

Role of Intrauterine Blood Transfusions in Management of Rh-Isoimmunized Pregnancies

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ABSTRACT

Background: Hemolytic disease of the newborn secondary to rhesus alloimmunization was once a major contributor to perinatal morbidity and mortality.

Aim: To describe the fetal outcome of the procedure and to calculate fetal survival rate after intrauterine transfusion in Sir Ganga Ram Hospital

Methods: This descriptive study was carried out in Sir Ganga Ram Hospital Lahore over a period of one year from January 2001 to December 2001. All the patients who require intrauterine transfusion (IUT) for Rh-incompatibility were included in this study. Those patients who require IUT due to causes other than Rh (D) incompatibility were excluded from the study. For intrauterine transfusion, canula was introduced in intrahepatic portion of umbilical vein under direct ultrasonic vision and fetal blood sample was taken before transfusion for blood grouping haemoglobin and haematocrit. Packed cells of compatible O-ve group were used for transfusion.

Results: Overall fetal survival rate after intrauterine transfusion was 62.5% for hydropic fetuses survival rate was 25% compared with non-hydropic fetuses which was 100%.

Conclusion: The response of non-hydropic and mildly hydropic fetuses was better as compared to severely hydropic fetus.

Keywords: Fetal outcome, Intrauterine transfusion, management, Rh-isoimmunization

INTRODUCTION

Hemolytic disease of newborn is an antibody mediated hemolytic anemia of fetus and newborn where aetiology being Rh-blood incompatibility. Attenuated life span of fetal RBCs is by the action of specific IgG antibodies coming from mother, producing fetal hemolytic anemia and hydrops fetalis¹. In the last century, the role of Anti-D immunoglobulins to prevent Rh-immunization, firstly postpartum and then antepartum is one of the major medical achievements as for preventive obstetric medicine is concerned.² Amongst many antigens included in Rh-system only D-antigen is the major antigen responsible for mismatch. Red cells harbouring 'D' antigen known as Rh-positive and when lacking it as Rh-negative.³ Severely sensitized fetuses due to Rh-immunization were used to managed in the past by intraperitoneal transfusion of blood with poor results as occurred before the intrauterine transfusion methodology arrived^{4,5}. In hydrops fetalis particularly IPT was rarely if ever, successful. In which lymphatics are waterlogged rendering the procedure ineffective. Procedural mortality also enhanced due to traumatic nature of IPT⁶.

Despite the fact that introduction and utilization of Rh-immunoglobulin prophylaxis, maternal Rh-alloimmunization is still a cause of hemolytic disease of fetus and newborn. However with appropriate monitoring and intervention, this disorder can successfully be managed in almost all cases, with no long term consequences in newborns.⁷ In severe Rh-isoimmunization cases management options have been very disappointing, and include termination of pregnancy, permanent sterilization or the highly controversial pregnancy with Rh negative donor semen. In most places even in teaching hospitals, management is only the preterm delivery and neonatal exchange transfusion as soon as the fetus is about 32-34 weeks old. Various techniques have been used historically to rectify fetal anemia in fetuses less than 32 weeks of age, cannulation of placental vessels at hysterectomy, plasmapheresis, fluoroscopic guided intraperitoneal transfusion, and fetoscopic guided intrauterine transfusion.⁴ The arrival of ultrasonography and ultrasound guided cord blood sampling enabled the present state of the art diagnosis and ultimately revolutionized treatment of fetal anemia by direct ultrasound guided fetal blood transfusion⁸.

PATIENTS AND METHODS

This descriptive study was carried out in Sir Ganga Ram Hospital Lahore over a period of one year from January 2001 to December 2001. Eight patients were included who require intrauterine transfusion for Rh-

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incompatibility. All the patients who require intrauterine transfusion (IUT) for Rh-incompatibility were included in this study. Those patients who require IUT due to causes other than Rh (D) incompatibility were excluded from the study. Each patient was evaluated by detailed history, clinical examination and related investigations. History included complete information about previous pregnancies, their outcome and history of anti-D prophylaxis. For intrauterine transfusion, canula was introduced in intrahepatic portion of umbilical vein under direct ultrasonic vision and fetal blood sample was taken before transfusion for blood grouping haemoglobin and haematocrit. Packed cells for compatible O-negative blood group were used for transfusion. Quantity of each transfusion to be given was calculated according to gestational age, pre-transfusion HCT and donor's HCT.

RESULTS

Out of eight, five patients delivered alive babies giving a success rate of 62.5% and 3 patients giving unsuccessful rate of 37.5% for this procedure (Table 1). According to fetal outcome of the procedure (IUT), 5 patients (62.5%) had alive babies. One patient had an abortion (12.5%), one patient had an intrauterine fetal death (12.5%) and there was one neonatal death (12.5%) [Table 2]. Non-hydropsic fetus respond better to IUT. In this study 50% of the patients had hydropsic fetuses at presentation, and 50% patients had non-hydropsic fetuses when survival rate of hydropsic and non-hydropsic fetuses was compared, it was 25% vs 100% (Table 3). Mostly the patients with Rh-incompatibility seek medical advise after multiple mishaps, so when parity of patients were observed. It was seen that 62.5% patients had previous 2-4 viable deliveries. 25% patients had parity of 5-8 and one patient was para 15(12.5%) [Table 4]. Fetal hydrops develops when there is hemoglobin deficit of 7 g/dl or more for gestational age. The lowest fetal hemoglobin at the time of first intrauterine transfusion was 3.0g/dl. Mean fetal hemoglobin was 7.56g/dl (Table 5). In postnatal period, babies who had IUT required mostly phototherapy for unconjugated hyperbilirubinaemia. Only one baby had a single exchange transfusion and three babies received simple top-up blood transfusion (Table 6).

Table 1: Fetal survival rate (n = 8)

Survival rate	n.	%age
Successful	5	62.5
Unsuccessful	3	37.5

Table 2: Frequency of fetal outcome (n = 8)

Outcome	n	%age
Live births	5	62.5
Abortion	1	12.5
IUD	1	12.5
Neonatal death	1	12.5

Table 3: Presence of hydrops at first IUT and survival rate

Condition	n	No. survived	%
Hydropsic fetus	4	1	25
Non-hydropsic fetus	4	4	100

Table 4: Parity of patients

Parity	n	%age
Para (2-4)	5	62.5
Para (5-8)	2	25.0
Para (10-15)	1	12.5

Table 5: Fetal hemoglobin before first intrauterine transfusion (n = 8)

Haemoglobin (g/dl)	n	%age
3.0 – 7.5	3	37.5
7.8 – 11.5	5	62.5

Table 6: Neonatal management (live births = 5)

Procedure	n	%age
Exchange blood transfusion	1	20
Blood transfusion	3	60
Phototherapy	5	100

DISCUSSION

Intrauterine fetal blood transfusion in the management of fetal anemia is however, a difficult procedure requiring a lot of skill and precision. It can not be done without ultrasound monitoring and ultrasound guided intervention, with high rate of procedure related fetal deaths.⁹ An assay of techniques, such as exchange, partial exchange or simple top-up transfusions, via different sites such as percutaneous, umbilical cord puncture at placental insertion site or free loop, the intrahepatic umbilical vein or IPT have been employed. Out of eight patients, five patients had healthy and alive babies after IUT, with a fetal survival rate of 62.5% which is favorably comparable with the results obtained in India 55.6%¹⁰ and 66.6% in France.¹¹ However, in Queen Charlotte's Maternity Hospital London the survival rate was 84%.¹² Eight patients were given a total of 26 IUT with a range of 2-5 per patient and mean of 3.25. Mean gestational age of fetuses requiring first intrauterine transfusion was 23 weeks. In Netherlands no difference was found in survival rate between children requiring first transfusion early (< or=26 weeks) or late (>26 weeks) in pregnancy¹³.

It was studied that non-hydropsic fetuses had a better prognosis as compared to hydropsic fetuses. Out of eight, four fetuses were hydropsic at the time of first IUT. Only one of them survived with a fetal survival rate of 25% as compared with 100% for those of non-hydropsic fetuses. This compared with results in Netherland¹³, where it was observed that non-hydropsic and mildly hydropsic fetuses had significantly higher survival rate than for those with severe hydrops (94% versus 53%). In France survival rate of hydropsic fetuses was found to be 50%¹¹.

Lowest fetal hemoglobin at the time of the first IUT was 3g/dl with hematocrit of 11 at 22 weeks. Total volume of 150 ml packed cells with donar's HCT of 55 was transfused to make the post-transfusion hemoglobin of 13.6 g/dl. This volume of blood was given to cover fetoplacental volume of blood, as fetal volume of blood at 22-24 weeks of gestation is 50-60 mls only.

Hydropic fetuses had transfusion hemoglobin in the range of 3-7.5g/dl, while hemoglobin of non-hydropic fetuses was in the range of 7.8-11.5 g/dl at the time of first IUT. Mean hemoglobin for all the fetuses was 7.5 g/dl. In France lowest pretransfusion fetal hemoglobin was found to be 3 grams at 25 weeks.¹¹ When fetal outcome of these eight patients was studied it was found that one patient had an abortion at 24 weeks, due to preterm premature rupture of membranes, this patient developed frank leaking and expelled a hydropic fetus. Vaginal leaking of amniotic fluid and preterm labour was found in 33% of patients after IUT as described in complications of IUT by Bock¹⁴.

Out of five live births, only one baby received an exchange transfusion after birth. Three babies received simple top-up transfusion, and all the five babies had phototherapy. These babies were discharged from nursery at 3-7 days. When different aspects of previous obstetric history, it was found that none of these patients had postpartum anti-D prophylaxis. There is 10% chance of mothers having Rh-isoimmunization after delivery of first Rh-positive baby if not given anti-D and 17% risk after second Rh-positive fetus. Risk of isoimmunization increases subsequently¹⁰. One patient received incompatible Rh +ve blood transfusion after delivering her first IUD baby. This patient had such a strong sensitization developed that in next pregnancies fetuses developed hydrops at 22-26 weeks gestation. This patient had her first intrauterine transfusion in 5th pregnancy at 20 weeks gestation.

Prevention of rhesus disease is very cost effective as compared to treatment of the disease. In developing countries like India it has studied that the prevention option of postpartum prophylaxis was found to be far less expensive than the treatment option.¹⁵ The postpartum prophylaxis to treatment ratio was 1:8 in this study. Initially IPT were started in most of the centers in world but with the introduction of intravascular approach, intraperitoneal transfusions became less popular. Intravascular transfusions are very effective, and can be started at an earlier gestation. Intravascular route is also preferred in hydropic fetuses, as ascites prevents adequate absorption of red cells through the lymphatics. In this study all IUTs were through intravascular approach and intrahepatic part of umbilical vein was selected for intrauterine transfusions. A new technique in practice is

intrauterine exchange transfusion¹¹. This technique is claimed to avoid fetal hypervolaemia and it also prolongs the intervals between transfusions. Intervals can be prolonged to 15 days to 60 days. But it is a complex procedure and is more time consuming. In Pakistan the success rate of the procedure is comparable with developed countries. Well-equipped fetal medicine clinics and trained staff can do miracles for Rh-isoimmunized pregnant women.

CONCLUSION

Intrauterine blood transfusion plays a very important role in the management of Rh-isoimmunized pregnancies. This study also highlights the importance of anti-D prophylaxis. Early detection of problem definitely improves the results as non-hydropic fetuses respond better than hydropic fetuses. Use of direct intravascular intrauterine transfusion is preferred method of management as compared with intrauterine intra-peritoneal transfusion.

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