ABO hemolytic disease of newborn : Does newborn's blood group a risk factor

Ictère hémolytique par incompatibilité ABO : Le type du groupe sanguin du nouveau-né constitue-t-il un facteur de risque?

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RÉSUMÉ

Introduction : Devant la régression de la fréquence de l'incompatibilité fœto-maternelle dans le système rhésus, l'allo immunisation érythrocytaire dans le système ABO est devenue la principale cause des maladies hémolytiques néonatales. L'incompatibilité ABO est retrouvée dans environ 15 à 25% des grossesses avec une vrai allo immunisation dans 1/150 naissances.

Objectifs : Un groupe sanguin néonatal de groupe B nous semble plus prédisposant à une hémolyse aigue et à un ictère intense, nous nous proposons de vérifier si ce groupe sanguin est un facteur de risque d'hémolyse sévère et/ou d'ictère intense.

Méthodes : Nous avons mené une étude rétrospective comparative au service de médecine infantile B de l'hôpital d'Enfants Béchir Hamza de Tunis sur une période allant de janvier 2011 à mars 2014. Nous avons comparé deux groupes d'incompatibilité ABO, les groupes OA et OB. Pour l'analyse statistique, le seuil de signification a été fixé à 0,05.

Résultats : Nous avons colligé 98 cas d'ictère hémolytique par incompatibilité ABO. Les deux groupes étaient comparables. Nous n'avons pas trouvé de différence statistiquement significative entre les 2 groupes pour l'intensité de l'ictère et le recours à l'exsanguino-transfusion. Toutefois, les transfusions étaient statistiquement plus fréquentes dans le groupe OB comparé au groupe OA (81,6‰ vs 10,2‰, p = 0,039, OR=2,9, IC95% (1,1 – 7,8)).

Conclusions : L'incompatibilité OB semble être un facteur de risque pour l'intensité de l'hémolyse comparé au groupe OA. Alors que le type de groupe sanguin du nouveau-né n'interviendrait pas dans l'intensité de l'ictère.

Mots-clés

Ictère néonatal, hémolyse néonatale, incompatibilité ABO

SUMMARY

Background: Due to the marked decline of maternal-fetal rhesus incompatibility, ABO alloimmunization has become the leading cause of the newborn hemolytic disease. It is estimated that 15–25 % of all pregnancies are concerned by ABO incompatibility.

Aim: Neonatal blood group B seems to be more predisposing to acute hemolysis and severe hyperbilirubinemia. We propose to find if the newborn's blood group B represents a risk factor for severe hemolysis and/or severe hyperbilirubinemia.

Methods: We conducted a comparative study in the pediatrics department "B" of the Children Hospital of Tunis. We collected retrospectively the medical files of the newborn hospitalized for ABO alloimmunization (January 2011 – March 2014), then we compared two groups, OA group with OA alloimmunization and OB group with OB alloimmunization. A significant threshold was fixed to 0.05.

Results: We collected 98 cases of newborn ABO hemolytic disease. Both groups, OA and OB, were similar for the onset of jaundice, age of hospitalization, initial hemoglobin and indirect bilirubin levels. There were no statistically significant difference in the severity of hyperbilirubinemia and the use of exchange transfusion for the two groups. However, transfusion was statistically more frequent in the OB group compared to OA group (81.6‰ vs 10.2‰, p = 0,039, OR=2.9, 95% IC (1.1 – 7.8)).

Conclusion: OB alloimmunization seems to induce more active hemolysis than OA one, with no difference for severe hyperbilirubinemia in both groups.

Key-words

Hemolytic disease of newborn, Neonatal hyperbilirubinemia, ABO incompatibility

INTRODUCTION

Hemolytic disease of newborn represents nearly 20% of neonatal jaundice, and it is caused by ABO and rhesus system incompatibility in 30% of cases. With the widespread prevention of rhesus alloimmunization, newborn ABO hemolytic disease has become more common, and occurs almost exclusively among A or B blood group infant born to O blood group mothers. Generally, 15 to 25% of all maternal/newborn pairs are ABO incompatible (2). The Nigerian cohort showed that 14.3% of all deliveries will result in a blood group O woman giving birth to a child who is blood group A or B, 30.3% and 18.6% of them will lead to respectively a newborn hemolytic disease and a moderately severe to severe hemolysis (3).

Several studies have focused on the ABO maternal-fetal incompatibility, and searched if the newborn blood group A or B was a serious risk factor for hemolysis and / or severe hyperbilirubinemia. It has often seemed that a neonatal blood group B was more predisposing to acute hemolysis and severe hyperbilirubinemia. We propose to test this hypothesis by comparing the morbidity associated with maternal-fetal incompatibility in the ABO system among maternal blood group O with A or B blood group new borns.

METHODS

This comparative study was conducted in the Pediatric Department "B" of Children's Hospital "Bechir Hamza" of Tunis, covering a three years period, from 1st January 2011 to 31 March 2014.

We studied retrospectively all the medical files of newborns hospitalized for neonatal jaundice. We included A or B blood group newborns whose mothers blood group is O, and without rhesus system incompatibility.

We excluded newborns with congenital malformation or another related etiology that could explain neonatal jaundice (lump or caput cephalohematoma, maternal-fetal infection, inborn error of metabolism, hypothyroidism, G6PD deficiency and hereditary spherocytosis).

we compared two groups: OA group including A blood group infant born to O blood group mother and OB group including B blood group infant born to O blood group mother; and an OB group involving a newborn of blood group B and a mother of blood group O.

For each file, we collected for the mother: delivery mode, blood group and rhesus; and for the newborn: gestational age, birth weight, gender, date of establishment of jaundice, physical examination data, blood group and rhesus, direct antiglobulin test (DAT), bilirubin rate and its evolution, hemoglobin level and its evolution as well as the received treatment.

Phototherapy and exchange transfusion thresholds were determined based on bilirubin level reported to the curves of the "American Academy of Pediatrics hyperbilirubinemia treatment guidelines 2004" (4).

The hemolysis was defined by a level of hemoglobin lower than 14g/dl during the first week of life and / or hemoglobin decrease higher than or equal to two points on two blood counts made 24 hours apart.

Statistical analysis of data was carried out by SPSS v.11 software. We used the Pearson chi-square test and Fischer test for the study of qualitative variables and t-student test for the study of quantitative ones. The significance level was set at 0.05. For multivariate analysis, the qualitative variables were compared with percentage comparison tests (chi-square test or Fisher exact test) and quantitative variables with mean comparison tests (Student test or rank test in case of parametric distribution). The alpha risk of first species was set at 0.05.

RESULTS

The study consisted of 98 newborns. Forty infants (40.8%) were male and 58 (59.2%) female, with a sex ratio of 0.7. Prematurity was found in 9.3% of cases and low birth weight in 8.1% of cases. Forty-seven newborns had blood group A, while 51 had blood group B. The average age of detection of jaundice was 39.5 ± 25.7 hours (1-130 hours). The mean age on the hospitalization was 69.4 ± 68 hours (1-400 hours). The average length of hospital stay was 5.48 ± 2.2 days (2-12 days). Both groups were comparable regarding sex ratio, the rate of prematurity, birth weight, age average of jaundice detection, age of hospitalization and hospitalization length (Table 1).

Clinically, jaundice had similar intensity in both groups. It was evaluated in zone IV in 13.2% for OB group and in 8.1% for OA group, without a statistically significant difference (Table 2 and Figure 1).

The study of hemolysis in OA and OB groups, comparing hemoglobin and bilirubin levels and DAT positivity, is shown in Table 3. We noted a significant drop in hemoglobin level in OB group compared to OA group (Figure 2).

Exchange transfusion was performed in 13.3% of cases. It was necessary in 5.1% of OA group cases and in 8.2% of OB group cases, without a statistically significant difference. While transfusion was more frequent in the OB

group compared to the OA group with p = 0.039, OR = 2.9 and 95%IC (1.1-7.8) (Table 4).

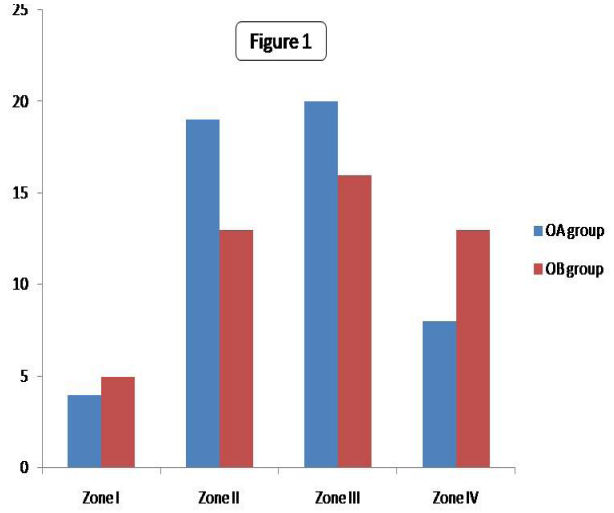

Figure 1: Distribution of OA and OB incompatibility groups according to the intensity of jaundice.

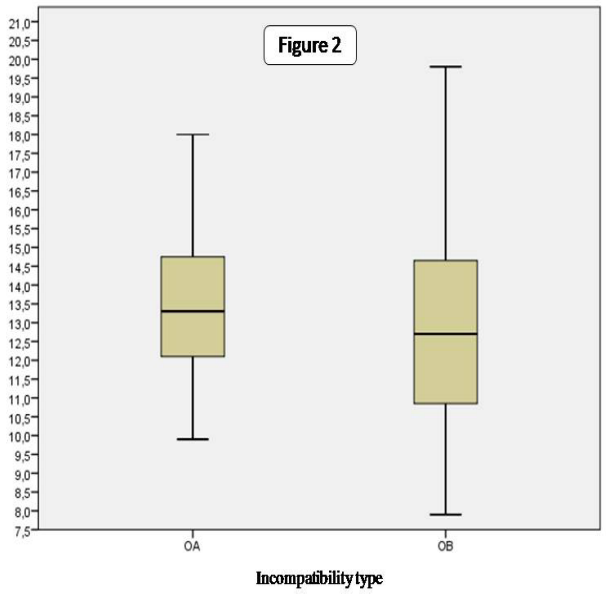

Figure 2: Study of the variation in hemoglobin depending on the incompatibility type OA and OB.

Table 1: Demographic profile of the population studied

		Total	OA Group	OB Group	p	OR	IC 95%
Number		98	51	47			
Sex	Male	40	22 (55%)	18 (45%)	0,6	1,2	0,5 – 2,7
Prematurity		9	4	5	0,1	0,8	0,6 – 1,0
Low birth weight (< 2500g)		8	5	3	0,3	1,4	0,6 – 3,0
Age of finding jaundice (hours)		39,5 (1-130)	43,4 +/- 28,1	35,1 +/- 22,3	0,1	0,9	0,9 – 1,0
Age of hospitalization (hours)		69,4 (1- 400)	65,8 (1- 280)	73,4 (5- 400)	0,5	1,0	0,9 – 1,0
Lenght of Hospital Stay (days)		5,48 (2-12)	5,27 (2-11)	5,27 (2-12)	0,3	1,0	0,9 – 1,3

Table 2: Intensity of jaundice according to the incompatibility type OA and OB

		OA group	OB group	Total	P	OR	$IC_{95\%}$
Jaundice Zone	Zone I	4 (4,1%)	5 (5,1%)	9 (9,2%)	0.448	1,2	0,7 – 1,1
	Zone II	19 (19,4%)	13 (13,2%)	32 (32,6%)	0.213		
	Zone III	20 (20,4%)	16 (16,3%)	36 (36,7%)	0.375		
	Zone IV	8 (8,1%)	13 (13,2%)	21 (21,3%)	0.116		
Total		51 (52%)	47 (48%)	98 (100%)			

Table 3: Study of hemolysis according to the incompatibility type OA and OB

		OA group	OB group	p	OR	$IC_{95\%}$
Initial hemoglobin (g/dl)		13,8 (+/- 2,1)	13,7 (+/- 2,5)	0,9	0,8	0,7 – 1,0
Lowest rate hemoglobin (g/dl)		13,5 (+/-2,0)	12,8 (+/- 2,6)	0,1		
Total bilirubin (µmol/l)		242,1 (+/-105,9)	271,0 (+/- 113,9)	0,1		
Anemia	No	28 (68,3%)	13 (31,7%)	0,006	3,1	1,3 – 7,4
	Yes	23 (40,4%)	34 (59,6%)			
Hemolysis	No	22 (66,7%)	11 (33,3%)	0,039	2,4	1,0 – 5,9
	Yes	29 (44,6%)	36 (55,4%)			
Direct antiglobulin test	Negative	37 (48,1%)	40 (51,9%)	0,1	0,4	0,1 – 1,2
	positive	14 (66,7%)	7 (33,3%)			

Table 4: Different therapeutic used in OA and OB incompatibility

	OA group	OB group	p	OR	$IC_{95\%}$
Conventional phototherapy alone	44 (57,9%)	32 (42,1%)	0,03	2,9	1,0 – 8,0
phenobarbital	4 (66,7%)	2 (33,3%)	0,6**	1,9	0,3 – 10,9
Albumin	3 (60%)	2 (40%)	1**	1,4	0,2 – 8,8
Blood transfusion	1 (11,1%)	8 (88,9%)	0,02***	0,09	0,01 – 0,8
Exchange transfusion	5 (38,5%)	8 (61,5%)	0,2	0,5	0,1 – 1,7

** Fisher test, *** Yates correction

Table 5: Factors associated with the type of jaundice: Multivariate Analysis

	OR_b ($IC_{95\%}$)	p	OR_a ($IC_{95\%}$)	p
Term	0,8 (0,5 – 1,1)	0,2		
Average age of finding jaundice	0,97 (0,95 – 0,99)	0,02	0,9 (0,95 – 0,99)	0,018
Anemia	1,4 (0,4 – 5,4)	0,5		
Hemolysis	3,1 (0,7 – 13,2)	0,1	2,9 (1,1 – 7,8)	0,031
Conventional phototherapy alone	7,8 (1,7 – 35,1)	0,007	11,1 (2,7 – 44,6)	0,001
Blood Transfusion	0,1 (0,016 – 1,6)	0,1		

OR_b : Odds Ratio brut ; $_{ORa}$: Odds Ratio ajusté

DISCUSSION

Newborn ABO hemolytic disease with OB incompatibility was significantly associated with a higher rate of hemolysis with no difference in the rate of severe hyperbilirubinemia compared to OA incompatibility.

In fact, in our cohort we didn't found a statistically difference in the intensity of jaundice and bilirubin levels between OB and OA groups. The treatment of jaundice with phototherapy and the use of exchange transfusions for severe jaundice with a high risk of kernicterus were reported in similar proportions in both groups without statistically significant difference.The South African study of Farrell (5) carried out in 1970 concluded that OB incompatibility lead more frequently to exchange transfusion, but the small size of this study (51 cases) and the lack of standardized criteria to indicate exchange transfusion, challenge these findings (5).The study of Quinn and al., made in 1988, hypothesized greater severity of hyperbilirubinemia in OB incompatibility but without statistical validation of the results (6). Contrariwise, the Serbian cohort of Bujandric and Grujic (7), showed a greater risk of servere neonatal hyperbilirubinea and exchange transfusion in blood group A infant of blood group O mother (68.7%) versus blood group B infants of blood group O mother (31.3%). However, two Turkish studies of large cohorts, of Bhat and al. (151 infants) and of Akgül and al. (166 infants), comparing two groups (OA and OB group) with similar general characteristics, found no statistically significant difference between the two groups for the intensity of jaundice and the use of exchange transfusion (8, 9), which joined our results.

The study of hemolysis and its severity caused by ABO incompatibility in our study showed a higher risk of hemolysis in OB incompatibility. We found no difference to the initial hemoglobin and the positivity rate of the DAT. However, we found a significant decrease in hemoglobin during evolution in group B, in fact, OA group had less hemolysis with p = 0.031, OR 2.9, 95% CI (1.1 to 7.8) and less anemia with p = 0.006, OR = 3.1 95% CI (1.3 -7.4). Concerning the use of blood red cells, it was statistically more frequent in the OB group in the univariate analysis (p = 0.02) but not significant in multivariate logistic regression analysis (p = 0.1). Both Turkish Studies Bhat and al. (8) And Akgül et al. (9) showed no statistically significant difference between the two groups for the intensity of hemolysis. However, in Ozgonenel study (10), OB incompatibility was significantly associated with a higher rate of hemolytic anemia (32.6% in OB incompatibility versus 14.0% in OA incompatibilty, p=0.001), but not with a higher rate of severe hyperbilirubinemia (p=0.981). These results are correlated with ours.

The Adewuyi and al. study (11) compared the hemolytic activity of anti-A and anti-B antibodies in two different racial groups living in the same conditions (black and white Zimbabwe). This study showed a greater anti-A and anti-B hemolytic activity in the black race, and for the two races, a higher hemolytic activity for anti-B antibodies. This may explain our findings about more significant hemolysis in OB group. This study also suggests that the hemolytic activity can differ from one racial group to another, which may explain the difference in results between our tunisian study and the turkish studies. Other studies in different ethnic groups would be useful to analyze and confirm this hypothesis.

Conclusions

In newborn ABO hemolytic disease, we showed that newborn blood group A or B has no major effects on the intensity of neonatal jaundice; however, the risk of hemolysis is greater in case of OB incompatibility. Further studies are needed to allow a better understanding of immunological mechanisms. More rigorous monitoring has to be implemented for newborn with blood group B born of blood group O mother.

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