Modern embryo transfer catheters and pregnancy outcome: a prospective randomized trial

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Objective: Embryo transfer (ET) is the final crucial step in IVF treatment. The type of catheter used can affect the pregnancy rate (PR). In this prospective, randomized trial we compared the clinical PR between the Wallace and the Cook K-Jet embryo transfer catheters.
Design: Prospective, randomized clinical trial.
Setting: A National Health Service Assisted Reproduction Unit.
Patient(s): One hundred fifty women undergoing a fresh ET. Age more than 40 years, a high basal FSH, a previous difficult ET, or more than six previous ETs were the exclusion criteria.
Intervention(s): Women undergoing a fresh ET were randomized at the time of ET to either the Cook K-Jet or Wallace embryo transfer catheter. The randomization was stratified according to age and the number of previous ETs.
Main Outcome Measure(s): Clinical PR.
Result(s): There was no significant difference in the clinical PR between the Wallace and the Cook catheters (22/75 [29.3%] and 23/75 [30.6%], relative risk [RR]: 0.96 [95% confidence interval 0.58–1.58]).
Conclusion(s): There is no significant difference in the PRs achieved by modern, soft, double-lumen ET catheters. (Fertil Steril® 2005;84:996–1000. ©2005 by American Society for Reproductive Medicine.)

Key Words: Catheter, embryo transfer, IVF, pregnancy rate, randomized controlled trial

Embryo transfer is the final crucial step in IVF treatment. There are many factors, in addition to the embryo quality, that have been shown to influence the success of embryo transfer (ET) such as the technique used (1), the experience of the operator (2), and the difficulty of the procedure (3).

The type of embryo catheter used is also important. Older style catheters such as the Tomcat (single-lumen) and TDT (metal obturator) have not performed as well in previous randomized controlled trials as the soft, double-lumen catheters (4, 5). Randomized prospective comparisons of different "modern" ET catheters have not shown as marked a difference in ongoing pregnancy rates (PR) (6, 7).

We compared the Wallace and the Cook K-Jet ET catheters. The objectives of this study were to evaluate the catheters for our own use and to further the information available regarding the impact of modern ET catheters on PRs.

MATERIALS AND METHODS

One hundred fifty fresh ETs in 142 women who underwent IVF/intracytoplasmic sperm injection (ICSI) treatment were randomized to either the Wallace or the Cook K-Jet transfer catheter at the Assisted Conception Unit at The Jessop Wing Sheffield. Enrollment occurred between September 2002 and May 2004. Women were excluded if they were older than 39 years, had a high basal FSH, a previous difficult ET, or more than six previous ETs. The study was discussed with eligible patients on the day of oocyte retrieval and written information given. On the day of ET those who agreed to take part gave written consent.

Tele-randomization using computer-generated random numbers was performed at the time of ET. The embryologist loading the embryos telephoned a designated secretary in the University department who consulted a randomization table drawn up by a statistician from the pharmacy department. The randomization was stratified according to age and the number of previous ETs. The patients were blinded to which group they had been allocated.

The local research and ethics committee approved the trial and all patients gave informed consent to participate.

The main outcome measure was the clinical PR, defined as the presence of fetal heart motion at ultrasound. A trained operator in the Assisted Conception Unit performed an ultrasound at 6 to 7 weeks gestation. The secondary outcome measures included the difficulty of transfer; whether an obturator, tenaculum, or change of catheter was required; the presence of blood or mucous on the catheter tip; and the time taken to perform the transfer.

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Statistical Analysis

A total of 150 patients were required (75 in each arm) to achieve a power of 80% with a type I error of 0.05 to detect a difference of 15%. This difference was based on unpublished work provided by Cook's sales representative of a randomized trial declaring a difference of 25%. As such a difference was not realistic we reduced it to 15%. Statistical analysis was carried out using SPSS (SPSS Inc., Chicago, IL) and a $P<.05$ was considered significant. The χ^2 and Fisher's exact tests were used to compare proportions and the analysis was carried out on an intention to treat basis. Nominal data were compared between the two groups using two-tailed unpaired Student's *t* test.

Catheters

The Cook Catheter (K-Jets-7019-SIVF; Cook IVF, Eight Miles Plains, Queensland, Australia) consists of a slightly stiff outer cannula with a bulb tip and a curved distal end to help negotiate the cervical canal. The outer guide catheter is 19 cm long. The Cook inner catheter is 23 cm long. It is thinner and softer than the Wallace but made of a similar material. In general the inner catheter does not negotiate the cervical canal directly but rather is introduced into the uterine cavity through the outer catheter.

The Wallace (Edwards-Wallace Embryo Replacement Catheter; Sims Portex Ltd., Hythe, Kent, UK) design consists of a soft inner polyurethane catheter that is introduced with a stiffer outer cannula. Generally the inner catheter is introduced directly through the cervix. If difficulty is encountered, a stiff inner obturator may be used before introduction of the inner catheter. The Wallace comes in lengths of 18 and 23 cm.

Stimulation Protocol

In the majority of cycles (114/150; 76%) a GnRH antagonist (GnRH-a) regime was used, as is the standard practice in our unit. Ovarian stimulation was started on menstrual cycle day 2 or 3 with recombinant FSH (Puregon; Organon, Cambridge, UK) at a dose determined by the patient's age and their previous response to treatment. An ultrasound scan assessment of the pelvis was carried out before starting the treatment on cycle day 2 or 3. Cycle monitoring was carried out using both ultrasound scanning and LH and E_2 assays. The GnRH-a (Orgalutran; Organon) was administered using a flexible start protocol. The antagonist was started once the serum E_2 level was 1,000 pmol/L or the lead follicle was 14 mm or greater in size (whichever occurred first). It was continued until the day of hCG administration. Final oocyte maturation was triggered by administering 10,000 IU of urinary hCG (Pregnyl; Organon) at 35 hours before oocyte retrieval. The criteria for administering hCG were the presence of three follicles $\geq$17 mm in diameter. Oocyte retrieval was carried out using ultrasound-guided transvaginal needle aspiration while the patient was receiving sedation and analgesia.

The remainder of cycles (30/150, 20%) were either short (9/150) or long (21/150) GnRH agonist down-regulation protocols using the same dose and monitoring strategy as under the antagonist regime.

Embryo Transfer Technique

Embryo transfer was performed 2 to 3 days after oocyte retrieval. A day 2 transfer was performed when only two embryos were available for transfer on day 2 or when day 3 fell on a Sunday. The routine practice of the clinic is to transfer two embryos. In exceptional circumstances (multiple previous failed attempts in older women) three embryos may be transferred. Only one patient in this study (Wallace group) had three embryos transferred. Single ETs were carried out under obligatory circumstances where only one embryo was available. No patient underwent a trial transfer.

Trained, experienced operators performed all the transfers. All operators had performed a minimum of 200 ETs each to be considered experienced. A plastic bivalve speculum was used to visualize the cervix, which was then cleaned with Hartmann's solution. The embryos were loaded once the operator had ensured the correct placement of the speculum. The embryologist flushed the selected catheter with 1 mL of Hartmann's solution and then primed it with culture medium. The catheter was loaded with (from tip) air gap, embryos in culture medium, air gap, then remainder of catheter with culture medium.

The loaded Cook catheter was handed to the clinician with the inner catheter retracted within the outer guiding catheter. The inner catheter was advanced into the uterine cavity once the bulb tip had negotiated the internal os.

The loaded Wallace catheter was handed to the clinician with the inner catheter already advanced. The inner catheter was directly introduced into the uterine cavity only using the outer catheter for extra rigidity. If difficulties were encountered using this technique, the inner catheter was retracted into the outer rigid catheter for negotiation of the cervical canal.

At the commencement of the trial embryo, placement within the uterine cavity was done using the clinician's judgment. After the first 30 patients were recruited ultrasound-guided replacement became standard practice at the clinic. This was due to the publication of evidence that ultrasound guidance improved PR (8, 9). With a full bladder transabdominal visualization of the endometrial cavity was performed throughout embryo placement. The embryos were injected once the tip of the catheter was judged or visualized to be 1–2 cm from the uterine fundus.

After deposition of the embryos the respective catheter was kept still for 30 to 60 seconds, then gently withdrawn. After inspection for the presence of blood or mucous on the tip, the catheter was then flushed and inspected by the embryologist for the presence of retained embryos. No embryos were retained in the study patients.