Research Article

Effect of exchange transfusion in bilirubin and calcium level in Neonatal Hyperbilirubinemia

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Abstract

Background: Hyperbilirubinemia is very common and usually benign in the term newborn infant and late preterm 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. **Methodology:** 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 calcium. **Result**: A significant decrease in serum bilirubin values was observed in both the groups after exchange transfusion. Also a significant elevation of blood calcium level was found in both the groups of infant studied. **Conclusion:** 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.

Keywords: Hyperbilirubinemia, Jaundice, Pre-Term Newborn, Exchange Transfusion.

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Introduction

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. 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 >340 µmol/L at any time during the first 28 days of life and critical hyperbilirubinemia occurs when the TSB concentration is >425 µmol/L during the first 28 days of life. It is estimated that 60% of the term newborns develop jaundice and 2% reach a TSB concentration >340 µmol/L [1]. Several risk factors have been identified for the development of severe hyperbilirubinemia in the newborns**.** These risk factors are all common and the attributable risk of each is therefore very low.

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Risk factors for the development of severe hyperbilirubinemia

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

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. In ET infant's blood is exchanged with adult blood by conventational 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 [2]. Exchange transfusion of blood collected with acid citrate dextrose (ACD) may produce calcium abnormalities [3]. To decrease the morbidity from chelation of divalent cations by citrate, injection of calcium gluconate during exchange transfusion was advocated [4].

An exchange transfusion soon after birth is indicated if:

1. Cord bilirubin is ≥ 5 mg/dl
2. Cord Hb is ≤ 10 mg/dl, PCV <30.
3. Previous sibling history and positive DCT

Subsequent exchange transfusion is indicated if:

1. Bilirubin ≥ 10mg/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.

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 [2, 4-7]. The most commonly reported adverse incidents during or soon after exchange transfusion: Hypo or hyperglycemia, hypocalcaemia, acidemia, arrhythmias, bradycardia, neutropenia, septicemia, Hypo or Hyperthermia [8].

Material and Method

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: Preterm 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, cephalhematoma, 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 calcium estimation. Serum bilirubin was estimated by Jendrassik colorimetric method. Serum calcium was done by OCPC method. Pre and Post Exchange values of the above described biochemical parameters were analyzed statistically applying the student's paired t-test.

Results

Table 1: Clinical details of Group A & B Infants studied

	Number and sex		Birth weight (grams)		Gestational age	
	Male	**Female**	**Range**	**No. Of infants**	**Weeks**	**Number**
Term infants	16	8	2500-2999	15		
			3000-3499	9		
Premature infants	20	16	<1000 gm. (up to 999gms)	0	----	----
			1000-1499 gms.	6	<28 wks	0
			1500-1999 gms.	17	28-31	5
			2000-2499 gms.	9	32-36	19
			>2500 gms.	4	37-41	12

Table 1 shows the clinical details of term (Group A) and preterm (Group B) infants studied. **Table 2** shows the etiology of jaundice in both Group A and Group B infants studied.

Table 2: 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

Table 3: Pre and Post Exchange Serum Bilirubin and calcium changes

Groups	**Serum Bilirubin levels (mg/dl)**	**'p' value**
	Pre Exchange and Post Exchange Difference (Mean± SD)	
Group A	8.51±9.61	<0.001
Group B	8.86±10.89	<0.001
Groups	**Serum Calcium levels (mg/dl)**	**'P' Value**
	Pre Exchange and Post exchange Difference (Mean ± SD)	
Group A	1.495±1.86	<0.001
Group B	2.62±2.93	<0.001

Highly significant ($p<0.001$) difference was observed in serum bilirubin level after Post Exchange transfusion in both the group of infants studied. In the present study mean Post Exchange total calcium level was significantly higher than the pre exchange total calcium level ($p<0.001$) in both the groups of infants studied **(Table 3).**

Discussion

Jaundice in the newborn is one of the most frequently encountered clinical problems in the neonatal period. This is the most common cause of deafness and mental retardation in children.

Exchange transfusion is the most reliable and rapid method of removing bilirubin from the body. The classical controlled clinical trial reported by Mollison and Walker [9] and subsequent clinical experience has established exchange transfusion as the standard treatment for preventing bilirubin encephalopathy in severe neonatal hyperbilirubinemia.

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 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.

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 Das et.al [10], Devarajan Verma M. et al. [11], 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. [12], Deshmukh et.al, Bajpai et.al [13]. In 50% cases the etiology of jaundice could not be determined. The present findings are in accordance with the study of Merchant and Abhyankar [14], Jackson J.C [15].

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. 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 [14], Zuelzer and Robinson [16, 17] suggested on extra vascular 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.

In the present study mean Post Exchange total calcium level was significantly higher than the pre-exchange total calcium level ($p<0.001$) in both the groups of infants studied. This transient rise of total calcium level was associated with routine use of intravenous administration of 10 % calcium gluconate after each 100 ml of blood exchange in order to counteract any fall in serum ionized calcium levels [18]. Such fall occurs due to calcium chelating properties of citrate which is present in high concentration in the donor's blood where it is used as an anticoagulant [19, 20]. Calcium level came within the normal range after 24 hours of exchange.

Conclusion

Kernicterus is still occurring but should be largely preventable if health care personnel follow the recommendations listed in this guideline. These recommendations emphasize the importance of universal, systematic assessment for the risk of severe hyperbilirubinemia, close follow-up, and prompt intervention, when necessary. 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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