among schoolchildren, young adults, and female schoolteachers suggests environmental associations with educational establishments and seasons of the year. Although numbers are small, they also suggest transmission between female subjects and from female to male subjects or vice versa, but not, as a rule, between male subjects.

Temporal clustering observed early in the course of the study might have been due to initial enthusiasm of the referring practitioners, but examination of their referral patterns suggested that this was not the case. A determined search for an infective organism and a transmission mechanism now seems justifiable.

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Ultrasound-guided fetal intravenous transfusion for severe rhesus haemolytic disease

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Abstract

Intrauterine, intraperitoneal transfusion is associated with a poor survival rate in fetuses with hydrops and low gestational age. A method of direct fetal intravenous transfusion was used in two fetuses. One fetus with severe rhesus haemolytic disease was given transfusions in the 29th and 30th weeks of gestation, using an ultrasound-guided needle through the hepatic part of the umbilical vein without fetoscopy. In another fetus, an experimental cannulation of the umbilical vein succeeded in the 23rd week of gestation.

Ultrasound-guided fetal intravenous transfusion avoids the use of fetoscopy, which has limitations, and may improve the prognosis for rhesus-sensitised fetuses.

Introduction

Intraperitoneal transfusion of unborn infants with severe rhesus haemolytic disease gives poor results when the fetus has hydrops and a low gestational age.¹ Probably the fetal ascites prevents adequate resorption of erythrocytes, so that in many cases early delivery remains the treatment of choice.²

Rodeck *et al*³ introduced a method of direct intravascular transfusion of fetuses under fetoscopic control at 23 to 26 weeks of gestation. Beyond that age, however, the method could not

be used because of problems with the fetoscopic technique. We have therefore tried direct intravenous transfusion of fetuses through the hepatic part of the umbilical vein using a thin needle guided by ultrasound. The procedures conformed with the Declaration of Helsinki 1975.

Materials and methods

Ultrasound scanning was performed with linear real-time equipment (Aloka). Gestational age was assessed from biparietal diameter and the fetus checked for hydrops and ascites. The intrauterine, intravenous transfusions were carried out under local anaesthesia.

A guide needle (1.2 × 150 mm) was introduced into the fetal abdomen 3-4 mm from the hepatic part of the umbilical vein, and through this a fine needle (0.6 × 180 mm) was inserted into the lumen of the umbilical vein. The procedure was visualised by ultrasound, the needle being passed through a special puncture transducer mounted on the scanner. The puncture transducer has a slit in the centre for introducing the needle, which may be fastened or released from the transducer with a wheel at the top. Also the puncture transducer was fitted with a movable scale calibrated in centimetres, by which the route of the needle could be monitored on the oscilloscope. When we scanned with the puncture transducer the scale was pointed directly at the umbilical vein and the tips of the guide needle and fine needle were visualised on the oscilloscope (figure).

Infusing blood into the umbilical vein produced some echoes, and the dispersal of the blood in the fetal vessels was seen on the oscilloscope. The fetal heart rate was measured before and after the transfusion.

Results

CASE 1

A 33-year-old woman, blood group O, rhesus-negative, was in her fifth pregnancy. The first had ended in spontaneous abortion, but the

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second (1974) had resulted in a normal delivery without rhesus isoimmunisation; she had not been given immunoprophylaxis. The third pregnancy was complicated by anti-D isoimmunisation, but the child was only slightly affected and no exchange transfusions were necessary. The fourth pregnancy was terminated.

The patient was transferred to this hospital from the local obstetric department at 29 weeks after heavily yellow-stained amniotic fluid had been obtained by amniocentesis. Ultrasonic assessment showed a fetus of normal size for 29 weeks. Fetal ascites was present, and the amniotic fluid bilirubin concentration was $14 \mu\text{mol/l}$ (0.8 mg/100 ml), which was in the "severely affected" zone of our prognostic chart.¹ The

Transverse section of fetal abdomen. C = Cord. A = Ascites in fetal abdomen. UV = Umbilical vein. N = Tip of needle in lumen of umbilical vein. L = Liver tissue.

patient was pretreated with betamethazone 12 mg daily for two days, ritodrine 10 mg four times daily, and phenobarbitone 100 mg daily.

We planned an intraperitoneal transfusion with 50 ml group O, rhesus-negative (cde/cde) erythrocytes suspended in sterile isotonic sodium chloride (packed cell volume 0.60 (60%)). To prevent immunological complications the cell suspension was irradiated with 2160 rads for four minutes before use. During the transfusion we observed a dilated umbilical vein and, with the informed consent of the mother, gave a further 10 ml blood into the hepatic part of the vein. A fetal blood sample, which looked like reddish serum, showed the fetus to be group A, rhesus-positive and gave a strongly positive reaction to a direct Coombs test.

A second intravenous transfusion of 25 ml was given one week later. A fetal blood sample before the second transfusion showed a ratio of fetal to adult erythrocytes of 37:63.

At 32 weeks a girl of 1700 g was delivered by caesarean section. The Apgar score was 3 at one minute and 10 at five minutes. The umbilical cord haemoglobin concentration was 6.4 g/dl and the bilirubin concentration $144 \mu\text{mol/l}$ (8.4 mg/100 ml). The ratio of fetal to adult erythrocytes was 22:78. The infant had a slight bluish discoloration around the umbilicus, possibly a slight haematoma. During the next two days five exchange transfusions were given because of high and rising serum bilirubin concentrations, the highest being $393 \mu\text{mol/l}$ (22.9 mg/100 ml). There were no further complications.

CASE 2

A 25-year-old woman in the 23rd week of pregnancy was transferred to this hospital for termination after a prenatal diagnosis of genetic disease (chromosomal abnormality). There was no evidence of rhesus isoimmunisation. The patient gave permission for an ultrasound-guided puncture for fetal blood sampling. Biparietal diameter was compatible with the age of gestation. Puncture of the hepatic part of the umbilical vein was performed under epidural anaesthesia. The tip of the needle was visualised on the oscilloscope in the lumen of the vein and 0.5 ml blood withdrawn. Analysis on a Coulter counter showed 100% fetal blood. Subsequently 40 mg dinoprost trometamol (Amoglandin) was instilled into the amniotic cavity for termination.

Comment

Intraperitoneal transfusion of unborn infants has a survival rate of 25-70%,¹⁻⁴ depending on the prevalence of fetal hydrops and the gestational age when the transfusion is started. Both fetal hydrops and low gestational age appreciably reduce the success rate, possibly because of poor resorption of erythrocytes due to ascites. Despite technical improvements in the transfusion procedure, primarily the use of ultrasound in placing the transfusion needle, rhesus isoimmunisation may be so severe in some cases that traditional intraperitoneal transfusions are not effective and fetal prognosis is poor. In an earlier study all 14 fetuses with amniotic fluid bilirubin concentrations above $10 \mu\text{mol/l}$ (0.6 mg/100 ml) died perinatally.¹

Direct intravascular fetal transfusion might theoretically solve these problems. This treatment could be established at an earlier stage of gestation and might prevent fetal ascites, and thus remove the problem of peritoneal resorption of erythrocytes. Furthermore, the technique permits precise evaluation of the haematological state of the fetus. Rodeck *et al*³ described direct intravascular transfusion with the use of fetoscopy. The authors believe that the fetoscopic technique has some limitations: by 26 weeks of gestation the uterus may be too large, the amniotic fluid too cloudy, and the quantity of blood needed for transfusion too great.

In our two patients we succeeded in obtaining fetal blood samples at 23, 29, and 31 weeks of gestation, twice performing a direct intravenous transfusion through the hepatic part of the umbilical vein.

In severe rhesus isoimmunisation the umbilical venous flow shows a negative correlation with the umbilical cord haemoglobin concentration.⁵ This suggests that the diameter of the umbilical vein increases in fetal anaemia, which, if so, would make cannulation of the umbilical vein possible at later gestational ages and without the elective risk and morbidity from fetoscopy.

Knowledge of various factors—for example, the size of transfusion, the cardiovascular effects of transfusion, the importance of different blood variables in fetal blood—should be established, but we hope that direct intravenous fetal transfusion will improve the prognosis of high-risk, rhesus-sensitised fetuses that cannot be saved by traditional methods.

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