The Effect of Ease of Transfer and Type of Catheter Used on Pregnancy and Implantation Rates in an IVF Program

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Purpose: To test the effects of type of embryo transfer catheter, transfer difficulty, and observations after the transfer procedure on pregnancy and implantation rates in an IVF programme.

Methods: Patients were prepared for IVF using standard protocols. Embryo transfer was performed using either Edwards-Wallace or TDT catheter. The difficulty of transfer was graded by a clinician and biologist. Blood observed inside the catheter after the transfer procedure was scored as endometrial damage. Pregnancy and implantation rates were scored.

Results: Type of embryo transfer catheter and the observation of blood did not significantly affect pregnancy and implantation rates when transfer was performed by a single operator.

Conclusions: In the hands of experienced, skilled operators, neither choice of transfer catheter and difficulty of transfer nor observations of blood on the transfer catheter caused any significant reduction in outcome to the patient.

KEY WORDS: Embryo transfer; human embryo; in vitro fertilization; pregnancy.

INTRODUCTION

In vitro fertilization (IVF) technology involves the aspiration of human oocytes followed by the consequent transfer of cleaving embryos into the patients' uterus. The transfer procedure is one of the most delicate procedures of assisted reproduction, and both the type of catheter used for embryo transfer and the skill of the clinician play a fundamental role in the success rate to the patient (1–8). General agreement on the indications for a successful transfer suggest that the use of standardized protocols is an important factor (9).

In fact, even within IVF units the success rate per clinician can vary widely (4). The outcome of a transfer procedure where uterine damage has resulted can lead to a continued series of contractions of the uterus, probably leading to the expulsion of the embryos (10).

Both choice of technique and choice of embryo replacement catheter play an important role in the embryo replacement. The use of ultrasound-directed embryo transfer has helped increase pregnancy rates significantly over "blind" techniques (11,12). Furthermore, the development of soft-tip embryo replacement catheters has been suggested to increase pregnancy rates by damaging the uterine wall less during the replacement procedure (12–14).

In this paper, we have compared pregnancy and implantation rates after 163 IVF-embryo transfer procedures, involving two types of transfer catheter and a variety of grades of difficulty in embryo transfer procedures. We show that neither transfer catheter nor the observation of blood are determinative of the success rate when the embryo transfer is performed by a single, experienced operator.

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MATERIALS AND METHODS

Patients

Patients were attending the IVF clinic for IVF protocols. Patients were prepared using standard controlled ovarian hyperstimulation protocols including downregulation of the pituitary gland with a GnRH agonist (Decapeptyl, Ipsen, Italy) followed by ovarian stimulation with exogenous FSH (Gonal-F, Serono, Italy). Oocyte retrieval was performed 36 h after the administration of 10,000 UI β -hCG when two to three follicles of 18–20 mm diameter were observed by ultrasound examination, and blood 17 β -oestradiol levels reached 150–200 pg/mL/follicle over 18 mm. Because the Italian State finances the IVF centre in Naples and therefore patients do not pay for IVF treatment, oocytes are routinely treated by ICSI to guarantee optimal fertilization rates. Oocytes were processed for ICSI, using commercial IVF medium (Medicult, Copenhagen, Denmark) preequilibrated to 37°C and 5% CO₂. Zygote quality was scored 16–20 h after ICSI. Embryo quality was assessed every 24 h and embryos were transferred on the second or third day after oocyte retrieval. Embryo transfer procedures involved the use of either soft catheters (Edwards-Wallace, SIMS Portex, UK) or catheters designed for difficult embryo transfer (TDT, Laboratories CCD, France) in a medium containing 75% patients serum: 25% embryo culture medium. Embryo transfer difficulty was graded by agreement between the clinician and biologist. The presence of blood within the tip of the catheter after transfer was interpreted as damage to the endometrium. The presence of blood outside the tip was interpreted as damage to the cervix and not the endometrium.

Study Design

The study is a retrospective trial of 163 patients treated in the Polyclinic of Naples between January and May 2000. Patients were unselected for age, BMI, and treatment protocol. Patients diagnosed for endometriosis or polycystic ovarian syndrome were excluded from the study. As stated above, all patients were treated by ICSI without reference to sperm quality in order to ensure the comparability of the assessments.

Statistics

All data is presented as mean $\pm$ standard deviation of the mean, except where stated. Statistical

analysis was performed with SigmaStat software (SPSS, Erkrath, Germany).

RESULTS

In total, 163 cycles of IVF technology were performed during the period from January 2000 to February 2001. A total of 1681 oocytes were retrieved of which 1439 were considered mature and therefore inseminated. We achieved a fertilization rate of 81% (1166 mature oocytes fertilized) and a total of 572 embryos were transferred to the patients' uterus. The type of transfer to be expected from each patient was tested a priori to the cycle of IVF by performing a false transfer during ambulatory monitoring of the patients' menstrual cycles. This enabled the avoidance of procedures where a change in catheter was required during the embryo transfer procedure, a variable that can cause further damage to the patients' uterus and so negatively affect the outcome without any signals visible to the operator. We achieved a total of 69 pregnancies, in which 80 embryos were implanted and 69 embryos are presently continuing to develop.

We analysed the results retrospectively to test whether the transfer procedure, type of catheter, and signs of damage to the uterus did affect the outcome of the procedure. We first tested whether the difficulty of the procedure, independent of other variables, influenced the outcome. The transfer difficulty was graded as easy, medium, or difficult by both the clinician and the biologist. In total, 111 easy transfers, 34 medium, and 18 difficult procedures were performed (Table I).

Table I. Pregnancy and Implantation Rates According to Ease of Transfer

	Easy	Medium	Difficult
No. of patients	111	34	18
Maternal age	32.7 $\pm$ 4.7	34.1 $\pm$ 4.3	32.0 $\pm$ 6.6
Total embryos transferred (mean per patient)	390 (3.5 $\pm$ 0.9)	121 (3.6 $\pm$ 0.9)	61 (3.6 $\pm$ 0.6)
Observations of blood on catheter (%)	20 (18)	6 (18)	3 (17)
Pregnancies (%)	49 (44)	14 (41)	6 (35)
No. of foetal heart beats (implantation rate %)	54 (14)	16 (13)	10 (16)
Ongoing pregnancies (clinical implantation rate %)	47 (12)	15 (12)	7 (11)

The pregnancy and implantation rates for easy transfers were 44 and 14% respectively (Table I). Medium transfers were characterized by a pregnancy rate of 41% and an implantation rate of 13% (Table I). Difficult transfers were characterized by highly similar outcomes to the easy transfers. In these cases, the pregnancy rate was 35% and an implantation rate of 16% was achieved (Table I). These data suggest that, when performed correctly, the difficulty of transfer does not influence the outcome to the patient.

In the present report, two types of embryo transfer catheter were used. The type of catheter differ in the hardness of the tip and hence the possibility of inducing damage to the uterus during the procedure. We examined whether the type of transfer catheter influenced the outcome of the IVF procedure by again comparing pregnancy and implantation rates. We performed 148 embryo transfer procedures with the soft-tip Edwards-Wallace catheter. The procedures resulted in a pregnancy rate of 44% and an implantation rate of 14% (Table II). When the TDT, a harder catheter recommended for difficult transfer procedures was used, 27% pregnancies with an implantation rate of 11% was achieved (Table II). The pregnancy and implantation rates suggested a trend to lower success rates with the TDT catheter, although the data were not significantly different (Table II). These data suggest that the type of catheter used during embryo transfer does influence the pregnancy rate, although the differences are not significant when embryo transfer is performed by an experienced operator.

Table II. Pregnancy and Implantation Rates According to Type of Transfer Catheter

	Edwards-Wallace	TDT	P
No. of patients	148	15	N/A
Maternal age	33.1 ± 4.6	31.1 ± 7.0	0.13 ^a
Total embryos transferred (mean per patient)	516 (3.5 ± 0.9)	56 (3.7 ± 0.5)	0.39 ^a
Observations of blood on catheter (%)	26 (17)	3 (20)	0.95 ^b
Pregnancies (%)	65 (44)	4 (26.6)	0.31 ^b
No. of foetal heart beats (implantation rate %)	74 (14)	6 (10.7)	0.97 ^b
Ongoing pregnancies (clinical implantation rate %)	65 (13)	4 (7)	0.79 ^b

^a Two-tailed *t* test.

^b *z* test.

Table III. Pregnancy and Implantation Rates According to Endometrial Damage

	No blood	Blood	P
No. of patients	134	29	N/A
Maternal age	32.9 ± 4.7	32.8 ± 5.6	0.92 ^a
Total embryos transferred (mean per patient)	471 (3.5 ± 0.9)	101 (3.5 ± 0.8)	1.0 ^a
Pregnancies (%)	60 (45)	9 (31)	0.24 ^b
No. of foetal heart beats (implantation rate %)	70 (15)	10 (9.9)	0.67 ^b
Ongoing pregnancies (clinical implantation rate %)	59 (13)	10 (9.9)	0.882 ^b

^a Two-tailed *t* test.

^b *z* test.

Damage to the endometrium inflicted during the embryo transfer procedure usually results in the observation of blood within the tip of the catheter. We tested whether such an observation was indicative of a negative outcome by comparing procedures where blood was observed against “clean” procedures. Where no blood was observed after embryo transfer, 45% pregnancies were achieved with a corresponding implantation rate of 15% (Table III). Thirty-one percent pregnancies with an implantation rate of 9.9% were achieved in cases where blood was clearly visible inside the catheter (Table III). Again, a trend to lower success rates was observed in cases where blood was present inside the transfer catheter, although no significant differences were noted.

DISCUSSION

The technique of embryo transfer is one of the most important stages during cycles of IVF. Damage to the uterine wall, resulting when the catheter tip touches the endometrium, may cause intrauterine bleeding which can lead to the rejection of the embryos and a negative outcome (15). Touching the uterine wall with any embryo transfer catheter has been shown furthermore to cause a long series of contractions in the uterus which probably lead to the expulsion of embryos and a negative outcome to the patient (10). In this work, we have tested whether difficulty of transfer procedure, type of catheter used, and signs of damage to the endometrium can be used to determine the outcome.

The difficulty of the transfer procedure is an empirical measure where both clinician and biologist must agree to a score. In the present analysis, the graded difficulty of the transfer procedure did not affect outcome in terms of pregnancies and the implantation rate of the embryos. These data suggest that, when performed with attention, the transfer difficulty per se does not affect pregnancy outcome. The difficulty of embryo transfer has been suggested to negatively affect IVF outcome in other cases (16,17). In the present work, no relation between blood on the catheter and transfer difficulty was observed (Table II). We suggest that transfer difficulty is not the negative variable in those cases, but the skill of the operator in avoiding uterine damage even in the most difficult cases.

We tested whether the type of embryo replacement catheter and the presence of blood in the transfer catheter affected the pregnancy and implantation rate. Factors such as maternal age and number of embryos transferred were equal in the two groups. The use of the TDT hard-tip catheter caused a trend towards reduced success rates, although the results were not significantly lower than for soft-tip catheters. This was not because of a high number of observations of blood on the catheter because the incidence of blood on the catheter tip was equal (Table II). Furthermore, the differences were not due to transfer difficulty as we have already shown that transfer difficulty is not an indicative variable in the present data. These data suggest that although the use of hard-tip catheters can cause a reduction in pregnancy and implantation rates in cycles of IVF, the differences are reduced to a minimum in the hands of experienced operators.

The presence of blood in the embryo transfer catheter at the end of the transfer procedure has been correlated with a reduction in the pregnancy and implantation rates (15). In the present data, we noted a rather more modest reduction than the six- to seven fold decrease in pregnancy rates reported by these authors (15). In fact, our results were not significantly different to the outcome in cases where no blood was observed. We cannot comment on the previous authors' experience, but state that in the present report the amount of blood at the tip of the catheter was never excessive. It is therefore highly possible that the amount of blood observed is correlated with pregnancy rates, and not simply the observation of blood.

The above data therefore suggest that transfer procedure and type of catheter used during the procedure does not significantly affect the outcome of IVF or

ICSI cycles when the same experienced operator performs the procedure.

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