Rh DISEASE: INTRAUTERINE INTRAVASCULAR FETAL BLOOD TRANSFUSION BY CORDOCENTESIS*

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A total of 49 cordocenteses, including 40 intrauterine intravascular fetal blood tranasfusions, were performed in 30 pregnancies complicated by red cell isoimmunization. Transfusions were started at 19-33 weeks' gestation and repeated up to five times, at one-to-four week intervals. The volumes of transfused blood were 20-110 ml, hematocrits were 58-82 percent and the rate of transfusions was 1-15 ml/min. The pretransfusion fetal hemoglobins were 3.5-11.6 g/dl and the posttransfusion fetal hemoglobins were 7.5-15.6 g/dl. There were three intrauterine deaths and two neonatal deaths. The overall survival rate was 83.3 percent including all cordocenteses. The survival rate for the intrauterine transfusions was 81 percent. *Key words: Rh disease, fetal blood transfusion, cordocentesis.*

Severe fetal anemia and fetal hydrops caused by blood incompatibilities are generally associated with poor perinatal outcome, especially if hydropic signs develop during the second trimester. Although intraperitoneal transfusion has been used efficiently to treat fetuses without hydrops, its results for treatment of hydropic fetuses have been disappointing[1,2].

Since first reported by Daffos et al.[3] in 1983, ultrasonographically guided percutaneous access to fetal umbilical circulation has become a popular technique. The potential applications of percutaneous umbilical blood sampling or funipuncture, previously called cordocentesis, have increased.

Here we report our experience in fetal intravascular blood transfusion by cordocentesis in the management of 30 pregnancies complicated by Rh isoimmunization between 1993 and 1996 in Hacettepe University Hospital.

Material and Methods

Nine patients had only fetal blood sampling. In the remaining 21 patients, 40 intrauterine intravascular transfusions were performed in total. Before cordocentesis, no maternal sedation or fetal paralysis was done. The site and direction of the umbilical cord at its placental insertion was defined by a high resolution real time ultrasound scanning with a curvilinear probe (3.5 MHz). The site of entry on the

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abdominal wall was cleaned with antiseptic solution (povidone iodine). With the transducer in one hand, a 22 gauge needle 15 cm long held in the other hand was guided sonographically. The tip of the needle emitted a clearly visible echo, which was followed on the scope toward the insertion of the cord.

Briefly, three situations were encountered: a) when the cord insertion was anterior, the needle was introduced by transplacental access, avoiding introduction into the amniotic cavity, and the cord was punctured at its base; b) when the cord insertion was lateral, the needle was introduced through the placenta and then through the amniotic cavity before penetrating the cord at about 1 cm from its insertion. c) when the cord insertion was posterior, the needle was introduced through the amniotic fluid and penetrated the cord at about 1 cm from its insertion. By certain experience the resistance of penetration of the cord was easily felt. It was necessary to push firmly but gently to penetrate Wharton's jelly.

After penetration of the cord the needle's stylet was removed, a syringe was attached to the hub of the needle and 2-3 ml of pure fetal blood was obtained. This fetal blood was used for the determination of fetal hematocrit and hemoglobin level and for blood group, Rh factor and direct Coombs. If the hemoglobin level was less than 2 SD below the normal mean for gestation (Table I)[4], the tip of the needle was kept in the lumen of the umbilical cord and a connecting tube, 10-15 cm long, was attached to the hub of the needle for intravascular transfusion. 0-Rh negative fresh, packed erythrocytes with at least a 60 percent hematocrit level were infused manually through a 20 ml syringe into the fetal circulation. The rate of transfusions was 1-15 ml/min. The sonographically detectable turbulence and echogenicity in the umbilical cord produced by the infused blood allowed identification of the punctured vessel whether it was artery or vein. The fetal heart rate and the flow of the infused blood were monitored continuously throughout the procedure by ultrasonography. At the end of the transfusion a further sample (2-3 ml) was aspirated for posttransfusion levels.

Table I: Normal Fetal Hemoglobin and Hematocrit Values

Weeks of Gestation	Hematocrit (%)	Hemoglobin (g/dl)
18-20	35.8 ± 7.3	11.4 ± 2.6
21-22	38.5 ± 8.1	12.2 ± 2.8
23-25	38.6 ± 6.5	12.4 ± 2.3
26-30	41.5 ± 7.1	13.3 ± 2.3

Results

Thirty patients with Rh isoimmunization had a total of 49 cordocenteses. On 19 occasions the umbilical cord was entered transplacentally and on 30 it was punctured transamniotically. In 40 of 49 cordocenteses, the fetal hematocrit was

below the normal range for gestation and fetal intravascular blood transfusion was given. At the time of the first transfusion, 12 (40%) fetuses were hydropic.

The mean gestational age at initial transfusion was 27 weeks (range 19-34 weeks) (Table II). The mean pretransfusion fetal hemoglobin was 6.23 g/dl (range 3.5-11.6 g/dl); postransfusion it was 12.5 g/dl (range 7.5-15.6 g/dl). The mean donor hematocrit was 68 percent (range 60-82%). The transfused blood volume was 20-110 ml (mean 64 ml). The mean interval between transfusions was 19 days (range 7-33 days). The rate of decrease of fetal hemoglobin following a transfusion was 0.12-0.42 g/dl/day (mean 0.30 g/dl/day). In four of 12 hydropic fetuses reversal of hydrops was observed after multiple consecutive transfusions. In eight patients severe hydrops did not resolve despite treatment.

Table II: Cordocentesis and Intravascular Transfusions (IVT) According to the Gestational Ages

Weeks of Gestation	FBS (N)	IVT (N)
18-20	–	1
21-24	–	8
25-28	–	10
29-32	2	14
> 33	7	7

There were three intrauterine fetal losses and two postpartum infant losses. The gestational weeks of the intrauterine losses were 22, 25 and 28 weeks, respectively, and all were hydropic at the time of admittance. One of the losses was directly related to the procedure. This case terminated by immature labor because of chorioamnionitis. The remaning two cases ended by intrauterine death at one and two weeks following the procedures. These two losses were probably related to inadequate transfusion volumes to correct the fetal anemia because of technical difficulties.

There were two postpartum losses. The first infant, to whom only fetal blood sampling was performed, was delivered at 33 weeks, was 1270 g and had intrauterine growth retardation. The mother had class II cardiac disease and preeclampsia. The infant died 19 days after the delivery because of pulmonary infection not related to the isoimmunization. The second infant, who had two successful transfusions at 23 and 28 weeks of gestation, was delivered at the 32nd week. He died eight days after delivery because of prematurity and acute renal failure.

Discussion

The results of this preliminary study show that intrauterine intravascular blood transfusion can be performed as early as 19 weeks of gestation and until the third trimester. It is a relatively safe and effective method of fetal therapy. The

overall fetal survival rate in our study was 83.3 percent including all fetal blood samplings. If only fetal intrauterine transfusions are taken into account this rate was 81 percent, which is comparable with those in the literature (Table III).

Table III: Comparison of Survival Rates After Straight Intravascular Transfusion in Seven Studies

	No. of Cases	Overall Survival (%)	Survival of Hydrops (N)
Rodeck et al.[5]	19	84	11/13
de Crespigny et al.[6]	4	75	1/4
Grannum et al.[7]	26	82	16/20
Berkowitz et al.[8]	16	76	–
Brass et al.[9]	23	85.7	5/6
Önderoğlu et al.	30	83.3	7/12

Most of our blood transfusions were done into the umbilical vein. The advantages of transfusing into the vein are: a) the sonographic observation of the intravascular flow of blood provides constant reassurrance that the tip of the needle has not slipped into the Wharton's jelly, where injection of 0.5 ml of blood could lead to cord tamponade and fetal death, and b) fetal bradycardias occur more often when transfusing into an artery than a vein, presumably as a result of a procedure-related spasm of the more muscular umbilical artery.

Transplacental rather than transamniotic entry to the umbilical cord reduces the risk of displacement of the needle by fetal movements. Furthermore, since the amniotic membrane is not punctured, transplacental cordocentesis avoids both leakage of amniotic fluid and intra-amniotic fetal bleeding. However, with this route, fetomaternal hemorrhage is more than in the transamniotic route and the severity of the disease can be increased.

One of the theoretical risks of the procedure is the possibility of fetal exsanguination from the puncture point on the umbilical cord. However, the duration of the bleeding from the puncture point after withdrawal of the needle was clearly visible on the scope and noted in each case. In our series there was not significant bleeding from the puncture site and no complication related to the puncture was observed.

A recent review of the literature suggested that 33 percent of fetal mortality was associated with isoimmune-induced hydrops[10]. In addition, most losses following intrauterine intravascular transfusion in hydropic fetuses did not appear to be procedure related[8, 11, 12]. Consistent with those reports, we observed that all the fetuses who died in utero were hydropic at the administration; only one in utero death was related to the procedure itself.

In conclusion, intrauterine intravascular fetal blood transfusion is the procedure of choice for Rh disease of the fetus. Especially it is the only procedure capable of treating the most severely affected fetuses, namely those with hydrops fetalis. It enables anemia to be corrected efficiently, hydrops to be reversed and in most cases, leads to a mature healthy newborn requiring minimal treatment during the neonatal period. As opposed to the intraperitoneal approach, it is possible with the intravascular route to obtain information about the hematologic and acid-base status and biochemical data of the affected fetus.

Cordocentesis and intravascular transfusion require an experienced team and a laboratory capable of performing a variety of tests on a small volume of specimen. It is not practical from the standpoint of personnel, costs, and experience for every hospital to offer a similar service. These facilities must be regionalized to maximize both safety and efficacy.

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