Selected Summaries

Prophylactic platelet transfusion in dengue: Blanket of false comfort?

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SUMMARY

This study was an open-label, randomized trial, which included adult patients with dengue in Singapore and Malaysia, to assess the utility of platelet transfusions in those with significant thrombocytopenia.

Admitted adults, ≥21 years of age, in whom a diagnosis of dengue was confirmed by either polymerase chain reaction, non-structural protein 1 positivity or serology and with a platelet count of <20 000/cmm were included in the study. Patients with significant active bleeding, pregnant or lactating women, those with a history of peptic ulcer or with anticoagulant use or those with a long-standing organic disease were excluded from the study. In addition, extremely sick patients who were not expected to live beyond 48 hours and those with a history of an adverse reaction to transfusion of blood or its products were also excluded from the study. Eligible patients (*n*=372) were randomized to two groups. The transfusion group received platelet transfusion and supportive care and the control group was managed with supportive measures in the form of intravenous fluids and antipyretics. Patients in the transfusion group were transfused 4 units of platelets every day, until the platelet counts were >20 000/cmm, in addition to supportive care. Since none of these patients had active bleeding from any site at the time of randomization, this strategy in the transfusion group was termed prophylactic platelet transfusion. Baseline blood investigations were done in all patients including haemogram and kidney and liver function tests. In addition, coagulation profile and a chest X-ray were also done.

Patients were monitored for bleeding, serositis and shock. In the transfusion group, platelet counts were done at 1, 12 and 24 hours after transfusion. Packed cell volume (PCV) was also monitored and an increase by 20% or more was considered indicative of plasma leakage. Based on these clinical and laboratory monitoring measures, various events in the study groups were measured. One of these was the number of days in which the baseline platelet count of 20 000/cmm or less increased to ≥50 000/cmm. The number of days of hospitalization was also noted. Major adverse events such as sepsis, adverse reaction to platelet transfusion, transfer to intensive care unit and severe bleeding manifestations and death were assessed.

In the transfusion group, by the fourth day of enrolment, almost all patients had platelet counts >50 000/cmm. Four units of platelets were transfused to the patients per day in the transfusion group and an average of 4.71 units of platelets was transfused per patient. No significant difference was found in bleeding rates, including severe bleeding, between the two groups. The number of patients with evidence of plasma leakage was also comparable. There was no significant difference in the occurrence of dengue shock syndrome between the two groups. The number of days of hospitalization was also not significantly different between the groups. The transfusion group had significantly higher number of adverse events compared to the control group, of which approximately 69% of events were attributable to the transfusion itself.

The authors concluded that the strategy of prophylactic platelet transfusion did not provide an advantage to supportive care in terms of risk of bleeding, hospital stay or prevention of non-haemorrhagic complications of dengue-like shock. Instead, platelet transfusion was associated with more adverse events as compared to those who were managed conservatively.

COMMENT

Dengue has become a major global health problem.[1] Thrombocytopenia which commonly accompanies dengue has become an inappropriate target of treatment.[2] There is a constant fear of increased risk of bleeding manifestations with low platelet counts which lead to inappropriate prophylactic platelet transfusions. This strategy actually does not serve any purpose and adds to the risk as evidenced by various studies. Further, prophylactic platelet transfusions increase the burden on the healthcare system by increasing the requirement of blood products during epidemics of dengue.

Studies in both children and adults have shown that platelet counts are not related to the risk of bleeding manifestations.[3–5] On the other hand, abnormality in platelet aggregation was noticed in dengue patients with bleeding in a large study from New Delhi,[4] suggesting that qualitative defects in platelet functioning rather than the number of platelets is responsible for bleeding manifestations. Other factors such as old age,[6] deranged coagulation profile,[7] higher PCV,[7] leucocytosis[8] and female gender[8] have been shown to be associated with increased risk of bleeding. A large retrospective study from Singapore has shown that prophylactic platelet transfusion is not helpful in preventing bleeding or in increasing platelet counts.[3]

A study from Bengaluru found that prophylactic platelet transfusion delayed the recovery of patients, in terms of increment of platelet counts and the time to discharge.[9] In another study of children from Malaysia, patients receiving prophylactic platelet transfusion had a significantly higher risk of developing pulmonary oedema.[10] The risk of transfusion-related adverse effects such as anaphylaxis, transmission of blood-borne infections and acute lung injury always exists with transfusion of blood products, including platelets.

This large randomized study was done on 372 adult patients with dengue and showed that prophylactic platelet transfusion had no added advantage over supportive care. Women, who are at higher risk of bleeding, constituted just 24% of the study population.[8] Severe bleeding was present only in a minority of patients, so the effect of prophylactic platelet transfusion on severe bleeding events could not be assessed. Another study from

Singapore measured outcomes similar to the current study but retrospectively.[11] It found that patients who were transfused prophylactically had a shorter duration of fever, higher pulse rate and more neutrophil percentage as compared to those who were not transfused. Further, platelet increment after 24 hours of admission was higher in the transfusion group.

The British Committee for Standards in Haematology has recommended a platelet count ≤10 000/cmm for prophylactic platelet transfusion in those with no other risk factors which would increase the risk of bleeding.[12] In high-risk groups, clinical practice guidelines from Singapore recommend a platelet transfusion threshold of 20 000/cmm.[13] There is an urgent need for randomized controlled trials which would help in the formulation of guidelines regarding platelet transfusion in dengue. This would reduce the huge variability in the practice of clinicians worldwide in terms of indications for platelet transfusion.[14]

Implications for India

Dengue is endemic in India, and every year we see outbreaks that concern healthcare providers, municipalities and the general population. Because of a huge population load, healthcare facilities are always overloaded with patients during times of outbreaks of dengue. Thrombocytopenia, which is a common feature of dengue fever, has been inappropriately correlated with bleeding risk, both by doctors and by the general public.

Due to the constant fear of major bleeding associated with uncorrected thrombocytopenia, pressure from patients and their family members on doctors for platelet transfusion and lack of formal guidelines on prophylactic platelet transfusion results in frequent, inappropriate transfusion of blood products. Further, because of increasing assaults on doctors by patients and their relatives these days, doctors tend to play it safe by transfusing platelets, even in the absence of strong indications. This adds up to a severe paucity of blood products during the peak dengue season all over the country. This deprives the more deserving sick patients with other diseases of blood products.

This study highlights the need to understand that platelet counts should not be the target of treatment in uncomplicated dengue and should not be used as a tool to assess disease severity. Other clinical and laboratory parameters such as blood pressure, pulse pressure, pulse rate, respiratory rate, consciousness level, third space fluid loss, haematocrit and total and differential leucocyte counts should guide treatment because the presence of breathlessness and impaired consciousness level have been shown to be factors predicting mortality in patients with dengue.[5] Patients dying of dengue haemorrhagic fever were found to be having lower levels of haematocrit compared to survivors, in a tertiary hospital-based setting in Delhi.[4] The results of this study should be made widely known not only to healthcare providers and planners but also to the lay public. It would go a long way in ending the platelet count-centred care of patients with dengue.

Conflicts of interest. None declared

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