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Severe neonatal hyperbilirubinemia leading to exchange transfusion

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Abstract

Background: Severe neonatal hyperbilirubinemia is associated with significant morbidity and mortality. This study was conducted to investigate the causes of severe hyperbilirubinemia leading to Exchange Transfusion (ET) from March 2009 to March 2011 in Bahrami children hospital, Tehran, Iran in order to establish guidelines to prevent profound jaundice & ET.

Methods: 94 neonates underwent ET for severe hyperbilirubinemia data for demographic data, and onset of jaundice, history of severe hyperbilirubinemia in siblings, blood group of both mother and neonate, G6PD activity, hemoglobin, hematocrite, reticulocyte count, peripheral blood smear, total and direct bilirubin before and after ET, direct and indirect Coombs, times of transfusion and the cause of hyperbilirubinemia were all recorded for analysis.

Results: Ninety four neonates (56.4% boys and 43.6% girls) underwent ET with a mean birth weight of 1950±40 g and a mean gestational age of 35.2±1.4 weeks. Premature labor, breastfeeding jaundice, ABO incompatibility and G6PDD with the frequency of 59(63%), 33(35%), 25(24/5%) and 12(12.8%) were of major causes of ET.

Conclusions Predisposing factors for severe hyperbilirubinemia in this study were premature labor, breastfeeding jaundice, ABO incompatibility and G6PDD. The authors recommend prevention of premature labor, reevaluation of successful breastfeeding education for mothers and screening infants for blood group and G6PD In the first of life. Arranging earlier and continuous visits in neonates with these risk factors during the first four days of life is also recommended.

Keywords: Severe hyperbilirubinemia, Neonatal jaundice, Exchange transfusion.

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Introduction

Pathologic neonatal hyperbilirubinemia is associated with significant morbidity and mortality. It is estimated to be the most common cause of neonatal hospital readmission in North America (1). It may lead to bilirubin accumulation in basal ganglia and brain stem nuclei and lead to kernicterus. If the infants survive the acute phase, which is marked by lethargy, hypotonia, poor feeding and opisthotonus, they may develop chronic encephalopathy. This condition is manifested by cerebral palsy,sensory neural hearing loss, dental dysplasia, upward gaze paralysis and mental retardation (2).

Causes of severe neonatal hyperbilirubinemia are categorized either as hemolytic (blood group mismatch, sepsis, G6PD deficiency) or non-hemolytic (breast feeding jaundice, internal hemorrhage, gestational diabetes, pyloric stenosis, hypothyroidism and some mutations in hepatic enzymes). Prematurity, jaundice in the first 24 hours of life, jaundice noted before discharge from hospital, a history of jaundice treated with phototherapy in siblings and Asian

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race are other predisposing factors for severe hyperbilirubinemia noted by various studies (3-5).

Phototherapy is the main method of treatment for neonatal jaundice. However, severe hyperbilirubinemia is mainly treated by Exchange Transfusion (ET).According to American Academy of Pediatrics (AAP), neonates with weight ≥ 2500 grams in healthy term, ET is indicated when indirect bilirubin level reaches≥ 25 mg/dl and ≥20 mg/dl and in cases with risk factors or gestational age of35-37 wk and well despite 6 hr of intensive phototherapy. In newborns of 35-37 wk and risk factors, ET is indicated when the indirect bilirubin level reaches ≥ 18 mg/dl despite 6 hr of intensive phototherapy (2). ET is associated with many complications such as hypersensitivity reactions, sepsis, catheter-induced vascular damage, hypotension, necrotizing enterocolitis, etc (5).

The present study has been conducted to investigate the causes of severe hyperbilirubinemia leading to exchange transfusion from March 2009 to March 2011 in Bahrami children hospital, Tehran, Iran. The aim was to identify neonatal predisposing factors that can be prevented by screening or other measures, thus reducing the incidence of kernicterus, which can be prevented and also to avoid ET and its side effects.

Methods

All infants below 30 days who underwent ET for severe hyperbilirubinemia in Bahrami Children Hospital during 2009-2011 were enrolled into this cross sectional study. A questionnaire prepared consisted of neonates' gender, gestational age, age at the time of admission, birth weight, time of jaundice appearance, history of severe hyperbilirubinemia in siblings, blood group and Rh of both mother and neonate, G6PD activity, complete blood count, reticulocyte count, peripheral blood smear, total and direct bilirubin before and after exchange transfusion, direct Coombs in mother and indirect Coombs in neonates, times of transfusion, any other diagnostic laboratory data based on attending neonatologist's decision and the cause of hyperbilirubinemia stated by the attending neonatologist. Criteria for diagnosis of ABO incompatibility were type O maternal blood group and A, B or AB neonatal blood group associated with neonatal Hb drop. Positive coombs, peripheral blood spherocytosis and high corrected reticulocyte count were other diagnostic criteria. Icteric breastfed newborns with the beginning of jaundice in the second or third day of life and 2% or more weight loss per day of life with or without uremia or hypernatremia were considered breastfeeding jaundice.

The data were analyzed with SPSS software, version 16.

Results

During the study period, 94 neonates (56.4% boys and 43.6% girls) underwent exchange transfusion due to severe hyperbilirubinemia. The infants had a mean birth weight of 1950±40 g and a mean gestational age of 35.2±1.4 weeks. Fifty nine (63%) of neonates were preterm, and history of neonatal jaundice in siblings was reported in 50% of cases. However, only 18(19%) had a history of severe hyperbilirubinemia leading to ET in their siblings.

Most cases (40.5%) of severe hyperbilirubinmia started to become icteric on the second day after birth.

First day jaundice was observed in 10 neonates, all of them due to hemolysis. Table 1 shows a summary of underlying factors for severe hyperbilirubinemia according to the onset of jaundice.

The majority of infants (91.5%) had only one episode of ET, and hemolysis was the sole underlying reason in the remaining who had 2 or 3 episodes of ET. Totally, after prematurity, the second most prevalent underlying factor for severe hyperbilirubinemia was breastfeeding jaundice that included 33(35%) of neonates. We found that the next most prevalent causes were ABO mismatch and G6PD deficiency (Table 2). No cases of cephalhematoma, hypothyroidism or metabolic cases led to blood

Table 1. Underlying causes of severe hyperbilirubinemia leading to ET according to the date of jaundice appearance

Start date of jaundice	Underlying causes	N (%)
First day after birth	ABO mismatch	7(7.4%)
	Rh mismatch	2(2.1%)
	G6PD deficiency	1(1.06%)
Second day after birth	ABO mismatch	13(13.82%)
	Rh mismatch	2(2.1%)
	G6PD deficiency	6(6.3%)
	Infection	8(8.5%)
	Breast feeding jaundice	9(9.6%)
Third day after birth	ABO mismatch	3(3.2%)
	Rh mismatch	2(2.1%)
	G6PD deficiency	2(2.1%)
	Infection	3(3.2%)
	Breast feeding jaundice	14(14.9%)
Forth day after birth	Rh mismatch	2(2.1%)
	G6PD deficiency	2(2.1%)
	Breast feeding jaundice	8(8.5%)
Fifth day after birth and later	G6PD deficiency	1(1.6%)
	Breast feeding jaundice	2(2.1%)

Table 2. Prevalence of predisposing factors of severe hyperbilirubinemia leading to ET

Predisposing factor		Numbers (%)
Hemolytic		
	ABO mismatch	23(24.5%)
	Rh mismatch	8(8.5%)
	G6PD deficiency	12(12.8%)
	Sepsis	11(11.7%)
Non-hemolytic		
	Breast feeding jaundice	33(35%)
	prematurity	59(63%)
Idiopathic		7(7.5%)

exchange. There was no kriglernajar cases in our study because no significant hyperbilirubinemia was found after discharging and fallow up.

Discussion

According to epidemiological studies, some risk factors are associated with severe hyperbilirubinemia in neonates. The risk factors are male gender, jaundice presenting in the first 24 hours after birth, jaundice noted at discharge from the hospital, previous sibling with jaundice, preterm labor, breast feeding, Rh and ABO incompatibility, G6PD deficiency and sepsis (4, 6).

According to the Canadian Pediatric Society, gestational age of 35-36 weeks is an important risk factor for hyperbilirubinemia (7). Kuzniewicz et al also reported gestational age to be the main predictor of severe hyperbilirubinemia (8). In our series, infants had a mean gestational age of 35.2

weeks and fifty nine (63%) of neonates were preterm.

Most cases (40.5%) of severe hyperbilirubinmia started on the second day after birth. This corresponds with views of American Academy of Pediatrics and Canadian Pediatric Society, which recommend clinical assessment of infants for jaundice within the first 48 hours of birth (6, 7). However, clinical assessment of newborns is not an accurate means of assessing the severity of hyperbilirubinemia (1).

In the present study, breastfeeding jaundice, as the most important factor associated with severe hyperbilirubinemia and according to Salas and Mazzi (9), is encountered in 33(35%) of cases. The data also corresponds with findings of Huang et al (6), who reported an odds ratio of 3.2 for severe hyperbilirubinemia in neonates who were breastfed (10). Inadequate intake may lead to dehydration, increased enterohepetic cycle and development of hyperbilirubinemia. Guidelines advise mothers to nurse their infants at least 8 to 12 times per day for the first several days, rooming in with night feeding, discouraging 5% dextrose or water supplementation and ongoing lactation support for reducing the incidence of breast feeding jaundice (2).

In this study, ABO mismatch was the third most common cause of severe hyperbilirubinemia and accounted for 24.5% of cases. This is similar to the reports of Badee and Sanpavat who reported ABO mismatch in 22% and 21.3% of cases, respectively (11, 12). However, according to Canadian surveillance program, the most common causes of severe hyperbilirubinemia were incompatibility ABO blood group and G6PD deficiency.

The G6PD deficiency was the fourth most prevalent risk factor for severe hyperbilirubinemia leading to ET and accounted for 12(12.8%) of cases. Badee also reported G6PD Deficiency in 19.1% of neonates who underwent ET (11). According to Johnson et al, G6PD deficiency was considered to be the main cause of hyperbilirubinemia in 19 of 61 (31.5%) infants who developed kernicterus (14).

Sepsis accounted for 11(11.7%) cases of severe hyperbilirubinemia. On the other hand, sepsis was the most common underlying cause for ET in the study performed by Koosha and Rafizadeh (15).

Conclusion

Prematurity was the most prevalent risk factor for severe hyperbilirubinemia. Thus following protocols for prevention of premature labor is recommended. Educating mothers for breast feeding in regard to the right times and method of feeding are important issue that should be considered. Since blood group mismatch and G6PD deficiency were the third and fourth most prevalent underlying factors, screening infants for blood group and if proven to be cost effective, G6PD activity in the first day of life are also recommended. Arranging earlier and continuous visits in neonates with these risk factors during the first four days of life are also mandatory.

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