

# COELOCENTESIS: A STUDY OF SHORT-TERM SAFETY

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## SUMMARY

Coelocentesis was performed in 20 singleton pregnancies at 6–10 weeks of gestation and 2–13 days before planned termination. The control group consisted of 100 women who were also undergoing planned termination and were matched with the study group for maternal age and gestation. During the follow-up period, there were five miscarriages (25 per cent) after coelocentesis and five in the control group (5 per cent) ( $\chi^2=6.68$ ;  $P<0.01$ ). The high risk of miscarriage following coelocentesis makes the technique unsuitable for early prenatal diagnosis. © 1997 by John Wiley & Sons, Ltd.

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## INTRODUCTION

Prenatal diagnosis in the first trimester of pregnancy provides early reassurance to most mothers that their fetus is not affected by the genetic disorder under investigation. In those with abnormal results, termination of pregnancy may be performed earlier in pregnancy when the surgical risks and psychological trauma are less than with late abortion. Both chorionic villus sampling (CVS) and amniocentesis can be performed very early in pregnancy. However, their use has been restricted to after 10 weeks due to concerns regarding the safety of these procedures. CVS performed earlier than 66 days' gestation is associated with limb reduction deformities (Firth *et al.*, 1991). Amniocentesis before 10 weeks' gestation has a high rate of diagnostic failure (Jorgenson *et al.*, 1992) and there is an increased risk of fetal loss if performed at 10–13 weeks' gestation when com-

pared with CVS at the same gestation (Nicolaidis *et al.*, 1994).

Coelocentesis, which involves aspiration of fluid from the extraembryonic coelom, can be performed between 6 and 12 weeks' gestation and is technically no more difficult than CVS or amniocentesis (Jauniaux *et al.*, 1991; Wathen *et al.*, 1991). Examination of coelomic fluid cells has enabled accurate prediction of fetal sex using fluorescent *in situ* hybridization techniques (Jurkovic *et al.*, 1993), detection of the sickle gene by DNA analysis (Jurkovic *et al.*, 1995), and, more recently, cytogenetic analysis (Crüger *et al.*, 1996). Aspiration of coelomic fluid can be performed without the needle traversing the placenta or amniotic membrane, providing a potentially safer invasive method for prenatal diagnosis. The aim of our study was to investigate the short-term safety of coelocentesis by examining the miscarriage rate within the week following the procedure.

## MATERIALS AND METHODS

This was a prospective controlled observational study of women due to undergo termination of

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pregnancy for psychosocial indications. In 20 cases, coelocentesis was performed 2–13 days before termination and the rate of miscarriage was compared with that in 100 matched controls that did not have coelocentesis.

#### Recruitment of patients

In our hospital, all patients requesting termination of pregnancy first have an ultrasound scan to determine the gestational age and the presence of fetal heart action. They are then seen by a specialist nurse and a doctor for counselling. Those who wish to proceed with a termination are asked to sign a consent form and are given a date for the operation. For this study, the patients were subsequently approached by a different doctor and offered the option of having coelocentesis for research purposes. The study protocol was approved by the Research Ethics Committee of King's College Hospital and written informed consent was obtained from all subjects.

#### Study group and controls

During an 8-month period, 320 patients with an uncomplicated singleton pregnancy of 6–10 weeks' gestation were approached. The study group consisted of 20 patients who agreed to have coelocentesis.

Blinded to outcome, each study patient was matched with five controls of similar maternal age and gestation from the group that declined coelocentesis.

#### Coelocentesis

0.5–2.5 ml of coelomic fluid was aspirated under ultrasound guidance using a 5 MHz transvaginal probe (Aloka SSD-500; Aloka Co., Tokyo, Japan) and a 20 G spinal needle as described previously (Jauniaux *et al.*, 1991). No local anaesthetic or sedation was used and participants were asked to evaluate the pain associated with the procedure using a verbal analogue score of 0–10. Following coelocentesis, the pregnancies were scanned continuously for 5 min to detect major changes in fetal heart rate or signs of bleeding into the gestational sac.

#### Follow-up

The ultrasound examination was repeated in all women at the time of admission for pregnancy

Table I—Comparison of demographic data and outcomes in the coelocentesis and control groups

	Coelocentesis (n=20)	Controls (n=100)
Maternal age (years)*	27.6 (17–41)	27.7 (15–40)
Gestational age (weeks)*	8.0 (6–10)	7.9 (6–10)
Interval to termination (days)*	7.4 (2–13)†	6.7 (1–20)
Miscarriage rate (%)	5 (25)	5 (5)‡

\*Mean and range.

†n=18.

‡ $\chi^2=6.68$ ,  $P<0.01$ .

termination. Those patients who developed pain or bleeding before their operation were seen immediately for clinical assessment and an ultrasound scan. The diagnosis of a missed abortion was made in the presence of an intact gestational sac that contained hypoechoic fluid and a clearly defined embryonic pole with no visible heart action. Other cases of pregnancy failure were classified as incomplete miscarriages.

#### Data analysis

Statistical calculations were carried out using the software package SPSS<sup>®</sup> for Windows (version 5.0) (SPSS Inc., Chicago, IL, U.S.A.). The means of unpaired groups were compared using the Mann-Whitney test. The frequencies of miscarriage in the study and control groups were compared using the chi-squared test with Yates' correction.

## RESULTS

Clear coelomic fluid was successfully aspirated in all 20 cases after a single puncture of the extraembryonic coelom. Eighteen patients underwent termination of pregnancy but two decided to continue with their pregnancies. There were no significant differences between the coelocentesis and control groups with respect to mean maternal age, gestational age, or interval from the initial scan to termination of pregnancy (Table I). The miscarriage rate was 5 per cent in the control group and 25 per cent following coelocentesis ( $\chi^2=6.68$ ;  $P<0.01$ ). All patients with failed pregnancies in the control group had missed abortions,

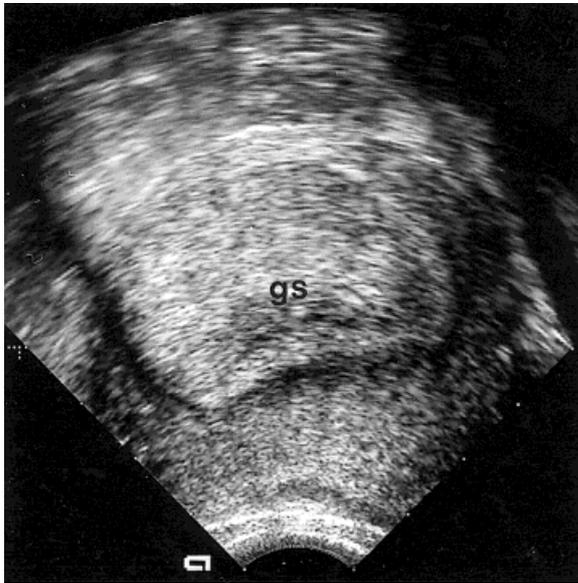


Fig. 1—Incomplete miscarriage following coelocentesis. The gestational sac (gs) is filled with echogenic material

whilst one patient in the coelocentesis group had a missed abortion and the other four, incomplete miscarriages. All cases of incomplete miscarriage had a specific appearance on ultrasound scan; the gestational sac was filled with echogenic material and the fetus was no longer discernible, although no products had been passed (Fig. 1). In patients undergoing sampling, one miscarriage occurred at 7 weeks and the remaining four during the eighth and ninth week. In the control group, all miscarriages occurred before eight weeks' gestation.

A comparison of patients with failed and viable pregnancies following coelocentesis is given in Table II. There were no significant differences in maternal age, gestational age, or the interval

between the procedure and termination of pregnancy. There were no significant differences in the volume of aspirated fluid between failed and viable pregnancies, and patients reported similar low levels of discomfort. One of the women who decided to continue with her pregnancy had a preterm delivery of a normal neonate at 25 weeks. The baby died after 3 days, due to immaturity and respiratory distress syndrome. The patient was subsequently diagnosed as having cervical incompetence and had an emergency cervical suture inserted in her next pregnancy, which proceeded to 36 weeks' gestation. The second patient had an uncomplicated pregnancy following coelocentesis and delivered a healthy neonate at term.

## DISCUSSION

This study has shown that coelocentesis is associated with a high rate of miscarriage following the procedure. In general, the risk of miscarriage increases with maternal age, is inversely related to gestational age, and is higher in women who experience bleeding in early pregnancy (Smith and Buyalos, 1996; Goldstein, 1994; Hill *et al.*, 1991). The reported rate of fetal loss in uncomplicated early pregnancies following the demonstration of cardiac activity by ultrasound is between 2 and 7 per cent, which is similar to the findings in our control group. The study was controlled for maternal and gestational age, and therefore the excess of miscarriages in the coelocentesis group could not be explained by the differences in these parameters between the study and control groups.

The ultrasound appearance of the miscarriages following coelocentesis was unusual and very different from that of spontaneously failed pregnancies seen in routine practice. In missed

Table II—Comparison of patients in the coelocentesis group with respect to outcome

	Miscarriage (n=5)	Non-miscarriage (n=15)
Maternal age (years)*	25.4 (24–28)	27.8 (17–41)
Gestational age (weeks)*	8.2 (7–9)	7.7 (6–10)
Interval to terminations (days)*	7.4 (2–11)	7.4 (2–13)†
Volume of aspirated fluid (ml)*	1.1 (0.5–2.0)	1.0 (0.5–2.5)
Pain score*	2.8 (2–4)	3.5 (1–6)

\*Mean and range.

†n=13.

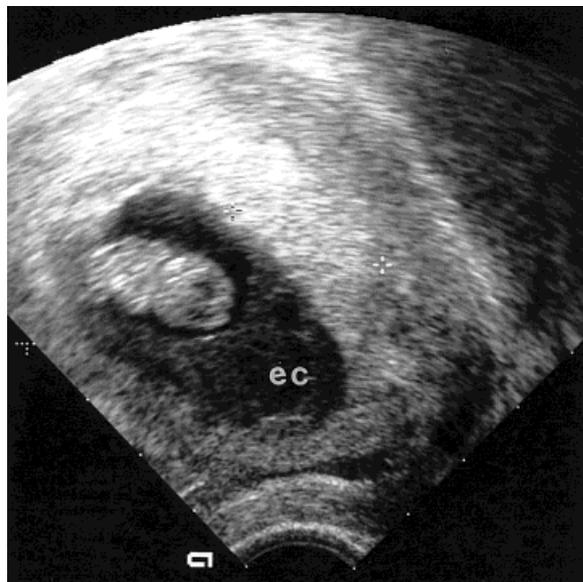


Fig. 2—Continuing pregnancy following coelocentesis. The exocoelomic cavity (ec) contains hyperechoic material

abortions, the embryo is usually at the bottom of the gestational sac with absent heart action. The sac itself is intact and the amniotic and coelomic fluids are hypoechoic, similar to normal pregnancies. In spontaneous incomplete miscarriages, the gestational sac is collapsed, the fetus is not visible, and there is a variable amount of echogenic retained placental tissue within the uterine cavity. Four out of five miscarriages following coelocentesis presented with an intact gestational sac which was filled with echogenic material. It was impossible to visualize the fetus within the sac and there were no cardiac pulsations on B-mode and Doppler examination. These morphological appearances are highly suggestive of a major haemorrhage inside the gestational sac.

The two cases where the women decided to continue with their pregnancy also provided evidence of the profound effect of coelocentesis on the coelomic cavity. In both cases, the exocoelomic space was filled with hyperechogenic material which persisted until the coelomic cavity was obliterated in the early second trimester (Fig. 2). These features are compatible with previous haemorrhage into the fluid and are similar to the appearance of amniotic fluid following amniocentesis or antepartum haemorrhage.

Miscarriages in the coelocentesis group did not only appear morphologically different, but also

occurred later in pregnancy compared with the control group. None of the spontaneous miscarriages occurred after 7 weeks of gestation whilst 80 per cent of the miscarriages following coelocentesis occurred during the eighth and ninth week. Both the morphology and the gestational age of miscarriages in the study group indicate that the increased rate of pregnancy loss following coelocentesis is a true rather than a chance finding.

Aspiration of coelomic fluid in all our patients was uneventful and we could not detect any technical problems during the procedure to explain why miscarriages occurred in some, but not other pregnancies. There were no blood-stained samples and the mean volume of aspirated fluid was around 1 ml. Considering the low density and poor viability of cells in coelomic fluid, it cannot be reduced further if cell culture or DNA analysis is to be attempted (Paton *et al.*, 1994). A 20-gauge needle was used in all cases, the finest that allows easy and successful aspiration of coelomic fluid, which is more viscous than amniotic fluid. We have tried very fine 22 and 23 gauge needles in the past and found that the aspiration of coelomic fluid is often impossible. Furthermore, these needles tended to bend whilst traversing the myometrium which led to an increased number of multiple punctures and a lower success rate of the procedure. Both of these factors may compromise the safety of coelocentesis more than the use of a larger-diameter needle.

The increased miscarriage rate following coelocentesis cannot be explained by the proportion of blood-stained samples or the number of uterine entries, which are parameters known to affect the outcome in CVS and amniocentesis. Haemorrhage into the gestational sac could have been caused either by partial detachment of the chorion or by influx of maternal blood into the sac following withdrawal of the needle. The negative pressure within the exocoelomic cavity generated during aspiration of the fluid could facilitate this process. Whatever the mechanism of haemorrhage, it could not be observed immediately following the procedure, nor was there any immediate change in embryonic heart rate.

It has been suggested that coelocentesis may be suitable for the diagnosis of single gene disorders (Jurkovic *et al.*, 1995). The risk of having an affected fetus in these cases is up to 50 per cent and therefore the procedure-related loss after coelocentesis could be relatively high, yet still be acceptable. However, a pregnancy loss rate of

25 per cent, including the procedure-related loss and background rate, is too high even for patients with autosomal dominant disorders.

This study also indicates that the first-trimester placenta and embryo may be more susceptible to the adverse effect of interventions which are unlikely to cause harm later in pregnancy. In that respect, our experience with coelocentesis confirms the concerns raised with early amniocentesis and CVS. Our observations also suggest that the coelomic cavity has an important physiological role in early pregnancy, disruption of which may have serious consequences on subsequent development.

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