Indian J Hematol Blood Transfus (Apr-June 2011) 27(2):70–74
DOI 10.1007/s12288-011-0059-1

ORIGINAL ARTICLE

Unfurling the Rationale Use of Platelet Transfusion in Dengue Fever

P. Pallavi · C. K. Ganesh · K. Jayashree · G. V. Manjunath

Received: 24 August 2010 / Accepted: 15 February 2011 / Published online: 11 April 2011

Abstract Dengue fever and dengue haemorrhagic fever have emerged as a global public health problem in recent decades. The practice of platelet transfusion has been adapted into the standard clinical practice in management of hospitalized dengue patients. The exact indications and situations in which platelet have to be transfused may vary greatly. Blood components especially platelet concentrates due to their short shelf life are frequently in limited supply. Hence, appropriate use of blood is required to ensure the availability of blood for patients in whom it is really indicated, as well as to avoid unnecessary exposure of the patients to the risk of transfusion reactions and transmission of blood borne infection. The present study was conducted to evaluate the appropriateness of platelet transfusion done in dengue patients with thrombocytopenia. The present study was conducted on 343 serologically confirmed dengue patients admitted at JSS University Hospital between 1st January and 30th August 2009. Clinical data, platelet count and platelet requirements were analyzed. Among the 343 serologically confirmed cases, the prevalence of thrombocytopenia (platelet count < 100,000/cumm) was 64.72% (222 patients) and bleeding manifestations were recorded in 6.12% (21 patients). 71 (20.7%) patients of dengue cases received platelet transfusion. Among them 34 (47.89%) patients had a platelet count <20,000/cumm, 28 patients (39.44%) had platelet counts in the range of 21–40,000/cumm while the remaining 9 (12.67%) patients had platelet count between 41–100,000/cumm. Out of 37 patients with a platelet count >20,000/cumm 11 patients had haemorrhagic manifestations such as petechiae, gum bleeding, epistaxis etc., which necessitates the use of platelet transfusion. However, the remaining 26 patients with platelet count >20,000/cumm and with no haemorrhagic manifestations received inappropriate platelet transfusion. Transfusion of 36.62% of platelet concentrate was inappropriate. The study emphasizes the need for development of specific guidelines for transfusion of blood components, constant interaction and co-ordination amongst clinicians and transfusion centre for implementation of these guidelines and a regular medical audit to review the optimal utilization of blood components.

Keywords Dengue · Haemorrhagic fever · Platelet count · Platelet transfusion · Rationale use

P. Pallavi (✉) · K. Jayashree · G. V. Manjunath
Department of Pathology, JSS Medical College and Hospital, JSS University, Mysore, India
e-mail: drpallavi123@gmail.com

C. K. Ganesh
JSS Medical College and Hospital, JSS University, Mysore, India

Introduction

Dengue infection is usually a benign syndrome caused by an arthropod borne virus. Dengue fever and dengue haemorrhagic fever have emerged as a global public health problem in recent decades. The South East Asian countries such as India, Indonesia, Myanmar and Thailand are at the highest risk of dengue accounting for nearly half of the global risk [1].

The role of platelet transfusion as a panacea for the management of dengue needs special mention since it is adopted into the standard clinical practice in many dengue endemic countries. Blood components especially platelet concentrates due to their short shelf life are frequently in limited supply. The collection, processing and testing of blood components is expensive and necessitates cost-containments, as in other areas of health care system [2]. A

poor health care system has led to under development of blood transfusion services which ultimately affect the transfusion practices [3]. Hence, appropriate use of blood components especially platelets is required to ensure the availability of the same for patients in whom it is really indicated, as well as to avoid unnecessary exposure of the patients to the risk of transfusion transmissible diseases [4].

There is a paucity of comprehensive data on the platelet usage from the developing countries which is reflective of their modest development in blood component therapy [3]. Our study aimed to know the appropriateness of platelet transfusion during dengue epidemic noting the platelet count in dengue patients and categorizing them as high risk (<20,000/cumm), moderate risk (20–40,000/cumm), low risk (40–100,000/cumm) and no risk (>100,000/cumm).

Materials and Methods

A retrospective study was conducted in blood bank, JSS University Hospital, Mysore, Karnataka during the epidemic of dengue fever between 1st of January and 30th of August 2009. Only dengue seropositive cases formed the subjects of the study. Patients clinical data, platelet count and platelet transfusion given to them were analyzed. Guidelines of platelet transfusion as suggested by WHO, followed at JSS Hospital (Table 1) was utilized as the criteria to assess the appropriateness of platelet transfusion during the study.

Results

During the study period, 343 patients had positive serology (IgM or IgM and IgG) to dengue virus by Elisa (Kit-Euro immune). Among these 343 patients with confirmed diagnosis, 199 (58%) were males while the rest 144 (42%) were females showing a male predominance. Majority of the dengue cases were children, with large proportion in the age group of less than 10 years (Table 2). Fever was the most common clinical presentation and was noted in all patients at the time of admission. Other common clinical features were headache, myalgia, vomiting and diarrhoea.

Table 1 Guidelines for platelet transfusion in dengue haemorrhagic fever

Indications:
• Prophylactic transfusion (in a non-bleeding patient)
Platelet count $< 20 \times 10^9$ l
• Therapeutic transfusion (in a bleeding patient)
Significant active clinical bleeding with platelet count $< 50 \times 10^9$/l
Proven disseminated intravascular coagulation

Platelet count of <100,000/cumm (thrombocytopenia) was detected in 222 (64.72%) patients. Haemorrhagic manifestation were present in 21 (6.12%) patients of dengue infections which mainly included petechiae, epistaxis, haematemesis, melaena and gum bleeding.

Seventy-one patients among 343 serologically confirmed patients (20.7%) received platelet transfusion. Among them 37 (52.11%) patients were male and 34 (47.89%) were female (Table 2). Out of 71 patients, 65 patients had only fever, four patients had features of dengue haemorrhagic fever while two patients had features of dengue shock syndrome. Dengue patients who received platelet transfusions with their respective platelet levels and clinical manifestations were noted (Table 3). Out of 23 dengue patients having platelet counts <10,000/cumm, 15 patients had received platelet transfusion. Of the 33 patients having platelet counts between 11–20,000/cumm, 19 patients received platelet transfusion where as 28 patients out of 76 having platelet counts in the range of 21–40,000/cumm had received platelet transfusion. Nine patients having platelet count in the range of 41–100,000/cumm received platelet transfusion. None of the 123 patients having platelet count >100,000/cumm received platelet transfusion (Table 3).

Out of 34 patients having platelet count <20,000/cumm who had received platelet transfusion, 15 patients had platelet count <10,000/cumm and the remaining 19 patients had platelet count between 11 and 20,000/cumm. Of these 19 patients, seven had haemorrhagic manifestations while 12 had no haemorrhagic manifestations. It has been observed that out of 37 patients having platelet count >20,000/cumm and having received platelet transfusion only 11 patients had haemorrhagic manifestations indicating a necessity of platelet transfusion while the remaining 26 patients had no haemorrhagic manifestations or signs of sepsis (Table 4).

Considering the guidelines of platelet transfusion, 26 (36.62%) patients with platelet count >20,000/cumm in absence of bleeding or sepsis received inappropriate transfusion. Only two patients died during hospitalization (mortality being 0.58%).

Discussion

Dengue viruses, belonging to the genus flavivirus of the family flaviviridae has antigenically four distinct serotypes, called DEN-1, DEN-2, DEN-3 and DEN-4. The virus is transmitted to the human beings by the bite of infected Aedes Egypti mosquito and few other members of Aedes species. Dengue virus causes a broad spectrum of illness ranging from mild undifferentiated fever to classical dengue fever, as well as dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). It has recently emerged as

Table 2 Age and sex distribution of patients with dengue fever and those who received platelet transfusion

Age group (in years)	Number of dengue cases			Number of cases who received platelet transfusion		
	Male	Females	Total	Males	Female	Total
0–10	78	54	132	12	13	25
11–20	37	27	64	3	8	11
21–30	44	16	60	14	5	19
31–40	16	15	31	4	3	7
41–50	14	17	31	3	4	7
>50	10	15	25	1	1	2
Total	199 (58%)	144 (42%)	343	37 (52.11)	34 (47.89)	71 (20.7%)

Table 3 Dengue patients who received platelet transfusion with their range of platelet count and haemorrhagic manifestation

Platelet counts (cells/cumm)	No of dengue patients	Number of cases who received platelet transfusion	Number of cases with haemorrhagic manifestation
<10,000	23	15	3
11–20,000	33	19	7
21–40,000	76	28	9
41–100,000	88	9	2
>100,000	123	0	0
Total	343	71 (64.72%)	21 (6.12%)

a major international health problem with an expanded geographic distribution and potential to cause major epidemics [5]. Our study showed that majority of dengue cases were children with the largest proportion in the age group of less than 10 years. In contrast to our study, Chuansumrit et al. [6] noted high percentage of dengue cases in age group of 10–14 years, while Ayyub et al. [5] and Lye et al. [7] noted adult preponderance in age group of 20–40 years.

Thrombocytopenia is a common problem in dengue, which causes a lot of concern not only to the patients but also to the relatives as well as the attending physicians [8]. In our study, thrombocytopenia (platelet count < 100,000/cumm) was found in 64.72% of the dengue confirmed cases which was low when compared to the findings of Makroo et al. [1] and Chairulfatah et al. [9] (84.88 and 83%, respectively). No clear guidelines exist for management of thrombocytopenia. The natural tendency is to transfuse platelets. Thrombocytopenia in dengue is primarily immune mediated and platelet transfusion are said to aggravate the thrombocytopenia by an exalted immune response by presenting a strong antigenic stimulus [8]. Besides, the short life span of transfused platelets result only in a transient non-sustained elevation of the platelet count [8, 10] they also evoke hypersensitivity reactions and fluid overload with complications such as pleural effusion, ascitis and pulmonary oedema [8].

In the present study, among the 71 patients who received the platelet transfusion only 21 patients (6.12%) presented with haemorrhagic manifestations. There was no correlation noted between the platelet counts and severity of symptoms, for only three patients out of 23 patients with counts below 10,000/cumm had signs of haemorrhage. Similarly, studies done by Lye [7] and Krishnamurty [11] found no correlation between bleeding score and platelet count. In paediatric dengue shock syndrome, thrombocytopenia did not predict severe bleeding in univariate

Table 4 Risk categorization of dengue

Risk category	PLT count cells/cumm	Treatment recommended	No of dengue cases	No of cases who received platelet transfusion	No of Inappropriate transfusion
High risk	<20,000	Prophylactic platelet transfusion	56	34	0
Moderate risk	21–40,000	Platelet transfusion for haemorrhagic symptoms (HS)	76	28 9—with HS	19
Low risk	41–100,000	Carefully monitor	88	9 2 with HS	7
No risk	>100,000	Supportive therapy	123	0	0
			343	71	26 (36.62%)

Table 5 Comparative Studies

Study	No of dengue cases	No of cases with platelet transfusion	No of cases with haemorrhagic symptoms	Inappropriate platelet transfusion	References
Kumar et al. [4]	1,837	208 (11.3)	65 (31.3%)	71 (34.1%)	4
Makroo et al. [1]	225	96 (42.6%)	34 (15.11%)	31 (13.77%)	1
Chaudary et al. [14]	245	–	–	21.5%	14
Present study (2009)	343	71 (20.7%)	21 (6.12%)	26 (36.62%)	

analysis, the only two independent predictors of severe bleeding were shock and low haematocrit [12].

Prophylactic platelet transfusion is defined as platelet transfusion without clinical bleeding, in contrast to therapeutic platelet transfusion with clinical bleeding [7]. The dengue patients can be categorized into the high, moderate, low and no risk groups based on their platelet count of <20,000, 21–40,000, 41–100,000 and >100,000/cumm, respectively at the time of admission. It is noted that patients belonging to high risk group are at high risk of bleeding and need prophylactic platelet transfusion [1]. But, Lye have shown in his study that prophylactic platelet transfusion did not improve relevant outcome measures, such as clinical bleeding, platelet increment and platelet recovery with no significant benefits among adult dengue patients [7]. Similarly in paediatric DSS, prophylactic transfusions of platelets and fresh frozen plasma did not reduce bleeding or expedite platelet recovery, instead, it caused fluid overload and prolonged hospitalization [13].

In our study 45 out of 71 patients received platelet transfusion, the norms laid down by the guidelines for the hospitalized dengue patients was followed. Among these, 34 patients had platelet count <20,000/cumm and 11 though their platelet counts were >20,000/cumm they presented with haemorrhagic manifestations and thus required therapeutic platelet transfusion. But in the remaining 26 patients though their platelet counts were >20,000/cumm and did not have any bleeding manifestations or signs of sepsis, they were transfused with platelets. Thus, the guidelines for platelet transfusion were ignored, exposing a significant number of 26 (36.62%) patients to unnecessary hazards of blood transfusion. Similarly other studies [1, 4, 14] have found inappropriate platelet transfusion during dengue epidemics (Table 5).

Sellahewa states that prophylactic transfusion for dengue are baseless and appear to be an irrational and inappropriate intervention. However, transfer of patients from peripheral hospitals to tertiary care hospitals primarily for platelet transfusions reflect the dilemmas confronting clinicians in managing thrombocytopenia in patients with dengue [8]. Makroo et al. [1] noted that many times the prescription for the platelet are not based on medical rationale, but as a response to an intense social pressure on the treating physicians by the patients and their relatives. Kumar et al. [4] also observed that the demands for platelet transfusion were mostly received as a panic reaction during the epidemic of dengue fever. Observing a fall in platelet count even if the count were above 20×10^9/l, the blood prescribing clinicians had sent requisition for platelet transfusion without any specific indications. This actually led to non-availability of platelet in a centre not geared to meet excessive requirements of platelets. The same 'chase' for platelet counts has been mentioned by Ahluwalia [15]. The crux in treatment of dengue patients is maintenance of good hydration, monitoring for any over bleeding and not 'panic' if the platelet count is more than 50,000/cumm. This 'syndrome' of chasing platelet count in dengue patients who are otherwise completely asymptomatic and improving can be labelled as 'Dengue panic syndrome'. This panic syndrome was also quiet evident in our study.

The efficacy of prophylactic platelet transfusion and the threshold for transfusion is questionable. Platelet transfusions are hardly ever required even with counts as low as 10,000/cumm because the circulating platelets are haematologically active and sufficient to prevent bleeding by thrombocytopenia per se [10]. In general, platelet transfusion are given only when there are serious haemorrhagic manifestations. Transfusion requirements correlate with the occurrence of bleeding in the gastrointestinal tract but not with the platelet count [6]. Mucosal bleeding may occur in any patients with dengue but, if the patients remain stable with fluid resuscitation/replacement, it should be considered as minor. In patients with profound thrombocytopenia, strict bed rest and protection from trauma to reduce the risk of bleeding is recommended [16]. According to the guidelines by Ministry of Health, Srilanka there is no place for prophylactic platelet even with a count below 10,000/cumm if there is no evidence of bleeding [17]. Considering the various guidelines and several studies done it is clear that platelet count alone does not predict the severity of bleeding. Hence before giving prophylactic platelet transfusion to high risk group patients with platelet count <20,000, their haemodynamic status and signs of sepsis must be considered. Thus, reducing the number of prophylactic transfusion to patients with platelet count >10,000 and with no signs of sepsis or haemorrhagic manifestations.

In developing world a considerable heterogeneity exists for platelet transfusion practices between countries and even within countries in hospitals where this precious resource is available [3]. As platelet products are scarcely available and expensive, there is a need to implement best platelet transfusion practices. Few interventions are emphasized in this study in the context of improving the status of platelet utilization in developing countries. A regular medical audit or a blood utilization review is an effective way of increasing the likelihood of improving transfusion practices. Constitution of a hospital transfusion committee, with a constant communication, interaction and co-ordination amongst clinicians and transfusion medicine specialist, as well as continuing medical education programmes for prescribing clinicians and blood transfusion personnel would also be helpful in promoting appropriate use of blood.

Conclusion

Transfusion of 36.62% of platelet concentration was inappropriate. The liberal use of platelets in the treatment of dengue may create a real danger to the patients in terms of fluid overload and transfusion transmitted infections in addition to unnecessary cost. The study emphasizes the need for development of specific guidelines for transfusion of blood components, constant interaction and co-ordination amongst clinicians and transfusion centre for implementation of these guidelines and a regular medical audit to review the optimal utilization of blood components.

References

1. Makroo RN, Raina V, Kumar P, Kanth RK (2007) Role of platelet transfusion in the management of dengue patients in a tertiary care Hospital. Asian J Trans Sci 1:4–7
2. Thomas A, Contreras M, Knowles S (1991) Blood component treatment: a retrospective audit in fine major hospitals. J Clin Pathol 44:734–739
3. Verma A, Agarwal P (2009) Platelet utilization in the developing world: strategies to optimize platelet transfusion practices. IJPM 41:145–149
4. Kumar ND, Tomas V, Singh B, Kela K (2000) Platlet transfusion practice during dengue fever epidemics. Indian J Pathol Microbiol 43:55–60
5. Ayyub M, Khazindar AM, Lubbad EH et al (2006) Characteristics of dengue in a large public hospital, Jeddah, Saudi Arabia. J Ayub Medical Coll Abbottabad 18:9–13
6. Chuansumrit A, Phimolthares V, Tardtong P et al (2000) Transfusion requirements in patients with dengue hemorrhagic fever. Southeast Asian J Trop Med Public Health 31:10–14
7. Lye DC, Lee VJ, Sun Y, Leo YS (2009) Lack of efficacy of prophylactic platelet transfusion for severe thrombocytopenia in adults with acute uncomplicated dengue infection. Clin Infect Dis 48:1262–1265
8. Sellahewa KH (2008) Management dilemmas in the treatment of dengue fever. Dengue Bull 32:211–218
9. Chairulfatah A, Setibudi D, Agoes R, Colebunder R (2003) Thrombocytopenia and platelet transfusion in dengue. Haemorrhagic fever and dengue shock syndrome. WHO Dengue Bull 27:141–143
10. Isarangkura P, Tuchinda S (1993) The behavior of transfused platelets in dengue haemorrhagic fever. Southeast Asian J Trop Med Public Health 24:222–224
11. Krishnamurti C, Kalyanaraj S, Cutting MA et al (2001) Mechanisms of haemorrhage in dengue without circulatory collapse. Am J Trop Med Hyg 65:840–847
12. Lum LC, Goh AX, Chan PW et al (2002) Risk factors for severe haemorrhagic in severe dengue infections. J Pediatr 140:629–631
13. Lum LCS, Abdel-Latif ME, Goh AYT et al (2003) Preventive transfusion in dengue shock syndrome is it necessary? J Pediatr 143:682–684
14. Chaudhary R, Khethan D, Sinha S, Sinha P, Sonker A, Pandey P et al (2006) Transfusion support to dengue patients in a hospital based blood transfusion service in North India. Transfus Apher Sci 35:239–244
15. Ahluwalia G, Sharma SK (2004) Dengue current trends and challenges–an Indian perspective. JAPI 52:561–563
16. World Health Organization (2009) Dengue: guidelines for diagnosis, treatment, prevention and control. World Health Organization, Geneva, pp 40–41
17. Ministry of Health, Sri Lanka (2005) Guidelines on clinical management of dengue fever/dengue haemorrhagic fever. Epidemiology Unit, Colombo