Case Series

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Intrauterine transfusion in hydropic fetuses: An outcome analysis

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Abstract:

The objective of this study is to determine the perinatal outcome in pregnancies with hydropic fetuses. The study was a retrospective evaluation of data on intrauterine transfusion (IUT) done in hydropic fetuses for correction of severe anemia from December 2017 to August 2021 in AIIMS Jodhpur. The retrospective case series involves five cases that underwent IUT for severe fetal anemia. All had a sign of hydrops at the time of presentation. Out of five cases, four were of alloimmunized pregnancies while one was of hydrops fetalis secondary to parvovirus infection. The presence of severe hydrops at the time of presentation is a poor prognostic factor affecting fetal survival post-IUT therapy.

Keywords:

Hydrops, intrauterine transfusion, perinatal outcome

Introduction

Fetal anemia contributes significantly to perinatal mortality and morbidity. Intrauterine transfusion (IUT) is one of the most successful treatment options for fetal anemia till now. As a fetus has a very small blood volume and is relatively immune-compromised, transfusion to the fetus should be rigorously monitored. As appropriate transfusion is lifesaving while over transfusion in severe anemic fetuses is also associated with risk and increases morbidity and mortality.

Due to the paucity of literature related to the specialized nature of these transfusions in severely anemic hydropic fetuses, and evidence to support specific steps in blood transfusion rate. Challenges with IUT are the selection of patients at the right time. Hence, monitoring of transfusion rate, frequency of transfusion events and diagnostic testing preceding the transfusion require consideration.

Here, we are reporting a retrospective case series of some IUT sessions that lead to an adverse neonatal outcome.

Materials and Methods

This is a retrospective case series of five pregnant women aged between 23 and 29 years who underwent IUT at our center. These five patients were selected after a review of the case records of the transfusion medicine department at our institution from December 2017 to August 2021. During the study period, there were 10 pregnancies in which IUTs were performed. Of these five cases were those who have hydrops at the time of presentation. Four pregnancies had immune causes, whereas one pregnancy had nonimmune causes affecting the pregnancy. All women presented between 22 and 31 weeks of gestational age with severe fetal anemia. To detect fetal anemia, middle cerebral artery peak systolic velocity (MCA-PSV) using Doppler ultrasound (USG) was used. Fetal anemia was suspected if the MCA-PSV is found to be ≥1.5 multiples of the median for gestational age.[1] Indication for IUT was if fetal hematocrit of <30% in

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fetuses <35 weeks gestation. At the time of IUT, fetuses were administered O–, leukoreduced, irradiated, and SAGM depleted packed red cell with hematocrit levels ranging from 75% to 80%.

Intravascular transfusion was the preferred choice of therapy, especially in hydropic fetuses. Intraperitoneal transfusion could be performed in situations when it is difficult to reach the cord like in the posterior placenta, during obesity, and during very early gestation. Blood is absorbed through the lymphatics in intraperitoneal transfusion. USG and color Doppler are done for fetal monitoring and to localize cord insertion, and accessible site. The needle path is mapped and the decision is taken on where to enter the cord – cord insertion/free loop/intrahepatic portion site. A 20 gauge long needle is inserted into the umbilical vein, and the first 2–3 mL of blood is aspirated to differentiate it from liquor. A pretransfusion sample from the fetus is used for the assessment of hematocrit and blood group. Based on that necessary volume of packed O negative, irradiated red blood cell (RBC) (hematocrit of 75%–80%) is then transfused. Fetal monitoring is done by serial USG for anemia, till the time of the next transfusion.

Severe fetal anemia was defined as a hemoglobin level 5 standard deviation or more below the mean for gestational age.[2] Severe fetal anemia is an indication for immediate transfusion. To avoid volume overload, the first transfusion aimed to obtain an increase in hemoglobin concentration of less than fourfold of the starting level. A second transfusion was always performed within 7–14 days.[3] After the second transfusion, the interval between transfusions is monitored by weekly monitoring of MCA-PSV values. Pregnancy should be allowed to continue until approximately 37 weeks, for reducing the risk of prematurity.

Prediction of fall in hemoglobin value and the likelihood of continuing fetal anemia indicated by an expected hemoglobin decrease of 0.3 g/dl/day from posttransfusion hemoglobin measurements following the second IUT procedure.[4]

The volume of the processed RBC units to be transfused was calculated as follows:[5]

$$\text{RBC volume} = (\text{FPBV} \times \text{TH} - \text{IH})/\text{HTB}$$

Where fetal placental blood volume (FPBV) is the fetoplacental blood volume in mL, TH is the target hematocrit proportion, IH is the initial fetal hematocrit proportion, and HTB is the hematocrit proportion of the transfused RBC unit.

The feta placental blood volume was calculated from the USG estimate of fetal weight (UEFW) in gram according to the following formula:[4]

$$\text{FPBV} = 1.046 + \text{UEFW} \times 0.14$$

Observations and Results / Outcome Analysis

Case 1

The first case is a 23-year-old female who presented at 25 weeks of gestation with polyhydramnios with MCA-PSV of 50.3. On immunohematology workup, the maternal antibody screen was negative. Mother was diagnosed with hydrops fetalis secondary to parvovirus and pure red cell aplasia. The patient was planned for IUT. Fetal weight at that time of presentation was 800 g and preprocedure hematocrit was 8.7%. On USG, the fetus has mild ascites, generalized skin edema, and bilateral pleural effusion. Postprocedure hematocrit was 26.5%. The second procedure could not be conducted as the fetus did not survive.

Case 2

The second case is a 29-year-old female G3P2 L1A0D1, first time presented at 26 weeks. Gestational age with a weight of the fetus was 1486 g with USG feature of pericardial effusion, gross ascites, and placentomegaly. Preprocedure hematocrit was 8.7%. On immunohematology workup, the antibody identified was anti-D with a titer of 512. MCA-PSV was 74.9 before the first IUT. After the first procedure hematocrit was 26.5%. The second procedure was done at 27 weeks of gestational age. Before starting the second procedure hematocrit was 8.7% and postprocedure hematocrit was 16.10%. The third procedure was done at 27 + 3 weeks gestational age and preprocedure hematocrit was 13.9%, but we were unable to get postprocedure hematocrit due to the replacement of

Table 1: Case summary

Patient's age (years)	Gestation age at the time of presentation (weeks)	Number of IUT session	Hydrops	MCA-PSV value at the time of presentation	Weight of fetus (g)	Preprocedure Hct (hb) value	Reason	Outcome
23	25	1	Yes	50.3	800	8.7 (3.1)	Parvovirus	Dead
29	26	4	Yes	74.9	1486	8.7 (2.8)	Anti-D, 512	Dead
28	26	2	Yes	67.6	1000	0.6 (***)	Anti-D, 512	Dead
23	22+4	1	Yes	60.7	493	1.5 (0.6)	Anti-D, 256	Dead
27	30+5	2	Yes	69.7	974	3.5 (1.3)	Anti-D, 256	Dead

IUT=Intrauterine transfusion, MCA-PSV=Middle cerebral artery peak systolic velocity, HCT=Hematocrit, Hb=Hemoglobin

the needle. The fourth procedure was planned at 28 weeks of gestation with preprocedure hematocrit was 5.10%. Before starting the fourth IUT session, MCA-PSV value was 77 at 28 weeks of gestation. The fetus did not survive.

Case 3

The third case is a 28-year-old female G3P2001, first time presented at 26 weeks of gestation with USG suggestive of pericardial effusion and placentomegaly, with MCA-PSV value of 67.6. On immunohematology workup, the antibody identified was anti-D with titer 512. The patient underwent three procedures of IUT. The first procedure was undergone intravascular route with preprocedure hematocrit was 0.6%. This may be due to sample error as contamination with liquor. Postprocedure hematocrit was 21.4%. The second procedure was done through the intraperitoneal route with an interval of 4 days. Postprocedure hematocrit could not be able to assess due to the intraperitoneal route. After that procedure, the fetus underwent bradycardia and did not survive.

Case 4

The fourth case is a 23-year-old female with G3P1100, first time presented at 22 + 4 weeks of gestation with fetal weight of 493 g. USG finding of fetus was suggestive of oligohydraminos, cardiomegaly with pericardial effusion and gross ascites. MCA-PSV was 60.7. On immunohematology workup, the antibody identified was anti-D with titer 256. The patient underwent one IUT procedure. Preprocedure hematocrit was 1.5%. We could not be able to assess postprocedure hematocrit due to slippage of the needle. The second procedure was planned. However, the fetus underwent bradycardia before the next procedure.

Case 5

The fifth case is a 27-year-old female with G5P2201, first time presented at 30 + 5 weeks of gestation with a fetal weight of 974 g. MCA-PSV was 69.7. USG finding was suggestive of of moderate to severe ascites with anasarca with placentomegaly and cardiomegaly. On immunohematology workup, the antibody identified was anti-D with a titer of 256. The patient underwent the first procedure of IUT with preprocedure hematocrit was 3.5%. Postprocedure hematocrit was 10.9%. The second procedure of IUT was planned 3 days after the first procedure with preprocedure hematocrit was 3.5% and postprocedure hematocrit was 9.8%. The third procedure was planned but the fetus underwent bradycardia before the procedure and did not survive.

Volume was calculated for each session as per gestational weight and preprocedure hematocrit.

Approximately, 40–70 ml blood volume is required during these procedures including tube wastage.

Brief summary of all cases is summarized in Table 1.

Discussion

Intrauterine blood transfusion is mainly done for fetal anemia secondary to red cell alloimmunization. Hence, the selection of patients based on diagnostic testing is crucial for predicting the perinatal outcome. The intravascular route is considered a safe method. The incidence of severe adverse long-term outcomes post-IUT ranges from 2.8% to 13%.[6-8] While perinatal survival of IUT for fetal anemia due to parvovirus ranges from 67% to 73%.[9-11]

Survivability decreases if the fetus is hydropic at the time of presentation or if the fetus requires early transfusion at 20 weeks or less. If severe anemia presents early in the second trimester, the treatment is technically challenging. Such cases have been associated with a higher loss of pregnancies.[12]

The survival rate in hydrops depends on their severity, the weeks of gestation at its first presentation, and prompt intervention.[13]

In our case series, a total of five patients were present with mean prehematocrit before the first IUT was 4.6% ± 2.86%. All are severely anemic with one or more features of hydrops at the time of presentation. Based on the grading of hydrops, gross ascites were present in three patients, one having moderate to severe and one having mild ascites. Pericardial effusion was in three patients, and bilateral pleural effusion was seen in one patient. Placentomegaly was in three patients and skin edema in two patients. All patients have more than one of the hydropic features [Table 2].

Hence, we advocate that IUT treatment should be started for the correction of fetal anemia before the onset of fetal hydrops. One review series reported a survival rate of 90% in nonhydropic fetuses compared to a survival rate of 70% in hydropic fetuses after IUT for fetal anemia secondary to maternal RBC alloimmunization. IUT therapy may be composed of an intravascular transfusion through the umbilical vessels, an intraperitoneal transfusion, or a combination of both. In general, most centers use intravascular transfusions to reach a target fetal hematocrit between 45% and 50%. Intraperitoneal transfusions are employed when the fetus is present in early gestation when it is difficult to find umbilical vessels. Alternatively, intraperitoneal transfusion is employed in conjunction with intravascular transfusion by a limited number of centers to prolong the interval between IUT procedures while still maintaining a stable fetal hematocrit.

The presence of hydropic features at the time of presentation in this case series may reflect the late referral of patients from other centers, although they all have

Table 2: Severity of hydrops according to cases

Case number	Ascites	Pleural effusion	Cardiomegaly	Pericardial effusion	Skin edema	Placentomegaly
1	Mild	Bilateral present	-	-	Generalized thickness 15.7 mm	-
2	Gross	-	-	Yes	-	Yes
3	Gross	-	-	Yes	-	Yes
4	Gross	-	Yes	Yes	-	-
5	Moderate to severe	-	Yes	-	Anasarca	Yes

previously affected pregnancy history too. Alloimmunized pregnancies having high antibody titers and causative antibody identifies were anti-D in our case series. The presence of hydrops fetalis is a major contributor to adverse post-IUT outcomes and worsens the rate of survival.[12-14] A recent study by Zwiers *et al*. reported improved post-IUT survival at a national referral center in New Zealand due to reduced severity of the disease at referral, lower rates of hydrops fetalis at presentation, and increased hemoglobin levels at the time of the first IUT.[15] These findings support the recommendation that high-risk pregnancies should be followed up in a tertiary care center between 15 and 20 gestational weeks.[16]

Conclusion

Hence, the presence of hydrops at the time of presentation is itself a poor prognostic factor for the perinatal survival of the fetus.[13,17] In addition, (alloimmune) fetal hydrops is considered a risk factor for long-term neurodevelopmental impairment.[18] Early and timely detection of suspected pregnancies with bad obstetric history, and their referral and treatment before the development of hydrops, improve the outcome of such pregnancies. Careful selection of patients based on grading or severity of hydrops also predict outcome and helps to assess the plan for IUT.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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