Does catheter choice during embryo transfer alter the pregnancy rate?

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ABSTRACT

BACKGROUND

Although every step in the in vitro fertilisation (IVF) procedure is important, the impact of embryo transfer (ET) on pregnancy rate (PR) is significant. Of all the crucial aspects of ET the type of catheter used and the technique of transfer on the PR has drawn the maximum attention and controversy. We aimed to compare the outcome of two different ET catheters on the PR.

METHOD

A prospective analysis comparing the classical Frydman (Laboratoire CCD, France) and the soft Cook (Cook Medical, Indiana, USA) ET catheters was performed. Primary end-point was clinical pregnancy rate (CPR); secondary end-points were rates of difficult transfer. A total of 1,446 ETs were performed in women undergoing IVF treatment, of which 723 cycles were randomised to the Cook catheter and 723 to the Frydman catheter.

RESULTS

It was observed that, although the Cook catheter was related to a slightly higher PR, the overall comparison failed to indicate a significant difference in CPR. It was also seen that the ease of transfer did not significantly affect the PRs.

CONCLUSION

Individual variables during ET may not contribute significantly to the success of an IVF programme; however, a holistic approach encompassing all the factors is quintessential to improve the PR.

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Key Words: catheter; embryo transfer; in vitro fertilisation

INTRODUCTION

A perfect embryo transfer (ET) in an in vitro fertilisation (IVF) programme is a challenge for many reasons. The transfer can make the difference between a successful cycle and a failed one. The ultimate goal of a successful ET is to deliver the embryos atraumatically to a location in the uterus where implantation is maximised. Although different factors influencing the pregnancy rate (PR) in an IVF programme have been studied extensively by many workers in an endeavour to improve results, like the age of the patient, the type of ovarian stimulation, the use of human chorionic gonadotrophin (hCG), the number of eggs collected, the number of embryos transferred, and the embryo quality; however, the ET technique has been found to be one of the most critical procedures in successful assisted reproduction.^{1,2}

Crucial steps reported to affect the success rate during embryo replacement are presence of blood or mucus on the catheter post transfer, catheter choice, dummy ET, ultrasonography-guided transfer, presence of uterine contractions, and difficulty encountered during ET.^{3–7}

Our study aimed to find out whether catheter choice influences the PR in an IVF–ET programme, so a prospective analysis of embryo replacement was carried out. We compared the performance of two different ET catheters namely the Cook and the Frydman catheters, and the ease of embryo replacement procedure in terms of PR.

MATERIALS AND METHOD

Around 1446 ETs were performed over a period of 18 months (January 2009–June 2010) at our centre. Data were collected from ETs done on infertile patients undergoing IVF after ovum pick up (OPU). All patients with even registration numbers were assigned to the Cook catheter arm while that with odd registration numbers underwent transfer by the Frydman catheter.

The difficult cases for transfer were identified based upon the following factors:

- Acute utero-cervical angulations.
- History of difficult intra-uterine insemination.
- History of difficulty during transfer in previous IVF–ET cycle.

Controlled ovarian hyperstimulation (COH) was carried out in all the patients with recombinant FSH (follicle-stimulating hormone), after downregulation, with gonadotrophin-releasing

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hormone (GnRH) agonist, in the preceding late luteal phase. Follicular growth was followed by transvaginal ultrasonography and once adequate follicular maturation was obtained, hCG was administered and oocyte retrieval was performed about 36 hours later under transvaginal sonography guidance and general anaesthesia. Embryo transfer was carried out on day 2 or day 3 after oocyte retrieval.

The Embryo Transfer Procedure

We carried out all the ETs in the operation theatre; however, it was done without anaesthesia, except in one case where the patient was very apprehensive and required general anaesthesia.

One, two, or three embryos were usually prepared for transfer. The subjects arrived with semi-filled bladder and were placed in the lithotomy position. After insertion of a sterile Sims speculum, the anterior lip of the cervix was held with the volsellum at 12'o clock position and cleaned with prewarmed saline. Visible mucous was removed by gentle dabbing. The ET was performed under trans-abdominal sonographic guidance. No mock ET was performed before the transfer.

Embryos were loaded into the classical Frydman (Laboratoire CCD, France) or the soft Cook (Cook Medical, Indiana, USA) catheter as per the study protocol.

The Frydman catheter (Figure 1) is a polyethylene open ended catheter with an external diameter of 1.6 mm. It has a 4.5 cm soft distal part and a 12.5 cm more rigid proximal part, and is graduated at 5.5 and 6.5 cm distances from the tip. The Cook catheter (Figure 2) is a double lumen catheter set. The guiding (outer) catheter is 19 cm long, has a polycarbonate hub, a bulbous tip and the distal end is angled. The transfer (inner) catheter is 23 cm long and the tip is 2.8 French size. The base of the transfer catheter fits onto a 1.0 mL plastic syringe. All catheters used in the study were from the same batch.

A day 2/3 ET with a 4–8 cell embryo was preferred. Air bubble technique was used to load the embryos.

Transfer of Embryos

The catheter was loaded with the embryo(s) and was smoothly introduced through the cervical canal up to 1–2 cm from the uterine fundus, while trying to avoid touching the fundus under ultrasound guidance. The embryos were then expelled gently, after which the catheter was slowly removed while being rotated. The catheter was checked under a microscope for embryo retention or the presence of blood.

Classification of the Type of Transfer

Depending upon the ease of transfer, the transfers were classified as

- Easy
- Difficult

An easy ET was one which took place smoothly, without the use of uterine sound and the catheter was clean of blood. Difficult transfers were those which required manipulation or sounding.

Patients were advised serum β -hCG levels on day 18 and transvaginal sonography on day 21 after the OPU.

Figure 1 The classical Frydman catheter.

Figure 2 Cook double lumen catheter set.

Outcome Measures

The primary end-point was clinical pregnancy rate (CPR). Clinical pregnancy was defined as a positive pregnancy test (β -hCG measured in venous blood >50 mIU/mL on day 18 following oocyte retrieval), followed by the presence of at least one foetal sac on transvaginal ultrasound four weeks after transfer. The secondary end-points were the rates of difficult transfer.

Statistical Analysis

Statistical analysis was done using χ^2 -test and SPSS software version 10.0.

RESULTS

Over a 18-month time period, 1,446 ETs were carried out in women undergoing IVF treatment. Around 723 cycles were transferred with the Cook catheter and 723 patients underwent transfer with the Frydman catheter. The mean age of women at the time of ET was 32.2 years. As summarised in Table 1, there were no significant differences between the two catheter groups as to baseline or cycle characteristics.

When Cook cycles were compared with Frydman cycles it was observed that there was no significant difference in overall

Table 1 Baseline and cycle characteristics of patients randomised to different catheters.

Patient characteristics	Cook (n=723)	Frydman (n=723)
Age (yr)	32.2 (4.4)	31.2 (2.9)
Primary infertility (%)	455 (62.93)	444 (61.41)
No. of oocytes retrieved (mean, SD)	13.4 (7.8)	13.4 (7.1)
Transfer of one embryo (%)	234 (32.4)	248 (34.3)
Transfer of two embryos (%)	413 (57.1)	395 (54.6)
Transfer of three embryos (%)	76 (10.5)	80 (11.1)
Transfer on day 2 (%)	472 (65.3)	481 (66.5)
Transfer on day 3 (%)	251 (34.7)	242 (33.5)

CPRs. Among 723 cycles subjected to the Cook catheter, 301 cycles led to a clinical pregnancy (301/723 [41.6%]). Among 723 cycles performed with the Frydman catheter, 2 cycles were lost to follow-up, and 285 clinical pregnancies were detected (285/721 [39.5%]).

It was also seen that the ease of transfer did not significantly affect the PRs. Transfers classified as easy amounted to a PR of 30.25% as opposed to a PR of 29.26% after a difficult transfer requiring various degrees of manipulation.

DISCUSSION

Embryo transfer, the final and most crucial step in IVF procedure requires a close collaboration between the clinician and the embryologist. Healthy, good quality embryos are required to be transferred in the most atraumatic manner. Therefore, the ultimate goal of a successful ET is to smoothly traverse the endocervical canal, internal os, and lower uterine segment of the uterus with a catheter that is not contaminated by bacteria, mucous, or blood, to eject intact embryos with the tip of the catheter placed in the middle third of the endometrial cavity, and to avoid the retention of embryos in the catheter and their expulsion from the uterine cavity.⁸

Various reasons have been postulated for a failed transfer, like disruption of the endometrium by the catheter, induction of uterine contractions, deposition of the embryos in a suboptimal location, or damage to the embryos during the transfer process.⁹ Therefore, numerous technical aspects of this procedure have been studied to minimise these complications and determine their effect on pregnancy outcome.

The myriad factors involved in the ET technique has been researched by different workers, of which the availability of an ideal ET catheter has been the subject of maximum controversy and the best catheter to be utilised for ET is still not resolved.

Several ET catheters are commercially available varying in catheter design and physical attributes. They may be of stiff or soft materials, with the presence or absence of an outer sheath, variable malleability, and quality of the materials and finish.¹⁰

An acceptable catheter for human ET should be easy to use, non-toxic and should ensure proper placement in the uterus. Stiff catheters and use of a rigid outer sheath make catheter placement easier but may cause more bleeding, trauma, mucous plugging, and stimulation of uterine contractions. Soft catheters allow the tip to follow the contour of the cervix and uterus and at the same time minimise trauma to the endometrium.¹⁰

Although published randomised control trials (RCT) comparing exactly the same pair of ET catheters rarely exist. Grunert et al¹¹ in a small study, directly comparing the Cook, Frydman and the Wallace catheters, reported a 32% (16/50) CPR for cycles transferred with the Cook soft coaxial catheter, 39% (20/51) with Frydman catheter, and 39% (19/49) with the Wallace catheter (Marlow, Willoughby, OH, USA). This study did not observe a significant difference in PRs among these three catheters.¹ Our analysis also did not show any statistically significant difference in success rate with the two catheters. Al-Shawaf et al in a randomised study, also inferred that there was no difference in the PR with the Wallace catheter (30.3%) when compared with the Frydman catheter (30.7%).¹²

The conflicting results emerging from RCTs and the lack of power caused by inadequate sample size in most RCTs brought about two meta-analyses comparing soft vs firm ET catheters. Both the meta-analyses by Abou-Setta et al¹³ and Buckett¹⁴ have demonstrated that softer catheters are associated with higher CPRs than firmer catheters by overall comparison. Therefore it is evident that the relationship between the type of catheter used in ET and the successful outcome remains elusive. Some studies have reported better results with soft catheters; other studies found the complete opposite and a third group reported no difference.

The technique of ET is also an important variable in the success of an IVF cycle and may explain the disparity between embryonic development and PRs. The inefficiency of embryo implantation may reside with the ET technique.¹⁵ Meldrum was one of the first investigators to suggest that meticulous ET technique is essential to IVF success.¹⁶ Subsequently, many studies have attempted to characterise variables and techniques associated with ET success or failure.

Embryo transfer considered difficult are those where greater resistance was met during negotiation due to uterocervical angulations, the procedure was time consuming, uterine sounding or cervical dilatation was carried out or there was blood in any part of the catheter as observed in 29.26% cases in our study.

Englert et al¹⁷ reported a 33.3% PR with transfers rated excellent, whereas “bad” transfers yielded a 10.5% PR. In contrast, Tur-Kaspa et al¹⁸ and Nabi et al¹⁹ found no difference in success between easy and difficult transfers. However, in our study there existed no significant difference in the PRs obtained irrespective of the ease of transfers.

CONCLUSION

Taking the results of our study into account, it might be proposed that catheter choice does not influence the success rate

in an IVF-ET programme nor does the ease or difficulty in transfer influence the implantation rate, nevertheless, individual variables when taken together definitely increase the success rate. Meticulous attention to the various details of ET technique is as important for in vitro fertilisation success as the efforts of embryologist in the laboratory. Therefore a holistic approach encompassing all the factors for the fruitful outcome of an IVF-ET cycle, on the part of, both embryologists and clinicians will serve to maximise PRs for patients.

Intellectual Contributions of Authors

Study concept: Lt Col Pankaj Talwar, VSM, Lt Col Sandeep K
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CONFLICTS OF INTEREST

None identified.

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