

FETAL OUTCOME FOLLOWING INTRAUTERINE INTRAVASCULAR TRANSFUSION IN RHESUS ALLOIMMUNIZATION

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ABSTRACT

The outcome of 14 pregnancies with severe rhesus alloimmunization was analyzed over a period of 16 months. Group A consisted of 7 cases who received ultrasound guided intravascular intrauterine packed red blood cell transfusions via the umbilical vein after determining fetal blood group and hematocrit. The outcome of these cases was compared with another 7 cases (Group B), who did not require intrauterine transfusions. The 7 cases in Group A received a total of 25 intrauterine transfusions between 25 to 33 weeks gestation. Procedure related complications encountered were transient fetal bradycardia on 4 occasions, difficulty in cord cannulation due to fetal movements in 2 cases and transient bleeding at puncture site in 2 cases. These complications were not associated with any maternal or fetal consequences. There was no procedure related mortality.

Mean cord hemoglobin in Group A (12.52 g/dl) was significantly higher ($p < 0.05$) than in Group B (8.5 g/dl), and mean cord indirect serum bilirubin was significantly lower ($p < 0.1$) in Group A (2.5 mg/dl) than in Group B (5.8 mg/dl). Three neonates in Group A required one exchange transfusion each, as compared to all 7 in Group B who required a total of 12 exchange transfusions. All neonates in Group B survived, whereas 2 expired in Group A, one of severe in-

travascular coagulopathy and the other due to prematurity and hyaline membrane disease.

In spite of the availability and widespread use of anti-D gammaglobulin prophylaxis, rhesus hemolytic disease of the newborn still poses an appreciable problem in our country. Before the advent of intravascular intraumbilical transfusion (IUT) fetuses severely sensitized due to Rh alloimmunization were managed by intraperitoneal transfusion (IPT) of blood, albeit with a poor outcome (1-3). Unfortunately IPT was rarely, if ever, successful particularly in a hydropic fetus wherein the lymphatics are waterlogged making the procedure ineffective. Also the traumatic nature of IPT increased the procedural mortality (4).

Rodeck *et al.* (5) introduced a method of direct intravascular transfusion of fetuses between 23 to 36 weeks of gestation under fetoscopic control. However, beyond 26 to 28 weeks gestation,

travascular coagulopathy and the other due to prematurity and hyaline membrane disease.

Percutaneous ultrasound guided umbilical blood transfusions directly into the vascular system appears to be safe in experienced hands and has the potential to improve the prognosis of the severely alloimmunized fetus.

Key words: Intrauterine transfusion, Exchange transfusion, Rhesus alloimmunization, Fetal therapy.

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fetoscopic transfusion becomes technically difficult(6). The use of real time ultrasound guided intrauterine intraumbilical blood transfusion has significantly improved the survival and outcome of such fetuses(7,8). This communication presents our experience following ultrasound guided IUT in severe rhesus hemolytic disease.

Subjects and Methods

During a 16 month period from November 1992 to March 1994, seven pregnant women with evidences of severe rhesus alloimmunization received a total of 25 IUT between 25 to 33 weeks gestation, after informed consent and explanation of procedural details and risks. Criteria for IUT were a peak Rh antibody titre $\geq 1:64$, amniotic fluid delta optical density (AOD) at 450 nm in Lileys upper zone II or in Zone III at about 24 to 30 weeks of gestation indicative of severe fetal hemolysis, and ultra-sonographic (USG) evidence of hydrops fetalis, if present.

After maternal sedation with 25 mg intravenous promethazine and 30 mg pentazocine and USG assessment of fetus, placenta and cord insertion, a 21 gauge 89 mm spinal needle was guided into the umbilical cord at its site of placental insertion. "O" negative packed red blood cells (RBC) previously crossmatched with maternal serum was then transfused. The volume of RBC to be transfused was calculated from a normogram based on donor and fetal hematocrit, fetoplacental blood volume and gestational age(8). The hematocrit of packed RBC transfused ranged from 40 to 65%, the volume transfused at a time ranged from 50 to 220 ml, and the proce-

dures time ranged from 30 to 60 minutes. Post transfusion blood sample was taken for hematocrit estimation to check adequacy of the transfusion. Close fetal surveillance was maintained during and for 48 hours following the procedure. IUT were repeated at 7 to 15 days intervals.

Outcome of fetuses in Group A was compared with another 7 Rh alloimmunized fetus (Group B) who were not severely affected before 30 to 32 weeks gestation, and hence did not require IUT. Premature induction of labor or delivery of fetus was done at about 34 to 36 weeks gestation, based on amniotic fluid bilirubin zone. The criteria for exchange transfusion (ET) in both groups was cord hemoglobin (Hb) ≥ 10 g/dl, cord indirect serum bilirubin (ISB) ≥ 4 mg/dl or a rise in ISB >1 mg/dl/hour and positive direct antiglobulin test (DAT).

Results in Groups A and B were statistically analyzed using the Chi square test.

Results

A total of 25 IUT were performed in the 7 cases in Group A (*Table I*). Six of these were delivered by elective Cesarean section between 34 to 36 weeks gestation and their birth weight ranged from 2008 to 2500 g (mean 2372 g); however, one case, who delivered spontaneously at 28 weeks gestation weighed 1.1 kg. Two cases were born with hepatosplenomegaly and anemia and had cord Hb of 5.9 and 8 g/dl, respectively. The cord fib in this group ranged from 5.9 to 18 g/dl (mean 12.52 g/dl), and cord ISB ranged from 0.8 mg/dl to 4.28 mg/dl (mean 2.5 mg/dl). The

TABLE I—Antenatal Details of Group A

Case No.	Previous deaths due to Rh disease	Peak Rh antibody titre	Gestation in weeks/ Lileys zone (amniotic fluid Δ OD)	Gestation in weeks at first IUT/ Initial USG findings	Number IUT performed/ Total volume (ml) of RBC transfusion	Hematocrit before first IUT/ After last IUT
1.	3	1:256	28/III (0.7)	29/Ascites	4/400	18/47
2.	1	1:1024	26/II (0.2)	27/N	5/300	24/36
3.	1	1:128	24/III (0.3)	25/N	5/300	18/45
4.	2	1:64	29/II (0.2)	30/N	3/350	22/46
5.	1	1:256	29/II (0.2)	30/N	2/265	10/55
6.	1	1:256	24/III (0.3)	25/N	2/280	22/45
7.	3	1:1024	24/III (0.3)	25/Ascites, pericardial effusion, hepatosplenomegaly	4/300	9/45

N = Normal

IUT = Intrauterine transfusion

Δ OD = Delta optical density at 450 nm

preprocedural direct antiglobulin test (DAT) was strongly positive in all cases, whereas at birth 6 of 7 cases had negative DAT while 1 had a weakly positive DAT.

In Group B (*Table II*), 6 cases delivered vaginally at term and had birth weight ranging from 2320 to 2680 g (mean 2510 g). The one case who was delivered by emergency Cesarean section for a nonreactive nonstress test at 38 weeks gestation weighed 2060 g. Three cases in this group were born with hepatosplenomegaly and anemia. Cord Hb ranged from 4 to 14.7 g/dl (mean 8.5 g/dl) and cord ISB ranged from 3.28 to 11.5 mg/dl (mean 5.8 mg/dl).

The mean cord Hb level in Group A

(12.52 gVdl) was significantly higher ($p < 0.05$) than Group B (8.5 g/dl) while mean cord ISB was significantly lower ($p < 0.1$) in Group A (2.5 mg/dl) as compared to Group B (5.8 mg/dl). Neonates in Group A required a total of 3 ET as compared to 12 ET in Group B (*Table III*).

In Group A, 2 of 7 cases expired (28.57%), one of disseminated intravascular coagulopathy and the other who delivered at 28 weeks gestation expired of hyaline membrane disease. There was no mortality in Group B.

Discussion

In 1963 Sir William Liley(2) performed the first IPT for severe rhesus sensitization. Blood placed in the fetal

TABLE II—Antenatal Details of Group B

Case No.	Previous deaths due to Rh disease	Peak Rh antibody titre	Gestation in weeks/ Lileys zone (Amniotic fluid Δ OD)	Gestation in weeks/ Initial USG findings
1.	1	1:128	35/II (0.2)	30/N
2.	2	1:128	33/II (0.2)	30/N
3.	2	1:64	32/I (0.1)	29/N
4.	2	1:32	34/II (0.1)	25/N
5.	3	1:128	34/II (0.2)	25/N
6.	0	1:128	32/II (0.15)	30/N
7.	1	1:32	33/II (0.16)	35/N

N = Normal

Δ OD = Delta optical density

peritoneal cavity can be absorbed via the subdiaphragmatic lymphatics from which it can gain access to the circulation. This procedure, however, does not allow determination of fetal anemia and the survival, success and complication rates have differed from one centre to another(9-12y.

Intravascular transfusion *in utero* is undoubtedly technically more exacting and inherently superior than IPT. By quantification of pre and post procedural hematocrit and checking fetal blood group, inappropriate transfusions can be avoided. Rodeck *et al* reported a survival rate of 84% with fetoscopic guided intravascular approach. The major problem with this approach is the technical difficulty as the amniotic fluid gets increasingly opaque with increasing gestation. Over the last decade a number of workers(13-17) have utilized the ultrasound guided approach for intrauter-

ine intraumbilical blood transfusion.

Although there is wide acceptance of intravascular transfusion into the cord vessels at its placental insertion site, problems with this technique may be encountered. The cord vessel may be rendered inaccessible by intervening fetal parts or while dealing with a posterior placed placenta in an obese patient it may be difficult to guide the needle with precision into the vessel. In the present series no patient had a posterior placed placenta: however, 2 patients had anterior placed placentae requiring crossing the placenta before entering the placental end of cord.

On 2 of 25 occasions we faced difficulty in cord cannulation due to the dislodgement of needle caused by fetal movements. Although direct injection of curare into the fetal thigh has been documented(7), maternal sedation prior to

TABLE III-Post-natal Details in Groups A and B

Group A Case No.	Gestational age (weeks)/ Birth weight (g) Condition at birth	Cord Blood		ET n=	Outcome	Group B Case No.	Gestational age (weeks)/ Birth weight (g) Condition at birth	Cord Blood		ET n=	Outcome
		Hb (g/dl)	ISB (mg/dl)					Hb (g/dl)	ISB (mg/dl)		
1.	34/2100 Good	12	3.05	Nil	Discharged	1.	37/2300 Hepatosplenomegaly and anemia	4.0	3.28	2	Discharged
2.	36/2500 Hepatosplenomegaly and anemia	5.9	3.77	Nil	Expired of DIC	2.	38/2700 Good.*	9.0	4.81	2	Discharged
3.	35/2500 Good	14.2	2.0	1	Discharged	3.	36/1800 Hepatosplenomegaly and anemia	5.0	11.5	3	Discharged
4.	35/2500 Good	13.6	0.8	Nil	Discharged	4.	35/2500 Good	14.7	3.6	1	Discharged
5.	35/2400 Good	18.0	2.1	1	Discharged	5.	33/2100 Hepatosplenomegaly and anemia	4.0	7.0	3	Discharged
6.	28/1100 Good	16.0	2.0	Nil	Expired of HMD	6.	35/2400 Good	10.0	4.0	1	Discharged
7.	34/2100 Hepatosplenomegaly and anemia	8.0	4.28	1	Discharged	7.	38/2800 Good	13.2	6.85	1	Discharged

DIC = Disseminated intravascular coagulopathy
 ISB = Indirect serum bilirubin
 ET = Exchange transfusion
 HMD = Hyaline membrane disease

the procedure is often sufficient to slow down or arrest fetal movements. Fetal bradycardia which was noted on 4 occasions and was transient has been documented(15,16) earlier. On 2 occasions transient bleeding from the puncture site was noted without apparent maternal or fetal consequence.

Of 7 cases who received IUT, 2 expired (28%). One died of severe hyaline membrane disease and prematurity and the other of intravascular coagulopathy. Hemorrhagic diathesis is a well recognized' complication of severe erythroblastosis and has been reported in a significant number of severely affected infants(18,19). Bleeding may occur as a result of bone marrow depression, or destruction of platelets on an immunological basis, or due to a coagulopathy secondary to hepatic dysfunction(20,21). There was no procedure related mortality in this study, although a procedural mortality of 2 to 3% has been reported earlier(17).

The timing of transfusion, and determination of the optimal amount of blood to be transfused need to be individualized on the basis of pretransfusion hematocrit and the subsequent rate of fall in hematocrit. There is usually an approximate drop of 1-2% per day in the hematocrit necessitating a transfusion interval of around 2 weeks in between IUT(22). In the present series, successive IUT were performed at 7-15 day intervals. In severe hydrops overtransfusion may aggravate the preexisting cardiac failure. In this series, the maximum volume of RBC transfusion given at one occasion was 220 ml but did not result in fetal cardiac failure as the fetoplacental unit can accommodate large volumes(15).

In the present study no effort was made to evaluate and compare the long term outcome in the two groups. An effort is, however, being made in an ongoing study to evaluate long term outcome of those who received IUT. The outcome of those fetuses who received IUT would have been uniformly poor had no antenatal intervention been done in them, given their previous bad obstetric history and present bad biochemical and hematological parameters.

Ultrasound guided intravascular intrauterine transfusion of blood into the umbilical circulation represents a significant step towards the management of the severely rhesus alloimmunized fetus. In most cases hydrops can be reversed well before delivery(16), which may be planned between 35-36 weeks. This improvement in antepartum management has greatly reduced fetal mortality due to rhesus alloimmunization as well as simplified the neonatal management as non hemolyzing babies are delivered at a mature stage.

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