EXCHANGE TRANSFUSIONS IN NEONATAL SEPSIS

R. Dalvi
S. Rao
J. Rangnekar
A. Fernandez

ABSTRACT

Between October, 1987 and October, 1988, 53 neonates with severe or unresponsive sepsis were subjected to therapeutic exchange transfusions (ET) using 170 ml/kg of citrated blood less than 24 hours old. The procedure was repeated upto a maximum of 4 times. The success of therapy was adjudged by resolution of sclerema and/or improvement in clinical features. There were 32 low birth-weight (LBW) and 21 non-LBW infants and 51/53 subjects had sclerema. The mean time for recovery following ET was 19.6 ± 12.4 h (range: 1-48 h). The overall survival was 77.4% and the survival rates for LBW and non-LBW infants were 73.6 and 68.2%, respectively, however, the difference was not statistically significant. No significant or fatal complications occurred during ET. The effects of other associated problems on outcome studied by multiple regression analysis showed that neurologic problems were associated with a poor chance for survival despite ET. Exchange transfusion may thus be an effective and safe therapeutic modality for severe neonatal sepsis.

Key words: *Exchange transfusion, Sepsis, Newborn.*

From the Department of Neonatology, LTM Medical College and LTM General Hospital, Sion, Bombay-400 022.

Reprint requests: Dr. Armida Fernandez, 53, Sea Springs, Bandstand, Bandra, Bombay-400 050.

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Over the last decade several reports have described the utility of exchange transfusions (ET) as an unconventional therapy in severe neonatal sepsis(1-4). Removal of endotoxin, improved tissue perfusion, diminished bleeding tendency, and augmentation of humoral and cellular immunity are the possible mechanisms of action of this therapeutic modality(1). Sclerema still remains an ominous sign of overwhelming sepsis and predicts a poor outcome with conventional therapy(5,7). This is a report of our experience with exchange transfusions in the treatment of newborns with severe septicemia and sclerema, unresponsive to appropriate antibiotics.

Material and Methods

Fifty-three neonates with severe or unresponsive sepsis treated with exchange transfusions during the period October, 1987 to October, 1988 formed the subject of this study. Their case histories were retrospectively analysed. Cases with inadequate data or where the primary indication for exchange transfusion was hyperbilirubinemia were excluded.

The clinical diagnosis of sepsis was based on a neonatal sepsis score followed at this centre, as shown in *Table I.* A score >5 suggested a clinical suspicion of sepsis. Supportive diagnostic evidence was provided by hematologic features such as leucocytosis or leucopenia, and an increased peripheral blood immature: total (I/T) neutrophil ratio >0.2(8). For confirmation of sepsis samples of blood, urine, stool, cerebrospinal fluid or pus were sent for bacteriological examination and culture, prior to antibiotic therapy. The initial choice of antibiotics was ampicillin and gentamicin. As soon as culture results were

TABLE I—*Clinical Sepsis Score*

Parameters	Score points
Maternal fever upto 1 week before delivery	1
Leaking membranes >24 h	3
Overt maternal vaginal infection	1
Fetal distress with meconium staining of liquor	1
Intubation/instrumentation	2
Prematurity/small for date	2
Top feeding	1
Refusal of feeds (local causes/tetanus, excluded)	2
Temperature <36°C or >38°C	2
Apneic spells	1
Local skin infection	2
Loose motions	1
Abdominal distension	1
Jaundice	1
Convulsions	2
Respiratory distress	2
Hypotonia (full-term infant)	2
Deterioration in reflexes	1
Activity (*i*) no spontaneous activity but responds to stimulus	1
(*ii*) no response to stimulus	2
Paralytic ileus	2
Sclerema	4
Disseminated intravascular coagulation	4
Decreased capillary filling time	2

available, the drugs were changed, if indicated. If no clinical improvement was seen within 24-36 hours, third generation cephalosporins and/or amikacin were administered.

Development of sclerema or rapid clinical deterioration was considered as indication for exchange transfusion. Sclerema was defined as "diffuse, rapidly spreading, non-edematous hardening of the subcutaneous tissues".

Exchange transfusions were performed after obtaining informed parental consent, using 170 ml/kg body weight citrated blood less than 24 hours old. The procedure was repeated every 12-24 hours upto a maximum of four times, or until clinical improvement or death of the patient occurred. The success of therapy was adjudged by resolution of sclerema and/or improvement in pre-exchange transfusion clinical features. The time interval between

diagnosis of sepsis and ET, and the time taken for improvement after last ET (as defined above) were noted. The patient related factors selected for correlation with outcome included, prematurity with <30 weeks gestational age, hyaline membrane disease, meconium aspiration syndrome, perinatal asphyxia, apneic spells, neurological problems, metabolic abnormalities and congenital anomalies. The effects of associated problems and the time interval before ET on the outcome of patients undergoing ET were studied by univariate analysis (χ^2 test) as well as multivariate regression analysis.

Results

One hundred and four exchange transfusions were performed for 53 septicemic neonates, with 1-4 ET per patient (mean 2.9±1.0). The data on gestational age, birth weight and sex of these patients is shown in *Table I*. A total of 29.4% of infants had a sepsis score >15 while the rest had a score >20. Fifty-one patients had sclerema while the 2 without sclerema had rapid clinical deterioration. All but 3 cases had early onset sepsis.

Positive bacterial cultures obtained in 29/53 patients showed Klebsiella (11 cases), Coagulase positive *Staphylococcus aureus* (7 cases), *E. coli* (3 cases), *Pseudomonas aeruginosa* (5 cases), and *Enterobacter* (3 cases). The remaining 24 infants had, in addition to clinical evidence of sepsis, hematological features in the form of leucocytosis (20 cases) with I/T ratio ranging from 0.3-0.8, and leucopenia with thrombocytopenia (4 cases). The time interval between diagnosis of sepsis and first ET, time taken for recovery, and the survival rates, were as shown in *Table II*. Three patients had apneic spells, one had congestive cardiac failure and one had hypothermia during ET, however, there were no deaths attributed to ET.

The mortality rates in culture-positive and culture-negative cases were 24.1 and 20.8%, respectively; the difference not being statistically significant ($p > 0.05$). On univariate analysis, presence of neurological problems was the sole factor correlating with poor outcome (*i.e.*, death) ($p < 0.001$). Multivariate regression analysis using the same factors, in order to account for interaction between variables showed similar results ($p < 0.0001$)

TABLE II—*Summary Data of Septic Newborns Treated with ET*

Feature		Total patients	Low birth weight	Non-low birth weight
No. of cases		53	32	21
Birth weight (kg)		2.2 ± 0.7	1.5 ± 0.3	2.6 ± 0.4
Male : female		1.5 : 1	1.7 : 1	1.3 : 1
Interval before ET (h)	Range	6 - 96	12 - 76	6 - 72
	Mean ± SD	37.2 ± 26.8	43.2 ± 20.2	40.6 ± 28.1
Time for recovery (h)	Range	1 - 48	5 - 40	1 - 48
	Mean ± SD	19.6 ± 12.4	16.2 ± 15.9	20.8 ± 13.2
Survival rate (%)		77.4	73.6	68.2

ET = Exchange transfusion

(Regression constant=0.0896, standard error of 'Y' estimation=0.3541, r squared=0.4870, degrees of freedom=44). No significant correlation was noted between time interval before ET and patient outcome.

Discussion

Despite advances in neonatal intensive care and availability of potent antibiotics, neonatal sepsis continues to be a major cause of morbidity and mortality(9,10). Especially in developing countries, newborns with overwhelming sepsis unresponsive to standard therapy, have poor chances of survival. Development of sclerema in neonatal sepsis almost invariably predicts a fatal outcome(5). Most of the experience with this therapeutic modality being without comparative controls, the efficacy of ET is not well-accepted(4). Likewise in this study too, with the significant improvement noted with ET, it was ethically not possible to have a controlled study when previously, sclerematous septic infants had a near 100% mortality.

Exchange transfusions in neonatal sepsis have been shown to effect removal of bacteria and endotoxins from the circulation. Elimination of the vasoconstrictive action of the endotoxin results in improved tissue perfusion producing immediate improvement in cardiac output, arterial blood pressure, urine output and acid base imbalance(1). The total leucocyte, polymorphonuclear and lymphocyte counts(11), as well as IgM, IgA, and serum opsonic activity in septic neonates, are reported to increase following ET(1). Gross and Melhorn(12) have also shown ET to be effective in treating neonates with disseminated intravascular coagulation.

The present study shows a survival rate of 77.4% in severe sepsis which is comparable to the 50-70% survival in previous reports(1,3). No significant or fatal complications occurred during ET, indicating the safety of this procedure. Central nervous system problems in the form of intracranial hemorrhage, meningitis, ventriculitis, and intractable convulsions were associated with a poor chance for survival.

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NOTES AND NEWS

XII ANNUAL CONFERENCE
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The XII Annual Conference of U.P. Chapter is being organised by IAP Gorakhpur Branch on 15-16 March,1991 at B.R.D. Medical College, Gorakhpur.

For further details please contact:

Dr. Y.D. Singh,
Head, Department of Pediatrics,
B.R.D. Medical College,
Gorakhpur 273013.

Phone: 334747