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Value of hysteroscopy after one in vitro fertilization failure

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Abstract

To investigate the relationship between abnormal findings and the cost effectiveness of performing a hysteroscopy after one in vitro fertilization (IVF) failure. The cases of 110 patients with a normal ultrasound of the endometrial cavity and a history of one IVF treatment failure who had been referred to the Inonu University School of Medicine Department of Obstetrics and Gynecology between June 2014 and November 2017 were recruited for this study. The median age of patients was 31.7 ± 5.7 years. Intrauterine pathologies were observed in 29 (26.3%) patients, whereas 81 (73.7%) patients exhibited a normal hysteroscopy. The distribution of the pathologies was as follows: a uterine subseptum existed in 9 (8.1%) women, an intrauterine adhesion existed in 8 (7.2%) women, a cervical stenosis existed in 4 women (3.6%), an endometrial polyp existed in 4 women (3.6%), and a submucosal myoma uteri existed in 3 women (2.7%). Two abnormalities (intrauterine adhesion and cervical stenosis) existed together in one patient. A routine hysteroscopy is necessary for women with a normal ultrasound of the endometrial cavity after one IVF failure, meaning that women with a normal ultrasound should be offered a routine hysteroscopy.

Keywords: Hysteroscopy, intrauterine pathologies, in vitro fertilization

Introduction

It is estimated that infertility affects 10–15% of women of a reproductive age in the world, and an increasing number of couples who have had difficulties conceiving are seeking in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) [1]. An estimated more than five million children have been born because of IVF/ICSI [2]. Since the first live birth after conception by IVF in 1978, a significant number of developments have occurred in both the basic science of IVF and clinical practices. Despite these technological advances, only 25–30% of cycles of IVF lead to birth of a child [3].

The cause of IVF failure is poorly understood but can be related to either embryonic or maternal factors [4,5]. Studies suggest the most frequent cause of implantation failure is chromosomal abnormalities in the embryo, but abnormalities of the uterine cavity, such as polyps, submucosal leiomyomas of the uterus, and intrauterine adhesions, are also thought to be associated with impaired implantation and a reduced chance of pregnancy after IVF [5,6]. Endometrial pathology has been reported in up to 20% of infertile women undergoing IVF treatments [7].

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Hysteroscopy is a very common tool that provides the gynecologist with the ability to diagnose and treat intrauterine abnormalities [8]. It allows for the visual assessment of the cervical canal and uterine cavity and provides an opportunity to operate when necessary during the same procedural setting. Hysteroscopy is thought to improve pregnancy rates in women scheduled for IVF through the detection and surgical removal of endometrial cavity disorders [9], the dilatation of the cervical canal to allow the forthcoming embryo transfer [10], or the stimulation of an inflammatory reaction of the endometrium by the procedure itself [11].

A hysteroscopy is often performed for infertile women starting IVF to improve their chances of having a baby. However, no evidence-based data are available to support this practice. Therefore, we aimed to evaluate whether a routine hysteroscopy after one IVF failure is necessary in women with a normal ultrasound of the endometrial cavity.

Material and Method

Study design and participants

This is a retrospective review of the hysteroscopic findings of 110 women with a normal ultrasound of the endometrial cavity and a history of one IVF treatment failure who were attending at the Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology at the Inonu University School of Medicine between June 2014 and November 2017. This study was approved by local ethical comitee (2017-27-15).

Before the hysteroscopy, the standard pre-operative preparations of a hemogram, biochemical analysis, β-hCG measurement, and a PAP smear were performed.

Procedures

The hysteroscopy was done using a rigid 2.9 mm in diameter and 300 view hysteroscope with an atraumatic tip (Karl Storz, Tuttlingen, Germany) in a vaginoscopic approach. Lighting was provided by a high-intensity cold light source via a fiber-optic lead, and all procedures were monitored using a video camera and monitor (Sony). Mannitol was used as a distending media. Uterine distention was accomplished by a 3000 ml Pressure Infusion Cuff (Karl Storz, Tuttlingen, Germany). The pressure was pre-settled to 100 mmHg.

All of the hysteroscopic procedures were carried out during the proliferative phase of the menstrual cycle. With the patient lying in the lithotomy position, a bimanual pelvic examination was performed. The cervix was inspected through a vaginal speculum, and the hysteroscope was guided through the endocervical canal into the uterine cavity. The tubal orifices were identified, and the endometrial lining was examined. The cervical canal was then observed in its entirety during the withdrawal of the hysteroscope.

All of the hysteroscopic examinations were performed by the same operator (GT). The median duration of hysteroscopy was 20 minutes (10–45 min.). A routine preoperative analgesia was used, and pre-operative antibiotics were not routinely administered. No hysteroscopy-related complications were reported. The findings were recorded on a standardized form. Uterine abnormalities were defined by the presence of polyps, submucosal myomas of the uteri, adhesions, or uterine malformations. Medical records were obtained, noted, and revised, and then the data were analyzed.

Statistical analysis

The data were analyzed using the Statistical Package for Social Science Software for Windows, release 11.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to evaluate normality. Variables with a normal distribution were shown as the mean ± standard deviation (SD), and variables with a skewed distribution were shown as the median and interquartile range (IQR). The groups were compared using the chi-square test with Yates correction, Fisher's exact test, the Student's t-test, and the Mann-Whitney U test. A p value of less than 0.05 was considered statistically significant.

Results

Baseline clinical characteristics of the study population are shown in Table 1. Of the 110 patients with one IVF failure, the mean age was 31.7 ± 5.1 years. Eighty-five (77.2%) patients were housewives, whereas only 25 (22.8%) patients were working. There were 82 (74.5%) women with primary infertility and 28 (25.5%) women with secondary infertility. Only 7 (6.3%) women had a live birth history and 6 (5.4%) women had children. Only 8 (7.2%) women smoked. The median duration of infertility was 5.5 years (IQR: 3–7.5 years).

Of the 110 hysteroscopic operations, no intrauterine cavity access failure was noted, and no hysteroscopy was incomplete due to inadequate visualization. Of the 110 cases, the hysteroscopy was normal in 81 (73.7%) women. A uterine cavity or cervical canal abnormality was reported in 29 (26.3%) women. Uterine subseptum existed in 9 (8.1%) women, and intrauterine adhesions existed in 8 (7.2%) women. Both cervical stenosis and endometrial polyps exist in 4 women (3.6%). Three (2.7%) women had a submucosal myoma uteri, and one patient had two abnormalities (intrauterine adhesion and cervical stenosis together; Table 2).

Table 1. Baseline characteristics of the study participants

Variable	Variable category	Cases [n (% of 110)]
Mean age (years)	<25	6 (5.4)
	25-29	30 (27.2)
	30-34	40 (36.3)
	≥35	34 (30.9)
Infertility Status	Previous livebirth	6 (5.4)
	Duration of infertility	5.5 (3.0–7.5)
	Primary infertility	82 (74.5)
	Secondary infertility	28 (25.5)
Cause of Infertility	Male factor	43 (39.1)
	Female factor	13 (11.8)
	Combined	4 (3.6)
	Unexplained	50 (45.5)
Hormone Levels (IU)	Basal FSH	7.08 (5.3–8.3)
	Basal LH	5.3 (4.1–6.5)
	Basal E2	45.8 (33.8–68.5)
	Basal Prolactin	13.8 (8.7–19.3)
	Basal TSH	1.6 (1.1–2.3)
Smoking Status	Smoker	8 (7.2)

Data shown as n (%), mean ± standard deviation or median (IQR)
FSH: follicle stimulating hormone, LH: luteinizing hormone, E2: estradiol; TSH: thyroid stimulating hormone

Table 2. Findings in women who received a hysteroscopy

Abnormality Location	Specific Abnormality	With Abnormality (n)
Cervical	Stenosis of external os	-
	Stenosis of internal os	4
	Cervical canal adhesion	-
	Cervical canal deviation (retroversion)	-
	Cervical canal polyps	-
	Shortened cervical canal	-
Uterine	Dysmorhic (arcuate) cavity	-
	Hemi-uterus	-
	Endometrial polyps	4
	Partial uterine septum	9
	Submucous fibroid	3
	T-shaped uterus	-
Subtle endometrial	Hypervascularization	-
	Mucosal elevation	-
	Micropolyps	-
	Pale endometrium	-
	Endometrial defect	-
	Single adhesion band	-
	Multiple adhesion	8

Discussion

In agreement with the findings of this study, some studies have suggested that women with a normal ultrasound should be offered a hysteroscopy. A meta-analysis from Pundir et al. [9] demonstrated that live birth rates increased after a hysteroscopy in women scheduled for a first IVF cycle. In addition, some studies demonstrated that a hysteroscopy before IVF treatment significantly increases the pregnancy chances in the consequent

IVF cycle in women who have already had one or more IVF cycles [12,13].

On the contrary, some studies have suggested that women with a normal ultrasound should not be offered a routine hysteroscopy. The findings from the inSIGHT trial [14], a multi-center, randomised, controlled trial conducted in the Netherlands, demonstrated that a routine hysteroscopy does not improve live birth rates in infertile women with a normal transvaginal ultrasound who are scheduled for their first IVF cycle. Additionally, the TROPHY study [15], a multi-center, randomised, controlled trial done across eight different European countries, investigated the role of hysteroscopy in women with recurrent IVF failure who have a normal uterine ultrasound scan. The TROPHY study identified cervical- or uterine-cavity abnormalities in 26% of women who had a hysteroscopy [15]. The results of this study do not suggest that a hysteroscopy could improve the success of IVF treatments.

Hysteroscopy is the gold standard for evaluating the uterine cavity. Previous studies have assumed that the beneficial effect of a hysteroscopy on the outcome of IVF treatment was due to the treatment of the unsuspected intrauterine pathology identified during the hysteroscopy [16]. Hysteroscopy is hypothesized to facilitate the impending embryo transfer via the removal of cervical canal obstructions and the optimization of the embryo transfer process, thus improving treatment outcomes [17]. It has been suggested that this procedure improves IVF outcomes by stimulating the endometrium through surface injuries, which is suggested to increase the chances of embryo implantation [18]. However, two-thirds of reported intrauterine abnormalities discovered during the hysteroscopy were not treated because they were considered either untreatable (such as a shortened cervical canal or a unicornuate uterus) or of undetermined clinical significance (arcuate uterus or subtle endometrial abnormalities) [19].

Conclusion

In conclusion, although randomised, controlled trials did not suggest that a hysteroscopy could improve the IVF results in infertile women with a normal ultrasound of the endometrial cavity prior to their first IVF cycle or after recurrent IVF cycle failure, our study showed that hysteroscopy identified intrauterine pathologies in 26% of infertile women with a history of one IVF failure. Hysteroscopy allows for an individualized therapeutic approach based on the individual needs of the patient. This study has several strengths, namely that a large number of women were recruited into trial. An important limitation of this study was its retrospective nature. Future studies including an assessment of the endometrial cavity are needed to address the effectiveness of surgical correction of specific uterine cavity abnormalities after IVF treatment failure.

Competing interests
The authors declare that they have no competing interest

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