

Is Office Hysteroscopy Potentially Beneficial for Infertile Patients Prior to IVF Cycles?

IVF Siklusları Öncesi İnfertil Hastalarda Ofis Histeroskopi Yapılması Faydalı mıdır?

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ABSTRACT Objective: The objective of our study was to evaluate the prevalence of uterine abnormalities detected by office hysteroscopy prior to in vitro fertilization in asymptomatic patients. **Material and Methods:** We performed a retrospective analysis to determine the prevalence of unsuspected uterine abnormalities detected by office hysteroscopy. A total 571 patients who applied for in vitro fertilization underwent office hysteroscopy. All patients were evaluated with a basic infertility work-up, consisting of medical history collection, a physical examination and hormonal status and semen analyses. Furthermore, transvaginal sonography, saline infusion sonography and office hysteroscopy were performed on all patients. **Results:** Between September 2008 and November 2010, 571 infertility patients visited our clinic. All patients were assessed for in vitro fertilization. We planned office hysteroscopy for all patients prior to in vitro fertilization. In particular, in this study, we aimed to evaluate the importance of office hysteroscopy in patients who have a normal ultrasonographic diagnosis. We determined 11.8% (n=59) endometrial polyps and 5.8% (n=27) septa by office hysteroscopy. We mostly found these abnormalities in primary infertility patients. **Conclusion:** The intrauterine environment is an important factor for implantation in in vitro fertilization cycles. Uterine cavity pathologies can decrease implantation rates. Congenital uterine malformations are also thought to play a role in delaying natural conception. Hysteroscopy usually enables a more accurate diagnosis than other uterine cavity screening methods. Office hysteroscopy may be a part of the routine evaluation of infertility patients, even in patients with a normal transvaginal ultrasound, and especially in secondary infertility patients. These patients' uterine cavity abnormality rate is higher than in primary infertility patients according to proportional measurement.

Key Words: Hysteroscopy; fertilization in vitro; infertility; uterus

ÖZET Amaç: Çalışmamızın amacı, asemptomatik hastalarda in-vitro fertilizasyon öncesi ofis histeroskopi ile uterin patolojilerin prevalansını değerlendirmektir. **Gereç ve Yöntemler:** Ofis histeroskopi ile, kuşkululanılmayan uterin patolojilerin prevalansını değerlendirmek için retrospektif bir analiz yapıldı. IVF için başvuran toplam 571 hastaya ofis histeroskopi yapıldı. Transvajinal sonografi ve salin infüzyon sonografi de bütün hastalara uygulandı. Bütün olgular temel infertilite değerlendirmesine alındı (öykü, fizik muayene, hormon profili ve semen analizi); takiben bütün hastalara transvajinal sonografi, salin infüzyon sonografi ve ofis histeroskopi uygulandı. **Bulgular:** 2008 Eylül ile 2010 Kasım tarihleri arasında kliniğimize başvuran ve in-vitro fertilizasyon planlanan 571 hasta çalışma grubu olarak belirlendi. Bu hastalar in-vitro fertilizasyon açısından ayrıntılı olarak değerlendirmeye alındı. İn-vitro fertilizasyon öncesi bütün hastalara ofis histeroskopi yapılması planlandı. Bu çalışmada özellikle normal ultrasonografik bulgulara sahip olan hastalarda ofis histeroskopinin önemini vurgulamayı amaçladık. Ofis histeroskopi ile %11,8 (n:59) endometrial polip, %5,8 (n:27) septum saptanmıştır. Bu anomalileri daha sıklıkla primer infertil hastalarda saptadık. **Sonuç:** IVF sikluslarında intrauterin çevre implantasyon için önemli bir faktördür. Uterin kavite patolojileri implantasyon oranlarını düşürmektedir. Konjenital uterin anomalilerin doğal konsepsiyonu engelleme açısından rolü olduğu da düşünülmektedir. Histeroskopi genelde diğer uterin kavite görüntüleme metodlarına göre daha doğru tanı sağlamaktadır. Histeroskopi, özellikle sekonder infertil hastalarda uterin kavite anomalileri primer infertil olgulara göre oransal ölçümlere göre daha sık olması nedeni ve normal transvajinal ultrasonografi bulguları olan infertil olan hastalarda rutin değerlendirmenin bir parçası olmalıdır.

Anahtar Kelimeler: Histeroskopi; in vitro fertilizasyon; infertilite; uterus

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The pregnancy outcome and implantation rate of patients who are undergoing an in vitro fertilization (IVF) program are influenced by several factors. One of the important factors that affects the implantation rate is the intrauterine environment. A good-quality intrauterine environment has a positive impact on the likelihood of conceiving through IVF. Uterine cavity abnormalities have been found in 34% to 62% of infertile women.¹ Due to this high prevalence, screening the uterine cavity for such possible pathologic structures as polyps, fibroids, adhesions and septa has been recommended. Diagnosing and treating these pathologies and optimizing the endometrial structure can improve the success of IVF treatment. In this situation, hysteroscopy (H/S) is major component of an infertility work-up and is used for uterine cavity visualization. To evaluate the uterine cavity, the basic work-up consists of transvaginal sonography (TVS), saline infusion sonography (SIS) and hysterosalpingography (HSG), which can detect several of the uterine pathologies. In particular, the World Health Organization (WHO) recommends HSG as a first-line approach in infertile women.² However, with HSG, only tubal patency, tubal blockage and the border of the uterus can be determined. Moreover, HSG has high false-positive and false-negative rates of identifying intrauterine pathologies.³⁻⁵ The role of H/S is important in that this method provides direct visualization of the intrauterine conditions. Additionally, H/S can be performed in an outpatient setting and without anesthesia. Due to these factors, H/S may be considered as one of the first-line approaches prior to an IVF program.⁶ In the current study, our aim was to evaluate the prevalence of uterine pathologies with office H/S prior to IVF in asymptomatic patients.

MATERIAL AND METHODS

In our retrospective study, 571 infertile patients who participated in an assisted reproductive technology (ART) program prior to IVF and visited our clinic between September 2008 and November 2010 formed the study population. All patients were

evaluated by a basic infertility work-up consisting of medical history collection, a physical examination and hormonal status and semen analyses. Furthermore, TVS was performed on all patients. During TVS, suspected lesions were assessed, and uterine abnormalities were recorded. HSG was performed on all patients to detect any uterine cavity pathologies. For uterine cavity evaluation, we also used SIS. Patients who had undergone H/S previously were not included in the study population.

Each H/S was performed at the follicular phase of the menstrual cycle. Before the procedure, detailed information was provided to the patients by the operating physicians and nurses. Informed consent was obtained. An outpatient setting was used for the H/S procedure, without anesthesia or dilatation. The office H/S was performed using a Storz Office Hysteroscopy Hopkins Forward-Oblique Telescope with a 30° direction of view and 3 mm diameters. We used a vaginoscopic approach. During the procedure, the endocervical canal, uterine cavity and tubal ostia were inspected in sequence. Uterine cavity distension was maintained at 25 to 35 mmHg with an electronic pump for irrigation and aspiration (Endomat; Karl Storz GmbH & Co.), and normal saline solution was used for distension.

Detected uterine pathologies, which were endometrial polyps, fibroids, intrauterine adhesions and septa, were recorded. In several cases, the H/S procedure could not be completed because of the intolerance of the patients. The procedure was completed in approximately 3 minutes.

The patients' age, duration of infertility and types of uterine pathologies were determined, and Fisher's exact test was used for statistical analysis. Sensitivity and specificity were evaluated for TVS. A value of $p < 0.05$ was considered to be statistically significant. All statistical analyses were performed using SPSS version 15.1 (SPSS Inc., Chicago, IL, USA).

RESULTS

Between September 2008 and November 2010, 571 infertile patients visited our clinic. All the patients

	Mean±SD
Age (years)	30.23±5.41
Cycle day	8.31±2.32
Duration of subfertility (years)	7.60±4.32
BMI (kg/m ²)	25.14±4.30

SD: Standard deviation; BMI: Body mass index.s

	n (%)
Infertility type	
Primary	465 (92.8%)
Secondary	36 (7.2%)
Cause of infertility	
Female factor	61 (12.2%)
Male factor	247 (49.4%)
Unexplained	193 (38.5%)

were assessed for IVF. We planned an office H/S for all of the patients prior to IVF. In 18 patients, the procedure was not successful because of patient intolerance. In total, 13 of these patients had normal findings based on ultrasound examination and SIS. Five patients had undergone operative H/S because of a suspicious uterine evaluation by ultrasound examination. Two Asherman’s syndrome and three normal uterine cavity findings were determined during the surgical procedure. Among the patients who underwent a successful office H/S procedure, 52 patients had an abnormal ultrasound examination, and 501 had a normal examination. In the abnormal ultrasound examination group, we found 23 endometrial polyps, five fibroids/myomas, seven uterine septa and 17 normal cavity findings by office H/S. For TVS, the sensitivity and specificity values were determined to be 24% and 95%, respectively. In particular, in this study, we aimed to evaluate the importance of office H/S in patients

who have normal ultrasonography findings. For this reason, 501 patients who had normal ultrasound results were investigated. The average age, cycle day, duration of subfertility and body mass index (BMI) and infertility types and causes of infertility were examined (Table 1). SIS was performed on all patients, whether ultrasound examination was normal. Infertility types were evaluated after all of the procedures, which were TVS, SIS and office H/S. All of the patients were assessed by these three methods.

According to the findings, the most frequent cause of infertility was a male factor, in 49.4% (n=247) of cases (Table 2). Office H/S was frequently performed on patients in the follicular phase. Most assessments were performed on day 8 of the menstrual cycle.

In the evaluation of patients whose ultrasonography was normal, 77.8% of patients (n=390) had normal cavity findings by office H/S, and the most frequent pathologic abnormality was endometrial polyps, affecting 11.8% (n=59). In total, 111 (22.2%) uterine pathologies were missed by TVS (Table 3).

Among these patients, 465 (92.8%) were primary infertility patients, and 36 (7.2%) were secondary infertility patients. The frequency of intrauterine pathologies varied between the primary and the secondary infertility patients. Endometrial polyps, followed by fibroids/myomas and septa, were determined most frequently in both primary and secondary infertility patients (Table 4).

In our study, diagnoses varied within infertility type. For example, we evaluated 52 (11.2%) polyps in primary infertility patients and 7 (19.4%) polyps in secondary infertility patients. Similar findings were determined for fibroids. Moreover, we found that intrauterine pathologies, and espe-

	Adhesion	Polyp	Fibroid	Septum	Hyperplasia	Septum + Polyp	Normal
Normal TVS n (%)	5 (1)	59 (11.8)	8 (1.6)	27 (5.4)	9 (1.8)	3 (0.6)	390 (77.8)

TABLE 4: Hysteroscopic findings in infertile women who have normal ultrasonographic examination by office hysteroscopy (Percentages assessed within infertility type).

Findings	Primary infertility (n:465) (%)	Secondary infertility (n:36) (%)	p value* (Within Infertility)	p value**
Adhesions	3 (0.6%)	2 (5.6%)	0.044	
Polyps	52 (11.2%)	7 (19.4%)	NS	
Fibroids	7 (1.5%)	1 (2.8%)	NS	
Septum	25 (5.4%)	2 (5.6%)	NS	0.043
Hyperplasia	7 (1.5%)	2 (5.6%)	NS	
Septum + Polyp	3 (0.6%)	0 (0%)	NS	
Normal	368 (79.1%)	22 (61.1%)	0.020	

* Two proportions Fisher's exact test within infertility ** Pearson Chi-square Test.

cially polyps and fibroids, were mostly identified in primary infertility patients by quantitative measurement. However, congenital abnormalities, such as uterine septa, were mostly detected in primary infertility patients. In total, 25 (5.4%) patients in the primary infertility group had septa. In contrast, two (5.6%) patients in the secondary infertility group had uterine septa. When we examined diagnoses in the infertility base, there were no significant differences between primary and secondary infertility patients. According to proportional measurement by infertility type, uterine pathologies were more likely to exist in patients who had secondary infertility. The reason for these results was our population distribution. In our study, 465 primary infertility patients and 36 secondary infertility patients were included. For this reason, we did not find any significant differences. In Particular for other uterine pathologies, several differences were found between primary and secondary infertility patients, but no significant differences were established. Both primary and secondary infertility patients had normal cavities in 79.1% (n=368) and 61.1% (n=22) of cases, respectively. When we evaluated all diagnoses by office H/S, we obtained a significant difference between the primary and the secondary infertility types using Pearson's Chi-Square test (p=0.043).

After the procedures, no complications occurred in the patients.

DISCUSSION

One of the basic steps in an infertility work-up is to evaluate the shape and regularity of the

uterine cavity. Acquired uterine lesions, such as uterine fibroids, endometrial polyps, intrauterine adhesions or all of these may cause infertility by interfering with proper embryo implantation and growth.⁷ Congenital uterine malformations are also thought to play a role in delaying natural conception.

TVS is used as a first-line noninvasive method to evaluate the uterine cavity. Several studies have demonstrated various sensitivities (from 20% to 100%) and specificities (from 33% to 100%) for TVS.⁸ Our data demonstrate that TVS was a specific (95%) but not sensitive (24%) method that misdiagnosed 111 (20%) patients and over-diagnosed 17 (3%) patients. TVS does not seem to be adequate for evaluating the endometrial cavity.

Office H/S is a gold-standard method for investigating the uterine cavity that is a safe and accurate for the direct and accurate diagnosis of intrauterine pathologies. Currently, the routine usage of office H/S in infertility assessment is controversial. Several studies have demonstrated that if the uterine cavity has to be investigated as a part of an infertility work-up, H/S is much more accurate than other diagnostic methods.⁹ In our study, we evaluated 571 infertile patients by office H/S, and 501 of these patients had normal ultrasonography findings. In total, 111 (22.2%) of these patients had abnormal office H/S. Studies have shown that the prevalence of uterine cavity pathologies diagnosed by H/S prior to IVF is between 20% and 45%, and our data confirmed this finding.

Only endometrial adhesion was statistically higher in the secondary infertility group ($p=0.044$). Patients with a history of abortion and infertility should be submitted to H/S to rule out intrauterine adhesion as a possible cause of infertility. There was no statistically significant difference in other endometrial cavity pathologies.

The most frequent pathologic finding was endometrial polyps (11.8%) in patients who had normal TVS findings. Uterine septa (5.4%) were the second frequent abnormality in primary infertility patients. Abnormal findings were significantly higher (20.8% vs. 38.9%) in the secondary infertility group.

The true incidence of endometrial polyps in the general population is difficult to determine because many polyps are clinically asymptomatic. Nevertheless, Shokeir et al. found that such lesions are more frequent in the unexplained-infertility population compared with fertile women.¹⁰ In our study, group endometrial polyp incidence was 11.2% and 19.4% in primary and secondary infertility patients, respectively.

The incidence of uterine malformations in other series of infertile patients varies between 1% and 26%, with a mean incidence of 3.4%.⁸ We observed an incidence of 5.4% and 5.6% for primary and secondary infertility, respectively.

The reported incidence of myomas in infertile women without any obvious cause of infertility is estimated to be between 1% and 2.4%.¹¹ In the current study, submucous myomas were diagnosed in 1.6% of patients.

A recent systematic review and meta-analysis of two randomized and three non-randomized controlled trials, including 1,691 patients with two or more failed IVF attempts, concluded that operative H/S significantly improves the pregnancy rate in the subsequent IVF cycle.¹²

However, the value of H/S as a routine investigation in the management of infertile women is a matter of debate. The European Society of Human Reproduction and Embryology (ESHRE) guidelines indicate that H/S is unnecessary unless the method is used for the confirmation and treatment of

doubtful intrauterine pathology. The two main problems with H/S are that this method is an invasive procedure and that there is a debate about the real significance of observed intrauterine pathology on fertility.¹³

In our study, there were certain limitations. There was no control group for untreated septa. Many women with an undiagnosed septum could have a perfect reproductive history. Randomized controlled trials are necessary, in which several patients with endometrial pathologies are treated, and the others are not.

TVS, SIS and H/S are important tools currently used to evaluate uterine cavity structural abnormalities, but H/S is the most valuable method in terms of diagnostic accuracy.¹⁴ In our experience, office H/S has many clear advantages. First, office H/S is a minimally invasive procedure with a low failure rate (3%). Second, patients do not undergo hospitalization or anesthesia. Third, the procedure allows assessment of the cervical canal and reliable visualization of the uterine cavity. In our study, office H/S diagnosed 111 (22.1%) patients, which was more than TVS, and excluded 17 (32.6%) patients who were assessed as abnormal by ultrasonography examination.

CONCLUSION

Office H/S is a minimally invasive, rapid and accurate method for evaluating the endometrial cavity. TVS is a specific but not sensitive method. Office H/S is well tolerated despite its invasiveness and had no complications in our study group. From our clinical perspective, office H/S may be a part of the routine evaluation of infertility patients and even patients with normal TVS, and especially secondary infertility patients because their rate of uterine cavity pathologies is higher than in primary infertility patients. There are no adequate prospective studies on the effectiveness of office H/S, so current evidence does not support routine office H/S. We aimed to detect the potential effect of office H/S in our retrospective study. Further prospective randomized studies are needed to confirm these findings.

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