



Is intrauterine exchange transfusion a safe procedure for management of fetal anaemia?



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ABSTRACT

Objective: To study modalities and complications of intrauterine exchange transfusion (IUET) for the management of severe fetal anaemia.

Study design: Retrospective study of all IUET procedures performed between January 1999 and January 2012 at a regional centre. Characteristics of each procedure were studied to identify risk factors for complications. Survival rates according to the different aetiologies of anaemia were evaluated.

Results: In total, 225 IUET procedures were performed in 96 fetuses. Major indications were fetomaternal erythrocyte alloimmunization ($n = 80/96$, 83.3%) and parvovirus B19 infection ($n = 13/96$, 13.5%). Twenty-six percent of the fetuses (25/96) had hydrops fetalis before the first IUET. Intrauterine fetal death occurred after 2.7% (6/225) of procedures, premature rupture of the membranes occurred after 0.9% (2/225) of procedures, and emergency caesarean section was required after 3.6% (8/225) of procedures. Fetal bradycardia [odds ratio (OR) 37, 95% confidence interval (CI) 8.3–170; $p < 0.01$] and gestational age up to 32 weeks (OR 3.67; 95% CI, 1.07–12.58; $p = 0.038$) were significantly associated with complications after IUET. Complications occurred in 17.7% of pregnancies (17/96) and 7.5% of IUET procedures (17/225). The overall survival rate in the study cohort was 87.5% (84/96): 90% (72/80) in the alloimmunization group and 76.9% (10/13) in the parvovirus-infected group (NS).

Conclusion: IUET has a higher complication rate than simple intrauterine transfusion, and should be performed by well-trained specialists.

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Introduction

Numerous techniques exist for the treatment of fetal anaemia, such as intraperitoneal, intravascular by intrahepatic venous puncture or funipuncture transfusion (simple or exchange) [1]. The choice of procedure depends on gestational age, accessibility of the umbilical cord, and the clinician's experience.

Transfusion is widely practised as it improves the survival rates of anaemic fetuses [2,3]. However, it is a risky procedure with a complication rate of 3.1% [4]. Some complications may occur

secondary to vascular overload, particularly in cases of hydrops fetalis complicated with heart failure [5]. As such, intrauterine exchange transfusion (IUET) was proposed to avoid the transfusion of large volumes of blood and thus decrease the risk of vascular overload [6,7]. In addition, in cases of alloimmunization, the efficacy of transfusion therapy is more important when exchange transfusion is performed because this allows removal of the anti-erythrocyte antibodies, and reduces the number of incompatible erythrocytes in the fetal circulation. This technique has been evaluated previously [8,9] but none since the clinical use of the measurement of the peak velocity of systolic blood flow in the middle cerebral artery [10].

At the study hospital, IUET is the elective procedure in cases of fetal anaemia. The objective of this study was to evaluate the complication rate of IUET and the factors affecting this rate.

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Materials and methods

This retrospective study included all patients who underwent IUET between January 1999 and January 2012 at the study hospital. Ethical approval was granted by the French Committee of Obstetrics and Gynaecologic Research Ethics (CEROG OBS 2012-02-04).

Data on the obstetric history for each pregnancy, aetiology of fetal anaemia (feto-maternal alloimmunization with the antigens involved, parvovirus B19, etc.) and neonatal outcomes until discharge from the neonatal intensive care unit were collected.

Characteristics and technical conditions for each IUET were evaluated, including duration, umbilical cord haemorrhage (defined as continuous bleeding visible on ultrasound for more than 30 s), needle displacement and fetal bradycardia (defined as bradycardia lasting for more than 60 s). Complications after IUET, such as premature rupture of membranes (PROM) or preterm delivery within 7 days of transfusion, chorioamnionitis, emergency caesarean section due to fetal distress within 24 h of the procedure, fetal death and neonatal death, were notified. If more than one complication occurred after the same procedure and it was obvious that the first complication induced the others, all were considered as a single complication in the final analysis. In cases of simple transfusion or intraperitoneal transfusion, fetuses were included but only IUET cases were analysed.

In the first few years of the study, IUET was indicated when the optical index at 450 nm (DOD450) fell in Zone III of Liley's diagram. Over the course of the study, this technique was replaced by measurement of the peak velocity of systolic blood flow in the middle cerebral artery [10,11].

IUET was performed as described by Poissonnier et al. [8] using a 20-gauge needle. The needle was inserted preferentially in the umbilical vein, proximal to the placento-umbilical junction, under ultrasound guidance. The severity of anaemia was assessed using the haemoglobin level and the haematocrit measured during the procedure. Vecuronium bromide (Norcuron[®]), 0.1 mg/kg fetal weight, was injected in order to limit complications linked to fetal movements. An initial volume based on fetal weight and gestational age was transfused before commencing exchange. Blood component statuses were evaluated during IUET. The objective was to

increase fetal haemoglobin to 14–16 g/dL, with a difference between transfused and withdrawn volumes close to 0 ml. Ultrasound monitoring of the fetus was performed continuously throughout IUET, and fetal heart monitoring was performed before and after IUET in cases where the gestational age was ≥ 26 weeks.

IUET was performed until 34 weeks of gestation. Beyond this age, the issue of delivery was discussed with the perinatal specialists. The overall survival rate is based on the number of live infants discharged from the neonatal intensive care unit.

Statistics

In order to study the risk factors associated with complications, patients were classified into two groups: patients with no complications and patients with complications secondary to IUET. Qualitative variables are expressed as frequency and percentage, and quantitative variables are expressed as median and interquartile range or mean and standard deviation depending on the size of the cohort. Chi-squared test and Fisher's exact test were used to compare the qualitative parameters of the two groups, and the Mann–Whitney test was used to compare quantitative variables. Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI). $p < 0.05$ was considered to indicate significance. SAS software version 9.3 (SAS Institute Inc., Cary, NC 25513, USA) was used for statistical analyses.

Results

In total, 225 IUET procedures were performed in 96 fetuses between January 1999 and January 2012. Characteristics of the study population are summarized in Table 1. The most common indication for IUET was feto-maternal erythrocyte alloimmunization ($n = 199$ in 80 fetuses). Other non-immune aetiologies were parvovirus B19 infection ($n = 20$ in 13 fetuses), primary cytomegalovirus infection ($n = 1$ in one fetus), pyruvate kinase deficiency ($n = 2$ in one fetus) and severe feto-maternal haemorrhage ($n = 3$ in one fetus). In addition to IUET, three intraperitoneal and five intravascular simple intrauterine transfusions were performed in four fetuses (all in the alloimmunization group).

Table 1
Characteristics of the study population.

	Total ($n = 96$)	Alloimmunization group ($n = 80$)	Parvovirus group ($n = 13$)	<i>p</i> -Value
Age (years)	30 (27–35)	30 (27–35.5)	30 (24–30)	0.081
Parity	3 (2–4)	3 (2–4)	3 (2–3)	0.395
Maternal antibodies				
RH1		66 (82.5%)		
RH3 (Anti-E)		3 (3.8%)		
RH4 (Anti-c)		2 (2.5%)		
Kell		9 (11.2%)		
Presence of two antibodies		45 (56.2%)		
Presence of three antibodies		14 (17.5%)		
In-utero transfer	56 (58.3%)	44 (55%)	10 (76.7%)	0.12
Hydrops fetalis	25 (26%)	12 (15%)	11 (84.6%)	<0.01
GA at first IUET	26 (22–24)	26 (22–29)	23 (23–24)	0.049
Number of IUET procedures:				
1		23 (28.8%)	6 (46.1%)	0.002
2		21 (26.2%)	7 (53.9%)	
≥ 3		36 (45%)	(0%)	
Other procedures:				
IPT	3	3	0	
Medium term	18.8 (16.9–20.7)	18.8 (16.9–20.7)		
IUT	5	5	0	
Medium term	23 (18–28)	23 (18–28)		

Results are presented as median (interquartile range) or n (%).

GA, gestational age; IUET, intrauterine exchange transfusion; IPT, intraperitoneal transfusion; IUT, intrauterine transfusion.

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