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Neonatal Hyperbilirubinemia Due to AB0 Incompatibility

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Abstract

Aim: ABO incompatibility is a common condition occurring in about 15-25% of all maternal/fetal pairs. The features of ABO incompatibility range from asymptomatic through to severe hemolysis with hyperbilirubinemia and anemia. The aim of this study is to assess the clinical course of ABO incompatibility and to evaluate the effect of blood groups on the severity of neonatal jaundice.

Material and Methods: Neonates with ABO hemolytic disease of newborn were retrospectively studied. Risk factors for the severity of jaundice were recorded. Demographic, clinic, and laboratory features were compared in infants with blood groups A and B.

Results: Within 13 months, 165 term infants with neonatal jaundice were treated. 32 (19.4%) of these patients had jaundice due to maternal-fetal ABO incompatibility. The O-A group included 23 infants (71.9%) while the O-B group included for 9 infants (28.1%). All the infants received phototherapy while none of the cases required exchange transfusion. Mean total bilirubin level was 15.6±4.5 mg/dl on the 2.9±2.1 days of mean age after the initiation of treatment. There were no differences between the infants with blood group A or B in terms of demographics, initial bilirubin level, anemia in first 24 hours, the rate of hemolysis, and direct Coombs test.

Conclusion: ABO incompatibility may have risks of significant hyperbilirubinemia and hemolysis in infants. Neonatal jaundice due to ABO incompatibility can be successfully managed with early admission of intensive phototherapy through close follow-ups. Blood type has no effect on the severity of jaundice.

Key Words: Neonate; Jaundice; ABO Incompatibility; Blood Group; Phototherapy.

ABO Uygunsuzluğuna Bağlı Neonatal Hiperbilirubinemi

Özet

Amaç: ABO uygunsuzluğu tüm maternal-fetal çiftlerde yaklaşık %15-25 oranda sık görülen bir durumdur. ABO uygunsuzluğu bulguları asemptomatikten hiperbilirubinemi ve aneminin görüldüğü ağır hemolize kadar değişebilir. Bu çalışmanın amacı ABO uygunsuzluğunun klinik gidişinin belirlenmesi ve yenidoğan sarılığının şiddeti üzerine kan grubunun etkisinin araştırılmasıdır.

Gereç ve Yöntemler: ABO hemolitik hastalığı olan yenidoğan bebekler geriye dönük olarak çalışmaya alındı. Sarılığın şiddeti ile ilgili risk faktörleri kaydedildi. A kan grubu ve B kan grubuna sahip olan bebekler demografik, klinik ve laboratuar bulgular açısından karşılaştırıldı.

Bulgular: Onüç ay içinde 165 zamanında doğmuş bebek yenidoğan sarılığı nedeni ile tedavi edildi. Bunların 32'si (%19.4) maternal-fetal ABO uygunsuzluğuna bağlıydı. O-A grubunda 23 bebek (%71.9) O-B grubunda ise 9 (%28.1) bebek vardı. Tüm bebekler fototerapi alırken hiçbir bebekte kan değişimine gereksinim olmadı. Ortalama tedaviye başlama zamanı 2.9 ± 2.1 gün ve total bilirubin düzeyi 15.6 ± 4.5 mg/dl idi. A ve B kan grubu olan bebekler karşılaştırıldığında demografik veriler, başlangıç bilirubin düzeyleri, ilk 24 saatte anemi görülen bebek sayısı, hemoliz ve direkt Coombs oranları arasında fark saptanmadı.

Sonuç: ABO uygunsuzluğu bebeklerde belirgin hiperbilirubinemi ve hemoliz yönünden risk oluşturabilir. ABO uygunsuzluğuna bağlı gelişen yenidoğan sarılığı yakın izlemle birlikte erken yoğun fototerapi uygulaması ile başarılı şekilde yönetilebilir. Kan grubunun sarılığın şiddeti üzerine etkisi saptanmamıştır.

Anahtar Kelimeler: Yenidoğan; Sarılık; ABO Uygunsuzluğu; Kan Grubu; Fototerapi.

INTRODUCTION

In contemporary neonatal practice, the spectrum of hemolytic disease of the newborn has changed. Within routine immunoprophylaxis, Rhesus (Rh) hemolytic diseases have decreased and ABO incompatibility has gained importance. The ABO blood group system is a well known surface antigen system, expressed on a wide variety of human cells. The spectrum of presenting features ranges from asymptomatic through severe hemolysis with hyperbilirubinemia and anemia. Hemolysis due to ABO incompatibility is not frequent though severe cases such as antenatal hydrops fetalis have been reported (1). We aim to seek whether there may be any regional differences on clinical course of neonatal jaundice due to ABO incompatibility and if neonatal blood group has any effects on the severity of hemolysis and neonatal jaundice.

MATERIAL AND METHODS

This retrospective study was conducted at Neonatology Unit, Gaziosmanpasa University, Tokat, Turkey between January 2013 and February 2014. The term newborn infants (gestational age ≥37 weeks) with neonatal jaundice receiving at least phototherapy and maternal-fetal ABO incompatibility were included in the study. The diagnosis of maternal neonatal ABO blood incompatibility was done in the presence of indirect hyperbilirubinemia in the newborn infant with blood type A or B and maternal blood type O. The other causes of pathologic hyperbilirubinemia including hemolytic processes such as Rh-isoimmunisation,

erythrocyte membrane and enzyme deficiencies, hemoglobinopathies, glucose-6-phosphate dehydrogenase deficiency, sepsis or urinary tract infections, cephalohematoma, polycythemia, dehydration, inherited metabolic diseases, and hypothyroidism were excluded. Early or late breast milk jaundice was also excluded from the study.

Neonatal details such as gender, birth weight, gestational age, day of phototherapy initiation, hemoglobin and hematocrit levels on admission, presence of positive direct antibody test, presence of anemia in first 24 hours, type of treatment, duration of phototherapy were all recorded. Evidences of hemolysis were determined with the presence of two following parameters: anemia (<13 g/dl), circulating normoblasts, spherocytosis, polychromasia, or peripheral blood smear. Neonates requiring phototherapy were considered to get significant hyperbilirubinemia according to 2004 American Academy of Pediatrics (AAP) hyperbilirubinemia treatment guidelines (2). All infants received intensive light emitting diode phototherapy (Novos Bililed Nova, Ankara, Turkey).

Statistical Analysis

All the variables were parametrical. The significance of differences between the means of the two groups were determined by independent t test samples. The categorical variables were analyzed by Chi-square test or Fisher's exact test with significance defined as $p<0.05$.

RESULTS

Within 13 months 165 term infants with neonatal jaundice were treated. 32 of them (19.4%) were due to maternal-fetal ABO incompatibility and had no other reason for indirect hyperbilirubinemia. They were all coming from the provinces of the city of Tokat. Nineteen infants (59.4%) were males and 13 infants (40.6%) were females. Birth weights ranged from 1870 to 4170 g (mean 3012±576 g) and the gestational ages ranged from 37 to 40.3 weeks (mean 38.3±1.5 weeks). The O-A group had 23 infants (71.9%) and the O-B group included 9 infants (28.1%). All infants received phototherapy with varying periods between 12 to 72 hours with a mean duration of 33.4±12.4 hours. Mean initial total bilirubin level was 15.6±4.5 mg/dl on the 2.9±2.1 days of mean age of blood sampling. Sixteen infants (50%) developed jaundice in the first 24 hours and 8 infants (25%) had anemia in the first complete blood count analysis. Seven infants (22%) had hemolytic findings on peripheral blood smear, and 5 (15.6%) had positive direct Coombs test. None of them received exchange transfusion while 3 (9%) of them received intravenous immunoglobulin (IVIG) treatment. Comparing the infants with blood group A and B, we were unable to determine any differences in terms of demographics, initial bilirubin level (15.5±4.5 mg/dl in group A vs 15.9 ± 4.1 mg/dl in group B, p=0.670), the number of infants who had anemia in first 24 hours, the number of infants who had hemolysis and direct Coombs test. Initial bilirubin levels were higher than 20 mg/dl in 2 infants who had blood group A (Table 1).

Table 1. Comparing the demographic and clinical characteristics of 32 infants with O-A and O-B incompatibility

	O-A incompatibility (n=23)	O-B incompatibility (n=9)	P value
Birth weight (g)*	3002±532	3041±712	0.39
Gestational age (weeks)*	38.4±1.7	38.1±2.1	0.43
Gender (Male/Female), n(%)	15/8 (65.2/34.8)	4/5 (44.4/55.6)	0.24
Day of hospital admission*	3±2.1	2.9±2.4	0.40
Initial hemoglobin (g/dl)*	15.1±2.5	14.8±3.3	0.37
Initial hematocrit (%)*	44.1±7.4	44.3±6.7	0.57
Positive direct Coombs test, n(%)	3 (13)	2 (22.2)	0.43
Anemia, n(%)	5 (21.7)	3 (33.3)	0.50
Presence of hemolysis, n(%)	4 (17.4)	3 (33.3)	0.30
Jaundice in the first 24 hours, n (%)	12 (52.2)	4 (44.4)	0.52
Duration of phototherapy (hours)*	34.2±12.7	31.3±11.9	0.83
Need for IVIG therapy	2 (8.7)	1 (11.1)	0.64

*mean ± standart deviation
IVIG: Intravenous immunoglobulin

DISCUSSIONS

ABO incompatibility is a common condition occurring in about 15-25% of all maternal/fetal pairs. It occurs almost exclusively in infants with blood groups A or B whose mothers are group O. Hemolytic disease due to ABO incompatibility is confined to the 1% of group O mothers that have high-titer IgG antibodies (1). The incidence of ABO incompatibility in infants with significant neonatal jaundice was 19.4% in our study. Management of ABO incompatibility is usually successful and exchange transfusion is rarely needed when intensive phototherapy is effectively used. Eighteen infants (10.8%) received exchange transfusion in a recent study in Turkey (3), whereas none of our infants required exchange transfusions. Also the mean initial bilirubin level was low and mean day of phototherapy initiation was fairly earlier in our analysis (2.9 vs 4.4 days) in comparison to Akgül et al.'s study (3). We think that this may be due to close follow-ups and early phototherapy administration. In a study from India consisting 46 infants with significant jaundice; none of them required exchange transfusion either. Timing of initiation was 45.6 hours in infants with hemolysis and 74.8 hours in infants without hemolysis in this latter study, which is in line with our findings (4). Although IVIG treatment in ABO hemolytic disease is considered arguable (5); it may be

beneficial in selected cases. It is shown that administration of IVIG to infants with significant hyperbilirubinemia due to ABO hemolytic disease with positive direct Coomb's test reduces the need for exchange transfusion (6). All three infants who received IVIG treatment share hemolytic similar findings and positive direct Coombs test in our study.

We found positive results for direct Coombs test in five infants (15.6%). Direct Coombs test was positive with a percentage of 10.2-12% in infants with ABO incompatibility requiring phototherapy in previous studies (3,4). Direct Coombs test will always not be positive in affected infants while positive predictive value of the test was already shown to be low in clinically significant ABO hemolytic diseases previously (7). The ABO surface antigen system is expressed on a wide variety of human cells. Anti-A or Anti-B antibodies that enter the fetal circulation bind many different fetal cell types and leave fewer antibodies available for binding onto erythrocytes. Also fetal erythrocyte surface A and B antigens are not completely developed during gestation. Thus, it is not reliable to definitively diagnose hemolysis based on only positive direct Coombs test in ABO hemolytic disease (8).

Several studies have pointed out that ABO hemolytic disease is more common in black people and in children of mixed racial origin than it is for white infants or other races (9,10). In the United Kingdom, the reported incidence of ABO hemolytic disease is 2% in all births, whereas severe hemolysis is present in only 0.03% of all the births (11). In Turkey, Sarici et al. (12) reported an incidence rate of 14.8% in ABO incompatibility. Of these infants, 21.3% showed significant hyperbilirubinemia and 4.4% exhibited severe ABO hemolytic diseases requiring intensive treatment. The severity between O-A and O-B incompatible neonates may vary. In some studies, it was shown that B group antibodies have high hemolytic activity in certain ethnic groups (1,13). Several cases of hydrops fetalis caused by anti-B antibodies were reported especially in African-originated patients (9,10). In a study by Aewuji et al. (13), hemolytic activity of anti-A and anti-B antibodies in black and white Zimbabweans showed the serum of black subjects to have greater hemolytic activity of anti-A and anti-B than that of white subjects. In each racial group, anti-B showed greater hemolytic activity than anti-A. In contrast, no significant relationship between the blood type and severity of hemolysis and jaundice could be found in other studies involving large number of infants (3,4). We did not find any association between the severity of jaundice and blood group antigens in Turkish newborns from the province of Tokat either. In conclusion, infants with ABO incompatibility may have a risk for significant hyperbilirubinemia and hemolysis. Neonatal jaundice due to ABO incompatibility can be successfully managed with early admission of intensive phototherapy through close follow-ups. Although blood type had no effect on the severity of jaundice in this study, further studies with larger number of patients from different ethnic groups are needed to improve our understanding.

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