

# Fresh Plasma Transfusion In The Management Of Septicaemia Complicating Neonatal Tetanus: A Preliminary Report

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## Abstract

**Objective:** To determine the effect of fresh plasma transfusion on the mortality among babies with neonatal tetanus complicated with septicemia.

**Method:** The hospital records of babies with Neonatal Tetanus (NNT) and complicating septicemia who had adjuvant fresh plasma transfusion were compared with those without transfusion.

**Results:** Between August, 2002 and December, 2004, 62 (5.0%) out of 1,236 babies admitted the Newborn Unit had Neonatal Tetanus (NNT). Of these, 12/62 (19.4%) were transfused with fresh plasma when septicemia was suspected or confirmed as against 50/62 (80.6%) who were not. The mortality among babies who were transfused was 3/12 (25.0%) compared with 24/50 (48.0%) among babies who were not transfused with plasma but this difference was not statistically significant ( $p = 0.149$ ) probably due to the small size of the study population.

**Conclusion:** Fresh plasma transfusion as a form of hyperalimentation or immunotherapy improved the survival of babies with NNT and septicemia.

## INTRODUCTION

The role of Neonatal Tetanus (NNT) as a major contributor to neonatal mortality has been repeatedly described over time.<sup>1,2,3</sup> Lately, it was estimated to cause about 400,000 deaths annually in the developing world<sup>4</sup> and that makes it a major public health problem especially in the developing world. The high mortality associated with NNT is most confounding despite the fact that its prevention by adequate immunization is one of the most cost-effective medical interventions known.<sup>1</sup> Studies have suggested an increasing incidence of NNT in Nigeria despite a virile childhood immunization program in most parts of the country. This was attributed to poor Tetanus Toxoid coverage as a result of lack of acceptability despite adequate awareness.<sup>5</sup> All these necessitated the renewed effort at eliminating NNT through the Maternal Neonatal Tetanus Eliminating Initiative in the African region by 2005.<sup>6</sup>

The global efforts at eliminating NNT notwithstanding, child health physicians in the developing world still grope with

embarrassingly high mortality among babies with NNT. Septicemia is one of the major killers in NNT and it commonly manifests with poor skin colour, feed intolerance and recurrent apnea<sup>7</sup> which may be indications for intensive care in form of assisted ventilation and hyperalimentation. Unfortunately, these are not routinely available in the developing world. Therefore, to improve the survival rate in NNT in our Newborn Unit, trials of fresh plasma transfusion (10ml/kg) as a form of immunotherapy and hyperalimentation in NNT cases with suspected or confirmed superimposed septicemia was commenced in August, 2002 in addition to the routine of using Diazepam, Chlorpromazine and Phenobarbitone to control spasms, anti tetanus serum (ATS) to neutralize circulating tetanospasmin, Penicillin G to eliminate *Clostridium tetani* and appropriate nursing care.

The indication for plasma transfusion was the suspicion of septicemia based on poor color, feed intolerance or recurrent apnea. Informed consent was obtained from parents before intervention. Caution was taken to prevent

over-inclusion of babies with apnea since this might be due to the effect of the sedatives being used. Phenobarbitone, because of its tendency to cause respiratory depression was usually stopped once apnea occurred and when it became recurrent, it was then taken to be a manifestation of sepsis. Almost always, at least one other feature of sepsis was usually present as well.

Some of these critically ill newborns with NNT were not transfused with fresh plasma for reasons like non-availability of suitable blood in the laboratory, the refusal of parents to give consent for the procedure and early demise before plasma could be made available.

## **METHODOLOGY**

Data of babies with NNT were obtained from the admission and discharge register of the Newborn Unit in the Wesley Guild Hospital, Ilesa, southwestern Nigeria between August 2002 and December, 2004. Additional information was also gathered from the individual case files of these infants. Patients with NNT who were transfused with plasma during this period were regarded as the cases while those who were not transfused were used as the controls. The following data were obtained from the records: age on admission, weight on admission, sex, result of blood culture (done with scrupulous skin preparation) where it was available, the duration of admission as at the time of plasma transfusion and the outcome of admission. The data obtained was analyzed by simple descriptive statistics using SPSS<sup>8</sup> and PEPI<sup>9</sup> software. *p* values equal to or less than 0.05 in two-tailed tests were taken to be significant in all cases.

## **RESULTS**

We recorded a total of 1,236 admissions and 212 deaths (17.1% mortality) during this period. Sixty two newborns (comprising of 44 males and 18 females) had NNT with 27 deaths (43.5% mortality); these newborns with NNT formed 5.0% of the total admissions but 12.7% of the total deaths recorded in this unit during this period ( $z = 5.46$ ,  $p = 0.000$ ). Twelve (19.4%) newborns with NNT were transfused with fresh plasma while 50 (81.6%) babies were not transfused with plasma.

The mean weight of the cases was  $2.85 \pm 0.6\text{kg}$  compared with  $2.75 \pm 0.75\text{kg}$  for the controls ( $t = 0.43$ ;  $p = 0.67$ ). The age on admission was also similar in the both groups ( $7.8 \pm 2.3$  days Vs  $7.5 \pm 3.2$  days;  $t = 0.34$ ,  $p = 0.73$ ). The mortality of 48.0% (24/50) among the controls was higher compared with 25.0% (3/12) among the cases but without statistical

significance ( $p = 0.149$ ).

At the time of plasma transfusion, the mean duration of the cases was  $4.2 \pm 2.5$  days. However, the mean duration of admission of the controls who died was  $3.3 \pm 2.4$  days. The cases stayed longer on admission with the mean duration of  $20.6 \pm 6.9$  days compared with  $9.5 \pm 8.7$  days for the controls ( $t = 4.11$ ;  $p = 0.0000$ ). One of the babies who were transfused with plasma but died had associated moderate hyperbilirubinaemia requiring phototherapy. Five (41.7%) infants among the cases had serial plasma transfusions but none of them died.

Blood culture was done among 9/12 (75.0%) of the cases: 8 had *Staphylococcus aureus* infections while one had Coliforms. Two (22.2%) of these cases with confirmed septicaemia died. Blood culture was not done for 18/50 (36.0%) of the controls for logistic reasons. Out of the remaining 32 babies with blood culture, only 10 (31.25%) babies had positive culture of *Staphylococcus aureus*. Five (50.0%) of these controls with confirmed septicaemia died. However, the difference in the mortality between the cases and the controls with confirmed septicaemia was not statistically significant ( $p = 0.210$ ).

## **DISCUSSION**

NNT has been reported to be a major contributor to neonatal morbidity and mortality in our center and other parts of the country.<sup>1,3</sup> The Case Fatality Rate (CFR) of 40.8% in this study was similar to 46.9% reported in Port Harcourt<sup>10</sup> but less than 57.5% and 77.3% reported in Ife and Ibadan respectively.<sup>2,11</sup> This CFR was also lower than 64% reported from Accra, Ghana<sup>12</sup> but higher than 22% reported from South Africa.<sup>13</sup> The lower mortality in South Africa may be attributed to the availability of intensive care facilities (ICF). The ICF improved the outcome in NNT over a period of 20 years as demonstrated in a Mexican study in which the mortality was 46.6% in a 10-year period without ICF and 12.9% over another 10-year period with ICF.<sup>13</sup>

Septicaemia has been reported to be a significant complication of NNT in Nigeria<sup>7, 15</sup> with *Staphylococcus aureus* and the Coliforms playing major roles. This, in our experience may be associated with the fact that all the babies were out-born. In this study, septicaemia was suspected among babies with poor skin colour, recurrent apnea and feed intolerance and these were the indications for plasma transfusion.

Although, the mortality rate among the controls was almost double the mortality rate among the cases, the lack of statistical significance can be attributed to the small number of the babies studied. The total duration of hospitalization was also shorter among the controls than the cases, probably because the mortality among the cases was converted to prolonged period of morbidity.

It is remarkable that, the mortality among the cases with proven septicaemia was minimal whereas, a large proportion of the controls who had confirmed septicaemia succumbed to the illness despite the routine change of antibiotics. This observation further strengthens the postulated efficacy of plasma constituents in serving immunotherapeutic purposes.<sup>16</sup>

In our experience, fresh donor plasma, usually that of an adult contains high levels of pre-formed immunoglobulins against infectious agents in the environment<sup>17,18</sup> especially, *Staphylococcus aureus* with which the donor must have come in contact.<sup>19</sup> We did not have a schedule on who had how many doses of plasma, but while some babies responded to single doses of plasma, others required multiple doses for unknown reasons. The case of the baby who was transfused with plasma and still succumbed to the illness can be explained in terms of the additional problem of moderate hyperbilirubinaemia requiring phototherapy which expectedly provoked more spasms and increased his chances of death. For the other two cases who also succumbed to the illness, the plasma transfusion was done late due to non-availability of appropriate blood.

The risks associated with the use of blood and blood products especially in terms of transmission of infections is minimized by routine screening of blood donors for common infectious agents especially the hepatitis B and C viruses, syphilis, microfilaria and the human immunodeficiency virus (HIV). As it were, the risk of infections is not peculiar to plasma transfusion but cuts across other conditions requiring blood use. This is more relevant in Nigeria where severe anaemia requiring blood transfusion constitutes the bulk of cases managed in most emergency wards.<sup>20</sup>

## CONCLUSIONS

In conclusion, the use of fresh plasma transfusion seems promising in the reduction of mortality mainly due to septicaemia among babies with NNT in developing countries. In this part of the world where NNT still features prominently as a cause of neonatal morbidity and mortality,

the use of adequately screened fresh plasma as an adjuvant to the antibiotic management of septicaemia among babies with NNT as a way of improving the survival rate may be a worthwhile venture. In the interim, this study continues as a randomized clinical trial with a large size study population.

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