PREVENTIVE TRANSFUSION IN DENGUE SHOCK SYNDROME–
IS IT NECESSARY?
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We compared 53 patients with dengue shock syndrome (DSS) who received preventive transfusions with 53 who did not. Significant differences in the development of pulmonary edema and length of hospitalization ($P < .05$) and none in hemorrhage ($P = .136$) were observed. Preventive transfusions did not produce sustained improvements in the coagulation status in DSS. (J Pediatr 2003;143:682-4)

Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) is characterized by increased capillary permeability, thrombocytopenia, and coagulopathy. Several workers have observed that the severity of thrombocytopenia does not predict bleeding, and that other factors such as platelet dysfunction and a prolonged duration of shock leading to potentiation of the disseminated intravascular coagulation state may play important roles. There are no clear guidelines on the role of transfusions of platelet concentrates (PC) and/or fresh frozen plasma (FFP) in DHF/DSS. Nonetheless, these have been prescribed for many DHF/DSS patients with thrombocytopenia and coagulopathy, in an attempt to prevent bleeding. There is, however, no evidence to support that transfusions are of any benefit. The risks of these therapies are fluid overload, prolonged hospitalization, and blood-borne infections. Hence, the liberal use of blood products in the treatment of DSS creates a real danger to the patient, in addition to the unnecessary cost and an incorrect focus in the treatment.

Before 1997, our practice was to give transfusions of PC and FFP for DSS in the case of platelet counts less than $30 \times 10^9/L$ and coagulopathy. This practice was stopped in 1997. We therefore are able to evaluate the effect of this change in transfusion practice in DSS patients.

METHOD

We reviewed cases of confirmed DSS with admission to the Department of Pediatrics, University of Malaya Medical Centre, Kuala Lumpur, between January 1991 and May 2000. Patients admitted between 1991 and 1996 were compared with those in 1997 and 2000 (period groups). These patients were again divided into group 1, which received transfusions of either PC and/or FFP, and group 2, which did not receive any blood products (treatment groups). Patients with significant bleeding, evidenced by a low/normal hematocrit at the time of admission were excluded. Percentage increase in hematocrit was the percentage of highest rise in hematocrit over the hematocrit at discharge. Outcomes measured were total fluid balance at 48 hours from onset of shock, duration of thrombocytopenia (platelet count <100 $\times 10^9/L$), incidence of pulmonary edema as indicated by presence of rhonchi/crepitations or radiologic evidence or pink frothy secretions, incidence of hemorrhage, and length of hospitalization.

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We also studied the effects of the transfusions of PC and FFP on platelet counts, prothrombin time ratio (PTR), and partial thromboplastin time (PTT) during the 48 hours from the onset of shock. Median percentage change in platelet count was the median of the post-transfusion platelet count divided by pre-transfusion level. Median percentage improvement in PTR and PTT were the median of the pre-transfusion level divided by the post-transfusion level.

A value of 100% means no change in the parameter, whereas a value of above and below 100% means an improvement and deterioration, respectively.

**Statistical Analysis**

Data was managed with SPSS statistical package version 10.0.1 for Windows 1998 (SPSS, Inc, Chicago, Ill). Dichotomous measures were compared using the $\chi^2$ test or the Fisher Exact test where appropriate. The Mann–Whitney $U$ test was used for continuous variables. A $P$ value of less than .05 was considered statistically significant.

**RESULTS**

Fifty-three patients admitted between 1991 and 1996 and another 53 between 1997 and 2000 were eligible for analysis. The predominant virus strains were DEN-3 and DEN-2, respectively. Shock with hemoconcentration, thrombocytopenia, and coagulopathy were observed in all patients. Patients received boluses of 0.9% sodium chloride solutions during shock, with subsequent infusions adjusted in accordance with the serial hematocrit. Blood products were administered according to the prevailing transfusion practice and at the discretion of the attending physician. Dextran and other colloids were not used.

Table I shows that patients in the two periods were similar except for the transfusion of blood products and length of hospitalization ($P < .05$). Treatment group 1 had 60 patients (45 in period 1 and 15 in period 2); 15 received FFP transfusions only, 6 received PC transfusions only, and 39 received both, whereas treatment group 2 had 46 (8 in period 1 and 38 in period 2). The baseline characteristics of the two treatment groups were comparable. Significant differences were observed in the total fluid balance, incidence of pulmonary edema, and length of hospitalization ($P < .05$). There was no significant difference in the incidence of hemorrhage, which was mild in all cases. No fatalities were observed in these two groups of patients. Figure 1 shows that improvement in platelet counts, PTR, and PTT after transfusions lasted less than 5 hours.

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**Table. Comparison of clinical and laboratory findings in patients by period and treatment groups**

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<tbody>
<tr>
<td>Age (y)</td>
<td>6.0 (0.1-11.7)</td>
<td>6.0 (0.1-12.0)</td>
<td>.795</td>
<td>6.0 (0.1-11.0)</td>
<td>6.0 (0.3-12.0)</td>
<td>.243</td>
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<tr>
<td>Male:Female ratio</td>
<td>1:0.9</td>
<td>1:1</td>
<td>.846</td>
<td>1:0.8</td>
<td>1:1.2</td>
<td>.448</td>
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<tr>
<td>Duration of shock (h)</td>
<td>4.0 (0.1-11.0)</td>
<td>6.0 (3.0-12.7)</td>
<td>.805</td>
<td>4.0 (0.1-11.4)</td>
<td>4.0 (0.1-9.8)</td>
<td>.918</td>
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<tr>
<td>Percentage increase in hematocrit</td>
<td>53.0 (15.5-96.7)</td>
<td>42.0 (11.0-100.0)</td>
<td>.539</td>
<td>53.0 (15.8-94.8)</td>
<td>42.0 (9.5-100.0)</td>
<td>.239</td>
</tr>
<tr>
<td>Lowest platelet count ($\times 10^9/L$)</td>
<td>22.0 (8.3-117.8)</td>
<td>21.0 (5.0-70.6)</td>
<td>.172</td>
<td>20.5 (5.0-75.7)</td>
<td>22.0 (8.1-120.6)</td>
<td>.127</td>
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<tr>
<td>Highest Prothrombin time ratio</td>
<td>1.2 (1.0-2.8)</td>
<td>1.2 (1.0-2.0)</td>
<td>.194</td>
<td>1.2 (1.0-2.7)</td>
<td>1.1 (1.0-1.5)</td>
<td>.207</td>
</tr>
<tr>
<td>Highest Partial Thromboplastin time (sec)</td>
<td>72.1 (35.4-124.7)</td>
<td>75.7 (45.0-202.0)</td>
<td>.395</td>
<td>77.7 (43.8-158.8)</td>
<td>71.3 (35.0-202.0)</td>
<td>.347</td>
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<tr>
<td>Total volume of FFP transfused (mL/kg)</td>
<td>20.0 (0.0-68.4)</td>
<td>0.0 (0.0-40.0)</td>
<td>.000</td>
<td>20.0 (0.0-66.2)</td>
<td>0 (0.0-0.0)</td>
<td>.000</td>
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<tr>
<td>Total platelets transfused (U/kg)</td>
<td>0.1 (0.0-0.9)</td>
<td>0.0 (0.0-0.6)</td>
<td>.000</td>
<td>0.2 (0.0-0.9)</td>
<td>0 (0.0-0.0)</td>
<td>.000</td>
</tr>
<tr>
<td>Total fluid balance (mL/kg)</td>
<td>119.5 (23.4-276.2)</td>
<td>110.0 (10.4-205.4)</td>
<td>.574</td>
<td>121.0 (47.7-273.1)</td>
<td>107.0 (53.5-185.3)</td>
<td>.045</td>
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<tr>
<td>Days of thrombocytopenia</td>
<td>5.0 (0.3-12.7)</td>
<td>5.0 (3.0-9.3)</td>
<td>.135</td>
<td>5.0 (2.0-9.0)</td>
<td>4.0 (0.4-13.8)</td>
<td>.395</td>
</tr>
<tr>
<td>Days of hospitalization</td>
<td>7.0 (4.0-19.6)</td>
<td>6.0 (3.0-12.7)</td>
<td>.023</td>
<td>7.0 (4.0-17.0)</td>
<td>5.0 (3.0-17.3)</td>
<td>.000</td>
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<td>Incidence (%) of bleeding (95% CI)</td>
<td>56.6 (43.3-69.0)</td>
<td>49.1 (36.1-62.1)</td>
<td>.559</td>
<td>60.0 (47.4-71.4)</td>
<td>43.5 (30.2-57.8)</td>
<td>.136</td>
</tr>
<tr>
<td>Incidence (%) of pulmonary edema (95% CI)</td>
<td>22.6 (13.5-35.5)</td>
<td>17.0 (9.2-29.2)</td>
<td>.626</td>
<td>30.0 (19.9-42.5)</td>
<td>6.5 (9.2-29.2)</td>
<td>.006</td>
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</table>

*Values are median (2.5-97.5 percentile) unless stated otherwise.

†Group 1 received transfusions of either PC and/or FFP, and group 2 did not receive any blood products.

‡Bleeding that did not contribute to hemodynamic instability and did not require blood transfusions.
DISCUSSION

The reasons for transfusions of PC and FFP in this series of DSS patients were the abnormal laboratory coagulation profile and the prevailing transfusion practice. It could be argued that transfusions of PC and FFP prevented severe bleeding in treatment group 1. However, patients in treatment group 2, with a similar severity of DSS did not develop severe bleeding despite not receiving blood products. Even though the predominant viruses were different in the two periods, both DEN-2 and DEN-3 are associated with severe disease. The main risk factor for severe bleeding in DSS, as analyzed in a previous study, was longer duration of shock. Thrombocytopenia and coagulopathy were not predictive of bleeding. The prevention of hemorrhage in DHF/DSS should be directed at early recognition of shock and its prompt correction rather than transfusions of PC and FFP.

Monitoring serial hematocrit, which reflects the degree of plasma leakage, rather than thrombocytopenia and coagulopathy resulted in reduced use of blood products, judicious intravenous therapy, a lower incidence of pulmonary edema, and a shorter length of hospitalization. Physicians who focused on thrombocytopenia and coagulopathy might prescribe multiple transfusions because of the temporary effect on platelet counts and coagulopathy, contributing to the increased total fluid balance. The platelet counts, PTR and PTT, improved after the period of vascular permeability, regardless of the transfusions.

CONCLUSION

Preventive transfusions did not produce sustained improvements in the coagulation status during the plasma leakage phase of DSS. Patients who were not transfused did not manifest severe bleeding when shock was adequately managed.

REFERENCES