Role of platelet transfusion in children with bleeding in dengue fever

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ABSTRACT

Background & objectives: The indications for platelet transfusion in dengue fever are clearly defined in World Health Organization (WHO) guidelines (2011) for dengue fever, but physicians face practical difficulty in its implementation in an epidemic setting. On one hand there is an intense social pressure created by the panic-struck parents to transfuse platelets in presence of bleeding and on the other hand there is a need for its judicious use as the requirement is more than its availability. The study was aimed to assess the clinico-hematological parameters, and the requirement and need for platelet transfusion in children with dengue fever.

Material & Methods: All children (0–12 yr of age) diagnosed and confirmed with dengue fever at a tertiary care hospital in Puducherry between 1 August 2012 and 31 January 2015 were reviewed retrospectively from hospital case records as per the revised WHO guidelines for dengue fever. The diagnosis was confirmed by NS1 antigen-based ELISA test or dengue serology for IgM and IgG antibodies and the data were analyzed using SPSS 16.0 statistical software.

Results: Out of 261 cases of dengue fever, hemorrhagic manifestations were observed in 52 children (19.9%), which mainly included petechiae (38.5%), gum bleeding (34.6%) and melena (26.9%). Thrombocytopenia was seen in 211 (80.8%) cases. Bleeding manifestations were present in 20 (39.2%), 8 (15.7%), 13 (25.5%) and 11 (21.6%) cases with platelet count <50,000/mm³, 50,000–100,000/mm³, 1–1.50,000/mm³, and >1.50,000/mm³ respectively. Bleeding manifestations did not always correlate with platelet count in non-severe dengue infection in comparison to severe dengue infection. The most common mode of presentation of severe dengue infection was shock with 102 (39.1%) cases and among them only 22 children (21.6%) had bleeding. About 17 children (6.5%) with severe dengue infection required platelet transfusion and out of them, 12 children (70.6%) had a platelet count <20,000/mm³ whereas five children (29.4%) had platelet count in the range of 20,000–50,000/mm³.

Interpretation & conclusion: Platelet transfusion was required in children with severe dengue infection in the form of significant spontaneous bleed, shock and severe thrombocytopenia. Bleeding should not be considered only indicator to transfuse platelets as it occurred in children even with normal platelet counts. The community and treating physicians should be educated regarding the judicious transfusion of platelets. Unnecessary and empirical use of platelets should be completely avoided especially during an epidemic when there is scarcity in its availability.

Key words Bleeding manifestations; dengue fever; platelet transfusion; thrombocytopenia

INTRODUCTION

Dengue fever has become a major public health concern. The disease is now endemic in more than 100 countries with very high case fatality rate and children are the most affected age group worldwide¹. An estimated 500,000 people with severe dengue require hospitalization each year and 90% of them are children <5 yr of age. Without proper treatment, the case fatality rates can exceed 20% and with timely intervention it can be reduced to < 1%.¹ Bleeding and shock are the most dreaded complications in children with dengue fever leading to high mortality².

The role of platelet transfusion in the management of dengue fever is recognized globally and indications and situations in which they need to be transfused are clearly defined in the 2011 guidelines given by the WHO. However, they are most often not practiced by the physicians, where they find it difficult to avoid giving platelets in presence of bleeding. There is an added intense social pressure created by the panic-struck parents on the pediatricians to transfuse platelets even when not indicated. The requirement for platelets during an epidemic is high and the availability is low. The objective of the study was to evaluate the clinico-hematological parameters, requirement and the need for platelet transfusion in children with dengue fever.
MATERIAL & METHODS

The present study was conducted on confirmed cases of dengue infection admitted in the Department of Pediatrics at a tertiary care hospital at Puducherry from August 2012 to January 2015. The case definition, diagnosis and management of dengue fever in children were as per the WHO guidelines1. Clinical data, hematological parameters and the requirement of platelet transfusion to the confirmed cases of dengue fever were retrospectively analyzed from hospital case records. The study protocol was approved by the Institute Ethics Committee of Indira Gandhi Medical College and Research Institute at Puducherry, India. The data were analyzed using SPSS for window version 16.0 (SPSS, Chicago, IL).

RESULTS

In total, 398 children were provisionally diagnosed as dengue fever and the diagnosis was confirmed in 261 (65.5%) children. The most common affected age group was 6-12 yr and the mean age of presentation was 6.9 yr. The cases were from Puducherry (72%), Tamil Nadu (23%), Karaikal (3%) and Yanam (2%). Male to female ratio was 1.2 : 1. The mean duration of hospital stay was 6.5 days.

The common clinical presentations included fever (94.3%), conjunctival congestion (89.7%), myalgia (81.8%), coryza (79.9%), vomiting (77.1%), headache (70.2%), palmar erythema (64.5%), retro-orbital pain (52.3%), pain abdomen (31.8%), joint pain (26.6%), rash (17.7%), peripheral circulatory failure (41.7%), hypotension (30.3%), seizures (1.3%), jaundice (2.6%), hepatomegaly (62.9%), splenomegaly (21.2%), ascites (7%) and pleural effusion (5.1%).

Hemorrhagic manifestations were present in 52 children (19.9%), which mainly included petechiae 20 (38.5%), gum bleeding 18 (34.6%), melena 14 (26.9%), epistaxis 12 (23.1%), hematemesis 5 (9.6%), intracranial bleed 2 (3.8%) and pulmonary bleed 4 (7.7%). Tourniquet test was positive for 33 (12.6%) cases.

The clinico-hematological profile among severe and non-severe dengue is given in Table 1. Non-severe dengue and severe dengue was present in 60.9 and 39.1% cases respectively. Among the children with severe dengue infection, shock was present in 102 (39.1%) cases, in which 22 (21.6%) children had bleeding. Thrombocytopenia was seen in 211 (80.8%) cases and hematocrit ≥40 were seen in 25.1% of cases. Platelet count <1,00,000/mm³ was detected in 101 (38.6%) cases and among them

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69 (68.3%) cases had severe dengue infection. Severe thrombocytopenia (platelet count < 50,000/mm\(^3\)) was seen in 35.4 and 4.4% cases in severe dengue infection and non-severe dengue infection respectively. All the children who had platelet counts < 20,000/mm\(^3\) had features of severe dengue infection (Table 1). 79.9% of cases with platelet count > 1,000,000/mm\(^3\) had non-severe dengue infection. 46 children (17.6%) had normal platelet counts and among them 95.7% had non-severe dengue infection. 78.8% of cases with spontaneous bleeding had thrombocytopenia but bleeding manifestations did not always correlate with platelet counts as it occurred in 21.2% of cases with normal platelet counts (Fig. 1). However, it was also observed that the bleeding manifestations correlated well with platelet counts in severe dengue infection in comparison to non-severe dengue infection (Fig. 2).

Platelet transfusion was given in 17 children (6.5%) with severe dengue infection and out of them 12 children (70.6%) had a platelet count < 20,000/mm\(^3\); whereas five children (29.4%) had platelet count in the range of 20,000–50,000/mm\(^3\) (Table 1). All the children with a platelet count < 10,000/mm\(^3\) with severe dengue received platelet transfusion and among them five had melena and two children had intracranial haemorrhage. 64.2% of children who received platelet transfusion recovered completely and the average platelet count at the time of discharge was 75,000/mm\(^3\). The mean platelet recovery time was 4.1 days. Two children developed platelet transfusion reactions in the form of fever and rash. Apart from platelet transfusion, blood transfusion was given in 10 (3.9%) cases, fresh frozen plasma in 6 (2.3%) cases, colloids in 3 (1.2%) cases, i.v. fluids in 96 (37.7%) cases and inotropes in 5 (1.9%) cases. A total of 250 children were discharged without complete recovery and there were six deaths (2.3%). The most common factors associated with poor outcome (death cases) were refractory shock, disseminated intravascular coagulation (DIC), encephalopathy and multiorgan failure.

**DISCUSSION**

In our study children > 6 yr were the most commonly affected age group which is similar to the previous studies of Agarwal et al\(^5\) and Hema et al\(^4\), however, Narayanan et al\(^5\) and Gurdeep et al\(^6\) showed < 6 yr of age as the commonly affected age group. The most common mode of presentation of severe dengue infection was peripheral circulatory failure without bleeding, indicating a changing pattern of presentation and there was difficulty in classifying them as dengue haemorrhagic fever as per 2007 WHO guidelines. Bleeding manifestations were seen in 19.9% and was lower in comparison to the previous studies\(^5, 7-8\). Melena was the most common form of gastrointestinal bleeding in our study, however, earlier studies\(^3, 5, 7\) showed hematemesis to be the most common form of bleeding. The tourniquet test in our study was positive in 12.6% cases and was much lower compared to that reported in the previous studies\(^4, 5, 8\). It did not correlate well with bleeding manifestations or with thrombocytopenia, similar to the finding reported by Wali et al\(^10\) and Narayanan et al\(^5\).

Thrombocytopenia was found in 80.8% of cases in our study and was lower compared to that in the previous studies by Hema et al\(^4\) and Makroo et al\(^11\). Severe thrombocytopenia with platelet count < 50,000/mm\(^3\) were seen in 16.5% cases which was much lower compared to the previous studies\(^4, 11, 12-13\). In our study 78.8% of children with spontaneous bleeding had thrombocytopenia and 75% cases of bleeding manifestations in severe dengue occurred in patients with platelet count < 20,000/mm\(^3\) correlating to the previous studies by Chairulfatah et al\(^14\), Ratageri et al\(^7\), Shivbalan et al\(^2\) and Makroo et al\(^11\).

Bleeding manifestations were highly variable and did not always correlate with thrombocytopenia as it occurred even with normal platelet counts. The correlation between thrombocytopenia and bleeding was more common in severe dengue infection than non-severe dengue infection. The mechanism for bleeding manifestations is multifactorial in dengue fever and the factors such as thrombocytopenia, coagulation defects, vasculopathy and hepatic derangement act synergistically. Therefore, other causes of bleeding needs to be evaluated before transfusing platelets\(^2, 14-16\). In case of deranged coagulation profile, fresh frozen plasma was given instead of platelets. Children who had features of shock with rising hematocrit, not responding to crystalloids, received fresh frozen plasma or colloids and with falling hematocrit received whole blood transfusion.

Platelet transfusion was given in children with severe dengue infection associated with significant bleeding and with severe thrombocytopenia (platelet count < 50,000/mm\(^3\)). Skin bleeds, single episode of epistaxis or mucosal bleed were not given empirical platelet transfusion. Platelet transfusion was given in 17 (6.5%) children and among them two children developed transfusion reactions. The inappropriate use of platelet transfusion was completely avoided in the study. The need for platelet transfusion was much lower compared to the previous studies\(^11, 17\). Makroo et al\(^11\) in their study showed that 42.6% were given platelet transfusion and 13.7% re-
ceived inappropriate platelet transfusion. Kumar et al\textsuperscript{17} reported that 56.2% patients received inappropriate platelet transfusion, and opined that low risk patients should not be given platelet transfusion and should be managed on i.v. fluids and supportive therapy. The mean platelet recovery time was 4.1 days and similar to the previous studies.\textsuperscript{7, 18} There were six deaths (2.3%) in this study and common factors for poor outcome were refractory shock, multiorgan dysfunction and disseminated intravascular coagulopathy. Children with severe dengue required longer recovery period and more supportive management in the form of blood component therapy, fluids and inotropic support.

As per the WHO guidelines (2011) the indication for platelet transfusion in children with dengue fever is the presence of severe dengue with significant bleeding with severe thrombocytopenia, which was followed in this study\textsuperscript{4}. The use of prophylactic platelet transfusion for very severe thrombocytopenia (platelet count <10,000/mm\textsuperscript{3}) has been recommended by WHO only in adults and not in children and was not given in this study. Blood transfusion requirement was much lower compared to the use of platelets in our study which was a deviation from the guidelines.

The clinicians find the WHO guidelines for platelet transfusion not pragmatic enough to be followed, especially during the present times when there is an intense social pressure on the treating pediatrics by the parents and their relatives. The need for platelet transfusion is often overemphasized, but it is a myth and the fact is that the platelet count alone is not a predictor of bleeding. So, it is extremely important to be selective in giving platelet transfusion in children. The crux in the treatment of dengue patient is maintenance of good hydration, monitoring for any overt bleeding, periodic check on peripheral pulses, blood pressure, well supported with estimation of serial hematocrit and platelet counts and no panicking on seeing lower platelet counts.

CONCLUSION

Children with severe dengue with significant spontaneous bleed and severe thrombocytopenia necessitated platelet transfusion in the study. Bleeding should not be the only indicator to transfuse platelets as it occurred in children even with normal platelet counts. The community and treating physicians should be educated regarding the judicious transfusion of platelet and the unnecessary and empirical use of platelets should be completely avoided especially during an epidemic when there is scarcity in availability of platelets.

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