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ORIGINAL ARTICLE – OPEN ACCESS

Effect of ABO Blood Groups on Patent Ductus Arteriosus Closure

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ABSTRACT

Objective: Although some ABO blood groups are known to be associated with risk in adult diseases, the data related to neonatal diseases remain insufficient. The aim of this study was to identify blood groups that may confer a risk of patent ductus arteriosus (PDA) in very low birth weight (VLBW; <1500 g) preterm infants.

Materials and Methods: The records of preterm infants admitted to our unit who weighed <1500 g at birth were reviewed retrospectively. The prevalence of PDA and the demographic and clinical characteristics were compared according to blood group.

Results: The study included a total of 497 infants: 155 (31.2%) in blood group O, 227 (45.7%) in blood group A, 83 (16.7%) in blood group B, and 32 (6.4%) in blood group AB. There were no significant differences in PDA, demographic characteristics, or clinical parameters according to blood group (p>0.05).

Conclusion: The results of this study did not suggest a relationship between PDA and blood group in VLBW infants. These findings represent a valuable first contribution to the literature on the role of blood group in premature infants.

Keywords: Blood group, morbidity, mortality, patent ductus arteriosus, premature

INTRODUCTION

Patent ductus arteriosus (PDA) can cause pulmonary hemorrhage, respiratory distress syndrome (RDS), long-term mechanical ventilation (MV), and serious morbidity and mortality in preterm infants. It occurs in approximately one-third of very low birth weight (VLBW; <1500 g) infants. The ductus is typically functionally closed within 1-2 days of birth and anatomically in the first 7 days. However, increased prostaglandin E2 and prostacyclin levels, and low oxygen saturation have vasodilatory effects on the ductus arteriosus and can reduce or delay physiological closure (1). Biochemical and hematological parameters may also affect ductal closure (1–3). Other risk factors for unresolved PDA include antenatal drugs, administration of large volumes of fluid in the first week, phototherapy, infections, and genetic predisposition (2). The increased frequency and survival of VLBW infants in recent years has resulted in a corresponding increase in morbidities of prematurity. Since PDA is the most common cardiovascular condition in preterm infants, it is important to determine the potential risk factors (4).

Landsteiner identified the ABO blood group system in 1901, and thereafter, the clinical significance of the blood groups began to extend beyond transfusion medicine and hematopoietic/organ transplantation. Studies of adults have revealed relationships between the ABO blood groups and gastric cancer, as well as periodontal, cardiologic, and metabolic diseases (5–9).

There are few studies in the field of neonatal science that have evaluated the correlation between ABO blood groups and morbidities of prematurity (10–13). PDA, in particular, is associated with metabolic and structural risk factors as well as genetic predisposition, and the absence of a clearly defined relationship between PDA and ABO blood groups suggested a need for further research on the subject. Therefore, this study was designed to investigate a potential relationship between ABO blood groups and PDA.

MATERIALS and METHODS

The Zekai Tahir Burak Women's Health Training and Research Hospital granted approval for this study on March 27, 2018 (no: 54/2018). The principles of the Declaration of Helsinki were observed throughout the research.

Study Design

This retrospective study examined the records of a single hospital from between January 2017 and March 2018. The data of preterm infants weighing <1500 g at birth were included in the study; infants born with major congenital anomalies and those weighing ≥1500 g were excluded. The blood group and demographic and clinical characteristics of the preterm infants included in the study were retrieved from the records and analyzed.

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Table 1. Demographic characteristics of all blood groups

Demographic characteristics	ABO blood groups (n=497)				ANOVA p	Chi-squared p
	O (n=155, 31.2%)	A (n=227, 45.7%)	B (n=83, 16.7%)	AB (n=32, 6.4%)		
Gestational age, weeks[a]	27.7±1.2	28.1±1.2	27.7±1.1	27.7±1.1	0.411	–
Birth weight, g[a]	1025±223	1087±223	1038±230	1045±205	0.058	–
Male sex, n (%)	89 (57.4)	116 (51.1)	43 (51.8)	17 (53.1)	–	0.453
1-min Apgar score[b]	5 (1–7)	5 (1–7)	5 (1–7)	5 (1–7)	0.059	–
5-min Apgar score[b]	7 (2–9)	8 (3–9)	7 (3–9)	8 (3–9)	0.051	–
Antenatal steroid, n (%)	110 (70.9)	146 (64.3)	56 (64.7)	22 (68.7)	–	0.549
SGA, n (%)	13 (8.3)	18 (7.9)	7 (8.4)	2 (6.2)	–	0.981

a: Mean±SD; b: Median (minimum–maximum). ANOVA: Analysis of variance; SGA: Small for gestational age

Table 2. Clinical features of all blood groups

Clinical features	ABO blood groups (n=497)				ANOVA p	Chi-squared p
	O (n=155, 31.2%)	A (n=227, 45.7%)	B (n=83, 16.7%)	AB (n=32, 6.4%)		
ENS, n (%)	5 (3.2)	5 (2.2)	2 (2.4)	1 (3.1)	–	0.194
LNS, n (%)	35 (22.5)	52 (22.9)	20 (24.1)	7 (21.8)	–	0.982
RDS, n (%)	104 (67.1)	139 (61.2)	62 (74.6)	18 (56.2)	–	0.11
NRS duration, days[a]	7.6±5.3	8.1±6.1	10.3±8.0	7.0±4.9	0.054	–
MV duration, days[a]	4.4±3.2	3.7±2.5	5.1±3.2	3.4±1.9	0.056	–
PDA, n (%)	57 (36.7)	112 (49.3)	38 (45.7)	15 (46.8)	–	0.827
Time to full enteral feeding, days[a]	16.3±6.5	16.3±6.9	17.2±8.2	15.5±4.5	0.465	–
NICU length of stay, days[a]	54.5±32.1	56.2±1.0	56.9±34.2	47.3±29.1	0.066	–
Mortality, n (%)	43 (27.7)	38 (16.7)	15 (18)	8 (25)	–	0.073

a: Mean±SD; b: Median (minimum–maximum). ANOVA: Analysis of variance; ENS: Early-onset neonatal sepsis; LNS: Late-onset neonatal sepsis; MV: Mechanical ventilation; NICU: Neonatal intensive care unit; NRS: Noninvasive respiratory support; PDA: Patent ductus arteriosus

Demographic and Clinical Characteristics

Demographic and clinical characteristics such as gestational age (GA), birth weight (BW), sex, 1- and 5-minute Apgar scores, antenatal steroid use, small for gestational age (<10th percentile) (14), early-onset neonatal sepsis (sepsis at postnatal ≤3 days), late-onset neonatal sepsis (sepsis at postnatal >3 days) (15), RDS (defined by need for surfactant) (16), duration of non-invasive respiratory support and mechanical ventilator support, presence of hemodynamically significant PDA demonstrated by clinical signs or echocardiography and requiring medical treatment (2), time to full enteral feeding, length of neonatal intensive care unit stay, and mortality were recorded. These characteristics were compared according to blood groups O, A, B, and AB.

Statistical Analysis

Statistical tests were performed using SPSS for Windows, Version 16.0 software (SPSS Inc., Chicago, IL, USA). The distribution of measured values was evaluated for normality using both graphical methods and the Shapiro-Wilk test. The results were presented as mean and SD or the median with minimum and maximum values. Analysis of variance (ANOVA) testing was used for normally distributed variables. The Levene test was applied to test the equality of variances assumption. The Levene test results confirmed equal variance (p value >0.05). Since the ANOVA assumptions were upheld, the group means were analyzed to determine statistical difference. The H0 hypothesis, which was an equal mean among the different blood groups, was not rejected because the p value of the F test was >0.05 (significance level). Since we did not reject the null hypothesis, we did not apply post hoc tests to compare group means. To compare groups, we used a chi-squared test for categorical variables. Kruskal-Wallis analysis was not used because normal distribution was present. Results with a p value <0.05 were accepted as statistically significant.

RESULTS

In accordance with the criteria, 8 premature infants with major congenital anomalies and weighing <1500 g at birth were excluded from the study. A total of 497 preterm infants (GA: 28±1.2 weeks, BW: 1057±224 g) were included. Of these, 155 infants (31.2%) were in blood group O, 227 (45.7%) were in blood group A, 83 (16.7%) were in blood group B, and 32 (6.4%) were in blood group AB. ANOVA used to compare the different blood groups revealed no statistically significant differences in demographic or clinical characteristics among the 4 different blood groups (p>0.05). In addition, there was no significant difference when the categorical variables were compared with a chi-squared test. All of the results are shown in Tables 1 and 2.

DISCUSSION

It has been established that some ABO blood groups pose a risk for certain diseases in adults; however, the information on the possible effect of blood groups on neonatal disease remains insufficient. In this study, we determined that VLBW preterm infants in the 4 ABO blood groups had similar demographic and clinical characteristics, including the prevalence of hemodynamically significant PDA. To our knowledge, this is the first study to evaluate the relationship between PDA and blood groups in premature infants.

ABO blood groups are determined by A and B antigens on the surface of red blood cells. In addition to red blood cells, these antigens are commonly expressed on the membranes of a wide variation of cells, including platelets, those of the vascular endothelium, and the epithelium, and may be secreted into the saliva and other body fluids. ABO blood group antigens are composed of terminal carbohydrate molecules synthesized through the activity of ABO glycosyltransferases. The ABO gene locus and glycosyltransferase function have been linked to cardiovascular disease. It has been reported that ABO glycosyltransferase activity has a role in modulating endothelial, platelet, and cardiometabolic pathways. However, it is not yet clear whether the effects are causal (5).

PDA, which is the most common cardiovascular disease in VLBW preterm infants, occurs mainly due to risk factors such as GA, BW, infections, RDS, and genetics. In addition, oxygen, nitric oxide, and hematological and metabolic causes may also affect closure of the ductal opening (1–4). Considering the relationship between blood groups and adult cardiovascular disease, there may be a possible relationship between PDA and blood groups. Studies evaluating the relationship between diseases of prematurity and blood groups are limited (12, 13, 17). Investigation of this issue may provide important information to help understand the underlying causes of PDA.

McMahon et al. (10) examined 3981 infants born at 220/7 to 426/7 weeks and found that the AB blood group had an increased risk of RDS compared to the other blood groups, but there was no difference between the blood groups in terms of PDA. The low GA in the AB blood group may explain the higher frequency of RDS (10, 16). In contrast, the incidence of PDA in blood group AB infants with a lower GA was found to be similar to that of the other blood groups. This may be because PDA is associated not only with GA but also postnatal risk factors (4). In addition, considering that the study included infants at all GAs and that PDA affects mainly VLBW infants, we believe conducting a subgroup analysis would be appropriate when evaluating the results. In a study that examined 1785 preterm infants with a BW of <1500 g, it was found that the frequency of PDA was significantly higher in blood group A when compared with the other blood groups. The GA and BW of the preterm patients were similar (11). In our study, the prevalence of PDA was highest in blood group A. However, the difference did not reach a level of statistical significance; therefore, our results indicated that none of the blood groups presented a risk in terms of PDA. This result may be due to the small sample size.

Another factor in PDA closure is the effect of calcium (2). Considering the effect of ABO antigens on cardiovascular disease and vascular tone (via calcium and nitric oxide), they are likely to have an effect on PDA (5, 18, 19). However, our results did not reveal a relationship between blood group and PDA.

Our study has some limitations due to its single-center, retrospective design. Other risk factors that may affect PDA closure could not be evaluated. Moreover, we were not able to evaluate the relationship between ABO blood groups and genome, alleles, secretor status, and biochemical parameters, in terms of genetics.

In this study, the prevalence of PDA was similar between the ABO blood groups. As not all of the biological functions of the A and B antigens are clearly understood, recognition of their role in the morbidity of preterm infants may help physicians predict possible adverse clinical outcomes. Therefore, further research is needed to elucidate the relationship between blood groups and preterm neonatal morbidities, including PDA.

Ethics Committee Approval: The Zekai Tahir Burak Women's Health Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 27.03.2018, number: 54/2018).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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