

Effect of Exchange Transfusion in Biochemical Parameters in Neonatal Hyperbilirubinemia

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Hyperbilirubinemia is very common and usually benign in the term newborn infant and late pre-term infant at 35-36 completed weeks' gestation. Critical hyperbilirubinemia is uncommon but has the potential for causing long term neurological impairment. The present study is designed to determine the effect of exchange transfusion in biochemical parameters in pre-term and full term infants. Sixty newborns who underwent double volume exchange transfusion for different indications were studied. The infants were divided into two groups, Group A containing Full term infants and Group B containing Preterm infants. Blood samples were obtained and the following tests were performed i.e. serum bilirubin and blood glucose. A significant ($p < 0.001$) decrease in serum bilirubin values was observed in both the groups after exchange transfusion. Also a significant ($p < 0.001$) elevation of blood glucose level when measured at 5 min. after exchange transfusion and rebound decrease in blood sugar levels when assessed 3 hours post exchange was documented in both the groups.

Key words: Hyperbilirubinemia, jaundice, Pre-term newborn, Term-newborn, Exchange Transfusion.

Neonatal hyperbilirubinemia with mild to moderate elevation of serum bilirubin levels is generally considered to be an innocuous state. However, if serum bilirubin levels exceed a dangerous limit, which varies with birth weight, gestational age, chronological age and internal milieu of the body, bilirubin may cross blood brain barrier and bilirubin encephalopathy results. Severe hyperbilirubinemia occurs when the total serum bilirubin (TSB) concentration is greater than 340 $\mu\text{mol/L}$ at any time during the first 28 days of life and critical hyperbilirubinemia occurs when the TSB concentration is greater than 425 $\mu\text{mol/L}$ during

the first 28 days of life. Kernicterus - the pathological finding of deep yellow staining of neurons and neuronal necrosis of the basal ganglia and brainstem nuclei occurs when serum bilirubin levels are below 18-20 mg% in term infants⁽¹⁾. It is estimated that 60% of the term newborns develop jaundice and 2% reach a TSB concentration greater than 340 $\mu\text{mol/L}$ ⁽²⁾. Several risk factors have been identified for the development of severe hyperbilirubinemia in the newborns (Table 1). These risk factors are all common and the attributable risk of each is therefore very low.

Table 1 Risk factors for the development of severe Hyperbilirubinemia.

Major risk factors

- Jaundice observed in the first 24 hours.
- Blood group incompatibility with positive direct antiglobulin test, other known hemolytic disease (e.g.: G6PD deficiency).

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- Gestational age 35-36 week.
- Previous sibling received phototherapy.
- Cephalohematoma or significant bruising.
- If breast feeding is not going well and weight loss is excessive.

Minor risk factors

- Gestational age 37-38 week.
- Jaundice observed before discharge.
- Previous sibling with jaundice
- Macroscopic infant of a diabetic mother.

Decreased risk factors

- Gestational age more than 41 week.
- Discharge from hospital after 72 hours.

Despite advent of phototherapy as a therapeutic modality, Exchange Transfusion (ET) plays a significant role in the treatment of neonatal hyperbilirubinemia by eliminating serum bilirubin quickly (Table 2 and 3). In ET infant's blood is exchanged with adult blood by conventional discontinuation technique in 10 ml aliquots. Total volume of donor's blood infused is usually double (170 ml/kg body weight) the total volume of Infant (85 ml/kg body weight) and it replaces about 87% of the infant's blood. A significant proportion of serum bilirubin is removed from the body which ensures immediate protection against the imminent bilirubin toxicity⁽³⁾.

Although ET is considered to be a safe undertaking, many changes takes place in various serum biochemical parameters, plasma osmolality and electrolyte profile in the recipient infants which may give rise to post-operative complications including death, syncope and serious ECG changes^(3, 4, 5, 6). The most commonly reported adverse incidents during or soon after exchange transfusion: Hypo or hyperglycemia, acidemia, arrhythmias, bradycardia, neutropenia, septicemia, Hypo or Hyperthermia⁽⁷⁾.

Table 2. Indications for exchange transfusion

An exchange transfusion soon after birth is indicated if: Cord bilirubin is ≥ 5 mg/dl Cord Hb is ≤ 10 mg/dl, PCV <30 . Previous sibling history and positive DCT
Subsequent exchange transfusion is indicated if:
1. Bilirubin ≥ 10 mg/dl within 24 hours of age.
2. Bilirubin ≥ 15 mg/dl between 25-48 hours of age.
3. Bilirubin ≥ 20 mg/dl after 48 hours of age.
4. Rate of rise of bilirubin is ≥ 0.5 mg/dl/hr.

MATERIALS AND METHODS

The present work was done in the Department of Biochemistry in association with the Department of Pediatrics in Gandhi Medical College Bhopal. 60 Newborn infants of both sexes with hyperbilirubinemia who underwent ET for any reason in neonatal unit were selected for the study and were divided in two groups for the study.

Group A: Term, healthy newborns who were appropriate for gestational age and were admitted solely for asymptomatic hyperbilirubinemia.

Group B: Newborns who had primary additional medical risk factors prior to exchange transfusion, i.e., ill newborns.

Complete history of pregnancy and delivery was elicited, birth weight of babies were recorded, complete examination of the babies was carried out regarding extent of jaundice, condition of body, cephalohematoma, etc.

ET was performed by ACD blood using standard method through umbilical route in NICU under strict aseptic precautions. Blood samples were collected before exchange and after exchange through the umbilical catheter after 5 minutes. Samples were collected in clean plain vial for serum bilirubin and serum glucose estimation. One more sample from each newborn was collected at 3 hours after exchange transfusion for blood glucose estimation.

Serum bilirubin was estimated by Jendrassik colorimetric method. Serum glucose was done by Glucose-Oxidase method.

Pre and Post Exchange values of the above described biochemical parameters were analyzed statistically applying the student's paired t-test.

Table 3. Management of neonatal hyperbilirubinemia in low birth weight babies based on bilirubin levels (mg/dl)

Weight (gm)	Consider Exchange transfusion
500-750	12-15
750-1000	>15
1000-1250	15-18
1250-1500	17-20
1500-2500	20-25

RESULTS

Table 4(a) and 4 (b) shows the clinical details of term (Group A) and preterm (Group B) infants studied respectively. Table 5 shows the etiology of jaundice in both Group A and Group B infants studied. Highly significant (p<0.001) difference was observed in serum bilirubin level after Post Exchange transfusion in both the group of infants studied (Table 6). Table 7 shows the blood glucose level in both the groups of infants studied. In both the groups a significant (p<0.001) elevation of blood glucose level is observed when measured at 5 min after exchange transfusion. Significant (p<0.001) decrease in blood glucose level was observed when assessed at 3 hours after

exchange transfusion in both the groups of infants studied.

DISCUSSION

Jaundice in the newborn is one of the most frequently encountered clinical problem in the neonatal period. Though majority of the times jaundice is physiological, it creates anxiety amongst clinicians and parents as bilirubin is toxic to the central nervous system, if the value is very high it leads to bilirubin encephalopathy. This is the most common cause of deafness and mental retardation in children.

The classical controlled clinical trial reported by Mollison and Walker⁽⁸⁾ and subsequent clinical experience has established exchange transfusion as the standard treatment for preventing bilirubin encephalopathy in severe neonatal hyperbilirubinemia. Exchange transfusion is the most reliable and rapid method of removing bilirubin from the body.

In the present study, out of 60 newborns, 64% (32) were low birth weight. 23 newborns were preterm while 9 newborns were full term (SGA). In group A, 62.58% newborns had their birth weights

Table 4(a). Clinical details of Group A Infants studied

Term infants	Number and sex		birthweight (grams)	
	Male	Female	Range	No. of infants
	16	8	2500-2999	15
			3000-3499	9

Table 4(b). Clinical details of Group B Infants studied

	Number and sex		Birthweight (grams)		Gestational age	
	Male	Female	Range	No. of infants	Weeks	Number
Premature infants			<1000 gm.(up to 999gms)	0	<28 wks.	0
			1000-1499 gms.	6	28-31	5
			1500-1999 gms.	17	32-36	19
			2000-2499 gms.	9	37-41	12

Table 5. Distribution of Newborns according to etiology of jaundice

S. No.	Etiology	Group A (n=24)	Group B (n=36)
1	Rh incompatibility	5	4
2	ABO incompatibility	9	10
3	Rh and ABO incompatibility	2	4
4	G6PD deficiency	0	2
5	Cephalhematoma	0	2
6	Unidentified	8	9

in the range of 2500-2999 grams, while only 37.5% were >3000 grams. All newborns in group A were term (37-41 weeks). In group B of ill newborns, maximum 47.22% newborns had their birth weight in the range of 1500-1999 grams and 25% in the range of 2000-2499 grams. Maximum newborns (52.77%) were between 32-36 weeks of gestational age.

Increased incidence of neonatal hyperbilirubinemia in preterm and low birth weight babies can be explained on the basis of hepatic

immaturity, increased bilirubin load, decreased synthesis of ligandin (Y protein) and decreased UDPG (T) activity. The present findings are in accordance with the study of Maisles M.J. ⁽⁹⁾, Narang et. al.

Our study found that maximum number of newborns who were exchanged for jaundice had ABO incompatibility i.e. 37.5% in group A and 27.27% in group B. Rh incompatibility was present in 20.9% newborns in group A and 11.11% newborns in group B. In the present study the ratio of ABO: Rh HDN is 2:1. The present findings are in accordance with the study of B.N.Das et.al ⁽¹⁰⁾, Malati Jadhav ⁽¹¹⁾ and L.V. Devarajan ⁽¹¹⁾, Verma M. et al. ⁽¹²⁾, M.R. Lokeshwar and Minaxi Mehta. In the present study, G6PD deficiency and Cephalhematoma were documented as the cause of jaundice in 5.55% newborns each. This is also reported by Kaplan, M. et al. ⁽¹³⁾, Deshmukh et.al., Bajpai et.al. ⁽¹⁴⁾ and Poonam Dutta et.al. Cephalhematoma as the cause of jaundice was reported by P. Chandra and Merchant et.al ⁽¹⁵⁾. In 50% cases the etiology of jaundice could not be determined. The present findings are in accordance with the study of Merchant and Abhyankar ⁽¹⁶⁾, Jackson J.C ⁽¹⁷⁾.

In the present study we found that in group A, 54.1% (13) newborns had their pre exchange bilirubin levels in the range of 20-25 mg/dl and in group B, 27.7% (11) newborns had their serum bilirubin levels in the range of 16-19 mg/dl.

Table 6. Pre and Post Exchange Serum Bilirubin changes

Groups	Serum Bilirubin levels (mg/dl) Pre Exchange and Post Exchange Difference (Mean± SD)	'p' value
Group A	8.51±9.61	<0.001
Group B	8.86±10.89	<0.001

To avoid the risk of bilirubin encephalopathy in group B, keeping in view their clinical status, the exchange transfusion was undertaken even at lower levels of serum bilirubin. The drop in serum bilirubin levels following exchange transfusion, when expressed as a percentage in relation to pre exchange serum bilirubin was 61% and 53% in Group A and Group B respectively ($p < 0.001$). So, exchange transfusion as a modality of treatment was equally effective in healthy as well as ill newborns. The present findings are in accordance with the study of Merchant and Abhyankar ⁽¹⁶⁾, Fernandez et al. ⁽¹⁸⁾ Brown, Zuelzer and Robinson ^(18, 19) suggested on extravascular bilirubin pool equilibrating with the plasma pool. The total clearance of bilirubin by an exchange is the result of two simultaneous processes, the rate of removal from the plasma and the rate of equilibration between the plasma and the extravascular pool.

There is a significant elevation of blood glucose levels when measured at 5 min. after exchange transfusion, in both the group of infants studied. Higher blood glucose levels at 5 min. after exchange transfusion can be explained on the basis of the fact that as adult donors have higher blood glucose level (90-120 mg/dl) as compared to newborns (40-90 mg/dl). The high glucose content of CPD blood (300mg/dl) used for exchange transfusion also contributes to Post Exchange rise in blood glucose. The blood glucose levels as measured, 3 hours Post Exchange, had fallen below the pre exchange one ($p < 0.001$) in both the groups of infants studied. This can be explained by the following phenomenon: the high glucose content of CPD blood may stimulate insulin secretion and cause hypoglycemia 1 to 2 hours after an exchange transfusion. The present findings are also supported by the studies of Schiff, D. et al, Cser ⁽²⁰⁾, Milner ⁽²⁰⁾, Nina N. et al ⁽²¹⁾.

Table 7. Blood Glucose Changes at 5 min. and 3 hours Post Exchange

Groups	Blood Glucose (mg/dl)			
	Pre Exchange and Post exchange Difference after 5 min. (Mean ± SD)	'P' Value	Pre Exchange and post Exchange Difference after 3 hours	'P' Value
Group A	64±67.76	<0.001	25.87±23.69	<0.001
Group B	49.69±52.69	<0.001	32.14±38.80	<0.001

CONCLUSION

Hyperbilirubinemia is the commonest morbidity in the neonatal period and 5-10% of all newborns require intervention for pathological jaundice. Severe hyperbilirubinemia in relatively healthy term or late preterm newborns (greater than 35 weeks' gestation) continues to carry the potential for complications from acute bilirubin encephalopathy and chronic sequelae. Careful monitoring of the risk factors involved, a systematic approach to the detection and follow up of jaundice with the appropriate laboratory investigations, along with judicious exchange transfusion when indicated, are all essential to avoid these complications.

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