Original Article

DOI: 10.17354/ijss/2015/281

Role of Platelet Transfusion and its Misuse in Managing Dengue Fever

S Irshad Ahamed[1], R Raj Bharath[2]

[1]Undergraduate, Sri Manakula Vinayagar Medical College and Hospital, Pondicherry, India, [2]Assistant Professor, Department of Transfusion Medicine, Sri Manakula Vinayagar Medical College and Hospital, Pondicherry, India

Abstract

Background: Dengue is a prevalent mosquito-borne acute viral infection with potential fatal complications caused by an arbovirus transmitted by the vector aedes aegypti. Thrombocytopenia is almost universally observed in dengue infection. These results from both reduced production and increased destruction of platelets. The guidelines stipulate that platelet transfusion should be given to patients with platelet count <20000. Platelet transfusion has a variety of risks including alloimmunization, platelet refractoriness, allergic reactions, febrile nonhemolytic reactions, bacterial sepsis, and less commonly transfusion-associated acute lung injury.

Materials and Methods: A retrospective study design was conducted in blood bank Sri Manakula Vinayagar Medical College Hospital, Pondicherry with about 41 dengue patients who were transfused with platelet as a supportive measure during epidemic of dengue from 2012 to 2013.

Results: Among the 41 dengue patients who have been platelet transfused, therapeutic transfusion with bleeding manifestation includes 12 patients and prophylactic therapy without bleeding manifestation constitutes 29 patients.

Discussion: The patients who were having a platelet count <20,000 and therapeutically transfused (who had bleeding manifestations) were around 50%. The percentage of therapeutically transfused decreases from 50% to 15% in patients having a platelet count more than 20,000. This puts them at more risk of getting transfusion-transmitted infections and also various transfusion related adverse events.

Key words: Dengue, Platelets, Transfusion

INTRODUCTION

Dengue is a prevalent mosquito-borne acute viral infection with potential fatal complications caused by an arbovirus (arthropod - borne virus) transmitted by the vector aedes aegypti.[1] The term "break bone fever" was coined for dengue because of the symptoms of myalgia and arthralgia.[2] Dengue viruses (DV) comes under family *Flaviviridae* and there are four serotypes of the virus referred to as DV-1, DV-2, DV-3, and DV-4. DV is a positive-stranded encapsulated RNA virus and consists of three structural protein genes which encode the nucleocapsid or core (C) protein, a membrane-associated (M) protein, an enveloped (E) glycoprotein, and seven non-structural (NS) proteins.[2] It is endemic in more than 100 countries worldwide where around 50-100 million infections occur every year. All four serotypes can cause the full spectrum of disease from a subclinical infection to a mild self-limiting disease, the dengue fever (DF) and a severe disease that may be fatal, the dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS).[3] Dengue is globally the most important arboviral infection and threatens an estimated 2.5 billion people worldwide. Thrombocytopenia is commonly observed in dengue infection. This result from both reduced production and increased destruction of platelets.[4] The epidemiology of DF in the Indian subcontinent has been very complex and has substantially changed over almost past six decades in terms of prevalent strains, affected geographical locations, and severity of disease. The first report of dengue in India was in 1946, and soon the whole country was involved with widespread epidemics,

Access this article online

www.ijss-sn.com

Month of Submission : 04-2015
Month of Peer Review : 05-2015
Month of Acceptance : 05-2015
Month of Publishing : 06-2015

Corresponding Author: Dr. R. Raj Bharath, Department of Transfusion Medicine, Triplicane, Chennai - 600 005, Tamil Nadu, India, Mobile: +91-9444338316. E-mail: rajrr.84@gmail.com

which was followed by the endemic prevalence of all the four serotypes of dengue virus.

Clinical presentation of DF is characterized by an abrupt onset of fever associated with frontal headache and retro-orbital pain, myalgia, arthralgia, vomiting, and weakness. A generalized maculopapular rash appears 1 or 2 days after fever defervescence. Minor hemorrhagic manifestations signs like petechiae may be observed in some patients. DF is generally self-limiting, and most patients recover without complications approximately 10 days after the onset of illness. However, some patients develop severe manifestations such as increased vascular permeability and plasma leakage that can lead to death. Signs of spontaneous bleeding are more frequent in severe forms of dengue.[5] Dengue patients generally have high levels of cytokines, chemotactic complement anaphylatoxins C3a and C5a, and histamine, which have the capability to induce vascular permeability. Evidence indicates that the endothelium itself plays a prominent role in immune-enhanced pathology, and that leads to increased vascular permeability in DHF and DSS. The detection of NS1 in dengue is the basis of commercial diagnostic assays.[6]

Dengue patients can be categorized into the four categories based on their platelet count at the time of admission:

1. High risk (platelet count <20,000/cu mm)
2. Moderate risk (platelet count between 21 and 40,000/cu mm)
3. Low risk (platelet count between 40 and 100,000/cu mm)
4. No risk (platelet count >100,000/cu mm).[7]

While the medical fraternity globally recognizes the importance of platelet transfusion in the management of hospitalized dengue patients, the indications to platelet transfusion may vary. The DHS guidelines state that platelet transfusion should be given to patients with platelet count <20000/cumm.[7] The optimal number of platelets in a prophylactic platelet transfusion is controversial. A standard dose for adults is considered to be approximately 3×10^{11} to 6×10^{11} platelets. Higher doses of platelets than these could also result in superior hemostasis.[8] Prophylactic platelet transfusion can result in various risks such as alloimmunization, platelet refractoriness, allergic reactions, febrile nonhemolytic reactions, bacterial sepsis, and less commonly transfusion-associated acute lung injury.[9]

MATERIALS AND METHODS

A retrospective study design was conducted in blood bank Sri Manakula Vinayagar Medical College and Hospital Pondicherry with about 41 dengue patients who were transfused with platelet as a supportive measure during an epidemic of dengue from 2012 to 2013. The ethical clearance was obtained from the ethical committee, and the patient consent was obtained for the study. Only dengue seropositive (NS1 positive) patients who have undergone platelet transfusion were taken for the study. Nondengue patients and dengue patients who are not platelet transfused were not included in this study. The main objective was to determine whether prophylactic platelet transfusion is necessary and appropriate in dengue patients who have no bleeding manifestations.

RESULTS

A total of 41 dengue patients who have been platelet transfused were taken in the study during the period of the epidemic. Among them, patients with age <10 years included 5 (12.2%) patients, of age group 11-20 includes 2 (4.9%) patients, 21-30 includes 15 (36.6%) patients, 31-40 includes 8 (19.5%) patients, and 41 and above includes 11 (26.8%) patients. Fever was the most common clinical presentation noted in all patients during the time of admission. Other clinical features included headache, bleeding gums, vaginal bleeds, myalgia, and bone pain. Hemorrhagic manifestations, which were seen in dengue patients includes epistaxis, hematemesis, and gum bleeding. Among the 41 dengue patients who have been platelet transfused therapeutic transfusion with bleeding manifestation includes 12 (29.3%) patients of which 6 (30.0%) were female patients and male were 6 (28.6%) patients. Prophylactic therapy without bleeding manifestation constitutes 29 (7.7%) patients of which 14 (70%) were female patients and 15 were (71.4%) male patients. In this study, patients with platelet count <10,000/cu mm, 2 patients have received prophylactic therapy and 2 patients have received a therapeutic transfusion. Between 10,000 and 20,000/cu mm 4 patients have received prophylactic therapy whereas 4 patients received a therapeutic transfusion. Patients between 20,000 and 40,000/cu mm 9 received prophylactic transfusion and 2 received a therapeutic transfusion. Moreover, patients with 40,000 and above 14 received prophylactic transfusion and 4 patients were therapeutically transfused.

DISCUSSION

Of the 41 patients who were platelet transfused 29 (70.7%) were prophylactically transfused and the remaining 12 (29.3%) had bleeding manifestations and were therapeutically transfused. Pallavi *et al.* in her study reported that only 21 patients (6.12%) presented with hemorrhagic manifestations.[10] The most common age

group for platelet transfusion in dengue patients was between 20 and 30 years (36.6%). Makroo *et al.* similarly reported the majority of dengue cases were between the age group of 21-30 years while Nagerakha *et al.* observed that most dengue patients were in the age group <10 years.[11] In our study, 18 (43.9%) of those who were platelet transfused were in the platelet range of more than 40,000 whereas in Makroo *et al.* study the majority of dengue cases who were platelet transfused was between 20,000 and 40,000. In our study, the patients who were having a platelet count <20,000 and therapeutically transfused (who had bleeding manifestations) were around 50%. The percentage of therapeutically transfused decreases from 50% to 15% in patients having a platelet count more than 20,000. This is 56% (prophylactic transfusion and platelet count more than 20,000) of the total number of dengue patients who were transfused inappropriately with platelets. Pallavi *et al.* reported 36.6% of dengue patients to have been inappropriately transfused platelets. Studies conducted by Chaudhary *et al.* and Kumar *et al.* showed the patients transfused platelets inappropriately were 21.5% and 56.2%, respectively.[12,13] If we compare between age group and patients who were therapeutically transfused it was 43% in the age group of 0-20 years. It gets lower to 27% in the age group more than 20 years. This shows that the probability of bleeding in a patient aged more than 20 years is very low (platelet count more than 20,000) and platelet transfusion could have been avoided. There was no significant difference between the male and female group among those who were prophylactically and therapeutically transfused.

Mass media play a very important role in hyping up the role of platelet transfusion in dengue patients. Dengue patients get admitted to the hospital for the sole reason of platelet transfusion after reading these unproven reports from the media. The reason for platelet transfusion are not based on medical rationale, but as a result of an intense social pressure on the treating physicians by the patients and their relatives.[7] Kumar *et al.* also observed that the increased use of platelet transfusion were mostly due to a panic reaction during the epidemic of DF.[13] Clinician awareness is low in not knowing the more risk associated with platelet transfusion than the benefits of it. The blood bank is put under a lot of stress in getting more donors for this irrational platelet transfusion. This leads to more replacement donation than a voluntary donation. As most of the blood banks do not have an apheresis machine for obtaining single donor apheresis platelets they have to depend on only random donor platelets. Random donor platelets (prepared from 350 ml of blood) results in a very low increment (corrected count increment - 5,000) so these patients have to be repeatedly transfused with more number of platelets from different donors. This puts them at more risk of getting transfusion-transmitted infections and also various transfusion related adverse events. In economically under-developed and developing countries where the highly sensitive nucleic acid testing (NAT) cannot be done due to its high cost, platelet transfusion should be made more stringent.[9] The cost factor plays a predominant role in determining the type of screening tests in developing countries like India where rapid and ELISA testing are commonly employed which are not highly sensitive when compared to NAT.

Randomized controlled trials conducted by Mohammed *et al.* revealed that Platelet transfusion, despite increasing platelet count in half the recipients, neither stopped the progression to severe bleeding nor shortened the time to cessation of bleeding. This proves that a high baseline platelet count and a successful platelet transfusion cannot prevent progression to severe bleeding.[14] Similar studies by Krishnamurti *et al.* showed that vascular alteration and platelet activation present in dengue infection which is a separate, underlying process was also responsible for bleeding as well as thrombocytopenia.[15] Rather, early recognition of dengue with prompt correction of hemodynamic parameters, remains the cornerstone of avoiding hemorrhage and ensuring good clinical outcomes. As platelet products are scarcely available and precious, rational use of platelet transfusion should be advocated.

CONCLUSION

Platelet transfusion could have been avoided in 56% of the dengue patients. Irrational use of platelets will put the patient at a huge risk from transfusion-transmitted infections as well as transfusion-related adverse events. In developing countries, platelet transfusion practices vary between clinicians, hospitals, and regions. There should be a clear set of guidelines regarding the use of platelets in dengue and proper co-ordination among clinicians and transfusion medicine specialist would be helpful in promoting rational use of platelets.

REFERENCES

1. Whitehorn J, Farrar J. Dengue. Br Med Bull 2010;95:161-73.
2. Gupta N, Srivastava S, Jain A, Chaturvedi UC. Dengue in India. Indian J Med Res 2012;136:373-90.
3. Lee IK, Liu JW, Yang KD. Fatal dengue hemorrhagic fever in adults: Emphasizing the evolutionary pre-fatal clinical and laboratory manifestations. PLoS Negl Trop Dis 2012;6:e1532.
4. Whitehorn J, Rodriguez Roche R, Guzman MG, Martinez E, Gomez WV, Nainggolan L, *et al.* Prophylactic platelets in dengue: Survey responses highlight lack of an evidence base. PLoS Negl Trop Dis 2012;6:e1716.
5. Rodriguez-Roche R, Gould EA. Understanding the dengue viruses and progress towards their control. Biomed Res Int 2013;2013:690835.
6. Dalrymple NA, Mackow ER. Endothelial cells elicit immune-enhancing responses to dengue virus infection. J Virol 2012;86:6408-15.

7. Makroo RN, Raina V, Kumar P, Kanth RK. Role of platelet transfusion in the management of dengue patients in a tertiary care hospital. Asian J Transfus Sci 2007;1:4-7.
8. Slichter SJ, Kaufman RM, Assmann SF, McCullough J, Triulzi DJ, Strauss RG, *et al.* Dose of prophylactic platelet transfusions and prevention of hemorrhage. N Engl J Med 2010;362:600-13.
9. Kurukularatne C, Dimatatac F, Teo DL, Lye DC, Leo YS. When less is more: Can we abandon prophylactic platelet transfusion in Dengue fever? Ann Acad Med Singapore 2011;40:539-45.
10. Pallavi P, Ganesh CK, Jayashree K, Manjunath GV. Unfurling the rationale use of platelet transfusion in dengue fever. Indian J Hematol Blood Transfus 2011;27:70-4.
11. Kulkarni N. Studies on the effectiveness of transfusion program in dengue patients receiving platelet transfusion. Int J Blood Trans Immunohematol 2012;2:11-5.
12. Chaudhary R, Khetan D, Sinha S, Sinha P, Sonker A, Pandey P, *et al.* Transfusion support to dengue patients in a hospital based blood transfusion service in north India. Transfus Apher Sci 2006;35:239-44.
13. Kumar ND, Tomar V, Singh B, Kela K Platelet transfusion practice during dengue fever epidemic. Indian J Pathol Microbiol 2000;43:55-60.
14. Khan Assir MZ, Kamran U, Ahmad HI, Bashir S, Mansoor H, Anees SB, *et al.* Effectiveness of platelet transfusion in dengue fever: A randomized controlled trial. Transfus Med Hemother 2013;40:362-8.
15. Krishnamurti C, Kalayanarooj S, Cutting MA, Peat RA, Rothwell SW, Reid TJ, *et al.* Mechanisms of hemorrhage in dengue without circulatory collapse. Am J Trop Med Hyg 2001;65:840-7.

How to cite this article: Ahamed SI, Bharath RR. Role of Platelet Transfusion and its Misuse in Managing Dengue Fever. Int J Sci Stud 2015;3(3):110-113.

Source of Support: Nil, **Conflict of Interest:** None declared.