Retrograde tubal embryo transfer in natural cycle in-vitro fertilization

A.Kumar, P.Benny, E.A.Lenton and I.D.Cooke

1Sheffield Fertility Centre, 26 Glen Road, Sheffield S7 1RA.
2Department of Obstetrics and Gynaecology, Christchurch, New Zealand and 3Department of Obstetrics and Gynaecology, University of Sheffield, Sheffield S10 2TN, UK
4To whom correspondence should be addressed

Two modes of embryo transfer, uterine and tubal, were compared following natural cycle in-vitro fertilization (IVF). Only patients with patent Fallopian tubes were included in the study. Tubal embryo transfer was performed by retrograde tubal cannulation without analgesia on an outpatient basis. Tubal transfer conferred no benefit compared with uterine transfer in male factor infertility with positive fertilization (pregnancy rates of 15.8% in both groups). Although tubal embryo transfer in the patients with unexplained infertility improved the pregnancy rates from 7.8% in uterine transfer (5/64) to 17.6% in the tubal transfer group (13/74), this improvement was not statistically significant.

Key words: natural cycle IVF/retrograde cannulation/tubal embryo transfer

Introduction

In-vivo fertilization takes place in the ampullary part of the Fallopian tube. Ciliary movements of the endothelial cells, contractions of the Fallopian tube and secretions of the tube then assist in the transport of the human embryo to the uterine cavity 96–144 h after the luteinizing hormone (LH) surge (Croxatto et al., 1978). In couples with unexplained infertility evidence of fertilization constitutes an important part of diagnosis, and replacement of the embryo back into the physiological environment may enhance its survival. This hypothesis was developed by various practitioners in the field of assisted reproduction who attempted to replace either the gametes [gamete intra-Fallopian transfer (GIFT)], or embryos [pro-nuclear stage transfer (PROST), zygote intra-Fallopian transfer (ZIFT)] directly into the Fallopian tubes (Asch et al., 1985; Yovich et al., 1987; Hamori et al., 1988). In 1987, Jansen and Anderson described a technique of retrograde tubal cannulation under ultrasound guidance, using a curved uterine guide cannula to reach the uterotubal junction prior to passing a tubal catheter through the isthmus of the Fallopian tube. They reported successful pregnancies after tubal insemination of cryostored semen and of embryos following IVF using the same technique of retrograde tubal cannulation (Jansen et al., 1988a,b). Diedrich et al. (1991) selected tubal embryo transfer for those patients with male factor infertility in order to take advantage of the physiological tubal environment for early embryonic development. The above studies have reported on the efficacy of tubal embryo transfer in ovarian stimulated IVF cycles. The present study reports on the efficacy of retrograde tubal embryo transfer in comparison with uterine embryo transfer in natural cycle IVF.

Materials and methods

All patients with patent Fallopian tubes (confirmed by laparoscopy and/or hysterosalpingography) who were undergoing natural cycle IVF between 1989 and 1994 were included in the study. Patients aged > 40 years, patients requiring the use of donor spermatozoa and patients where an abnormal oocyte was obtained were excluded from the study. A total of 126 patients were booked for tubal embryo transfer; 112 patients had successful tubal embryo transfers, and 102 patients had an equivalent uterine transfer of a single embryo. Uterine transfer was performed for all patients with patent Fallopian tubes at the beginning and the end of the study period while tubal transfer was offered to all patients in the middle of the study period with the aim of having at least 100 patients in each arm of the study. On retrospective analysis the patients were allocated to two subgroups according to the aetiology of infertility. The number of couples presenting with unexplained infertility were 74 and 64 in the tubal transfer and uterine transfer groups respectively; the remainder of the couples having male factor infertility according to the World Health Organization (1980) criteria. Only patients with normal fertilization were included in the study. The mean age of patients is shown in Table 1.

The spontaneous menstrual cycle was monitored with twice daily blood samples to detect the endogenous LH surge as previously described (Lenton et al., 1992). Oocyte collection from the single follicle was performed by transvaginal ultrasound guided follicular aspiration 36 h after the start of the LH surge. A normally-fertilized, 2–4 cell stage embryo was replaced 40–60 h after oocyte collection into the Fallopian tube or the uterus. The feasibility of the study was determined by trial catheterization in women volunteers with patent Fallopian tubes. Initial experience with the method described by Jansen and Anderson (1987) revealed that the use of a vaginal ultrasound probe (Vaginal probe 7.5 MHz; Kretz-technic, Ziph, Austria) made manipulation of the catheter difficult. We therefore adopted the technique with a partially full bladder and transabdominal ultrasound scanning (Abdominal probe 4.0 MHz; Kretz-technic) as described by Hurst et al. (1993) in their pilot study, while confirming the correct placement of the tubal catheter by laparoscopy. The tubal catheter (KJITS 5000; William Cook Europe Ltd, Letchworth, UK) consists of five parts: (i) an outer 5.5 cm French opaque teflon uterine guide cannula with a fixed lateral curve at the tip; (ii) a malleable metal obturator; (iii) a 33 cm long size 3 teflon French inner catheter with a 3 cm tapered tip; (iv) a platinum-tipped guidewire to fit within the inner catheter; and (v) a small afterloading cannula.
Table I. Summary of clinical characteristics of patients and results of tubal and uterine embryo transfer in natural in-vitro fertilization. Figures in parentheses are percentages

<table>
<thead>
<tr>
<th>Tubal transfer</th>
<th>Uterine transfer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of infertility</td>
<td>Unexplained</td>
</tr>
<tr>
<td>No. of patients</td>
<td>74</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>33</td>
</tr>
<tr>
<td>Duration of infertility (years)</td>
<td>6.2 ± 3</td>
</tr>
<tr>
<td>No. with positive HCG</td>
<td>13 (17.6)</td>
</tr>
<tr>
<td>No. of live births</td>
<td>11 (14.9)</td>
</tr>
</tbody>
</table>

HCG = human chorionic gonadotrophin.

The tubal catheterization procedure was performed with the patient in a dorsal lithotomy position with a partially filled bladder. The uterine guide cannula with obturator was inserted just above the internal os and then pushed further away from the obturator thus regaining its curve in the selected cornu. The correct positioning of the guide cannula was confirmed by ultrasound scanning in the sagittal plane, firstly to confirm that the cannula had reached the fundus and then in the transverse plane at the level of the cornua. After removing the obturator, the inner tubal catheter with guidewire was then inserted via the guide cannula and gently fed ~3 cm into the selected Fallopian tube. Normally either no or minimal resistance was felt as the catheter entered the Fallopian tube, and the patient often felt a lateralizing sensation on the same side as the catheter. The absence of any deformity in the guidewire on removal confirmed the correct positioning of the catheter. It was often possible to confirm the correct placement of the catheter and guidewire in the Fallopian tube by ultrasound. The embryo was then retrieved in the after-loading cannula and injected with 30 µl of culture medium. No analgesia was required during the transfer. The patients were not given any special instructions. The procedure of tubal cannulation was abandoned in 14 patients after two failed attempts and the embryo was transferred into the uterine cavity. These patients were excluded from the analysis.

Uterine embryo transfer was performed using Friedman’s catheter (Solco Basle (UK) Ltd, High Wycombe, UK) or Cook’s catheter (KJITS-3025; William Cook Ltd.) under ultrasound guidance using a standard technique. Luteal support was given in both groups according to protocol: dydrogestrone 30 mg daily (Duphaston; Duphar Ltd, Southampton, UK). A pregnancy was diagnosed when a plasma human chorionic gonadotrophin (HCG) concentration >40 IU/l was detected ~14 days after oocyte retrieval.

Statistical analysis

The data from the two groups and subgroups were analysed and compared using the χ² test.

Results

A total of 214 patients were included in the study; all of the patients had their natural cycle monitored and an oocyte was collected. Those patients with failed fertilization were excluded from the study since its aim was to assess the implantation efficacy of different transfer sites. Uterine transfer was performed in 102 patients at the beginning and towards the end of the study while tubal catheterization was performed in the middle of the study period, thus avoiding any bias caused by improvements in technical and laboratory techniques over time. In the tubal transfer group, 74 couples presented with unexplained infertility and 38 couples with male factor infertility. In the uterine transfer group, 64 couples were considered to be in the unexplained group while 38 couples had male factor infertility.

Implantation was successful in 19 of the 112 tubal transfer cycles (16.9%) in comparison with 11 implantations which occurred in 102 treatment cycles (10.8%) following uterine transfer. Details of pregnancies in each subgroup are given in Table I. In the group of couples with male factor infertility there was no statistically significant difference in the pregnancy rates of 16% (6/38 in both groups) and the live birth rate of 13% (5/38 in both groups) following the use of different embryo transfer sites. In patients with unexplained infertility, tubal embryo replacement was associated with an 18% (13/74) implantation rate compared with only 8% (5/64) in the equivalent uterine transfer group. Live birth rates were 15% (11/74) and 6% (4/64) respectively. Again, however, these differences were not statistically significant.

There were no ectopic implantations in either group in this series of natural cycle IVF. None of the tubal cannulation procedures was abandoned due to pain. The suspected causes of failed tubal cannulation were tubal spasm or uterine cavity direction, i.e. acute retroversion or anteversion. The duration of a successful tubal embryo transfer procedure was 10–45 min, with a mean duration of 16 min. The duration of the uterine embryo transfer procedure was not recorded. In one of the 14 failures, the platinum-tipped guidewire became embedded in the tissues and an attempt to pull the wire led to uncoiling of the distal coiled tip. The tubal catheter and the guide wire were eventually removed, and a uterine embryo transfer followed. There were no other complications recorded during the procedure of retrograde tubal cannulation.

Discussion

The objectives of natural cycle IVF in couples with unexplained infertility are: a detailed endocrinological assessment of the woman’s spontaneous cycle; a timed oocyte recovery and a test of the capacity of fertilization with her partner’s spermatozoa. With the use of the transvaginal ultrasound-guided techniques, oocyte recovery has become a relatively simple procedure which can be performed without analgesia (Ramsewak et al., 1990). The standard method of uterine embryo transfer yields poor implantation rates in ovarian stimulated IVF cycles; these have shown improvement with the use of laparoscopic tubal embryo transfer, but this is an operative procedure requiring a general anaesthetic (Yovich et al., 1987). To avoid the need for anaesthesia, a retrograde approach to tubal cannulation has been attempted. Jansen and Andersen (1987) described such a technique which involved intermittent transvaginal scanning during the cannulation. This prolonged the procedure and caused additional stress to the patient. Bauer et al. (1990) performed retrograde cannulation without ultrasound guidance, but they routinely used a tenaculum and cervical dilator. We have performed transvaginal tubal cannulation using transabdominal transvesical scanning with
a partially full bladder. The partially full bladder also helped to straighten the anteversion of the uterus and reduced the requirement for a tenaculum, cervical dilator and uterine sound. Without ultrasound guidance, unexpected anomalies of uterine shape and direction of the uterine cavity may also lead to cannulation failure. In our experience, lateralizing sensation was not felt by all women, and this was particularly so if they had experienced discomfort during entry through the internal cervical os.

The methods described by Jansen et al. (1988a,b) and Bauer et al. (1990) involved pre-loading the embryo into the tubal catheter so that it was likely to be in the catheter for a long time, and hence exposed to environmental cooling. Another disadvantage of the preloading system is that either incorrect placement or uterine placement of the catheter are only noted after the embryo transfer by a kink in the catheter as described by Risquez et al. (1990b). An after-loading system of cannulation (KJITS 5000) was used in the present study, thus enabling the tubal placement of the catheter to be confirmed prior to embryo transfer and also limiting the period of cooling of the embryo. The replacement of the embryo into the favourable milieu of the Fallopian tube did not improve the success rate from natural cycles in those patients with only male factor infertility. These observations contradict the results reported by Diedrich et al. (1991). In their series of male factor infertility patients, tubal embryo transfer was performed in stimulated IVF treatment cycles. However, they did not compare these results with those from uterine transfer of embryos.

There were no ectopic pregnancies in our large series of tubal embryo transfers. This may reflect the advantage procured by proper selection of patients with patent Fallopian tubes and no previous history of pelvic inflammatory disease or surgery. Risquez et al. (1990a) reported that two out of five pregnancies were ectopic implantations in their study of tubal embryo transfer: a new treatment of male infertility. Hum. Reprod., 6, 672–675.

References


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