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Does rotation during catheter withdrawal in embryo transfer increase pregnancy rates?

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Abstract

Background: The aim of this study was to determine whether there is a difference in pregnancy rates between groups that we removed directly and removed by rotating the embryo transfer catheter 360°.

Methods: The study group consisted of 552 patients who were withdrawn by 360° rotation and 797 patients who were withdrawn without catheter rotation. All patients underwent one or two fresh ETs on day 3 or 5. Groups were compared in terms of cycle characteristics and clinical pregnancy rates.

Results: There were no significant differences in demographic and clinical characteristics of both groups, such as age, body mass index (BMI), duration of infertility, causes of infertility, and basal hormone levels. Clinicals pregnancy rate, in the study group, 48% (265/552) and in the control group, 50.8% (405/797) were similar in both groups. When the implantation rate and miscarriage rate were examined, both groups were found to be similar.

Conclusion: It was found that 360° rotation while pulling catheter during embryo transfer had no effect on pregnancy and clinical pregnancy.

Keywords: Catheter rotation; Embryo transfer; Implantation; Pregnancy rate

1. INTRODUCTION

There are three components to success in assisted reproduction techniques: improving embryo quality, appropriate endometrial receptivity, and efficient embryo transfer (ET). Several studies have been conducted to improve the ET technique, but the results to date have been disappointing.[1,2] A survey in the United States showed that in vitro fertilization centers have adopted different ET methods.[3] The American Society for Reproductive Medicine has developed simulation programs and published guidelines for standardization of ET.[4]

Many factors influence the success of ET, including use of soft catheters, mock (dummy-trial) transfer, operator experience, use of ultrasonography during ET, a full bladder, location of the embryo in the uterine cavity, and cervical mucus cleaning.[2] Cervical mucus may block the end of the catheter and prevent expulsion of the embryo by a mechanical effect. In addition, mucus contaminating the tip of the catheter can adhere to and pull the embryo out of the uterine cavity.[5–7] Cleaning with a cotton swab and saline or medium is recommended, as uncleaned mucus can cause microbial contamination in the cavity. Uterine contractions can sometimes be stimulated when cleaning. A randomized controlled trial showed that the removal of cervical mucus resulted in improved rates of clinical pregnancies and live births.[8] In a cohort study, the clinical pregnancy rate was significantly higher when mucus aspiration was used compared with no mucus aspiration.[9]

After ET, waiting before catheter withdrawal is thought to be beneficial; however, it was reported that this did not increase pregnancy rates.[10,11] A recent study reported that after ET, rotating the catheter by 360° while withdrawing it ensured that the embryo remained in the uterus, rather than being removed due to adherence to the cervical mucus in the catheter tip, thereby improving the pregnancy rate.[12]

The present study was performed to determine whether there is a difference in pregnancy rate according to use of ET catheter rotation by retrospectively examining the files of patients in whom the ET catheter was removed either directly or by rotating 360°.

2. METHODS

2.1. Study design and participants

We retrospectively analyzed patients who underwent in vitro fertilization (IVF) for the first time between June 2016 and November 2018 at the Novafertil IVF Center. Written informed consent was obtained from all patients for both the IVF treatment and scientific use of their data. This study was approved by the institutional ethics committee (NEKN: 2019-012).

The criteria for inclusion in the study were (1) age 20 to 42 years and (2) body weight >50 kg. The exclusion criteria were (1) severe endometriosis (presence of endometrioma or diagnosis of stage 3/4 endometriosis with surgery), (2) serious systemic disease, (3) azoospermia, (4) uterine infertility, and (5) difficult ET or use of a hard catheter

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Among the patients undergoing IVF treatment and ET, the study group consisted of patients in whom the catheter was removed by rotating it 360°, whereas the control group consisted of patients in whom the catheter was removed directly without rotation. ET was performed by a single physician. Treatment cycles from the two groups were matched using patients' variables in the following order of priority: female age, antral follicle count, body mass index (BMI), infertility duration.

2.2. Description of interventions

A gonadotropin-releasing hormone (GnRH) antagonist protocol was started in all patients. The antral follicle count and basal hormone results were recorded on day 2 or 3 of the menstrual cycle. Gonadotropin (150–375 IU; Gonal-F; Merck, Istanbul, Turkey or Merional; IBSA Turkey, Istanbul, Turkey) was started according to the antral follicle count, basal hormone level, and BMI. The first folliculometry was performed on day 5 or 6 after ovarian stimulation, and the dose was adjusted according to the response. A GnRH antagonist (Cetrotide; Merck) was started on day 6 or when the leading follicle was 14 mm. A dose of 250 μg recombinant human chorionic gonadotropin (Ovitrelle; Merck) or 10 000 IU urinary human chorionic gonadotropin (Choriomon; IBSA, Istanbul, Turkey) was administered when at least three follicles exceeded 17 mm in size. Oocyte retrieval was performed 35 to 37 hours later. All patients received 8% vaginal progesterone gel applied twice daily. Intracytoplasmic sperm injection (ICSI) was applied. All patients underwent one or two fresh ETs on day 3 or 5 by a single clinician.

In the operating room, the cervix was observed using a vaginal speculum when the patient had a full bladder and was in the lithotomy position. Cervical mucus was removed with a cotton swab and saline solution. All transfers were performed under ultrasound guidance. Embryo loading was performed by the biologist using a Wallace soft catheter. Following slow insertion of the stiffer outer sheath of the catheter, the softer inner cannula carrying the embryos was set in position. The embryos were gently discharged after determining the appropriate location. After the transfer procedure, the catheter was gently removed by rotating at least 360° in the study group (Fig. 1) or without rotation in the control group. All catheters were checked for retained embryos, mucus, and blood by the embryologist at the end of the procedure.

2.3. Primary and secondary outcome measures

The primary outcome of the study was the clinical pregnancy rate. Pregnancy was detected by measuring the level of serum human chorionic gonadotropin at least 15 days after oocyte retrieval. Clinical pregnancy was diagnosed by ultrasonographic visualization of one or more gestational sacs or definitive clinical signs of pregnancy, including ectopic pregnancy.

2.4. Statistical analysis

Descriptive summary measures, expressed as the mean ± SD, were used for continuous variables, and categorical variables were expressed as numbers (percentage). Statistical analysis was performed based on the intent-to-treat population, defined as all enrolled participants. Data are presented as the mean ± SD, percentage. Student's *t* test was used to compare normally distributed continuous variables. The Mann-Whitney *U* test and Kruskal-Wallis test were used to compare variables with a non-normal distribution. The chi-square test was used to compare categorical variables. In all analyses, $p < 0.05$ was taken to indicate statistical significance. All data were analyzed using SPSS for Windows (version 20.0; SPSS Inc., Chicago, IL).

3. RESULTS

There were no statistically significant differences in age, BMI, the duration or cause of infertility, or basal hormone levels between the two groups (all $p > 0.05$) (Table 1).

There were no statistically significant differences in endometrial thickness on the trigger day, number of retrieved, mature, or fertilized oocytes, number of transferred embryos, or ET days (day3 or day 5) between the two groups (all $p > 0.05$). The biochemical pregnancy rate per ET was 53.9% (298/552) in the study group and 58.2% (464/797) in the control group, and the difference was not significant ($p = 0.112$). The clinical pregnancy rate per ET was similar between the study and control groups (48% (265/552) and 50.8% (405/797), respectively, $p = 0.310$). The implantation and miscarriage rates were not significantly different between the two groups ($p > 0.05$) (Table 2). In both groups, remaining embryos were detected after the catheter was removed in only three patients, and these embryos were transferred again.

4. DISCUSSION

The pregnancy, clinical pregnancy, implantation, and miscarriage rates were similar between the two groups in the present study. There was no evidence that catheter rotation following ET had a positive effect on pregnancy outcomes. These results were different from those reported by Yayla Abide et al,[12] and we attributed this discrepancy to the small number of samples in their study. On average, ET is performed on day 5 after ovarian stimulation in our clinic at the present time.

Some studies have indicated that cervical mucus interferes with ET by blocking passage of the embryos through the tip of the catheter, pulling embryos back from the site of expulsion, or contaminating the intrauterine environment with cervical flora. There have been several reports regarding the clearance of cervical mucus to increase the success of ET. Most of these studies had a small sample size.[8,13,14] Some of these studies showed

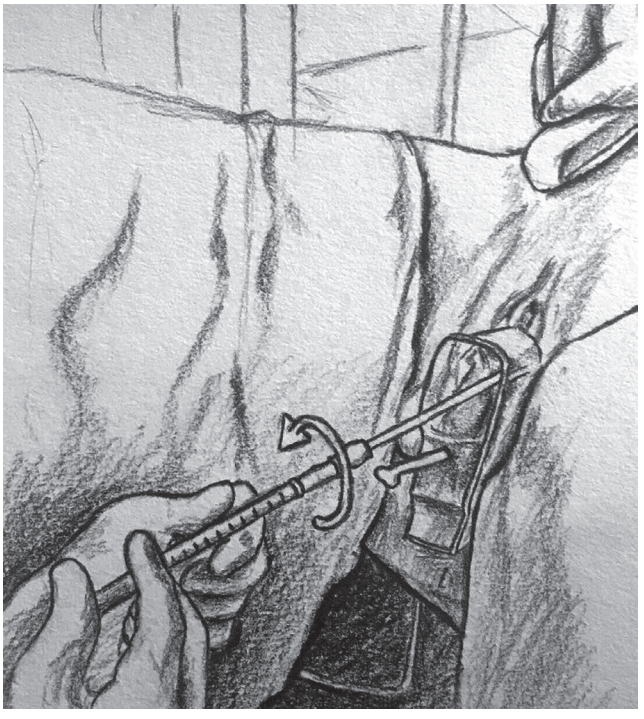

Fig. 1 Rotation of embryo transfer catheter during withdrawal.[12]

Table 1

Baseline characteristics and hormonal profile of patients (mean±SD)

	Study group (n:552)	Control group (n:797)	*p*
Baseline characteristics			
Age (y)	30.94 ± 5.91	30.58±5.84	0.273
BMI (kg/m^2)	25.64 ± 3.70	25.65 ± 3.59	0.954
Duration of infertility (y)	3.84 ± 1.93	3.76 ± 1.73	0.386
Day 3 FSH (IU/L)	5.97 ± 2.01	6.05 ± 2.05	0.447
Day 3 LH (IU/L)	5.92 ± 2.24	5.89 ±2.03	0.844
Day 3 E2 (pg/mL)	42.34 ± 21.70	43.17 ± 23.21	0.505
Day 3 P (ng/mL)	0.58 ± 0.38	0.57 ± 0.35	0.365
Indication for IVF (n)			
Male factor	162	205	
Tubal factor	104	137	
Male + tubal factor	23	40	
Mild endometriosis	1	3	
PCOS	93	149	
Hypogonadothropic hypogonadism	21	23	
Male+PCOS	2	2	
Mild endometriosis + PCOS	2	2	

BMI = body mass index; E2 = estradiol; FSH = follicle stimulan hormone; IVF = in vitro fertilization; LH = luteinizan hormone; P = progesterone; PCOS = polycystic ovary syndrome.

Table 2

Pregnancy outcomes and embryonic characteristics of the patients.

Characteristic	Study group (mean±SD)	Control group (mean±SD)	*p*
Endometrial thickness on trigger day (mm)	10.39±2.07	10.46±1.93	0.519
No of oocytes retrieved (n)	7.73±5.37	7.74±4.87	0.957
No. of MII oocytes (n)	5.83 ± 3.95	5.94 ± 3.60	0.600
No. of fertilized oocytes (n)	4.63±3.32	4.44±2.74	0.262
No of transferred embryos (n)	1.65±0.47	1.67±0.46	0.308
Day 3 transferred embryos (%)	66	69	0.401
Day 5 transferred embryos (%)	34	31	0.401
Pregnancy rate per ET(%)	53.9 (298/552)	58.2 (464/797)	0.112
Clinicals pregnancy rate per ET(%)	48 (265/552)	50.8 (405/797)	0.310
Implantation rate (%)	35.5 (324/912)	38 (509/1338)	0.254
Miscarriage rate (%)	8.6 (23/265)	10.8 (44/405)	0.357

MII = mature.

that aspiration of cervical mucus through the endocervical canal using sterile cotton swabs or a catheter improved clinical outcomes,[8,9] and others showed no change in pregnancy results with the use of cervical brush removal.[13]

A meta-analysis of Craciunas of medium- and low-quality studies showed that removing cervical mucus before ET was of little benefit.[14] However, significantly increased pregnancy rates were reported in two retrospective studies that performed cervical mucus removal by cytobrush and vigorous irrigation of the cervical canal, respectively.[15,16]

A recent study suggested that rotation of the catheter during withdrawal may result in increased implantation rates by preventing the remaining mucus from becoming entangled and causing mucus-related embryo displacement. Analyses of their data confirmed this hypothesis; they observed significantly higher pregnancy and clinical pregnancy rates but similar ongoing pregnancy rates when using catheter rotation.[12]

Mechanically stimulating the uterus and endometrium may initiate uterine contractions.[17,18] In particular, touching the fundus of the ET catheter or 360° rotation after transfer may apply such mechanical stimulation. It should be kept in mind that uterine contractions may have played a role in the similarity between the study and control groups in the present study.

Another expected effect of catheter rotation was the small rate of embryo retention in the catheter (only three in each group). We could not conclude that catheter rotation reduced the rate of embryo retention in the catheter due to the already low number of patients in our control group. Even in the case of embryo retention, the embryos retained in the transfer catheter were immediately retransferred, with no adverse impact on clinical pregnancy or implantation rates in the absence of other previously reported indicators of difficult transfer.[19]

Some studies attempted other interventions to prevent mucus-related embryo displacement. In a recent study, the ET catheter was kept in the cavity for an additional 30 s after transfer to prevent the embryo from being withdrawn during catheter withdrawal upon completion of the ET process, but this did not show any positive effect on pregnancy rates.[20] Cleaning the cervical mucus, either with a fine brush or with saline and a cotton swab, may result in bleeding of the cervix. In a study evaluating the effect of blood on the catheter tip, it was proposed that blood found outside the transfer catheter after ET was associated with lower rates of embryo implantation and clinical pregnancy following assisted reproductive technology.[21]

We found that the rotation idea, which we thought would be useful, was ineffective because of uterine contractions caused by the presence of a foreign material, such as a catheter, in the uterine cavity for an excessive duration, or movement, such as rotation. A recent case-control study by Eftekhar et al, [22] also found that catheter rotation during withdrawal increased the implantation rate and clinical pregnancy. Their result is different from our study. The main different is the nature of this study, retrospective, single-center. Therefore, a randomized study should be considered.

Due to the retrospective nature of the study, some values, such as antimullerian hormone (AMH), could not be determined in all patients, and day 3 embryos were transferred in some patients, whereas day 5 embryos were transferred in others. The strengths of the study were that a single physician performed the ETs, and the number of patients was much higher than those in previous studies.[12] During the planning stages of this study, rotation was considered to have potential to increase ET efficiency and result in higher pregnancy rates. However, the results of this study suggest that this technique was ineffective.

The results of the present study indicated that rotation of the catheter before its removal had no effect on pregnancy and clinical pregnancy rates.

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