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ORIGINAL ARTICLE

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Embryo transfer technic – role of transfer catheter

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OBJECTIVE(S) : To analyze the performance of four different embryo transfer catheters viz. Wallace, Frydman, Labotect and TDT in an IVF-ET Program.

METHOD(S) : The embryo transfer cycles were grouped into four according to the catheter used and the pregnancy rates were compared in each group. Woman's age, diagnosis, ovulation induction method and number of embryos transfered were similar in all the four groups. The ease or difficulty in transfer was also noted and pregnancy rates compared.

RESULTS : The pregnancy rates were better (P<0.001) with soft catheters (Labotect 39.4%, Wallace 41.4%) as compared to stiff ones (Frydman 24.2%, TDT 31.4%) but when the number of embryos transferred in each group was taken into account and relationship between type of catheter and success rate was analyzed keeping the number of embryos fixed in each group, there was no statistically significant difference in pregnancy rates between the four groups. The ease or difficulty in transfer does not appears to influence the implantation rate.

CONCLUSION(S) : Catheter choice in an IVF-ET program does not influence success rate. Most important variable affecting success rate is the number of embryos transferred.

Key words : embryo transfer, embryo transfer catheters, pregnancy rate

Introduction

The different factors influencing the pregnancy rate in an IVF-ET program had been studied by many investigators in an endeavor to improve results [1,2]. These include age of the patient, the type of ovarian stimulation, the use of human chorionic gonadotrophin, the number of eggs collected, the number of embryos transferred [1] and the embryo quality [2]. It is estimated that 85% of the embryos replaced during in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) fail to implant [3]. The exact cause of this low implantation rate is unknown, but it may depend upon multiple factors including embryo quality, endometrial receptivity and the technique of the embryo transfer itself.

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Although every step in the IVF-ET procedure is important, the impact of embryo transfer (ET) procedure on pregnancy rate is significant. The fact that embryo transfer technique is one of the most critical procedures in successful assisted reproduction has recently drawn attention of many investigators. Crucial aspects of embryo replacement such as presence of blood or mucus on the transfer catheter [4], catheter choice [5], dummy embryo transfer [6], ultrasonography guided transfer [7], presence of uterine contraction [8], difficulty in embryo transfer [6] and practitioners differences [9] have been reported to affect success rate in an IVF-ET program.

The most commonly used and effective route of embryo replacement till date is transcervical. In order to find out whether catheter choice influences the pregnancy rate in an IVF-ET program, a retrospective analysis of embryo replacement was carried out. We compared the performance of four different ET catheters and the ease of embryo replacement procedure in terms of pregnancy rate.

Material and Methods

Seven hundred and seventy embryo transfers were included in this study. Transfers of cryopreserved embryos were not included. The patients were grouped into four groups, according to the catheter used for embryo transfer. The ease or difficulty in transfer and whether traction was used during the procedure were noted in all four groups. The performance of these catheters was compared and the results of IVF-ET in terms of pregnancy rate were evaluated.

The age of these patients ranged from 22 to 34 years. Ovarian hyperstimulation was done by down regulation and induction by clomiphene citrate (Table 1). Cycles were monitored by using serial follicular ultransonography and measurement of serum estradiol levels. Once adequate follicular maturation had been obtained, human chorionic gonadotrophin was administered and oocyte retrieval was performed about 36 hours later under tansvaginal sonography guidance and general anesthesia. Follicular fluids were examined immediately under the microscope for oocytes, which were then graded for maturity and incubated in a humidified atmosphere of 37^0 C and 5% CO_2 (Heraus, Germany; Forma Scientific, USA). The oocytes were placed in insemination medium (IVF-20, Scandenavian IVF sciences, Sweden or Universal IVF medium, Medicult, Denmark) and inseminated with 50,000-100,000 total motile spermatozoa, about 4 to 6 hours postretrieval. Approximately 18 hours later the oocytes were examined for evidence of fertilization and transferred to fresh media under oil (prepared overnight). Each and every procedure was done under preequilibrated liquid paraffin oil (Ovoil, SIVF or Liquid petroleum oil from medicult).

ET Procedure

In a cycle preceding the IVF-ET, hysteroscopy and trial transfer were done to determine any endometrial abnormality and the direction and length of the uterine cavity. Embryo transfer was usually done (not under sonography guidance) 48 to 72 hours after oocyte retrieval. To reduce uterine contractility and anxiety, the patients were given 5 mg of midazolam intramuscularly 30 minutes before the embryo transfer.

All patients were placed in lithotomy position and no anesthesia was given. A maximum of three or four embryos were transferred. A sterile bivalve Cusco's speculum was inserted into the vagina and cervix was exposed. The exocervix was cleansed of cervical mucus with sterile cotton swab and a small amount of culture medium. Meanwhile in the adjacent embryo culture laboratory, the embryos were evaluated for the morphological appearance and the best three or four embryos selected for transfer were put together in a multi well (Nunc; Denmark) containing small amount of culture medium (IVF – 20).

In every kind of catheter, the catheter was rinsed twice with the transfer medium and then loaded in the following sequence: 15 to 20 □L of transfer medium, 10 □L of air, the embryos in 15-20 □L of transfer medium, and 10-15 □L of air to seal the catheter.

The embryologist passed the loaded catheter to the gynecologist performing embryo transfer. The tip of the catheter was placed about 1 cm from the uterine fundus and the embryos were gently released in the uterine cavity. The catheter was kept in place for about 10-15 seconds, gradually rotated to 180^0 and then withdrawn keeping the plunger tightly pressed. The catheter was immediately checked for the presence of blood, mucus or retained embryos.

The transfer was recorded as easy whenever the catheter could be passed easily into the uterine cavity. The uterocervical axis was corrected by maneuvering the speculum or by applying traction to the cervix using a tenaculum whenever the catheter could not be passed easily. In still difficult cases, further manipulation such as dilatation of the cervical canal was done. After ET, the patients remained supine in a slightly trendelenberg position for approximately half an hour. They usually stayed overnight in the hospital and were discharged the next morning. Serum βhCG was estimated 14 days after ET and values > 10 mIU/L were considered to be positive for pregnancy.

ET Catheters

The Wallace catheter (Wallace Ltd, Colchester, England) is a 17.5 cm long soft open ended silicone catheter with 1.6 mm external diameter. It has a more rigid outer Teflon sleeve that is used as an introducer through the cervical canal.

The Frydman catheter 4.5 (Laboratoire CCD; France) 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 TDT catheter consists of two sets. The first set has a metal mandrel coated with plastic, which fits into the Frydman catheter. This set serves as an introducer through the cervix. It is introduced through the cervical canal into the uterine cavity after adjusting or bending it according to the curvature of the cervical canal. Once in position the inner metal mandrel is removed from the introducer and a second set consisting of a thin catheter on a microsteel tube, with embryos loaded in it, is introduced through the Frydman catheter (introducer) into the uterine cavity.

The Labotect catheter is a 150 mm long atraumatic catheter having a precurved guiding cannula with spherical finish. It can be used reliably in difficult anatomical conditions and is easy and safe to handle through metal reinforced shaft inside the catheter.

Statistical Analysis

Because the data were retrospectively analyzed, sample size was determined by a defined period of time and was not prospectively determined using power analysis. The data of averages like age of the patients and the number of embryos transferred were expressed as mean ± standard deviation. Analysis was performed using Z test (as sample size was large). The association among non-parametric variables, such as the type of catheter and success rate, was analyzed using chi square test at 5% and 1% level of significance.

Results

The 770 embryo replacement procedures performed after IVF resulted in 272 clinical pregnancies i.e. 35.3% per embryo replacement. All the embryo replacements were done by the same gynecologist. Patients in the four groups showed no difference in terms of age, cause of infertility and ovulation induction protocol etc. (Table 1). In all cases of male factor infertility intracytoplasmic sperm injection was performed.

Table 1. Patient characteristics.

	Catheter used			
	Wallace n=287	**Frydman n=157**	**TDT n=156**	**Labotect n=170**
Age (mean ± SD)	31.7±4.07	32.92±4.94	32.14±4.99	31.62±4.53
Indication				
Male Factor	117 (40.77%)	67 (42.68%)	66 (42.31%)	73 (42.94)
Tubal factor	128 (44.6%)	71 (45.22%)	68 (43.59%)	86 (50.59%)
Endometriosis	3 (1.05%)	3 (1.91%)	5 (3.21%)	4 (2.35%)
Unexplained	39 (13.59%)	16 (10.19%)	17 (10.90%)	7 (4.12%)
Ovulation induction				
CC/hMG	41 (14.29%)	20 (12.74%)	30 (19.23%)	28 (16.47%)
Down regulation and hMG/FSH	246 (85.71%)	137 (87.26%)	126 (80.77%)	142 (83.53%)

As shown in Table 2, most of the transfers in the four groups were easy but the Frydman catheter had the highest number of transfers where cervical traction was used (P<0.05).

Table 2. Types of transfer and catheter used [e]

	Easy	Easy with traction	Difficult
Labotect[a]	157	11	2
Frydman[b]	135	21	1
TDT[c]	144	11	1
Wallace[d]	263	22	2

[a] Chi-square = 0.801; NS

[b] Chi-square = 6.257; P<0.05 Significant

[c] Chi-square = 0.391; NS

[d] Chi-square = 0.267; NS

[e] Chi-square = 7.190; NS

The pregnancy rate for different catheters is shown in Table 3. The Frydman catheter has shown a significantly lower pregnancy rate when compared with the other catheters. The usage of Frydman catheter has a highly significant effect on success. It is in negative direction i.e. the success rate is only 24% with Frydman catheter whereas with others (other than Frydman) it is 38%. The difference is about 14% which is reflected in Chi-square value, which is showing high significance. The TDT, Labotect and Wallace catheters scored better than the Frydman catheter, with Wallace showing best result (P<0.01). The pregnancy rate per embryo transfer was slightly higher in the Wallace group than in the Labotect group, but this difference was not significant.

Table 3. Type of catheter and success [e]

	Pregnancy	Percent
Labotect [a]	67/170	39.4
Frydman [b]	38/157	24.2
TDT [c]	49/156	31.4
Wallace [d]	118/287	41.4

[a] Chi-square = 1.620; NS

[b] Chi-square = 10.149; P<0.01 Significant

[c] Chi-square = 1.268; NS

[d] Chi-square = 7.031; P<0.01 Significant

[e] Chi-square = 14.776; P<0.01 NS

As shown in Table 4, the pregnancy rate was compared after easy transfer (252/699), after transfer where traction was used (17/65) and after difficult transfer (3/6). Although the pregnancy rate appeared to be slightly higher in patients who had easy transfer than in those where cervical traction was used, the difference was not statistically significant.

Table 4. Type of transfer and success

	Pregnancy	percent
Easy [a]	252/699	36
Easy with traction [b]	17/65	26
Difficult[c]	3/6	50

[a] Chi-square = 1.70 [b] Chi-square = 2.646 [c] Chi-square = 0.756

None of the differences were significant

Table 5. Number of embryos transferred

	Wallace[a] n=287	Frydman[b] n=157	TDT[c] n=156	Labotect[d] n=170
Embryos transferred (mean ± SD)	3.08 ± 0.90	2.38 ± 1.03	2.68 ± 1.07	2.85±0.96

[a] Z test = 6.19; P<0.01 [b] Z test = 5.91; P<0.01

[c] Z test = 1.68; P<0.05 [d] Z test = 0.70; P>0.05

Table 6. Pregnancy rate

No. of embryos Transferred	Wallace	Other than Wallace	Frydman	Other than Frydman
1	1/10	13/73 [a]	4/34	10/49 [e]
2	27/75	38/156 [b]	15/61	50/170 [f]
3	37/84	45/128 [c]	9/31	73/181 [g]
4	53/117	57/123 [d]	10/31	100/209 [h]

[a] Chi-square = 0.725 [b] Chi-square = 3.521

[c] Chi-square = 2.083 [d] Chi-square = 0.067

[e] Chi-square = 1.407 [f] Chi-square = 0.442

[g] Chi-square = 1.433 [h] Chi-square = 1.342

All the differences are nonsignificant

Discussion

The results of this study show that the performance of soft catheters (Labotect, Wallace) was best in IVF-ET program. The Frydman catheter yielded the lowest pregnancy rate. Most of the transfers where cervical traction with a tenaculum was required belonged to the Frydman catheter group (Table 2). Wallace catheter appears to have a statistically significant effect on success rate (Table 3). This improved success rate with Wallace catheter could be explained by two factors. One is the catheter itself has a significant effect on pregnancy rate and the other could be the number of embryos transferred in the four groups of patients. To determine the significance of number of embryos transferred upon pregnancy rate, we analyzed the relationship between the type of catheter and success rate, keeping the number of embryos fixed to one, two, three and four (Table 6). This analysis shows no statistical difference in success rate with any of the catheters. Since this was a retrospective study, the four study groups were not homogenous in term of number of embryos transferred. The apparent high success rate with Wallace catheter and low rate with Frydman catheter could be explained by the statistically significant difference in the number of embryos transferred in the two groups.

Several ET catheters are commercially available. Variations in catheter design include stiff or soft materials, end or side openings, the presence of an outer sheath, malleability, and quality of the materials and finish [10]. An acceptable catheter for human ET should be easy to use and should ensure proper placement in the uterus. Also it should be made of nontoxic material, and should be simple and cheap [5]. Stiff catheters and use of a rigid outer sheath make catheter placement easier but may cause more bleeding, trauma, mucus plugging, and stimulation of uterine contractions. Soft catheters allow the tip to follow the contour of the cervical and uterine access and minimize trauma to the endometrium [10].

The benefit of one catheter over another is controversial. While some studies [1,11-14], reveal no significant difference in the performance of various ET catheters in terms of pregnancy rate, others [5],[7],[15] find significantly better performance of one catheter over other in relation to success rate. Ghazzawi et al [11] compared the (rigid) Erlangen catheter to the (soft) Wallace catheter in 320 patients in a randomized controlled trial. The pregnancy rate per ET was apparently higher in the Erlangen group than in the Wallace group, but the difference was not significant. In a similar study, Urman et al [12] compared the (soft) Wallace catheter to (rigid) TDT catheter in 428 patients undergoing ET. In this retrospective study, the authors found that both catheters performed similarly, although there was a slight, but non-significant, increase in clinical pregnancy and implantation rates with Wallace catheter (41.6% vs 36.0% and 16% vs 14.4% respectively). Similarly, Al-Shawaf et al [13]. showed that there was no difference in the performance of the (soft) Wallace and the (rigid) Frydman catheters with regard to pregnancy rates (30.03% vs 30.7% respectively). Burke et al [14] in a retrospective study analyzed 46 frozen and 159 fresh embryo transfers and found that the catheter type (Wallace vs Tefcat) did not affect the outcome.

On the contrary, Wisanto et al [5], in a prospective randomized study of 400 consecutive ETs, recommended the use of the Frydman set over the Wallace catheter and TDT catheter because of higher pregnancy rates (32.3% vs 19.2% and 19.4% respectively). In a prospective, randomized, clinical study, Meriano et al [15] compared 32 patients who had embryo transfer using the Tomcat catheter with 34 patients using the TDT catheter. They found that the Tomcat catheter resulted in higher implantation (25.2% vs 8.4%) and clinical pregnancy rates (47% vs 14.7%) compared with those with TDT catheter. In another study, Wood et al [7] compared clinical pregnancy rates in 518 cycles in women undergoing embryo transfer. The clinical pregnancy rate in women using soft catheters (Wallace and TDT) were significantly higher than in those using hard catheters (Tomcat and Tefcat) viz., 36% vs 17%, respectively.

In our study, transfers where manipulation or cervical dilatation was required, seem to have adverse effect on the out come of IVF-ET. Although three out of six patients conceived after difficult transfer (Table 4) our number of difficult transfers is too small to draw any valid conclusion. Mansour et al [6] showed that difficult embryo transfers had a significantly lower pregnancy rate and implantation rate (4% and 1% respectively) compared with easy transfers (20.4% and 6.7% respectively). In contrast, Wisanto et al [5] and Burke et al [14] found no difference in success rates between easy and difficult transfers.

Taking the results of our study into account, we propose that catheter choice does not influence the success rate in an IVF-ET program. The ease or difficulty in transfer also does not influence the implantation rate.

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