Brief Reports

Role of Platelet Transfusion in Dengue Hemorrhagic Fever

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Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) are life threatening clinical manifestations of infection due to dengue virus. The clinical features of DHF/DSS are due to bleeding diathesis and increased capillary leak(l). The mechanisms of hemorrhagic manifestations in DHF/DSS are not well understood. The suggested factors contributing to bleeding include thrombocytopenia, coagulopathy and vasculopathy(2). Suggested mechanisms for thrombocytopenia include maturational arrest of megakaryocyte production in the bone marrow(3-5), platelet destruction by the virus itself(5,6) or disseminated intravascular coagulation (DIC)(6,7).

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Since the pathogenesis of bleeding manifestations and thrombocytopenia is poorly understood, there are no guidelines about the use of platelet transfusions in DHF/DSS. The World Health Organization (WHO) manual(8) and text books of Pediatrics^) and infectious diseases(10) recommend infusion of fresh whole blood, fresh frozen plasma and/or platelet concentrates; the last two are recommended in the presence of consumption coagulopathy. However, laboratory evaluation for DIC is not routinely available in most small and middle level hospitals. Platelet counts are more easily available. The above mentioned texts do not suggest any threshold platelet counts for platelet infusion in this illness. Theoretically, the risk of spontaneous bleeding becomes significant at a platelet counf of < 20 x 107ML(H)-

Does the infusion of platelet concentrates (PC) in severely thrombocytopenic patients (platelet count < 20 x 10^3/|J) with DHF/DSS affect their survival? We addressed this question by assessing the outcome of severely thrombocytopenic patients with DHF/DSS at our center in the 1996 Delhi epidemic.

Subjects and Methods

Delhi witnessed an epidemic of DHF/DSS during 1996. Two hundred and forty children were admitted in the pediatric wards of our hospital in this epidemic. Clinical details were prospectively recorded on the proforma for surveillance suggested by WHO(8). The case definition, monitoring and treatment were carried out according to WHO guidelines(8). Baseline packed cell volume (PCV) and absolute platelet counts were determined by use of microhematocrit method and by Coulter

blood cell counting machine, respectively. The PCV was repeated every 2-4 hours and platelet counts done at least once a day for the next 48 hours or till the PCV dropped below 40. An attempt was made to do a coagulation profile where feasible. Acute and convalescent samples were drawn for viral isolation and serology. IgM antibodies against dengue virus was detected by MAC ELISA technique and viral isolation was carried out in C6/36 Aedes cell line followed by indirect immunofluorescence for identification using the type specific monoclonal antibodies. The management of patients included infusion of intravenous crystalloids, colloids and plasma. The decision to administer platelet concentrates (PC) depended upon the attending pediatrician and the availability of PC in the blood bank. If administered, platelet concentrates were infused in a dose of one bag (5-7 x 10^9 platelets) per 10 kg body weight over 30 minutes aiming to increase the platelet count above 40 x l

Case records of all severely thrombocytopenic (< 20 x 10^3/|uL) children with DHF/DSS (n = 37) were examined for clinical staging, disease severity, infusion of PC and clinical outcome. Tests of significance for difference in proportions between two groups using Chi-square test with Yates correction were applied.

Results

Out of 240 admitted children 37 (15.4%) had platelet counts < 20 x 10^3/|^L. Eight children presented in Stage IV (21.6%), 17 in Stage III (45.9%), 9 in stage II (24.3%) and 3(8%) were diagnosed as dengue fever with unusual bleeding. Eighteen children (48.6%) with different stages of illness received PC infusion (Group I) in addition to standard case management while 19 patients (51.4%) were not given any PC infusion (Group II). The mean age, stage of illness, mean platelet counts, abnormal prothrombin time, mucosal bleeds and need for FFP, blood transfusion and mean hospital stay were comparable in the two groups *(Table I).* Twelve patients received PC infusion once only, 3 patients required twice and 3 patients required three times.

There were 4 deaths (11%) among these 37 children. Three of these received PC infusion, while one patient did not. This difference was not significant, {p = 0.34, Fisher exact two tailed test; OR 3.6 (95% CI 0.25-199.28)] *(Table I).* All 4 children who died presented in clinical stage IV and had refractory shock. One out of three patients in Group I who died also had uncontrolled bleeding in addition to profound shock.

Discussion

In the present study we analyzed patients with an absolute platelet count of < 20 x 10^3/(xl because these patients are at risk of spontaneous bleeding. These patients should have shown greatest benefit with PC infusion. The benefits of PC infusion can be demonstrated by decrease in bleeding or the overall survival. In our study the incidence of major bleeds were comparable in two groups. The number of days of hemorrhage were not affected by PC transfusion and the outcome was also not affected.

The baseline platelet counts were comparable in the two groups. As expected the platelet counts on subsequent days were higher in those who received PC infusion. No significant effect on the duration of bleeding even with higher platelet counts suggests that thrombocytopenia alone may not be responsible for bleeding in DHF/DSS. Further studies on cause of bleeding in DHF/DSS may suggest some effective treatment for control of bleeding.

The limitation of the present study is

TABLE I *Comparison of Clinical and Laboratory Characteristics in Children with DHF and Platelet Counts ≤ 20 × 10³/μl*

Clinical & laboratory characteristics	Group I (n = 18)	Group II (n = 19)
Mean age (years)	6 65 ±2 87	7 410 ± 2 32
Sex (M/F)	11/7	9/10
Severity stage IV	4	4
III	9	8
II	4	5
DF, bleeds	1	2
Hospital stay (days)	4 94 ±2 07	4 15 ± 1 46
Major bleeds*	13	12
Duration of bleeding (days)		
≤ 1	6	6
2	4	3
3	1	1
4	2	2
Mean duration of bleeding (days)	1 92 ±1 11	1 91 ± 1 16
Mean platelet counts (× 10³)		
Day I	17 11 ± 2 90	15 52 ± 4 46
Day II	27 13 ± 7 34	26 90 ± 16 05
Day III	51 73 ± 19 50	38 45 ± 17 22
Abnormal prothrombin time	3/8	2/4
Recieved FFP	10	10
Received blood transfusion	6	5
Mortality	3	1

Group I received PC infusion and supportive care
Group II received only supportive care
* Hematemesis/malena
PT was done in 8 and 4 patients in Groups 1 and II, respectively
Difference between two groups for all variables was not significant.

that the use of PC infusion in children with severe thrombocytopenia was not studied in a prospective randomized control design. There being no clear guidelines, the decision to use PC infusion was dependent on the treating pediatrician and availability of PC. As the two groups are comparable for known risk factors, any systematic bias is unlikely to have crept in. However, the amount and severity of blood loss could not be compared due to the retrospective nature of the study,

A prospective controlled study on a larger number of patients is desirable to confirm our results. The preliminary results of our study suggests that a prospective controlled trial can be ethically justified.

However, we would require at least 550 patients in each group to ascertain a decrease of mortality from 10% to 5%.

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A Nursery Outbreak of Multidrug Resistant *Salmonella typhimurium*

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Salmonella infection in the neonatal period is associated with high morbidity and mortality, with the development of septicemia in 5% of all salmonella infections(l). Amongst the nontyphoidal salmonella sero-types, *S. typhimurium* is the most common organism responsible for nursery outbreaks. The emergence of multidrug resistant salmonella serotypes over the past few years has become a major problem, because

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