Transvaginal ultrasound-guided embryo transfer improves pregnancy and implantation rates after IVF

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BACKGROUND: Attempts are constantly being made to improve clinical pregnancy rates after IVF and embryo transfer. Since November 1998, we have gradually been adopting transvaginal ultrasound guidance during embryo transfer. We retrospectively examined the efficacy of this method on pregnancy and implantation rates. METHODS: The results of 846 cycles from our IVF–embryo transfer programme were analysed and comparisons were made between those carried out using ultrasound guidance and those by the clinical touch method. RESULTS: Higher pregnancy and implantation rates (28.9 and 15.2% respectively) were found in the group using the transvaginal ultrasound guidance during embryo transfer compared with those in the group using the clinical touch method (13.1 and 7.0% respectively). The differences were statistically significant ($P < 0.01$). There was no significant difference in ectopic pregnancy rates between the two groups. CONCLUSION: The use of transvaginal ultrasound-guided embryo transfer significantly improved both pregnancy and implantation rates. Although technically difficult, we suggest its use may maximize the chances of achieving a successful pregnancy outcome.

Key words: air bubble/embryo transfer/IVF/pregnancy rate/transvaginal ultrasound guidance

Introduction

Many factors influence clinical pregnancy in the IVF cycle: patient selection, ovulation induction method, oocyte retrieval technique, embryo quality, uterine receptivity and embryo transfer technique. Embryo transfer, the last step, is a critical part of the IVF cycle and is thought to be the most inefficient step. Although embryo transfer techniques had been relatively unexplored, Kovacs demonstrated possible important factors for successful embryo transfer after IVF, based on questionnaires distributed amongst highly experienced IVF clinicians (Kovacs, 1999). Ultrasonic monitoring of embryo transfer was referred to in this report, however, the rank of this factor was not high.

Transabdominal ultrasound-guided embryo transfer has been described by various authors since 1985 to improve the pregnancy rate (Strickler et al., 1985; Leong et al., 1986; Al-Shawaf et al., 1993; Kan et al., 1999). However, significantly higher pregnancy rates following transabdominal ultrasound guidance have not been consistently demonstrated. Lindheim et al. first reported that ultrasound guidance improved pregnancy outcomes only in easy transfers (Lindheim et al., 1999). Subsequently, two studies demonstrated significant differences between the clinical touch method and transabdominal ultrasound-guided embryo transfer, retrospectively (Wood et al., 2000) and prospectively (Coroleu et al., 2000).

Transvaginal ultrasound is now routinely used to monitor follicle growth and to assist in oocyte retrieval. High frequency transvaginal ultrasound has provided significantly improved resolution of the fine details of pelvic anatomy and removed the necessity for a full bladder. Hurly et al. tried transvaginal ultrasound-guided embryo transfer; however, they could not demonstrate improved results using the new method (Hurly et al., 1991) and no subsequent study has been done. The problem is how to simultaneously and adequately place the ultrasound probe, the speculum and the catheter during embryo transfer.

The present study was undertaken to assess whether transvaginal ultrasound-guided embryo transfer could become a routine technique in the IVF–embryo transfer programme, whether pregnancy and implantation rates were improved by this method, and whether this technique could change the incidence of ectopic pregnancy. This is the first report that has revealed a significant importance of transvaginal ultrasound-guided embryo transfer in the IVF–embryo transfer programme.

Materials and methods

Figure 1. Diagram of transvaginal ultrasound-guided embryo transfer. After the ultrasound probe was inserted in the speculum, the outer sheath was advanced under real time ultrasound guidance to a point approaching, but not touching, the uterine fundus. The inner catheter containing the embryos was then inserted into the outer sheath.

Figure 2. Transvaginal ultrasound-monitored embryo transfer. (a) Before embryo transfer. The arrow indicates the tip of the outer sheath. The arrowhead indicates the tip of the catheter. (b) After embryo transfer. The arrow indicates two air bubbles.

The clinical touch method was performed according to the following regimen. After inserting the speculum and exposing the cervix, the outer sheath was inserted through the cervical internal os and advanced to the fundus by gently touching the fundus. When the outer sheath was withdrawn 2 cm, the embryologist was notified to load the embryos. The embryo transfer catheter was loaded with 6 µl of medium (HTF medium; Irvine, CA, USA) between air bubbles (~2 µl). Then the softer inner stylet was removed and the inner catheter containing the embryos was inserted into the outer sheath. The tip of the catheter was placed ~15 mm from the fundal limit of the uterine cavity with the scale on the catheter. The embryos were then injected over 30 s.

The transvaginal ultrasound-guided method was performed according to the following regimen. At first, the uterus and endometrial cavity were visualized in a sagittal plane using a 6.5 MHz transvaginal microconvex probe, MTZ (Yokogawa RT4600, Tokyo, Japan). The diameter of the transvaginal probe was 2.0×2.2 cm. The ultrasound probe was removed and a bivalve speculum was inserted, exposing the cervix. The outer sheath was inserted into the cervical canal, and placed around the internal os, not advanced into the uterine cavity. After an ultrasound probe was reinserted in the speculum, the outer sheath was advanced gradually under real time ultrasound guidance to a point ~20–25 mm from the uterine fundus. Care was taken not to touch the uterine fundus. Then, the softer inner stylet was removed, and the inner catheter containing the embryos was inserted into the outer sheaths in the same manner as for the clinical touch method (Figure 1). The catheter was identified in the uterine cavity and moved to a point 15 mm from the fundal limit of the uterine cavity (Figure 2). The transfer volume was gently expelled as the air bubbles...
were visualized moving through the catheter. The embryos were injected over 30 s, allowing observation of the movement of the air bubbles into the uterine cavity. Removal of the catheter was also monitored by ultrasound and retention of the air bubbles was observed in the fundal position. The catheter was carefully checked under a microscope and the embryos retained within the lumen or adherent to the surface of the catheter were reharvested. The embryos can be clearly identified by the air bubbles inserted on either side, which are seen as bright echoes on the ultrasound image.

The data obtained were compared using $\chi^2$ analysis and Student’s t-test. $P$ values $< 0.05$ were considered to be statistically significant.

### Results

A total of 444 embryo transfers were performed using the clinical touch method, including 247 IVF cycles and 197 intracytoplasmic sperm injection (ICSI) cycles, and a total of 402 transvaginal ultrasound-guided embryo transfers were carried out, of which 240 were IVF cycles and 162 ICSI cycles. No significant difference was observed between the two groups in the mean age of patients, mean number of oocytes retrieved, mean number of zygotes fertilized, mean number of embryos transferred or the days after retrieval (Table I). There were also no significant differences in the distribution of indications for IVF and in the rate of difficult cases of the procedure between the two groups (data not shown). Despite all conditions being similar, the pregnancy rate in the group of transvaginal ultrasound guidance (116/402: 28.9%) was significantly higher than that in the clinical touch group (58/444: 13.1%) ($P < 0.01$) (Table II). Furthermore, the ongoing pregnancy and implantation rates in the transvaginal ultrasound guidance group (90/402: 22.4% and 145/953: 15.2% respectively) were also significantly higher than those in the clinical touch group (47/444: 10.6% and 71/1015: 7.0% respectively) ($P < 0.01$) (Table II). However, there was no significant difference in ectopic pregnancy rate between the two groups (2.7 and 0.7% respectively).

The tip of the catheter was placed at a point 15 mm from the fundal limit of the uterine cavity under transvaginal ultrasound guidance. However, endometrial movement sometimes displaced the location of the air bubbles during or after transfer. The air bubbles were sometimes withdrawn with the catheter when it was removed, although these cases were rare. In the majority of transfers, the air bubbles remained at 6–15 mm from the fundus (232/389: 59.6%) (Table III). The relationship between the position of the air bubbles and the subsequent pregnancy rate is illustrated in Table III. The air bubbles could not be identified in 13 (3.3%) of the 389 transfers, and in four of the 13, embryos were found within the lumen of the catheter or on its surface. There was no pregnancy in the 13 cases in which the air bubbles could not be identified. The ectopic pregnancy rate among the cases in which the air bubbles located in the cornua of the uterus was similar to that in the other cases (data not shown).

### Discussion

Clinical pregnancy is influenced by many factors in the IVF cycle. Since the first IVF pregnancy was achieved, some aspects of the technique have remained largely unchanged, whilst others have been constantly evolving, the most significant developments being in ovulation induction, the use of ICSI and in the development of culture media. Despite these improvements, the majority of transferred embryos fail to implant. This failure may be due to poor embryo quality, lack of uterine receptivity, or the technique of embryo transfer itself.

Defining the factors that are important for successful embryo
transfer after IVF has been a major issue. Based on questionnaires distributed amongst highly experienced IVF clinicians, Kovacs summarized the answers (Kovacs, 1999). The need to revisit the embryo transfer technique was highlighted by an embryo transfer workshop held in Sweden in 1997. A number of conclusions were made at this workshop, and it was decided to compare the opinions amongst highly experienced IVF clinicians. A questionnaire was devised, based on the number of possible critical factors that make up the ‘embryo transfer matrix’. The factor that got the highest votes was the need to remove hydrosalpinges before treatment. The other important factors were in order of absence of bleeding/blood on the catheter, catheter used, not touching the fundus, avoiding the use of a tenaculum, removal of all mucus from the cervix, ultrasound details of the cavity before treatment, leaving the catheter in place for at least 1 min, 30 min rest after transfer, dummy transfer before treatment, ultrasonic monitoring of transfer, and antiprostaglandins to prevent contractions.

Although the clinicians rated the importance of ultrasound guidance as 11th of 12 factors, the role of ultrasound monitoring during transfer should receive more emphasis. The cause of the low priority of this factor might be due to the inconvenience and inaccuracy of transabdominal ultrasound guidance. Ultrasound-guided embryo transfer is technically difficult, as the best way to view the uterine cavity ultrasonically is by the transvaginal approach. The use of high frequency transvaginal ultrasound has provided significantly improved resolution of the fine details of pelvic anatomy and removed the necessity of a full bladder. However, it is very difficult to simultaneously place the ultrasound probe, the speculum and the catheter during embryo transfer. It was reported in a pilot study that transvaginal ultrasound-guided embryo transfer was difficult and there were no significant differences between this technique and the clinical touch method (Hurly et al., 1991). However, we believe the advantages of the transvaginal ultrasound-guided embryo transfer are significant, since it enables the precise placement of the embryos, hence permitting atraumatic procedures. Consistent with this view, Anderson et al. recently reported that transvaginal ultrasound-guided embryo transfer improved outcome in patients with failed IVF (Anderson et al., 2001).

Generally, the position of the air bubbles indicates the position of the embryos. It was recommended that the tip of the catheter be positioned 15 mm from the fundus of the uterine cavity to avoid placement of embryos close to the uterine fundus (Coroleu et al., 2000). In our study, the point of the placement of embryos was also 15 mm from the fundal limit of the uterine cavity. Further, the air bubbles were distributed ~15 mm from the fundus when embryo transfer was performed under transvaginal ultrasound guidance. We could transfer the embryos to the precise place under transvaginal ultrasound guidance because it can more clearly delineate the tip of the catheter than transabdominal ultrasound guidance.

There was no pregnancy among the 13 cases in which the air bubbles could not be identified. It is likely that these embryos were misplaced, probably due to uterine contraction or technical errors. In four cases, embryos remained in or on the surface of the catheter. In the other cases, we suppose that the catheter was inadvertently abutting the internal tubal os and the bubbles disappeared in the tubal canal. Furthermore, we experienced some cases in which the air bubbles moved towards the cornua or the cervix from the position of the tip of the catheter. These observations also suggest that adequate monitoring by ultrasound guidance is very important during embryo transfer.

Lesny et al. reported a study to assess whether embryo transfer can alter junctional zone contractility (Lesny et al., 1998). According to their report, a small force applied twice by the soft end of the catheter was sufficient to cause a turbulent uterine response. The degree of difficulty of embryo transfer also caused strong random contractions in the fundal area, which at first relocated mock embryos towards the cornua and then pushed them into the intramural segment of the Fallopian tube. It was also stated that high frequency uterine contractions on the day of embryo transfer hinder IVF–embryo transfer outcome, possibly by expelling embryos out of the uterine cavity (Fanchin et al., 1998). We must avoid uterine contraction induced by the technique of embryo transfer, except in cases inclined to have frequent uterine contractions by nature.

Under transvaginal ultrasound-guided embryo transfer, the course of the catheter and the air bubbles can be found in real time, although they cannot be identified under the clinical touch method. It was reported that tactile assessment of catheter placement was unreliable (Woolcott et al., 1997). The outer guiding catheter inadvertently abutted the fundal endometrium or the internal tubal os and indented the endometrium. The transfer catheter was seen to be embedded within the endometrium. Transvaginal ultrasound-guided embryo transfer can minimize these endometrial traumas. As transvaginal ultrasound can supply fine pictures of the flexion of the uterus and the curve of the uterine endometrial midline compared with

### Table III. Intrauterine pregnancy rate according to the position of the air bubbles

<table>
<thead>
<tr>
<th>Air bubble in cornual uterus</th>
<th>Distance of air bubble from fundus (mm)</th>
<th>No air bubbles</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–5</td>
<td>6–10</td>
<td>11–15</td>
</tr>
<tr>
<td>Pregnancy (n)</td>
<td>19</td>
<td>67</td>
<td>130</td>
</tr>
<tr>
<td>Pregnancy rate (%)</td>
<td>26.3</td>
<td>26.9</td>
<td>33.1</td>
</tr>
</tbody>
</table>

Thirteen cycles were excluded from this analysis because there was no description of the location of air bubbles in these cases.
transabdominal ultrasound guidance, the clinicians can insert the catheter smoothly without endometrial trauma under the monitoring, and stop the catheter before reaching the fundus. If the curve of the uterine endometrial midline is sharp, we stop the outer sheath before indenting the endometrium and advance only the inner catheter, which is softer than the outer sheaths, up to 15 mm from the uterine fundus. These atraumatic procedures probably contributed to successful embryo transfer in the present study because bleeding from the endometrium or the uterine cervix is a significant negative factor for embryo transfer, as suggested by Kovacs (Kovacs, 1999).

In conclusion, highly favourable pregnancy and implantation rates were obtained with the use of the transvaginal ultrasound-guided embryo transfer method compared with the clinical touch method. Based on the results obtained from the present study, transvaginal ultrasound guidance appears to be an essential factor for improving the results of embryo transfer. Moreover, it might represent the maximum possibility for successful pregnancy. Although transvaginal ultrasound-guided embryo transfer has been technically difficult, we have become used to this technique and it is now routinely used at our institution.

References

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