transmission and alloimmunization associated with platelet transfusion needs to be considered while transfusing platelets. Hence proper guidelines for platelet transfusion are needed considering the long term effects rather than the immediate benefit to patient. We also saw that RDP have similar efficacy and outcomes as SDP. This will not only reduce the number of inappropriate platelet transfusions, but will also reduce the financial burden on the hospital and the patients.

References

1. Lane DA, Philippou H, Huntington JA (2005) Directing thrombin. Blood 106: 2605.
2. Furie B, Furie BC (2008) Mechanisms of thrombus formation. N Engl J Med 359: 938.
3. Boon GD (1993) An Overview of Hemostasis. Toxicologic Pathology 21: 170-179
4. Bussel JB, Kuter DJ, George JN, McMillan R, Aledort LM, et al. (2006) AMG 531, a Thrombopoiesis-Stimulating Protein, for Chronic ITP. New England Journal of Medicine 355 : 1672-1681.
5. Blajchman MA, Slichter SJ, Heddle NM, Murphy MF (2008) New Strategies for the Optimal Use of Platelet Transfusions Hematology Am Soc Hematol Educ Program.
6. The Trial To Reduce Alloimmunization To Platelets Study Group (1997) Leukocyte reduction and ultraviolet B irradiation of platelets to prevent alloimmunization and refractoriness to platelet transfusions. N Engl J Med.
7. DeSancho MT, Rand JH (2001) Bleeding and thrombotic complications in critically ill patients with cancer. Crit Care Clin: 599-622.
8. Webert K, Cook RJ, Sigouin CS, Rebulla P, Heddle NM (2006) The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia. Haematological 91: 1530-1537
9. Gmur , Burger J, Schanz U, Ferh J, Schaffner A (1991) Safety of stringent prophylactic platelet transfusion policy for patients with acute leukemia. Lancet 338: 1223-1226
10. Webert K, Cook RJ, Sigouin CS, Rebulla P, Heddle NM (2006) The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia. haematologica 91: 1530-1537.
11. Gmur , Burger J, Schanz U, Ferh J, Schaffner A (1991) Safety of stringent prophylactic platelet transfusion policy for patients with acute leukemia. Lancet 338: 1223-1226
12. DeSancho MT, Rand JH (2001) Bleeding and thrombotic complications in critically ill patients with cancer. Crit Care Clin 17: 599-622.
13. Mahmood N, Rana MY, Qureshi Z, Mujtaba G, Shaukat U (2012) Prevalence and molecular characterization of dengue viruses serotypes in 2010 epidemic. Am J Med Sci 343: 61-64.
14. Kakar Q, Khan MA, Bile KM (2010) Malaria control in Pakistan: new tools at hand but challenging epidemiological realities. East Mediterr Health J: S54-60
15. Metha SR, Joshi V, Lazar AI (1996) Unusual acute and chronic complications of malaria. J Assoc Physicians India 44: 451-453.
16. Slichter SJ (2007) Evidence based platelet transfusion guidelines. Hematology Am Soc Hematol Educ Program: 172-178.
17. Kumar ND, Tomar V, Singh B, Kela K (2000) Platelet transfusion practice during dengue fever epidemic. Indian J Pathol Microbiol 43: 55-60.
18. Slichter SJ, Kaufman RM, Assmann SF, McCullough J, Triulzi DJ, et al. (2010) Dose of prophylactic platelet transfusions and prevention of hemorrhage. N Engl J Med 362: 600-613.
19. Slichter SJ (2004) Relationship between platelet count and bleeding risk in thrombocytopenic patients. Transfus Med Rev18: 153-167.

20. Heddle NM, Cook RJ, Sigouin C, Slichter SJ, Murphy M, et al. (2006) A descriptive analysis of international transfusion practice and bleeding outcomes in patients with acute leukemia. Transfusion46: 903-911.

21. Tinmouth A, Tannock IF, Crump M, Tomlinson G, Brandwein J, et al. (2004) Low-dose prophylactic platelet transfusions in recipients of an autologous peripheral blood progenitor cell transplant and patients with acute leukemia: a randomized controlled trial with a sequential Bayesian design. Transfusion 44: 1711-1719.

22. Heddle NM, Cook RJ, Tinmouth A, Kouroukis CT, Hervig T, et al. (2009) A randomized controlled trial comparing standard- and low-dose strategies for transfusion of platelets (SToP) to patients with thrombocytopenia. Blood 113:1564-1573.