



Does Placement of the Catheter Guide Through the Cervical Canal Influence the Embryo Transfer Outcome?

Kateter Gaydının Servikal Kanaldaki Yerleşimi Embriyo Transfer Sonuçlarını Etkiler Mi?

Placement of Catheter Guide and Embryo Transfer Outcome

Fatma Devran Bildircin¹, Ali Sertac Batioglu², Emel Kurtoglu³, Davut Guven¹
¹IVF Center, Ondokuz Mayıs University, Samsun, ²IVF Center, Medical Park Hospital, Izmir, ³Obstetrics and Gynecology Department, Ondokuz Mayıs University, Samsun, Turkey

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Özet

Amaç: Bu çalışmada, embriyo transferi işlemi esnasında embriyo transfer kateteri gaydının servikal kanaldaki yerinin, gebelik sonuçlarını etkileyip etkilemediğini araştırılması amaçlandı. **Gereç ve Yöntem:** Embriyo transfer kateteri gaydının servikal kanaldaki yerleşimine bağlı olarak in-vitro fertilizasyon sonuçları retrospektif olarak incelendi. Çalışma grubu ikiye ayrıldı: yalnız iç transfer kateterin servikal kanal boyunca yerleştirildiği grup (Grup 1, n= 55); çift kateter seti ile transfer yapılan grup (Grup 2, n= 58). **Bulgular:** İn-vitro fertilizasyon sonrası toplam 113 embriyo transferi uygulandı. Yalnız iç transfer kateteri ile transfer yapılan grupta gebelik oranları daha fazla tespit edilse de istatistiksel olarak iki grup arasında anlamlı bir fark bulunmadı (odds ratio: 1.644, %95 güven aralığı, p>0.05). **Tartışma:** Embriyo transferi esnasında transfer kateteri gaydının servikal kanal içindeki yerleşiminin, in-vitro fertilizasyon-embriyo transfer sonuçları üzerinde etkisi olmayabilir.

Anahtar Kelimeler

İn-Vitro Fertilizasyon; Embriyo Transferi; Kateter Gaydı; Servikal Kanal; Gebelik Oranı

Abstract

Aim: Our aim was to find out whether placement of the embryo transfer catheter guide through the cervical canal at the time of embryo expulsion influences pregnancy rates. **Material and Method:** We retrospectively compared in vitro fertilization (IVF) outcomes related to the placement of the embryo transfer catheter guide through the cervix. Subjects were divided into two groups: embryo transfers (ET) performed with the inner catheter alone through the cervical canal (n=55, Group 1) and transfers performed with the double catheter set through the cervix (n=58, Group 2). **Results:** A total of 113 ETs were carried out in women undergoing IVF treatment. Although the pregnancy ratio seemed to be higher among the transfers carried out with the inner catheter alone inserted through the cervix, no statistically significance for this was detected (odds ratio: 1.644, 95% confidence bound, p>0.05). **Discussion:** Placement of the catheter guide through the cervical canal at the time of embryo expulsion may not have any effect on the IVF-ET outcome.

Keywords

In Vitro Fertilization; Embryo Transfer; Catheter Guide; Cervical Canal; Pregnancy Rate

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Corresponding Author: Fatma Devran Bildircin, IVF Center, Ondokuz Mayıs University, Samsun, Türkiye.

T.: +90 3623121919/2468 GSM: +905324823472 E-Mail: drfdevran@hotmail.com

Introduction

In vitro fertilization and embryo transfer (IVF-ET) procedure is a long pathway that involves many important steps and is always expected to be perfect by clinicians. However, it is well known that there are several factors influencing the success of the IVF-ET treatment cycle, such as the age of the woman, the type of ovulation induction, the number of eggs collected, and the quality and number of the embryo transferred [1-3]. Embryo transfer (ET) is the final and crucial step affecting the success of the IVF procedure [4]. On the other hand, a perfect ET technique remains controversial as a result of studies reporting different effects of many factors, such as the type of catheter, blood at the catheter tip, easy or difficult transfer, ultrasound-guided transfer, uterine contractions, and also physician factor [5,6].

Among these critical steps, during embryo transfer, the type and placement of the tip of the catheter have recently been studied by many clinicians to determine their effect on pregnancy rate [7-10]. However, the ideal position of the catheter guide related to the cervical canal has been of little interest. Possible mechanisms have been suggested by some authors, but optimum procedures in this respect remain unclear [11,12].

In this study, we aimed to find out whether placing the ET catheter guide through the cervical canal at the time of embryo expulsion influences pregnancy rates.

Material and Method

In this study, we tested the placement of the catheter guide through cervical canal. The charts of 113 patients who underwent IVF-ET cycle from September 2012 to June 2013 in a single center were retrospectively analyzed. The study was approved by the Ethics Committee of Ondokuz Mayıs University, Samsun, Turkey. Women under the age of 21 or over 38 and transfers of cryopreserved embryos were not included.

Patients were divided into two randomized groups. In the first group, the inner catheter was inserted alone through the cervical canal, whereas in the second group, a double catheter set was inserted through the cervix.

The patients were stimulated using gonadotrophin-releasing hormone (GnRH) follicle-stimulating hormone (FSH) protocol. The dose of gonadotropins was individualized based on the patient's age, history, and response to medication. The GnRH agonist (Lucrin 5mg/ml; Abbote) was administered in the preceding late luteal phase for down-regulation of the pituitary gland. Then, recombinant FSH (GONAL-f 450 IU/0.75 ml) was used to carry out the controlled ovarian hyperstimulation. Cycles were monitored using serial transvaginal ultrasounds to chronicle follicular growth and the measurement of serum E2 levels. Administration of hCG (Ovitrelle, 250 mcg; Serono) occurred when follicular size and E2 levels were appropriate and oocyte retrieval was performed by ultrasound-guided puncture under general anesthesia 36 hours later. The all metaphase II (M II) oocytes obtained were fertilized by standard intracytoplasmic sperm injection (ICSI), and embryo transfer was carried out on Day 3 or Day 5 after oocyte retrieval [13]. Transvaginal progesterone (Progestan 200 mg Kocak) was initiated from the day of the oocyte pick-up and continued until the assessment of pregnancy (12 days after ET) to support the luteal phase.

On the day of ET, all patients were placed in the lithotomy po-

sition without any anesthesia, and a sterile bivalve speculum was inserted into the vagina to expose the cervix. The exocervix was gently cleaned of visible mucus with a sterile cotton swab and a small culture medium. Concurrently, in the adjacent embryo culture laboratory, embryos were evaluated according to morphology and cleavage criteria, the best one or two embryos were selected and loaded into a Cooks catheter, and a double lumen catheter set (K-JETS-7019-SIVF; Cook IVF, Eight Miles Plains, Queensland, Australia). Before the transfer, the features of the endometrial cavity and cervix in terms of the length, the angle between the internal os and the cavity were assessed by transabdominal ultrasonography.

The embryo transfer was carried out with a full bladder by the same experienced physician (ASB) with the assistance of the embryologist under transabdominal USG guidance. The inner catheter was gently inserted through the cervical canal in the first group, while in the second, the double catheter set was inserted. In both groups, the ET catheter was advanced through to 1 cm from the fundus under transabdominal ultrasonography guidance. The embryos were slowly released, then the catheter was left in situ for about 30 seconds and gently removed while being rotated. Next, the catheter was checked under a microscope for retained embryo or presence of blood. The patients were asked to remain in bed for 30 minutes.

The ET was assessed as easy whenever the catheter could be passed easily into the uterine cavity through the cervical canal. Difficult cases were recorded if further manipulations such as dilatation of the cervical canal, using a stylet or grasping the cervix with a tenaculum were performed.

Clinical pregnancy was defined as a positive pregnancy test (beta-hCG measured in venous blood >50 mIU/mL on day 12 following embryo transfer) followed by the presence of at least one gestational sac on transvaginal ultrasonography four weeks after transfer.

Data were analyzed using the SPSS for Windows version 11.5 software. In all tests, $p < 0.05$ was accepted as statistically significant.

Results

A total of 113 ETs were carried out in women undergoing IVF treatment, and data was analyzed retrospectively to determine whether the placement of the catheter guide had a significant influence on pregnancy rates. The subjects were divided into two groups: Group 1, consisting of embryo transfers performed by insertion through the cervical canal of the inner catheter alone ($n=55$), and Group 2, comprising transfers provided by insertion through the cervical canal of the double catheter set ($n=58$).

There was no significant difference between the groups in terms of ages of the women, number of oocytes retrieved and fertilized, embryo quality, or embryo transfer days (Table I).

Although the pregnancy ratio seemed to be higher in the transfers carried out with the inner catheter placed alone through the cervical canal, no statistically significance was detected (odds ratio: 1.644, 95% confidence bound, $p > 0.05$) (Table I).

Since all embryo transfers in the first group were recorded as easy whereas there were both easy and difficult transfers in the second group, we couldn't compare the catheter positions regarding ease of the transfers. But, no significant difference

Table I. Features of women undergoing ET with inner catheter alone and double catheter set

Variables	Inner catheter insertion alone through the cervical canal (n:55)	Double catheter set insertion through the cervical canal (n:58)	P-value
Mean age	30.9±4.4	30.4±4.0	0.547 ^a
Picked-up oocytes	13 (2-32)	11 (1-33)	0.153 ^b
Fertilized oocytes	6 (1-20)	5 (1-22)	0.434 ^b
Embryo grade	5 (1-20)	5 (1-22)	0.451 ^b
Embryo transfer			0.853 ^c
One embryo	37 (67.3%)	41 (70.7%)	
Two embryos	18 (32.7%)	17 (29.3%)	
Day of transfer			0.692 ^d
Day 3	48 (87.3%)	52 (89.7%)	
Day 5	7 (12.7%)	6 (10.3%)	
Pregnancy rate	28 (50.9%)	20 (34.5%)	0.077 ^c

a: Student's t test, b: Mann Whitney U test, c: Pearson's Chi-Square test, d: Fisher's Exact test.

was found in pregnancy rates between the easy transfers of both groups and the transfers in the second group including both difficult and easy applications. ($p > 0.05$) (Table 2) (Table 3)

Table 2. Pregnancy rates regarding the ease of transfer and the position of the catheter

	Pregnancy rate	P value
Easy transfer		0.180 ^a
Before internal os	28 (66.7%)	
After internal os	14 (33.3%)	
Difficult transfer		-
Before internal os	-	
After internal os	6 (100.0%)	

a: Pearson's Chi-Square test

Table 3. Pregnancy rates regarding ease of transfers with the catheter positioned after internal os

	Pregnancy rates	P value
After internal os		0.602 ^a
Easy	14 (70.0%)	
Difficult	6 (30.0%)	

a: Pearson's Chi-Square test

Discussion

Despite the fact that the possible mechanisms of failed embryo transfer remain controversial, the catheters, in terms of their features and intrauterine positions, have been the most discussed parts of the procedure. In this study, we tested whether the choice of insertion of the inner catheter through the cervical canal alone or together with the guide has any effect on pregnancy rates. Our data showed no statistically significance between the two placements, supporting the idea that contact of the catheter guide with the cervical canal and the internal os may not cause significant damage to the cervix and uterine contractions, and thus may not influence the outcome of the transfer. Congruently, Silberstein et al. performed ETs with both soft inner catheter and malleable outer sheath component when a resistant internal os was experienced, and they reported that passing internal os with the outer sheath of the soft inner

catheter may not influence the implantation or pregnancy rates [14].

In contrast, studies supporting the negative effect of the placement of the catheter on the pregnancy rates suggested possible effects, such as trauma, on the cervix during the embryo transfer may cause uterine contractions that can lead to damage to implantation [6,15,16]. Another hypothesis suggested by researchers is that the passage of the catheter guide through the cervix and internal os may create a wide space through which the released embryos may escape from the uterine cavity [11]. Nonetheless, more than one possible mechanism, including trauma to the cervix and creating a wide escape tunnel inside the cervical canal, may play a role in the impaired pregnancy rates reported by some studies [12,14].

We used soft, double-lumened Cook catheters, placing the tips 1 cm from the fundus under transabdominal guidance in all ETs. There have been many publications reporting conflicting results related to the use of soft versus stiff catheters. ET catheter properties vary in several ways, such as design, presence of an outer sheath, and quality [11]. While some studies have supported the benefit of one catheter type over another in terms of pregnancy rates [17-19], other studies found no significant difference between the catheters [7-9,20,21]. Meanwhile, the position of the tips has been evaluated by some researchers, leading to the suggestion that they be placed at least 5 mm from the fundus, without touching it [22,23]. In addition, the use of ultrasound-guidance, first reported by Strickler et al. in 1985, has facilitated the embryo transfers and been accepted as improving the outcomes in many published studies [24-27]. Studies supporting operator influence on the success of the procedure have been attracting more attention in recent years. The clinician factor was reported to be more important than the transfer itself in some published studies, although debate on the subject continues [28-31]. In the present study, the same operator and embryologist participated in the IVF-ET cycle, hence eliminating this confounding factor.

The correlation of technical difficulty, such as the necessity of using a cervical manipulator or a stylet during the ET, with the pregnancy outcome also remains as a controversial topic of the procedure. It is evident that, ET should be performed in the most atraumatic manner, therefore many studies reported the reduced pregnancy rates after difficult transfers probably due to more damage to the uterine wall [4,32]. In contrast, some researchers didn't found significance difference with regard to the ease of transfer [21,32]. In the present study, the whole transfers performed by placing the catheter guide just before the internal os were recorded as easy, whereas there were both difficult and easy ones in the second group with catheter located beyond the os. As a result, we couldn't compare the difficult transfers between the two groups, but, there wasn't significant difference regarding pregnancy ratio in easy transfers.

The definition of a perfect ET technique seems to remain controversial because of several factors contributing to the success of the procedure. This study suggested that the placement of the catheter guide through the cervical canal may not be one. This may not have any effect on the outcome, here. Nevertheless, further studies seem to be required for more definitive comments on this topic.

Competing interests

The authors declare that they have no competing interests.

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