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Predictive Role of Blood Group, Rh Factor and Gestational Age in Transfusion Reaction in Neonates

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Background. Transfusion therapy represents a rational model of therapy which is frequently used in neonatal period. Aim. to investigate predictive role of blood group, Rh factor and gestational age in transfusions reaction in neonates.

Patients and methods. We evaluated 95 neonates gestational age between 28 and 42 weeks treated with blood components. All neonates were treated in the Unit of Neonatology at Department of Gynecology and Obstetrics at University Clinical Center Tuzla in the period of 01.01.2006.-31.12.2008.

Results. During the period of investigation there were 12 526 born neonates gestational age from 28 to 42 weeks. Incidence of transfusion reaction was 0, 37%. The median of gestational age in the complete sample was 38 weeks, with interquartile range from 35 to 39 weeks, with 28 weeks minimum and 40 weeks maximum. The incidence of transfusion reaction in relation with the blood group was most evident in recipients in blood group type A, but there were no statistically significant differences in incidence of transfusion reactions between four blood groups ($X2=6.352$; $df=3$; $p=0.097$). There was no statistically significant difference in incidence of transfusion reaction according to the Rh factor ($X2=0.755$; $df=1$; $p=0.385$). Investigation of transfusion reaction according to the blood group and Rh factor showed no statistically significant difference ($X2=8.063$; $df=7$; $p=0.327$). The logistic regressional analyses showed that the gestational age is significant predictor of appearance of transfusion reaction (OR=0.867; %95 CI=0.756 do 0.993; p=0.04).

Conclusion. Transfusion reactions in neonates are not rare. The blood group and Rh factor are not valid in prediction of transfusion reaction while the gestational age is good predictor in appearance of transfusion reaction.

Keywords. *transfusion reactions, neonates, gestational age*

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Competing interests
The authors declare no competing interests.

INTRODUCTION

A neonate is an infant in first four weeks of life whose immediate and long term diagnosis depend on three basic features: gestational age, birth weight and functional maturity; Gestational age means duration of intrauterine life during which fetus grows and getting functional maturity; it is a term which expressed days or weeks of pregnancy[1]. Essential improvement of perinatology importantly changed the structure of morbidity and mortality of neonates in the last decades. Significant efforts have been made and today from modern perinatology is expected to provide a quality of life for infants with low gestational age. The new diagnostic and therapeutic possibilities have imposed often use of blood and blood derivates among neonates in different gestational age.

Karl Landsteiner in 1901. described ABO blood group and this discovery was awarded with the Nobel Prize. Specifically, he examined the interaction of erythrocytes and serum of different individuals and the resulting reaction explains with existence of three blood groups, which marked with symbols A, B, O. After above mentioned this study Landsteiner's associates Decastello and Sturli announced the discovery of fourth blood group AB[2]. Later, it was discovered several hundred of blood group systems[3].

Transfusion therapy still represents a realistic and rational therapeutic modality that is increasingly applied in the neonatal period. Transfusion of blood component can save a life, but like any other medical intervention is not without risk because it is invasive method of treatment and unexpected consequences are possible. When is the time to make decision on transfusion treatment, regardless of whether is a neonate, an older child or the adult, it is important to think of all possible harmful effects of such treatment for patients that may endanger expected results and useful effect of transfusion[4].

Over the past decade the quality and safety in all aspects of transfusion was significantly improved by systematic control of

Table 1. The incidence of blood groups with Rh factor in neonate

	Blood group and Rh factor								
	A-	A+	B-	B+	AB-	AB+	0-	0+	Total
Number	8	39	2	16	3	2	3	22	95
Percentage	8,4	41,1	2,1	16,8	3,2	2,1	3,2	23,2	100,0

Table 2. The incidence of transfusion reactions in neonates in relation to blood group

			Blood group			
			A	B	AB	0
Reaction	No	N	18	9	4	16
		%	38,3%	50,0%	80,0%	64,0%
	Yes	N	29	9	1	9
		%	61,7%	50,0%	20,0%	36,0%

X^2=6,352; df=3; p=0,097

Table 3. The incidence of transfusion reactions in neonates in relation to Rh factor

			Rh factor	
			Negative	Positive
Reaction	No	N	10	37
		%	62,5%	46,8%
	Yes	N	6	42
		%	37,5%	53,2%

X^2=0,755; df=1; p=0,385

Table 4. The incidence of transfusion reactions in neonates in relation to blood group an Rh factor

			Blood group and Rh factor							
			0-	0+	A-	A+	AB-	AB+	B-	B+
Reaction	No	N	2	14	4	14	3	1	1	8
		%	66,7%	63,6%	50,0%	35,9%	100,0%	50,0%	50,0%	50,0%
	Yes	N	1	8	4	25	0	1	1	8
		%	33,3%	36,4%	50,0%	64,1%	,0%	50,0%	50,0%	50,0%

X^2=8,063; df=7; p=0,327

transfusion treatment, but the reactions still occur. It is estimated that in the United States during 2000 occurred 0.0003 transfusion reactions in 1000 hospital discharge of patients aged 0-17 years[5]. According to the annual report SHOT (Serious Hazards of Transfusion) in Great Britain there was an increase in adverse events related to transfusion of blood and blood products, in relation to previous year in 32%, and two patients died as a direct results of errors during blood transfusion6.

Considering the occurrence time the transfusion reactions are divided into early (acute), which occurred

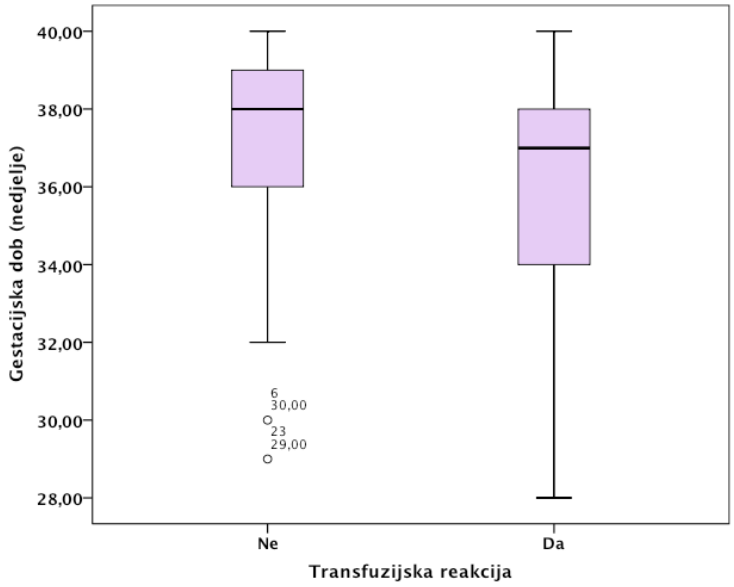

Figure 1. The frequency of transfusion reaction between experimental and control group in neonate in relation to gestation age

during first 24 hours after transfusion and late, which can occur even several months after transfusion. With regard to the etiology of transfusion reaction may be immunological and non/immunological[7]. Immunological reactions can occur in all transfusion recipients, regardless of age. Unlike older children and adults, immunological reactions are very rare among neonates.

Namely, among neonates due to immaturity of their immune system rarely are produced aloantibodies on blood cells. Therefore, immunologic transfusion reactions are often result of passive transfer of antibodies infused containing plasma, rather than antibodies produced by the child[8]. Hemolytic transfusion reaction is caused by intravascular (IgM antibody) or extravascular immune destruction of red blood cells (IgM antibody) and can be acute or delayed reactions.

Non-immunological transfusion reactions are caused either by metabolic changes or transmission of infectious diseases. Neonates, especially premature infants, are at risk group for occurrence of a group of metabolic complications such us hyperkalemia, hypocalcaemia, hyperglycemia, hypothermia, non-immune haemolysis and abnormality of acid base status[9]. The exact incidence and symptoms of transfusion reactions in neonates is not known, because there are few factors causing occurrence, starting with blood components, speed of transfusion and clinical condition of the newborn.

It is unusual to find classical signs of transfusion reactions in neonates. Besides general bad health condition during and after blood transfusion, other clinical symptoms are difficult to notice. Clinical manifestation, especially in premature neonates, are often hidden and very different from anxiety, apnea, cyanosis, heart rhythm disturbance, hypotonic, gastrointestinal symptoms, lethargy, to convulsion.

The aim of study was to examine the prediction of blood group, Rh factor and gestational age in the occurrence of transfusion reactions in neonates and to determine the frequency of transfusion reactions in neonate by blood group, Rh factor and gestational age.

MATERIAL AND METHODS

The study included 95 neonates of both sex, different blood group and Rh factors, gestational age from 28 to 42 weeks, and those who had received blood products, one or more times. All neonates were treated at the Unit of neonatology, Department of Gynecology and Obstetrics, University Clinical Center Tuzla, in period from 01.01.2006. to 31.12.2008. The study protocol included 95 neonates, of which 48(50, 5%) with transfusion reactions (study group) and 47 newborns (49,5%) without the same transfusion reaction (control group).

The diagnosis of transfusion reactions is determined in accordance with the guideline of the (European Haemovigillance Network)[2,10] and included the presence of some of the following disorders: respiratory disorder, cardiovascular disorder, gastrointestinal disorders, metabolic disorder, neurological disorders, disorder in regulation of body temperature and skin changes.

STATISTICAL ANALYSIS

Statistic analysis was performed by SPSS 18.0 (Chicago IL, USA). Basic tests of descriptive statistics were made with review of measures of central tendency and dispersion. It was tested each variable for qualification of normal distribution, using Kolmogorov-Smirnoff test and histogram display. Quantitative variables were compared by t-test with correction for unequal variance, or related t-test in cases of related samples.

For variables that were not normally distributed, it was performed non parametric Mann-Whitney analysis. Categorical variables were analyzed by X2 test and Fisher exact test. Non parametric correlation according to Spearman was used in testing the presence of significant relations among varaibles. Invariant binomial logistic regression was used to test the level of influence of individual variables on the presence of transfusion reactions. All statistical tests were carried out with statistic probability of 95 %. ($p<0,05$).

RESULTS

In the studied period 12 526 newborns were born in gestational age from 28 to 42 weeks. The frequency of transfusion reactions was 0.37%. Of 95 newborns, 65 of them were male (68, 4%) while remaining 30 (31,6%) were female, with the ratio of male and female from 2,16 : 1

Median gestational age in the total sample is 38 weeks, with inter-quartile range 35-39 weeks, with a minimum of 28 weeks and maximum of 40 weeks of gestation. In total 43 neonates (45,3%) had a birth weight below 2500 grams, while 52 of them (54,7%) was above this weight limit. Median length of newborns was 52 cm with inter-quartile range of 47-55 cm and a minimum of 34,5 cm and maximum of 58 cm.

Median Apgar score in the full sample, and according to the values in the first minuets of delivery was 8, with inter-quartile range from 5- 9, or with a minimum of 1 and maximum of 9. Median of Apgar score in fifth minute was equal to those in first minute and total 8 with inter-quartile range from 7 to 9, and with proper range (minimum–maximum) from 2 to 9. The frequency of certain blood groups, along with Rhesus factor is shown in Table 1.

When it comes to type of trans-funded preparation, 93 patients (97, 9%) had transfusion of plasma, while 1 examinee (1,1%) had a plasma transfusion combined with erythrocytes and plasma with full blood. Anamnesis of previously mentioned transfusions had 46 (48, 4 %) of examiners, while 49 (51, 6%) did not have the same anamnesis. There was no statistically significant difference in the number of newborns in comparison to previously transfusion (p= 0.664%). The study compared the frequency of transfusion reactions by blood group and Rh factor. Frequency of transfusion reactions according to blood group is shown in Table 2.

Although, there was tendency for more often reactions in patients receiving transfusion with blood group A, but still there was no significant differences in frequency of transfusion reaction between 4 main blood group (X2=6,352; df=3; p=0,097).

Analogous to this analyze, we compared the frequency of transfusion reactions according to Rh factor. Table review of frequency is given in Table 3.

There were no statistically significant differences in frequency of transfusion reactions in relation to Rh positivity (X2=0,755; df=1; p=0,385). The examined frequency of transfusion reaction combined regarding to the blood group and Rh factor is shown in Table 4. and there is no significant difference in frequencies of transfusion reactions (X2=8,063; df=7; p=0,327).

Gestation age was compared between examiners with and without reaction by using non-parametric Mann-Whitney test. In group of examiners with reactions, median of gestation age was 37 week of gestation (interquartile range : from 34 to 38), while in the group of those without reaction median was 38 weeks (interquartile range from 36 to 39 weeks). This difference was statistically significant (Z='2,054; p=0, 04) and graphically presented in Figure 1.

In order to additional explore relation between gestation age and presence of transfusion reactions, it was performed non-parametrical Spaearman's correlation which proved presence of weak and negative (ρ=-0,21), but still statistical significant correlation (p=0,039). Additionally, in order to quantify the influence of gestation age on presence of reactions, logistic regression analyze was performed which proved that gestation age is significant predictor of transfusion reactions (OR=0,867; %95 CI=0,756 do 0,993; p=0,04). This effectively means that with each additional week of gestation age, the risk of transfusion reaction is reduced by 1/0,867 or 1,153 times.

DISCUSSION

During three-year period we examined the prevalence of transfusion reactions in neonates according to blood group, Rh factor and gestational age. Our research shows that transfusion reaction is not as rare as once thought. Frequency of transfusion reaction in our study is 0,37 % and it is similar to recent reports from the USA, where reported frequency of transfusion reaction was from 0,4 %[4,11]. In period from 1996. to 2005. were analyzed 3239 reported unexpected transfusion reaction in Great Britain, and 10% were related to children under 18 years and 4,5 % on children under 12 months[12].

The National program for collecting and analyses of unexpected transfusion reactions in New Zealand made conclusion that in 2007. had increased the number of transfusion reactions for 8% in relation to 2006. what is explained by improvement of reporting system. The most often unwanted transfusion reaction was febrile non-hemolytic transfusion reaction (FNHTR), than allergic reaction in 34% of patients (in total there were 133 allergic and 22 anaphylactic / anaphylactic reactions[13]. During the past decade, several studies have shown that there is inequality in the world in applying the indication of blood and blood preparations in neonatal intensive care units. In those studies were mentioned that transfusions of platelets were used in 2%, 3% and 8,2% of neonates in some units of neonatal intensive care in Mexico, England and USA. A different approach of transfusion is explained by differences in gestational age of treated neonates and severity of the disease[14].

In our study, gestational age was a better predictor of transfusion reaction than blood type, Rh factor and both parameters together. Examined frequency of transfusion reactions combined by blood group and Rh factor were not significant predictors of transfusion reactions. We found a slightly negative but statistically significant correlation between gestational age and the occurrence of transfusion reactions. Additionally, with the aim of quantifying the influence of gestational age on the presence of a reaction was performed by logistic regression analysis, which showed that gestational age was significant predictor of the existence of transfusion reactions. This effectively means that with each additional week of gestation age, the risk for transfusion reactions reduced by 1 / 0, 867, or 1.153 times.

CONCLUSION

The average gestational age of our examiners was 38 weeks. Transfusion reactions in newborns of different gestational age are rare. Blood type and Rh factor individually and together are not valid in the prediction of transfusion reactions, while the gestational age is a good predictor of the incidence of transfusion reactions. This connection between gestational age and occurrence of transfusion reactions suggests more frequent occurrence of reactions in the lower gestational age.

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