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Perinatal outcomes of intrauterine transfusions performed for RhD alloimmunization

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Abstract

The aim of this study was to assess perinatal outcomes of intrauterine transfusions (IUT) which were performed for Rh alloimmunization. We retrospectively analyzed 109 consecutive intrauterine transfusions, which included 28 pregnancies and 29 fetuses (one dichorionic-diamniotic twin pregnancy) between 2017 and 2019, from the hospital records. The study cohort was compared by means of the presence of hydrops before the beginning of intrauterine transfusions, the severity of fetal anemia, and Doppler parameters before consecutive transfusions. We evaluated perinatal outcomes, which consisted of fetal complications due to intrauterine transfusions and neonatal outcomes. Before the first IUT, 48,3% of the fetuses had hydrops fetalis, and 82,8% had severe anemia. The highest number of IUTs for the same fetus was eight. Overall survival rate was 72%. We divided our cohort into two groups by means of the presence of hydrops fetalis upon first admission. We found that the fetal hemoglobin levels before the first IUT were significantly lower in the hydropic fetuses. Intrauterine transfusion is a safe and effective treatment even in high-risk populations.

Keywords: intrauterine transfusion, pregnancy, neonatal, outcome

1. Introduction

Despite the introduction of anti-D immune globulin prophylaxis in 1968 and the establishment of a non-invasive diagnosis of fetal anemia, Rh alloimmunization continues to complicate pregnancies (1, 2). It is estimated that the incidence of hemolytic disease in the newborn due to alloimmunization is around 0.5% in developed countries (3). The current incidence of Rh alloimmunization has yet to be depicted in Turkey. On the other hand, there are studies from different regions of Turkey reporting high rates of severe alloimmunization, so we are of the opinion that alloimmunization is still a relatively frequent and severe complication leading to neonatal morbidity and mortality (4, 5).

In this study, we aimed to analyze the outcomes of intrauterine transfusions, which were performed in our Perinatology department in regards to the complications related to the procedure itself and perinatal/neonatal consequences.

2. Materials and Method

This is a retrospective cohort study of a continuous series of fetuses with suspected anemia undergoing IUT between 2017 and 2019 at the Perinatology Unit of Cengiz Gokcek Maternity Hospital, Gaziantep. We initially analyzed 30 fetuses in this study period (one dichorionic twin pair), and 109 IUTs were performed on them. All cases were assessed and counselled by the authors (A.O. and T.Y). Doppler measurements, presence of hydrops fetalis during the first admission, hematocrit (Htc) value of the donor blood, fetal hemoglobin (Hb) levels before and after the procedures, intervals between repetitive transfusions in order to calculate daily drop in fetal Htc levels were all recorded. Intrauterine transfusions (IUTs), outpatient follow ups and deliveries of the cases were also performed by the authors. Data regarding demographic characteristics, obstetric history, perinatal and neonatal outcomes were extracted from the electronic database of the hospital and the patient registry of the Perinatology Unit. MCA-PSV multiple of median (MoM) in prediction of severe fetal anemia were calculated for the first IUT. For the consequent IUTs a combination of estimated daily decrease in fetal Hb levels and MCA-PSV MoM were assessed. Degree of fetal anemia, technique of IUTs, and preparation of Rh D negative door blood were performed under the previous guidelines (2, 6, 7). Variables were characterized as means with standard deviation or medians where appropriate. The statistical analysis was conducted using SPSS for Windows 25.0 (SPSS Inc., Chicago, IL, USA).

Fetal anemia cases which were associated with conditions other than Rh immunization such as twin-twin transfusion syndrome or other conditions associated with monochorionic twin pregnancies; congenital parvovirus infections; or other alloimmunizations related to subgroup incompatibilities were excluded from the analysis. One case, which was later diagnosed with congenital leukemia, was also excluded from the analysis.

All the patients gave informed consent and were counseled for every step of medical or surgical interventions.

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3. Results

We analyzed 28 consecutive pregnancies for this study. Among those pregnancies, 10 were Syrian refugees, and 18 were Turkish women. 29 fetuses were included in the study population (one dichorionic twin pair), to whom 109 IUTs were performed. Maternal and fetal characteristics are presented in Table 1. Earliest transfusion was made at 20 weeks and 5 days of gestation. Nearly half of the study population (48,3%) had hydrops fetalis upon first admission to the Perinatology Unit. Severe anemia occurred during the first visit among 82,8% of the cohort. Eight cases had their first IUT before the completion of 24 gestational weeks. Twenty-one fetuses required a second IUT, and 17 required a third. The highest number of IUTs for the same fetus was eight (in one fetus).

Table 1. Maternal and fetal characteristics

Maternal Age (years)	29.1 (±5.8)
Gravida	4.3 (±1.3)
Parity	2.4 (±1.2)
Gestational age at first IUT	25.2 (±1.6)
IUT before 24 weeks of gestation	%28 (N=8)
Presence of hydrops fetalis on admission	%48.3 (n=14)
Severe fetal anemia on admission	%82.8 (n=24)
Total number of transfusions	3 (1-8)

Neonatal outcomes are presented in Table 2. The median value for the gestational age at birth was 34 weeks 2/7 days. The birth rate was 79% percent with 23 live-born fetuses. There were six cases which ended up with intrauterine demise and another two died in the neonatal period. Those two fetuses had fetal distress during the IUT. They both underwent emergency delivery but ended up with early neonatal death in the neonatal intensive care unit. The preterm birth rate was 44%, and the overall survival rate was 72%. Four cases were delivered before the completion of 34 weeks of gestation. Two of them were associated with acute fetal distress complicating IUT, and the other two had preterm premature rupture of membranes (PPROM).

Table 2. Neonatal outcomes

Gestational week at birth	**34,2 (±2.5)**
Livebirth	**%79 (n=23)**
Preterm birth	**%44 (n=13)**
Preterm birth <34 weeks	**%14 (n=4)**
Fetal distress related to IUT	**%6 (n=2)**
Intrauterine exitus	**%20 (n=6)**
Neonatal death*	**%6 (n=2)**
Survival rate	**%72 (n=21)**

*Two cases which were complicated with fetal distress

We compared our study group according to the presence of hydrops fetalis upon the first admission to the Perinatology department (Table 3). There were 14 cases who had hydrops before the first IUT. The number of IUTs and the survival rates were similar between the two groups. However, we found that the fetal hemoglobin levels were statistically lower in the hydropic fetuses (p=0,042).

Table 3. Comparison of cases in terms of presence of hydrops fetalis

	No Hydrops Fetalis (n=15) median, min-ma	Hydrops fetalis (n=14) median- min-max	p value
Number of IUTs	4 (1-7)	5 (1-8)	0.84
Fetal Hb on first IUT	4.6 (2-7.5)	2.7 (1.6-7)	**0.042**
Survival rate (%, n)	80% (n= 12)	57% (n=8)	0.19

4. Discussion

Despite developing anti-D immune globulin prophylaxis, Rh alloimmunization is still estimated to complicate around 1 percent of live births (8, 9). In addition to that, with the introduction of non-invasive screening and diagnosis of fetal anemia, the development of intrauterine blood transfusions has profoundly modified the prognosis of the condition (2, 10).

In this study, we aimed to conclude the obstetrical and neonatal outcomes of the IUTs between 2017 and 2019. The hospital in which this study was performed is located in a highly populated region; there are 11.500 births per year. About 40 percent of those births are consisted of Syrian refugees. Likewise, our study cohort of 28 women consisted of 10 Syrian refugees and 18 Turkish citizens. In this two years, we had performed 109 IUTs in our Perinatology department with a survival rate of 72 percent.

The overall survival rate after IUT with the indication of alloimmunization has been found to be over 95 percent in a large series (11, 12). The authors also mention that this survival rate is dependent on the center's experience, the presence of hydrops, and the gestational week hydrops fetalis develops. It has been shown that when severe fetal anemia develops before the gestational week of 20, survival is reduced (13). In our cohort, 82,8% had severe fetal anemia before the first IUT. Besides, nearly half of the fetuses (48%) had hydrops fetalis. Furthermore, 8 cases had their first IUT before 24 weeks of gestation. Those rates are higher compared to the aforementioned studies. We are in the opinion that low socioeconomic status of the study population is the most probable explanation for this condition. A relatively lower rate of survival in our cohort could be associated with the high rates of severe anemia and hydrops fetalis. In another study from Turkey, Savkli et al. analyzed their center's 3 years experience, and the overall survival rate was 80,95% (4). They also found that the survival rate was significantly lower in the hydropic fetuses (4).

The preterm birth rate was 44% in our study population. Four cases were delivered before the completion of 34 weeks of gestation (14% of the population). Those rates are comparable to the literature (14).

We also compared our cases with respect to the presence of hydrops fetalis. Nearly half of the cases (15 fetuses) did not have hydrops, whereas 14 of them had. The number of IUTs was similar between the two groups. Overall survival rate in

the no hydrops group was higher (80% vs 57%), but this difference was not statistically significant. This could be explained by the relatively low number of cases. In addition, we found that the fetal hemoglobin levels before the first transfusion were significantly lower in the hydrops fetalis group (p=0,042). Likewise, in a previous study with a similar population, the authors attributed the low level of overall survival in their cohort to the very high rate of severe anemia and hydrops fetalis before the first IUT (5).

The main limitation of our study is the retrospective design and the limited number of cases. On the other hand, we are of the opinion that the performance of all the diagnostic and invasive procedures and the meticulous recording of all the data by the two authors were the main strengths of this study.

In conclusion, we are of the opinion that even with screening and anti-D prophylaxis, severe fetal anemia associated with hydrops fetalis still continues to complicate pregnancies, especially in the lower socioeconomic status populations. On the other hand, intrauterine blood transfusion is still an effective and safe procedure, even in complicated cases.

Conflict of interest

The authors declared no conflict of interest.

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None to declare.

Authors' contributions

Concept: M.A.O., Design: M.A.O., Data Collection or Processing: M.A.O, Analysis or Interpretation: M.A.O, T.Y., Literature Search: M.A.O., T.Y., Writing: M.A.O., T.Y.

Ethical Statement

Approval was obtained from Gaziantep Health Directorate Ethics Board the study started. The ethics committee decision date is 06/01/2023 and the number of ethical committee decisions is 2023/02/B.

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