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Evaluation of Complications Related to Exchange Transfusion due to Hyperbilirubinaemia in Newborns with or without Comorbidities

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Abstract:

Introduction: Exchange transfusion (ET) is the first successful treatment introduced for severe neonatal jaundice considered to be a safe procedure but not risk free. Present study aimed to determine the complications related to exchange transfusion and to compare the incidence of severe complications between healthy and ill newborns.

Methods: This cross sectional study was done in Neonatal Intensive Care Unit (NICU), Dhaka Shishu Hospital and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, over 6 months from January to June 2010, included 50 newborns who underwent exchange transfusion due to hyperbilirubinaemia. Newborns with hyperbilirubinemia alone were classified as healthy, while hyperbilirubinaemia associated with other medical problems were classified as ill. Adverse events were analyzed and compared between two groups.

Results: Out of 50 patients who underwent ET, 27 were healthy had jaundice only and 23 were ill. Most of the newborns with comorbidities (87%) developed at least one complication following exchange transfusion (p<0.001). Newborns with co-morbidities developed hypoglycemia (13%), hypocalcaemia (17.4%), thrombocytopenia (26.1%), sepsis (26.1%), apnoea (4.3%) and in newborns without co-morbidities, hypoglycemia, hypocalcaemia, thrombocytopenia each was found in 7.4% cases and septicemia (14.8%). Thrombocytopenia was significantly higher in ill newborns (p = 0.039). About 9% of newborns died in ill group compared to 3.7% in healthy group (p = 0.439).

Conclusions: Complications and mortality were significantly higher in newborns having hyperbilirubinemia with co-morbidities. Thrombocytopenia was the most frequent complication. Majority of the hyperbilirubinemic neonates with comorbidities develop at least one complication after exchange transfusion.

***Key words*: Exchange transfusion, hyperbilirubinemia, comorbidities, adverse events.**

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Introduction

Neonatal jaundice is a common phenomenon affecting approximately 60% of full-term newborns in first 7 days of life.[1] Bilirubin, a breakdown product of haemoglobin, lead to hyperbilirubinaemia, may be due to an imbalance between production and elimination, increases the risk of encephalopathy and long-term sequelae.

Exchange transfusion was introduced in the late 1940s to decrease severe hyperbilirubinemia in neonates that can lead to acute bilirubin encephalopathy or permanent neurological sequelae in survivor[2]. The level of bilirubin concentration at which ET is indicated is controversial.[3-6] Because the risk of bilirubin encephalopathy is very difficult to determine with different variables of patients, such as with or without haemolysis, with or without comorbidities, gestational age[5]. Exchange transfusion is the treatment of choice in neonates with high risk of kernicterus, though proven benefit this procedure may give rise to different serious complications and mortality rates vary from 0.5-3.3%.[7-10] Neonates with hyperbilirubinaemia associated with comorbidities like convulsion, altered consciousness, reluctant to feed, respiratory distress, infection and their outcome after exchange transfusion is comparatively poor with those

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having no associated comorbidities[11].One study done in Bangladesh showed that nearly half (48%) of the babies who had undergone exchange transfusion developed some form of adverse events.[12]Adverse events like thrombocytopenia, hypoglycaemia, hypocalcaemia, septicemia were found in 78% of newborns with co-morbidities vs 30% without co-morbidities.[12] The present study was conducted to find out the adverse events related to exchange transfusion and to compare the incidence of complications in healthy and ill group.

Methods

This study was a hospital based cross sectional study carried out in NICU, Dhaka Shishu Hospital and BSMMU, over a period of 6 months from January to June 2010.Newborns who underwent ET due to hyperbilirubinaemia were included in this study. Fifty (50) cases were enrolled consecutively in this study after taking informed written consent from the parents or legal guardians. Ethical clearance was taken from the Institutional Ethical Review Board (IRB) of Bangladesh Institute of Child Health before doing the study. Data were collected using a structured questionnaire (research instrument) containing all the variables of interest.

History and thorough physical examination were done. Information like gestational age, sex, weight of the newborn, onset and duration of jaundice, time elapsed between onset of jaundice and admission, clinical presentation and associated co-morbidities like convulsion, reluctance to feed, hypertonicity, respiratory distress, fever etc were recorded and were determined in terms of sepsis, asphyxia, complications of hyperbilirubinaemia or hypocalcaemia. Complete blood count, peripheral blood film, reticulocyte count, blood group of the baby and the mother, Coomb's test (when suggested), serum bilirubin, serum calcium, electrolytes and random blood sugar were done before ET in all cases. C-reactive protein, blood culture and arterial blood gas analysis were performed when needed. Patients were divided into two groups depending on the presence or absence of associated medical problems on admission. Newborn infants admitted solely for hyperbilirubinemia were classified as healthy and allocated to Group-1, while the newborn infants with hyperbilirubinaemia associated with other medical problems were classified as sick and allocated to Group-2. Medical problems included were reluctant to feed, convulsion, respiratory distress, fever, hypertonicity etc.

Double volume exchange transfusion (DVET) is defined as exchange of twice the circulating blood volume of the newborn (2x80 ml/kg). DVET was done by small aliquots of blood (5-7 ml/kg) according to standard protocol using single line umbilical vein. Some investigations like

Hb%, serum bilirubin, platelets, serum calcium, electrolytes and blood glucose were done immediately after DVET and serum bilirubin was monitored 6-8 hourly until safe level and patients were assessed clinically.

The following conditions were considered as adverse events associated with exchange transfusion if they occur during or up to 48 hours after the procedure:

- Metabolic disorders: Hyperkalemia (potassium > 6 mEq/dL), hypocalcemia (serum calcium < 8mEq/dL), hypoglycemia (random blood sugar < 40mg/dL) and hyponatremia (serum sodium < 130 mEq/dL).
- Thrombocytopenia: Platelet counts <50,000/cmm after exchange transfusion.
- Sepsis: Patients admitted with a negative blood culture and/or negative CRP who developed clinical features compatible with infection and a positive blood culture and/or positive CRP after exchange transfusion.
- Cardiorespiratory decompensation: Abnormal cardiac (tachycardia, bradycardia or arrhythmia) and respiratory function (tachypnea or apnea) or hypotension during or soon after exchange transfusion. These types of problems were included in this group.
- Death occurring during or up to 6 hours after the procedure

Statistical Package for Social Sciences (SPSS), version 12.5 was used for analysis of collected data. Descriptive statistics and Chi-square (c^2) or Fisher's Exact Probability Test were used and p-value < 0.05 was considered as statistically significant.

Results

During the 6-months study period, total 50 ET were done due to hyperbilirubinemia. Characteristics of the

study population are shown in Table I. Among the studied newborns 27 were otherwise healthy and had no medical problems other than jaundice (Group-1). The remaining 23 patients were classified as sick because of their additional medical comorbidities (Group 2).

Table2 showed about one-third (32%) were preterm baby (< 37 weeks of gestation) and the remaining 68% were term baby (=>37 weeks of gestation). The mean gestational age was 36.4 ± 2.5 weeks. Among the 50 studied babies 23(46%) were of low birth weight and 27(54%) were of normal weight. The mean birth weight was 2452.2 ± 553.7 gm. More than two thirds (68%) babies were male and rest (32%) were female giving a male to female ratio roughly of 2:1.

Table-I

Characteristics of the study population

	Group I (n = 27)	Group II (n = 23)	All infants (n = 50)
Gestational Age (week± SD)	37.2 ± 2	36.1 ± 3.6	36.4 ± 2
Birth weight (g)	2510 ± 374	2346 ± 283	2452 ± 558
Age at admission (day)	3.3 ± 1.5	3.7 ± 2.3	3.4 ± 1.8
Age at onset of jaundice (hours)	15.8±2.1	14.7±1.4	15.9±2.3

Table-II

Distribution of baby by age, sex and birth weight (n = 50)

Gestational age (weeks)	Frequency	Percentage
<37 (Preterm)	16	32.0
≥37 (Term)	34	68.0
Birth weight (gm)		
Low (<2500)	23	46
Normal (≥2500)	27	54
Sex		
Male	34	68
Female	16	32

Mean birth weight = (2452.2 ± 553.7) gm;
Range = (860 – 3700) gm.
Mean gestational age = (36.4 ± 2.5) weeks;
range = (30 – 40) weeks

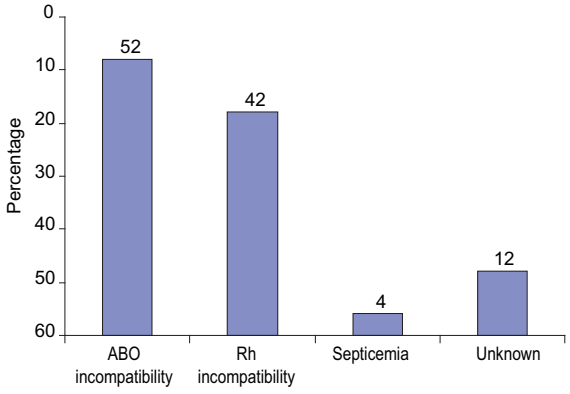

Fig.-1: *Distribution of babies by cause of jaundice (n = 50)*

Table-III

Distribution of medical problems on admission (n = 23)

Medical problems on admission	Frequency	Percentage
Convulsion	14	60.8
Reluctant to feed	09	39.2
Fever	04	17.4
Hypertonicity	02	8.7
Respiratory distress	04	17.4
Others	01	4.3

Table-III

Comparison of complications after exchange transfusion

Complications	Group-I (n = 27)	Group-II (n = 23)	P-value
Hypoglycemia*	2(7.4)	3(13.0)	0.422
Hypocalcaemia*	2(7.4)	4(17.4)	0.259
Thrombocytopenia*	2(7.4)	6(26.1)	0.039
Sepsis #	4(14.8)	6(26.1)	0.321
Cyanosis and apnoea*	00	1(4.3)	0.460
Hyperglycemia	00	00	
Feed intolerance	00	00	
Comparison of adverse events			
Developed	8(29.6)	20(87.0)	<.001
Not developed	19(70.4)	3(13.0)	

Figures in the parentheses denote corresponding percentage.
Chi square (c^2) Test was employed to analyse the data
*Fisher Exact Test was done to analyse the data.

Table-V

Outcome of studied newborns following exchange transfusion

Outcome	Group		p-value
	Group-I (n = 27)	Group-II (n = 23)	
Improved/ Discharged	26(96.3)	21(91.3)	0.439
Death	1(3.7)	2(8.7)	

*Fisher Exact Test was done to analyse the data;

Main cause of hyperbilirubinaemia that required ET was ABO incompatibility (52%), Rh incompatibility (42%), and septicemia (4%). In 12% of the cases no known cause of jaundice was revealed (fig.1). Out of 50 neonates, 23 had associated co-morbidities at admission e.g convulsion 60.8%, reluctant to feed 39.2%, respiratory distress and fever each 17.4% (Table III).Table IV showed that 13% of babies of Group-II (with co-morbidity) exhibited hypoglycemia after exchange transfusion, 17.4% hypocalcaemia, 26.1% thrombocytopenia and 26.1% sepsis. In Group-I (without co-morbidity), hypoglycemia, hypocalcaemia and thrombocytopenia each was found in 7.4% cases and 14.8% sepsis (CRP positive).Of the complications developed, thrombocytopenia was significantly higher in group-II than that in group-I (p = 0.039). These complications were attributable to ET as they occoured within 48 hours after the procedure and laboratory tests were normal before the procedure. These biochemical abnormalities resolved within 48 hours of ET regardless of intervention. Table IV also demonstrates that majority (87%) of the neonates with comorbidities developed at least one complication following exchange transfusion as opposed to 29.6% of the neonates without having comorbidites (p < 0.001). Majority of the babies with and without co-morbidity improved after exchange transfusion. About 9% of babies in group-

II died compared to 3.7% in group-I. There was no significant difference between the groups with respect to outcome of exchange transfusion (p = 0.439) Table V.

Discussion:

Exchange transfusion remain the gold standard for effective treatment of severe neonatal

hyperbiirubinaemia. Although reports show a progressive decline over the years in the number of neonates needing ET, a prospective study done in Nepal reported 6% (29/481) over 14 months' period.[13-14]However, the ET rate in developing countries is high.

The result from the study demonstrated that about one-third (32%) of the babies was preterm with mean gestational age being 36.4 ± 2.5 weeks. A male preponderance was observed with male to female ratio being 2:1. About 46% of the babies had low birth weight for their gestational age with mean weight being 2452.2 ± 553.7 gm. Hoque and colleagues[12] in a similar study in 2004 found that 40% their babies were of low birth weight and 34% were preterm.

The mean age at onset of jaundice was 15.9 ± 2.3 hours and the mean age of baby at admission was 3.4±1.8 days. Over half (52%) babies had a history of ABO incompatibility, 42% Rh incompatibility, 4% septicemia and 12% had no known cause of jaundice. One study done in Bangladesh by Hoque & his associates reported 39% of the jaundice due to ABO incompatibility and 34% due to Rhesus incompatibility.[12]Bujandric[15]found 76% of exchange transfusion were done because of acute hemolysis due to ABO and RhD incompatibilities.The higher ABO incompatibility than Rh incompatibility in the present study might be due to prophylactic use of Anti D in case of Rh -ve mother. ABO haemolytic disease has been reported as the cause of ET by Badiee[16],Davutoglu et al.[17],Bhat et al.[18] And Sanpavat[19] at the rate of 22.5%, 38% ,25% , and 21.3% ,respectively.

As neonates come late after the onset of jaundice, they usually develop some complications along with jaundice before admission. Hoque and associates[12] reported that 17 of the 38 patients (45%) who underwent exchange transfusion were ill and had one or more medical problems, singly or in combination with other problems, viz, convulsions (59%), reluctance to feed (23.5%), hypertonicity (11.8%), respiratory distress (29.4%) and fever (11.8%). In the present study out of 23 babies who had comorbidities, more than 60% had convulsion, about 40% were reluctant to feed, 17.4% had fever, another 17.4% had respiratory distress, 8.7% hypertonicity and 4.3% other comorbidities which are nearly consistent with those in Hoque and associates' study.

There are limited data regarding the adverse events of ET in newborn infants with indirect hyperbilirubinaemia. In the present study, 13% of babies with co-morbidity exhibited hypoglycemia after exchange transfusion, 17.4% hypocalcaemia, 26.1% thrombocytopenia and

26.1% CRP positive compared to 7.4% of the babies without co-morbidity had hypoglycemia, 7.4% hypocalcaemia, 7.4% thrombocytopenia, 14.8% positive CRP. Cyanosis and apnoea was found in 4.3% of babies with co-morbidity while none of the babies without co-morbidity exhibited such complications. Steiner et al.[14]in their detailed study covering 21 years, reported a rate of hypocalcemia 38% and thrombocytopenia 38%. Hosseinpour Sakha et al. [20]described adverse events of ET during 2006-2008. According to their study, the most common events were thrombocytopenia (36%), and hypocalcemia (25%). These findings are consistent with our study.

Majority of the babies with and without co-morbidity improved after exchange transfusion. About 9% of newborns with comorbidities died compared to 3.7% of neonates without comorbidities. Patra et al.[21] in 2004reported high rate of ET related adverse events (74%) and a mortality rate of 2%attributable to exchange transfusion. Hoque[12] reported 8% of patients died

after exchange transfusion in comorbid group, while none of the patients without co-morbidity died which is not consistent with present study.

Conclusion:

Complications were more among the hyperbilirubinaemic newborns with co-morbidities than those without comorbidities. Thrombocytopenia occoured significantly in babies with co-morbidities. Death rate also is comparatively higher following exchange transfusion in same newborns group having co-morbidities.

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