Postnatal Outcomes of Intrauterine Transfusion Infants Due to Immun-Hemolytic Disease

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İntroduction:

Immune-hemolytic disease of fetus and newborn is the clinical picture where maternal specific IgG autoantibodies passing through placenta bind to erythrocytes and result in progressive fetal hemolysis. This hemolysis can lead to fetal anemia. In severe cases, can cause hydrops fetalis and intrauterine death. The use of Rh immune globulin to prevent susceptibility of Rhesus (Rh) negative pregnant women has reduced the immune-hemolytic disease of the fetus to 1 / 300-1 / 600 live births (1). Despite advances in the use of Rhesus immunoglobulin prophylaxis, perinatal mortality remains approximately 1% in high resource countries and as high as 14% in low resource countries (2,3). These outcomes are preventable with fetal blood sampling and intrauterine transfusion (IUT), which have greatly im- proved survival in affected pregnancies, including those with fetal hydrops, and those with an onset < 22 weeks' gestational age. The aim of this study was to evaluate the postnatal outcomes of newborns who received transfusion in the intrauterine period due to immun-hemolytic disease.

Method:

This study was performed retrospectively between March 2018 and July 2019. Infants who underwent erythrocyte transfusion during the intrauterine period with the diagnosis of immune-hemolytic disease and followed in the neonatal intensive care unit were included. Demographic data of the patients, APGAR scores at 1 and 5 minutes, prenatal erythrocyte transfusion, exchange transfusion and postnatal erythrocyte transfusion requirement, birth hemoglobin and bilirubin levels and reticulocyte count, highest bilirubin level, intrauterine transfusion number, duration of phototherapy, hydrops status, discharge status duration and mortality rate were recorded. Data analysis and report writing operations were performed on computer. Median (min-max), frequency distributions and percentages were used to summarize the data. Mann-Whitney U test was used for comparisons between the groups and $p < 0.05$ was accepted for statistical significance.

Results:

A total of 16 infants were included in the study. The median gestational week was 34 (28-37) and the median birth weight was 2395 (1420-2985) grams. Nine (56.25%) of the babies were female and 7 (43.75%) were male. All were born by cesarean section. The median Apgar 1st and 5th minute scores were 5 (0-6) and 6 (3-10), respectively.

The median hemoglobin median was 8 (4-18), reticulocyte count 8.5 (0-52), the highest bilurubin level median was 10 (4-20) and median phototherapy time was 4.5 (1-6) days. Ten patients had 3 or less intrauterine transfusions and 6 patients had more than 3 intrauterine transfusions. Exchange transfusion was performed a maximum of 2 times in 10 (62.5%) infants. Postnatal erythrocyte transfusion was performed to 6 (37.5%) infants due to anemia during the period until discharge. 10 (62.5%) of the infants had hydrops findings. The median discharge time was 19 (1-78) days. A total of 2 infants (12.5%) died (Table-1).

According to Mann-Whitney U test between groups, there was a significant difference in apgar 1 and birth hemoglobin due to non-exchange infants (U = 12.500, p = 0.049; U = 6500, p = 0.01) (Table-2).

Discussion:

Red-cell alloimmunization is an immune disorder due to an incompatibility between maternal and fetal red blood cell antigens (4). Antigen D incompatibility is the most frequent cause of red-cell alloimmunization because of its high prevalence and immunogenicity. Fetal erythrocytes coated with IgG antibodies become attached to the Fc receptors on macrophages in the reticuloendothelial system, primarily in the spleen, and become phagocytosed. This results in varying degrees of hyperbilirubinemia, fetal anemia, tissue hypoxia, extramedullary hematopoiesis, hepatosplenomegaly, fetal hydrops, and possibly intrauterine fetal demise. Nowadays, mid-cerebral artery peak systolic velocity is measured by Doppler ultrasound, which is a non-invasive method, and the severity of fetal anemia is determined and IUT is applied when necessary. Antigen D incompatibility is the most frequent cause of red-cell alloimmunization because of its high prevalence and immunogenicity. However, red blood cells have more than 400 other surface antigens, at least 43 of which being capable of producing hemolytic disease (5). Routine administration of antenatal and postpartum Rhesus (Rh) immunoglobulin has resulted in a shift of cases of red-cell alloimmunization to other antibodies. In our study, most patients experienced hemolysis due to Rh incompatibility.

1 and 5 minute apgar scores were correlated with the severity of hemoslysis. Therefore, the first minute Apgar score was significantly lower in infants receiving exchange transfusion after delivery. It is suggested that Rh hemolytic disease, which is severe enough to require IUT in intrauterine period, is also seen as severe hemolytic disease in postnatal period and the need for blood exchange is higher in them. The result is similar in the study of Çetinkaya et al. (6). However, in retrospective studies of Gobalakichenane et al. Rh hemolytic disease was detected in 28 infants and 6 patients were treated with UT and only 1 infant (1 infant). 17%) postnatal blood. It was reported that the need for change. In the same study, it was reported that there were 22 infants without UT and 6 (27%) had postnatal blood exchange, and that blood exchange decreased during postnatal period due to antenatal treatment. Differences between these studies may be due to differences in patient numbers and study criteria (7).

Most of the patients (62.5%) did not need erythrocyte transfusion in the postanatal period. There was no difference in the frequency of transfusion between the exchange and non-exchange groups. In the study of Şavklı et al., A similar rate of transfusion was performed. This was not needed in all patients. In our opinion, this is related to the severity of hemolysis and the success of IUT. Our mortality rate is similar to the literature (87.5%) (8,9). Here we should emphasize that we only evaluate postnatal outcomes of live-born babies.

Conclusion:

Infants who receive intrauterine transfusion due to immune-hemolytic disease are born to preterm birth and cesarean rate is high in these infants. Exchange requirement is increased in patients with more severe hemolysis. Patients who will need to exchange are coming to a worse world. The frequency of intrauterine transfusion does not increase mortality.

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Table 1. Demographic, laboratory and clinical data of patients

Characteristics	**Patients (n=16)**
Gestational Age (week) *	34 (28-37)
Birth weight (gr)*	2395 (1420-2985)
Gender**	
Famele (n;%)	9 (56,25)
Male (n;%)	7 (43,75)
Length of stay in NICU (days)	19 (1-78)
Cesarean section, (n;%) **	16(100)
Apgar score 1st minute	5(0-6)
Apgar score 5.min	6(3-10)
Birth hemoglobin, median (min-max) *	8 (4-18)
Reticulocyte count, median (min-max) *	8.5 (0-52)
Highest bilurubin level, median (min-max) *	10 (4-20)
Phototherapy time, median (min-max) *	4.5 (1-6)
Number of intrauterine transfusions (more than 3), (n;%) **	6 (%37,5)
Exchange transfusion, (n;%) **	10(%62,5)
Postnatal erythrocyte transfusion, (n;%) **	6 (%37,5)
Hydrops, (n;%) **	10(%62.5)
Mortality (n;%) **	2(%12.5)

* Data were expressed as mean±SD

**Data were expressed as number and percent

Table 2. Comparison of patients with and without exchange

	Exchange Patients (n=10)	Patients without Exchange (n = 6)	*p*
Apgar 1st Minute, median (min-max) *	4	5,5	**.049**
Birth hemoglobin median (min-max)	7.5	11.5	**.01**

* Data were expressed as median.