Severe Neonatal Hyperbilirubinemia; Causes and Contributing Factors Leading to Exchange Transfusion at Ghaem Hospital in Mashhad

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Abstract- Hyperbilirubinemia is common in neonates; it can have a serious rising course. Due to its critical morbidity called "kernicterus", severe neonatal hyperbilirubinemia causes which lead to exchange transfusion, should be clarified. This descriptive cross sectional study performed with reviewing of files of 118 neonates weighting 2kg and more who had exchange transfusion in pediatrics ward at Ghaem training hospital in Mashhad from April 2004 to March 2007. Among 118 patients, 75 (63.6%) were male, and 43 patients (36.4%) were female. The most common cause of exchange transfusion was ABO incompatibility (38.1%). In order of frequency, unknown etiology (25.4%), Rh incompatibility (16.1%) with no immune hydrops, Sepsis (8.5%), urinary tract infection (5.1%) and others (3.4%) (Including Crigler-Najjar and cephalohematoma) were next ones. Vaginal delivery and exclusive breast feeding were detected as associated factors. Mean serum bilirubin levels was 28.7 mg/dl (SD. 9.2) ABO incompatibility. ABO incompatibility was the main cause of exchange transfusion. Male gender, vaginal delivery and exclusive breast feeding were seen more among patients who need to be exchanged. So in case of ABO incompatibility especially when delivery route is vaginal, newborns should be visited soon again after early discharge from hospital.

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Key words: Hyperbilirubinemia; exchange transfusion, whole blood; kernicterus; blood group incompatibility

Introduction

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Severe hyper bilirubinemia can cause neurotoxicity called kernicterus in which, patients suffer from long term morbidities consisting of developmental delays, sensorineural hearing impairments, mental retardation and other significant brain damages (1). But at first, acute neurotoxicity can cause poor feeding and lethargy then irritability and high-pitched crying with arching back may appear. To avoid from bilirubin encephalopathy in such a severe cases, exchange transfusion (ET) is recommended (2).

In one report from Canada, ABO incompatibility was the major cause of exchange transfusion among those patients who had identified cause of hyperbilirubinemia, but most cases had jaundice with unknown origin (2).

In one other report, common causes of exchange transfusion in icteric neonates were idiopathic, sepsis and hemolysis (3).

Also, another study detected that ABO incompatibility was the most common cause of ET (4). So, to identify the distribution of main causes of exchange transfusion at Ghaem hospital in Mashhad and also clarification of some probable related factor(s), this study was arranged.

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Patients and Methods

With reviewing among 643 files of neonates who had received blood in pediatrics ward at Ghaem teaching general hospital in Mashhad from April 2004 to March 2007, this descriptive cross sectional study was performed on records of 118 neonates weighting 2kg or more with severe jaundice who had exchange transfusion. All patients had serum bilirubin levels, blood group and rh (including his/her mother), reticulocyte count, coombs test, CBC, G6PD and peripheral blood smear. Data was brought to the detailed questionnaire by physician. This was consisted of demographic information, route of delivery, mother age, type of feeding of neonate, Apgar score in minute 1 and 5, serum bilirubin levels, mean age of neonate at admission, cause of ET and rate of weight losing of neonate during first week of life.

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Complications of severe neonatal hyperbilirubinemia, consisting of kernicterus, were not included in this study.

Those neonates (first 28 days after birth) who had indirect hyperbilirubinemia weighting 2kg or more and got exchange transfusion (according to guideline tables printed in Nelson Text book of pediatrics), included in the study. Excluding criteria was incomplete record of patient(s), newborn weighting below 2 kg and those patients that had above 28 days old.

Data was analyzed statistically with SPSS 11.5. t.Student, Chi-square and non parametric tests were used. P <0.05 was considered significant. CI 95% was calculated.

This study was confirmed by Research center and Ethics Committee of the Mashhad University of Medical Sciences.

Results

Mean age of mothers was 24.7 years old (16-40 years old).

Mean Apgar score in minute 1 and 5 had not statistically significant differences among our patients (P>0.05). 68 cases (57.6%) fed exclusively breast milk, 31 patients (26.3%) fed breast milk and formula, 13 cases (11%) took formula alone and 4 patients (5.1%) had not oral feeding and only got intravenous fluid therapy (P= 0.000 DF: 3).

The mean age of admission was 4.5 days in ABO and rh incompatibilities but was 7.5 days in unknown cases and 10.5 days in sepsis cases (P=0.002).

Table 1. Some risk factors in our patients

	Number	Percent	*P* value
Cesarean section	43	36.4%	0.003
Vaginal delivery	75	63.6%	
Weight loss above 10% after 1 week	19	16.1%	0.000
Weight loss below 10% after 1 week	99	83.9%	
Birth weight above 2500 grams	77	65.3%	0.001
Birth weight 2000-2500 grams	41	34.7%	
Male gender	75	63.6%	0.003
Female gender	43	36.4%	

df=1

Table 2. Serum bilirubin levels in our patients

Total bilirubin (*mg/dl*)	No	Percent
15-19	8	6.8
20-25	35	29.7
26-30	39	33.1
>30	36	30.5
Total	118	100

Mean: 28.7, SD: 9.2, P: 0.000, df: 3

Table 3. Causes of severe neonatal hyperbilirubinemia requiring ET

Cause	Number	Percent
*ABO incompatibility	45	38.1
Un known	30	25.4
**Rh incompatibility	19	16.1
Sepsis	10	8.5
Urinary tract infection	6	5.1
G6PD deficiency	4	3.4
Others (cephalohematoma, Crigler-Najjar)	4	3.4
Total	118	100

P= 0.000, DF: 7

*It is diagnosed with evidences of hemolysis including, positive direct and/or indirect coombs tests, hemoglobin decrement and reticulocytosis.

**It is diagnosed with detecting positive direct coombs test in rh positive neonate who delivered to rh negative mother.

It was not mixed etiologies leading to ET in our cases.

Some risk factors are shown in table 1.

Serum bilirubin levels of our patients are shown in table 2.

Causes of hyperbilirubinemia requiring ET are seen in table 3.

Discussion

According to our findings in this study, the most common cause of ET was ABO incompatibility, and male gender, vaginal delivery and exclusive breast feeding were significant contributing factors. Similarly, a report from Isfahan revealed ABO incompatibility as the most common cause of ET (4). In patients with ABO incompatibility, O blood group mothers have IgG antibodies that can pass through placenta and cause hemolytic events in A or B blood group offspring.

In some other studies, most patients (from 36.4% to 71%) with severe jaundice had unknown etiology (5-7).

This difference may be in some extent due to some difficulties in diagnosing ABO incompatibility. Our information came from rather complete laboratory tests including direct coombs test and indirect coombs test which helping ABO diagnosis and excluding those files in which the data was incomplete.

Rhesus incompatibility was responsible for 16.1% of ET in our cases. It is near to other report that revealed rh incompatibility in 12.7% of cases (8). But it is on opposite to other studies that ranging from 2.8% to 9.2% (3, 9, 10). If Anti D Ig use appropriately between 28-34 weeks of gestation and also as soon as possible after birth, it can effectively decrease the chance of rh incompatibility. It seems that poor medical cares during pregnancy and immediately after delivery including not taken Anti D Ig to unsensitized rh negative mothers have had a serious role in occurring hemolytic disease in our cases.

Sepsis was another cause (8.5%). It was next to other studies ranging from 4% to 9.15% (9, 11) .But in other study it was much higher than ours (24.1%) (3). Prenatal and post natal cares and regular revisiting of newborns after discharging from hospital can reduce the chance of infections.

A few of our patients had G6PD deficiency like other study that revealed 2.1% of their cases had G6PD deficiency (5). But in another report G6PD deficiency was the main cause of ET (38.1%) (12).

This obvious difference may be explained with ethnicity and geographic factors that in some region G6PD deficiency is more common.

In our study as like as others it was detected that most patients had vaginal delivery (2, 11, 13 and 14). Perhaps, early hospital discharge in addition to oxytocin use during this route of delivery can contribute to develop extreme jaundice.

Male gender is known as a risk factor for hyperbilirubinemia, similarly most of our patients were male (1).

According to our results, most of our patients fed breast milk exclusively. It was similar to other studies (11, 13, 15, 16). Breast feeding newborns may show an early onset jaundice in which lack of enough breast feeding can lead to lack of adequacy of intaking calories and as a result rise serum bilirubin levels.(breast feeding jaundice). So it may be partially due to ineffective lactation in first few days after birth resulting in dehydration or in some instances use of water or glucose in water finally cause aggravation of jaundice (14, 16-19).

But also it can be seen in successful feeding as well. In breast milk jaundice, it is estimated that glucuronidase containing breast milk may have a role in increased serum bilirubin levels in newborns.

As like as other report, most patients had serum bilirubin levels between (26-30 *mg/dl*) (20). In conclusion, in cases of severe hyperbilirubinemia, ABO incompatibility was the most common cause of ET and unknown etiology was the next one. Male gender, vaginal delivery mode and exclusive breast feeding were identified more in these cases.

So, it is regional that in case of ABO incompatibility, especially when the delivery is vaginal, neonates revisit as soon as possible after an early discharging from hospital.

Also, to prevent of rh incompatibility an appropriate antenatal care, consisting of administration of Anti D Ig to unsensitized rh negative mothers, can reduce neonatal hemolytic disease profoundly.

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References

1. Porter ML, Dennis BL. Hyperbilirubinemia in the term newborn. Am Fam Physician 2002;65(4):599-606.
2. Sgro M, Campbell D, Shah V. Incidence and causes of severe neonatal hyperbilirubinemia in Canada. CMAJ 2006;175(6):587-90.
3. Narang A, Gathwala G, Kumar P. Neonatal jaundice: an analysis of 551 cases. Indian Pediatr 1997;34(5):429-32.
4. Badiee Z. Exchange transfusion in neonatal hyperbilirubinaemia: experience in Isfahan, Iran. Singapore Med J 2007;48(5):421-3.
5. Koosha A, Rafizadeh B. Evaluation of neonatal indirect hyperbilirubinaemia at Zanjan Province of Iran in 2001-2003: prevalence of glucose-6-phosphate dehydrogenase deficiency. Singapore Med J 2007;48(5):424-8.
6. Sanpavat S. Exchange transfusion and its morbidity in ten-year period at King Chulalongkorn Hospital. J Med Assoc Thai 2005;88(5):588-92.
7. Martin TC, Shea M, Alexander D, Bradbury L, Lovell-Roberts L, Francis V. Did exclusive breast-feeding and early discharge lead to excessive bilirubin levels in newborns in Antigua and Barbuda? West Indian Med J 2002;51(2):84-8.

8. Arif MA. Neonatal jaundice in Pakistan. J Trop Pediatr 1984;30(4):213-6.
9. Dzinović A, Heljić S, Maksić H, Hrnjić Z. Neonatal hyperbilirubinemia: evaluation and treatment. Med Arh 2002;56(3 Suppl 1):44-5.
10. Tamook A, Salehzadeh F, Aminisani N, Moghaddam yeganeh J. Etiology of Neonatal Hyperbilirubinemia at Ardabil Sabalan Hospital, 2003. J Ardebil Uni Med Sci 2006;5(4):316-20.
11. Manning D, Todd P, Maxwell M, Jane Platt M. Prospective surveillance study of severe hyperbilirubinaemia in the newborn in the UK and Ireland. Arch Dis Child Fetal Neonatal Ed 2007;92(5):F342-6.
12. Abu-Ekteish F, Daoud A, Rimawi H, Kakish K, Abu-Heija A. Neonatal exchange transfusion: a Jordanian experience. Ann Trop Paediatr 2000;20(1):57-60.
13. Newman TB, Liljestrand P, Escobar GJ. Infants with bilirubin levels of 30 mg/dL or more in a large managed care organization. Pediatrics 2003;111(6 Pt 1):1303-11.
    Ebbesen F, Andersson C, Verder H, Grytter C, Pedersen-Bjergaard L, Petersen JR, et al. Extreme hyperbilirubinaemia in term and near-term infants in Denmark. Acta Paediatr 2005;94(1):59-64.
15. Salas AA, Mazzi E. Exchange transfusion in infants with extreme hyperbilirubinemia: an experience from a developing country. Acta Paediatr 2008;97(6):754-8.
16. Maisels MJ, Newman TB. Kernicterus in otherwise healthy, breast-fed term newborns. Pediatrics 1995;96(4 Pt 1):730-3.
17. Ebbesen F. Recurrence of kernicterus in term and near-term infants in Denmark. Acta Paediatr 2000;89(10):1213-7.
18. Johnson LH, Bhutani VK, Brown AK. System-based approach to management of neonatal jaundice and prevention of kernicterus. J Pediatr 2002;140(4):396-403.
19. Bhutani VK, Johnson LH, Jeffrey Maisels M, Newman TB, Phibbs C, Stark AR, et al. Kernicterus: epidemiological strategies for its prevention through systems-based approaches. J Perinatol 2004;24(10):650-62.
20. Newman TB, Liljestrand P, Jeremy RJ, Ferriero DM, Wu YW, Hudes ES, et al. Outcomes among newborns with total serum bilirubin levels of 25 mg per deciliter or more. N Engl J Med 2006;354(18):1889-900.