

Prophylactic platelet transfusion in dengue: A dilemma

Marium Rehman, Muhammad Armughan Ali, Muhammad Adil Siddiqui

Madam, dengue fever is a vector borne viral haemorrhagic fever associated with substantial cost to the health care sector in endemic countries. Thrombocytopenia, a major feature of dengue fever results from decreased platelet production from bone marrow suppression or increased platelet destruction.¹ The pathogenesis of bleeding in dengue is multifactorial and has not been fully elucidated. Clinical evidence guiding the management of thrombocytopenia with prophylactic platelet transfusion is debateable. Several retrospective studies have been conducted over the years regarding the efficacy of prophylactic platelet transfusion in thrombocytopenic dengue patients showing no increased benefit.^{2,3} A small randomised controlled trial (n=87) reported that platelet transfusion did not stop the development of severe bleeding nor reduce the time to cessation of bleeding but lead to severe transfusion reactions and two deaths.⁴

David Lye et al conducted a multicentre, open-label, randomised, superiority trial which included two groups: prophylactic platelet transfusion plus supportive care (transfusion group) versus supportive care alone (control group).⁵ The patients were adult, presenting with dengue and thrombocytopenia. This has been the only trial conducted on such a large scale. Out of the 372 enrolled patients, 188 were included in the transfusion group and 184 were included in the control group. Patients in the transfusion group with platelet counts of 20,000/ μ L or less received four units of pooled platelets each day. The primary endpoint was clinical bleeding (excluding petechiae) by study day 7 after randomisation or hospital discharge (whichever occurred earlier). It was observed that clinical bleeding occurred in 40 (21%) patients in the transfusion group and 48 (26%) patients in the control group showing no significant difference between the two. Incidence of clinical bleeding by day 21 (follow-up visit) also occurred similarly among the two groups with no statistically significant difference (42 [22%] vs 49 [27%]; $p=0.34$). Severe bleeding by day 21 was also observed to be similar between the two groups (3 [2%] vs 7[4%]; $p=0.21$). In

order to assess the efficacy at lower platelet counts, a post hoc sub group analysis was done which disclosed similar results in patients with platelet count of less than 10,000 per μ L and 5000 per μ L. However, adverse effects were noted significantly more in the transfusion group and included urticarial, maculopapular rash, pruritus, chest pain, anaphylaxis, transfusion related acute lung injury and fluid overload.

This trial reports that prophylactic platelet transfusion is not superior to supportive care in the management of thrombocytopenia in adult dengue patients. Conversely this study did not address the effects at different doses of platelet transfusion which entails further investigation. Since all the patients (transfusion group) in the trial received a similar dose (4 units per day), the efficacy of higher doses of platelets could not be elucidated. For now, these findings provide a substantial evidence to call for a cessation of prophylactic platelet transfusions in dengue so as to reduce the burden on already limited resources of blood banks and hospitals and spare the patients from potential adverse events.

Declaration: The letter has not been previously presented or published in a conference.

Conflict of Interest: None.

Funding Disclosure: None.

References

1. Azeredo EL, Monteiro RQ, de-Oliveira Pinto LM. Thrombocytopenia in dengue: interrelationship between virus and the imbalance between coagulation and fibrinolysis and inflammatory mediators. *Mediators Inflamm.* 2015; 2015: 313842.
2. Whitehorn J, Roche RR, 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.
3. Lee TH, Wong JG, Leo YS, Thein TL, Ng EL, Lee LK, et al. Potential harm of prophylactic platelet transfusion in adult dengue patients. *PLoS Negl Trop Dis* 2016; 10: e0004576.
4. Assir MZ, Kamran U, Ahmad HI, Bashir S, Mansoor H, Anees SB Akram J. Effectiveness of platelet transfusion in dengue Fever: a randomized controlled trial. *Transfus Med Hemother* 2013; 40: 362-8.
5. Lye DC, Archuleta S, Syed-Omar SF, Low JG, Oh HM, Wei Y et al. Prophylactic platelet transfusion plus supportive care versus supportive care alone in adults with dengue and thrombocytopenia: a multicentre, open-label, randomised, superiority trial. *Lancet* 2017; 389: 1611-8.

.....

Dow University of Health Sciences, Karachi.

Correspondence: Muhammad Armughan Ali.

Email: armughanali8@hotmail.com