

Clinical profile and outcome of newborns who underwent double volume exchange transfusion in the neonatal intensive care unit at B.P. Koirala Institute of Health Sciences, Nepal

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Abstract

Introduction: About 50% term and 80% preterm babies develop neonatal jaundice. Treatment to prevent bilirubin encephalopathy consists of phototherapy or exchange transfusion (ET). ET is not risk free, and mortality rates vary from 0.5 to 3.3%.

Objective: To report our observations on efficacy, adverse events and factors contributing to mortality related with ET performed for the treatment of neonatal hyperbilirubinemia at a tertiary-care centre.

Method: This retrospective study was conducted at the neonatology division of B.P. Koirala Institute of Health Sciences, Nepal. All neonates who required ET for jaundice from January 2013 to December 2014 were included.

Results: Sixty four neonates underwent double volume ET. Predominant causes of hyperbilirubinaemia were ABO incompatibility (32.8%), Rh incompatibility (17.2%) and idiopathic (20.3%). There was a mean reduction in serum bilirubin levels to 13.1±3.82 mg/dl in the post-ET and 14.63±3.16 mg/dl in the 6 hour post-ET period. The common adverse events were hypocalcaemia in 50% and thrombocytopenia in 35.9% of neonates. Other events such as hypoglycaemia (17.2%), apnoea (18.8%) and mortality (3.1%) occurred following ET.

Conclusions: ABO incompatibility was the commonest cause for ET. Most of the complications were transient. Mortality rate was 3.1% in this study.

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(Key words: Exchange transfusion, neonatal hyperbilirubinemia, adverse events)

Introduction

Neonatal hyperbilirubinemia is a common cause of admission to the neonatal intensive care unit (NICU)¹. About 50% of term and 80% of preterm babies develop jaundice during the neonatal period² but only 0.02-0.16% develop extreme hyperbilirubinaemia³. Breast milk jaundice, ABO incompatibility, Rh incompatibility, Glucose-6-phosphate deficiency (G-6-PD), East Asian ethnicity and cephalhaematoma are conditions associated with severe jaundice⁴. The serum bilirubin level varies with birth weight, gestational age, chronological age and internal milieu of the body. When total serum bilirubin level exceeds a critical limit, it crosses the blood brain barrier and results in bilirubin encephalopathy⁵. Treatment is always given to prevent bilirubin encephalopathy by phototherapy or exchange transfusion (ET)⁶. Although ET is considered to be a safe procedure, it is not risk free, and mortality rates vary from 0.5 to 3.3%^{4,7,9}. Recently, the number of ETs has been significantly reduced due to the availability of highly effective double surface and LED phototherapy and intravenous immunoglobulin G (IVIg) in prevention of isoimmunization / blood group incompatibility¹⁰. ET is sufficient to minimize brain damage, despite the adverse event¹¹.

Objectives

To report our observations on efficacy, adverse events and factors contributing to mortality related with ET performed for the treatment of neonatal hyperbilirubinemia at a tertiary-care centre.

Method

This retrospective study was conducted at the Neonatology Division of B.P. Koirala Institute of Health Sciences (BPKIHS), Nepal. All neonates who required ET from January 2013 to December 2014 were included. The criteria for ET for the management of hyperbilirubinaemia were followed as per American Academy of Paediatrics 2004 guidelines¹². Cases of ET for conditions other than jaundice were excluded from the study. The study

was approved by the Institute Ethical Review Board. Detailed baseline characteristics and clinical findings were recorded in a pre-designed proforma. Investigations such as blood glucose, total and indirect serum bilirubin (SB), ionized calcium, haematocrit, haemoglobin, total and differential leucocyte counts, platelet counts and peripheral blood smear, reticulocyte count and direct Coombs test were performed. ABO and Rh blood grouping of both baby and mother were done. Rh disease was defined as jaundice in Rh positive newborns born to Rh negative mothers with elevated antibody titre to the Rh antigen and evidence of haemolysis. ABO disease was attributed as a cause of jaundice in newborns with positive direct Coombs test against the A or B antigens from type O mothers. Infant's blood volume was taken as 80 ml/kg and so 160 ml/kg of blood was required for ET, which replaces 87% of the infant's blood volume with new blood. Exchange was done under a servo-controlled radiant warmer with monitoring of vital parameters. Exchanges were done by the push-pull technique with stored whole blood of less than 5 days duration. Umbilical catheter was inserted as far as required to permit free blood exchange. Blood was removed in aliquots tolerated by the infant, which was 5 ml for infants <1,500g, 10 ml for infants 1,500 to 2,500g, 15 ml for infants 2,500 to 3,500g, and 20 ml for infants >3,500g. If jaundice was the only problem and the baby was active and taking feeds adequately, the baby was

considered as a healthy newborn, as opposed to sick neonates who had ongoing illnesses such as birth asphyxia, meconium aspiration syndrome or respiratory distress syndrome that required treatment prior to or at the same time as ET. The adverse events which occurred during and within 3 days of the procedure were observed and managed accordingly. The catheter was removed after the procedure. In sick neonates, supportive treatment in the form of intravenous fluids, oxygen inhalation and empiric antibiotics (ampicillin + amikacin) were given. The antibiotics were changed after culture report as per antimicrobial sensitivity pattern. Biochemical abnormalities such as hypoglycaemia and hypocalcaemia were corrected before doing the ET. However, no intermittent infusions of calcium were given during the procedure as per our NICU protocol. IVIg was not used in any neonate with Rh isoimmunization because of high cost and non-affordability by the parents. Data were analysed using the SPSS version 20.0. Chi-square and Fisher Exact tests were applied to compare the data of proportions and Student's *t*-test was used for quantitative variables. A 'p' value less than 0.05 was considered as statistically significant.

Results

ET was performed in 64 neonates. Basic characteristics of the study subjects are shown in Table 1.

Table 1: Basic characteristics of study subjects

Characteristics		Gestational age		P value
		37 weeks or > (n=48)	< 37 weeks (n=16)	
Body weight (Kg) (mean ± SD)		3.01±0.47	1.587±0.47	<.001
Age at ET (days) (mean ± SD)		3.67±2.24	4.25±1.39	0.226
Gender	Male	31 (64.6%)	08 (50.0%)	0.300
	Female	17 (35.4%)	08 (50.0%)	
Race	Mongolian	24 (50.0%)	08 (50.0%)	1.000
	Non-Mongolian	24 (50.0%)	08 (50.0%)	
Place of delivery	Inborn	27 (56.2%)	05 (31.2%)	0.083
	Outborn	21 (43.8%)	11 (68.8%)	
Mode of delivery	SVD	30 (62.5%)	14 (87.5%)	0.62
	LSCS	18 (37.5%)	02 (12.5%)	

SVD: Spontaneous vaginal delivery; LSCS: Lower segment caesarean section; SD: Standard deviation

There were 16 preterm and 48 term neonates. Term neonates had significantly higher mean body weight than preterm neonates (*p*<0.001). Other parameters such as age at exchange transfusion, gender, race and place of delivery were comparable between preterm and term neonates.

Causes of hyperbilirubinaemia included ABO incompatibility (32.8%), Rh incompatibility

(17.2%) G6PD deficiency (1.6%) and idiopathic (20.3%). ET was done once in 62 (96.9%) and twice in 2 (3.1%). Mean serum bilirubin levels were 13.1±3.82 mg/dl post ET and 14.63±3.16 mg/dl 6 hour post-ET period. The mean serum bilirubin levels in study subjects are presented in Table 2.

Table 2: Serum bilirubin levels (mg/dl) in study subjects (mean \pm SD)

Group	Gestational age		P value
	>37 weeks (n=48)	<37 weeks (n=16)	
Pre Exchange Transfusion	24.12 \pm 4.01	22.55 \pm 2.45	0.70
Post Exchange Transfusion	13.51 \pm 3.93	11.84 \pm 3.26	0.102
6 hours post Exchange Transfusion	14.91 \pm 3.36	13.8 \pm 2.35	0.154

Bilirubin levels declined in post-ET and 6 hour post-ET period in comparison to pre-ET values. The term neonates had higher levels of mean SB at all stages (pre-ET, post-ET & 6 hour post-ET) when compared with preterm but this was not statistically significant. The neonates had more than one adverse event and thus 70 adverse events occurred in 64 babies during three days following ET, as shown in Table 3.

Table 3: Adverse events following 3 days of ET

Adverse event	Complication
Hypocalcaemia	32 (50.0%)
Thrombocytopenia	23 (35.9%)
Apnoea	12 (18.8%)
Hypoglycaemia	11 (17.2%)
Death	02 (03.1%)
Total	70

Discussion

Prevention of bilirubin encephalopathy is essential and ET is an emergency procedure. In the present study the mean age for ET was 3.7 days and 4.3 days in term and preterm newborns respectively. At BPKIHS newborns come from far off and there are late referrals from peripheral health centres. The common causes of hyperbilirubinaemia were ABO incompatibility (33%), idiopathic (20%) and Rh incompatibility (17%). Steiner *et al.*¹⁰ and Behjata *et al.*¹¹ found ABO incompatibility in 28% and 52% respectively. However, Behjata *et al.*¹¹ also reported Rh incompatibility in 12%. Idiopathic aetiology was the second common cause because we are unable to find any attributable cause in neonates with indirect hyperbilirubinaemia. In different studies idiopathic aetiology varied from 13.9% to 36.4%¹³⁻¹⁵. In our study ET was performed once in 97% of neonates and more than once in 3% of cases. Multiple ET was also reported by other workers^{14,16}. The mean SB level in post ET (13.1 \pm 3.82) and 6 hour post-ET (14.63 \pm 3.16) samples showed a decrease from the pre-ET value but this was not statistically significant. Further, there was a rise in the SB level in the 6 hour post-ET period despite continued phototherapy. Thus, ET removes about 60% of bilirubin from plasma, resulting in a clearance of 30 to 40% of bilirubin¹⁷. Following 3 days of ET, hypocalcaemia (50%) and thrombocytopenia (35.9%) were the major adverse events. In our study the high incidence of hypocalcaemia was because we did not use prophylactic calcium during the procedure unless it became symptomatic. Whilst 0.5-1.0 ml of 10%

intravenous calcium gluconate, given after each 100 ml of exchange blood, may reduce incidence of hypocalcaemia¹⁸, its use is controversial. Thrombocytopenia (36%) was another major adverse event. Besides ET, phototherapy can also cause thrombocytopenia. The other events were hypoglycaemia, respiratory distress, apnoea and cardio-respiratory arrest posing additional problems, which require close monitoring during procedure. Two neonates (3%) died within 24 hours of ET in contrast with other studies which have low mortality rates (0.5- 2.8%)^{19,20}. Newborns undergoing ET need close monitoring and prompt treatment for adverse events.

Conclusions

In our study ABO incompatibility was the commonest identified cause of ET. Adverse events remain common after ET. Most complications were transient. Mortality rate was 3% in this study.

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