Article

A prospective randomized controlled trial of Wallace and Rocket embryo transfer catheters

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Abstract

The aim of this study was to compare the efficacy of two embryo transfer catheters: Wallace® and Rocket Embryon® in an IVF programme of a tertiary referral university centre. A total of 308 patients undergoing embryo transfer were prospectively randomized to either a transfer with the Wallace catheter or a transfer with the Rocket catheter. The main outcome measure in this study was the clinical pregnancy rate, and secondary outcome measures included implantation rate, visibility of the catheter under ultrasound, number of retained embryos post transfer, and whether change of catheter was required. In addition, patient discomfort during the procedure was recorded. Pregnancy and implantation rates were similar when Wallace or Rocket catheters were used. However, for the Rocket catheter, the tip was more often clearly seen on ultrasound and it had a lower rate of retained embryos in the catheter after transfer ($P < 0.05$). Experience with different transfer catheters is recommended for difficult cases.

Keywords: *embryo transfer, pregnancy, Rocket catheter, Wallace catheter*

Introduction

Embryo transfer is a crucial step in IVF–embryo transfer treatment cycles, but it is probably the most inefficient (Buckett, 2006). Ovarian stimulation, oocyte retrieval, fertilization and embryo culture have been extensively studied and are performed under tight control, while improvements in embryo transfer are less often considered. There are many factors, in addition to the embryo quality, that have been shown to influence the success of embryo transfer, such as the technique used, the experience of the operator, and the difficulty of the procedure (McIlveen *et al.*, 2005). Several studies have shown increases in clinical pregnancy rate (PR) resulting from improvements in the various aspects of embryo transfer, including cervical cleaning, a full bladder, dummy transfer, pretreatment cervical dilatation in difficult cases, and ultrasound guidance (Buckett, 2005).

It has also been suggested that catheter choice influences pregnancy rates (Meriano *et al.*, 2000), and several surveys in the UK and Australia have shown that embryo transfer catheters rank high as an important independent factor in the success of an IVF programme (Abou-Setta *et al.*, 2005). A recent systematic review has suggested that the ideal embryo transfer catheter should avoid any trauma to the endocervix and/or the endometrium as it is introduced into the uterine cavity (Abou-Setta *et al.*, 2005).

In the search for the ideal catheter, many large retrospective studies (Burke *et al.*, 2000; Choe *et al.*, 2001; Wood *et al.*, 2002; Sallam *et al.*, 2003) have looked into the catheter type used, and have reported higher PR with soft catheters such as the Cook (Cook Medical, USA), and the Wallace (Marlow Technologies, USA) compared with firm ones such as TDT (Laboratoire CCD, France), Frydman (Laboratoire CCD), Tomcat (Kendell Health care, USA), Tefcat (Kendell Healthcare, MA, USA), and Rocket (Rocket Medical, UK) (Buckett, 2006). However, there are also several reports of the choice of catheter not influencing PR (Urman *et al.*, 2000; Karande *et al.*, 2002; De Placido *et al.*, 2002).

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It was, therefore, decided to evaluate the performance of the Wallace and Embryon catheters in a prospective randomized controlled trial (RCT) using clinical PR as the main outcome measure, in continuing efforts to determine the optimal embryo transfer device.

Materials and methods

Over a period of 8 months, 308 patients undergoing IVF–embryo transfer at the assisted conception unit of the Hammersmith Hospital were included in the study after the approval of the Hammersmith, Queen Charlotte and Chelsea Hospitals Research Ethical Committee. Patients having fresh embryo transfers were recruited on the day of transfer, after obtaining their informed written consent, and were then randomized to either the Wallace group or the Rocket group using a dark sealed envelope technique. Patients having single embryo transfers were excluded, as well as those having IVF treatment for preimplantation genetic diagnosis, gamete donation, or prior to chemo/radiotherapy and patients with repeated IVF failures (>6), or a previously difficult embryo transfer.

Ovarian stimulation for IVF

Ovarian stimulation was performed using recombinant FSH (Puregon NV; Organon, The Netherlands) after pituitary down-regulation with the gonadotrophin-releasing hormone (GnRH) analogue buserelin (Suprecur; Shire, Andover, UK). When at least three follicles had reached a diameter of 18 mm and serum oestradiol concentrations were appropriate, human chorionic gonadotrophin (HCG, Profasi; Serono, Welwyn Garden City, UK) was administered, and 34–36 h later transvaginal oocyte retrieval was performed under ultrasound control.

Embryo transfer catheters

The Rocket Embryon transfer catheter (Rocket Medical plc, Watford, UK)a firm embryo transfer catheter, consists of an outer sheath with 1 cm markings to indicate depth of penetration into the endocervix. The inner catheter is made of soft polyurethane with a hot-formed tip profile to minimize endocervical trauma. The outer and inner diameters of the inner transfer catheter are 1.5 and 1 mm respectively (Rocket Product information leaflet). The Wallace catheter (Sims Portex Ltd, Hythe, UK), a soft embryo transfer catheter, also has a flexible marked outer sheath to indicate depth of penetration and a soft inner catheter, which is made from a non-toxic biocompatible medical polymer. The outer and inner diameters of the Wallace inner catheter are 1.6 and 0.75 mm respectively (Wallace Product information leaflet).

Embryo transfer

All patients had mock embryo transfers performed prior to their IVF cycle, as this is routine practice in the study unit. On the day of actual embryo transfer, 160 patients were randomly allocated to the Wallace group and 148 to the Rocket group. For embryo transfer, patients were placed supine in the lithotomy position. The cervix was exposed using a Cusco bi-valve speculum. Any cervical mucus encountered was gently removed with a simple swab soaked in phosphate-buffered saline (PBS; Gibco, Paisley, Scotland). Patients had a full bladder for embryo transfer, and the uterus was visualized using ultrasound with an abdominal probe (Combison 311; Kretz Technic, Zipf, Austria). Under ultrasound control, the catheter was introduced into the mid-uterine cavity, taking care to avoid touching the uterine fundus. The embryos were then gently expelled with the aid of a tuberculin syringe. The catheter remained in place for 20–30 s after the embryos were expelled. The transfer catheter was then flushed with medium under light microscopy to ensure that no embryos were retained in the catheter. Experienced competent operators (all the authors) performed all transfers, each having performed a minimum of 200 transfers independently prior to the commencement of the study, and all familiar with the two catheters investigated in this study. Following embryo transfer, patients were kept in bed for 20–30 min before being discharged. Luteal phase support was given in the form of progesterone pessaries (Cyclogest; Hoechst, Frankfurt, Germany). Serum HCG concentration was measured 14 days after oocyte retrieval, and if positive, an ultrasound was performed 14 days later, i.e. at 6 weeks gestation.

Details describing the number of embryos available and the number transferred, the grade of the embryo transfer, whether any embryos remained in the catheter after transfer, whether a change of catheter was necessary, and the visibility of the catheter under ultrasound were recorded. Additionally, the patient was asked to score any discomfort during the transfer using a visual linear analogue score.

Statistical analysis

Statistical analysis was performed using the Mann–Whitney test for comparison of means and the chi-squared test for proportions; values of $P < 0.05$ were considered significant. Analysis was performed using STATA 6 statistical package (Statacorp 1999, College Station, Texas, USA).

Results

Results were analysed on an intention to treat basis. There were no statistically significant differences in patient demographics. Embryo transfer details between the two study groups as shown in **Table 1**. The patients were also comparable with regard to the cause and duration of infertility. Difficult transfers occasionally required the use of a malleable stylet, grasping of the cervix with a tenaculum or change of catheter to an alternative model. These details were carefully recorded as well as the incidence of bleeding and excessive manipulation. There was no statistically significant difference in the difficulty of transfer between the two catheters. None of the transfers in either group required sedation. Use of tenaculum was needed in one transfer in the Wallace group (0.6%), and in four cases in the Rocket group (2.7%), whereas cervical dilatation was required in four (2.5%), and five transfers (3.4%) respectively.

Clinical PR (fetal heart seen on transvaginal ultrasound) was the primary outcome measure, and is presented in **Table 2** with the other secondary outcome measures. Embryos were retained in the catheter post-transfer in a significantly greater number of cases using the Wallace catheter than the Rocket catheter ($P < 0.05$). In addition, the catheter tip was clearly seen on ultrasound in a significantly greater number of cases with the Rocket catheter than with the Wallace catheter ($P < 0.05$). The level of patient discomfort was similar in both groups.

Table 1. Patient characteristics and embryo transfer details for patients in the two study groups.

Parameter	*Catheter type*	
	Wallace (n = *160*)	*Rocket* (n = *148*)
Mean age in years ± SD	35.1 ± 4.9	35.4 ± 4.4
Mean body mass index ± SD	22.7 ± 3.3	22.6 ± 3.1
Nulliparity *n* (%)	129 (80.6)	117 (79.1)
Smoking *n* (%)	19 (11.9)	18 (12.1)
Race *n* (%)		
Caucasian	125 (78.1)	118 (79.7)
Black	9 (5.6)	5 (3.4)
Asian	20 (12.5)	19 (12.8)
Other	6 (3.8)	6 (4.1)
Mean no. of previous IVF cycles ± SD	1.9 ± 1.2	2.2 ± 1.6
Median no. of embryos transferred (range)	2 (2–3)	2 (2–3)
No. of embryos transferred on day 2 (%)	127 (79.4)	116 (78.4)
No. of embryos transferred on day 3 (%)	33 (20.6)	32 (21.6)
Mean no. of embryos available ± SD	5.8 ± 3.0	5.9 ± 3.1

There were no statistically significant differences between the two groups.

Table 2. Primary and secondary outcome measures in the two study groups.

Outcome measure	*Catheter type*	
	Wallace (n = *160*)	*Rocket* (n = *148*)
Clinical pregnancy	37 (23.1)	34 (23.0)
Implantation	21 (13.1)	17 (11.5)
Change of catheter required	7 (4.4)	6 (4.1)
Embryos retained in catheter	22[a] (13.8)	4[a] (2.7)
Catheter tip clearly seen on ultrasound	118[b] (73.8)	124[b] (83.8)
Mean patient discomfort measure ± SD	12.3 ± 14.2	14.2 ± 16.9

Values are *n* (%), unless otherwise stated.
[a,b]Values with the same superscript letter are significantly different ($P < 0.05$).

Discussion

Embryo transfer remains a critical step in achieving pregnancy following IVF. Changes in transfer technique and catheter design aim to improve implantation rates following this least understood and least efficient step in assisted reproduction. It is also known that catheter choice has largely remained a matter of personal/institutional choice, availability, and implied cost–effectiveness (Abou-Setta *et al*., 2005), rather than a consequence of evidence-based medicine. This prospective RCT was therefore initiated in order to discover whether a difference exists in terms of PR between two frequently used catheters. For the most part, the present study appears to be well designed, with a good patient distribution between the two embryo transfer catheter groups, as well as lack of major differences and confounders between the study groups, including stimulation protocol, and various transfer aspects such as embryo characteristics, and transfer details.

A recent Cochrane review has indicated that ultrasound guidance during embryo transfer appears to improve the chance of clinical pregnancy and live birth compared with clinical touch methods (Brown *et al*., 2007). Some units reserve ultrasound guidance for difficult cases only, but in the study unit ultrasound guidance is now routine for all transfers. Thus, visibility of the catheter under ultrasound became an important secondary outcome parameter in the present study. This study has revealed that Rocket transfer catheter was clearly seen in significantly more transfers than the Wallace catheter ($P < 0.05$). Interestingly, there was not a concomitant statistically significant difference in implantation or PR between catheters.

The PR in all transfers performed in this study when the catheter tip was visible (73/308, 23.7%) was higher than when the tip was not clearly seen (59/308, 19.2%). Moreover, the PR when the catheter was clearly seen in the Wallace and Rocket groups was 23.8 and 24.3% (n = 38/160 and 36/148 respectively), and this fell to 21.9 and 14.9% (n = 35 and 22) respectively when the catheter was not clearly seen. All these data, although statistically non-significant, confirm that good visibility on ultrasound is associated with higher pregnancy rates, and conforms to the findings of other investigators, who suggest that the use of an echogenic Wallace catheter simplifies ultrasound-guided embryo transfer (Coroleu *et al*., 2006), and improves PR (Brown *et al*., 2007). The findings of the present study are, however, at odds

with the recent plausible conclusions of a systematic review indicating that there is a definite statistical trend for higher clinical pregnancy rates using soft catheters, even though they are associated with more traumatic events (Abou-Setta *et al.*, 2005). The latter review has, however, still indicated the need for more randomized controlled trials to support the development of an 'ideal' soft embryo transfer catheter. Moreover, no statistically significant differences were found in the incidence of traumatic events between the two study groups.

It is well recognized that one of the most important predictors of clinical PR is the number of embryos transferred per number available (Templeton and Morris, 1998). The majority of embryo transfers performed in the study unit involve two embryos, and there was no significant difference in the number of embryos transferred per number available in the two groups. Residual embryos were noted in significantly more cases following Wallace transfer (13.8%) than those following Rocket transfer (2.7%; $P < 0.05$), with no subsequent effect on PR. The overall average rate of retained embryos in the study unit is usually in the range of 2–5%. This compares with 3.9% reported by Lee and colleagues in a study involving >1000 transfers (Lee *et al.*, 2004). The latter found that immediate retransfer of embryos retained in the catheter following the initial transfer attempt did not have an adverse effect on pregnancy outcome. This in accordance with the results of this study, although the overall numbers are still too small for this to have any impact on PR. It is possible that the difference in inner catheter diameter (Wallace 0.75 mm; Rocket 1 mm) may influence this finding. It is interesting that in a recent systematic review, and using the random effects model, there was a non-significant trend towards increased likelihood of retained embryos using the soft catheters (56/644; 8.7%) versus firm ones (16/634; 2.5%) (Abou-Setta *et al.*, 2005), which again conforms to the overall findings of the present study.

The impact of the 'physician factor' is known to affect embryo transfer results (Angelini *et al.*, 2006). The distribution of catheter use was similar between operators in this study, but the numbers involved were too small to allow for any meaningful statistical analysis. Analyses of independent practitioner performance within a programme may enhance patient autonomy, fairness and efficiency, but is particularly prone to the biases of patient selection, random variations and lack of performance standards (Lu, 1999). Patient discomfort was found to be similar in both groups, and is usually attributed to a full bladder around the time of embryo transfer.

Of importance is the finding that a change of catheter was required in a similar number of cases in both study groups. It is also worth noting that when data were pooled in a recent systematic review, there was a non-significant trend towards increased likelihood of catheter failure using soft catheters (Abou-Setta *et al.*, 2005). This highlights the need for physicians to be familiar with several different types of catheter in case of difficult transfers. When implantation rates and pregnancy results are equivalent, cost benefit may become the most influential factor in catheter selection. More high quality, adequately powered RCT are still needed to improve embryo transfer catheter technology, and optimize the final process by which women undergoing IVF can achieve a successful pregnancy.

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