

Clinical Research



Our Office-Based Diagnostic Hysteroscopy Results of Pre-IVF Patients

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ABSTRACT

Objective: To evaluate the intrauterine pathologies using office-based hysteroscopy (OH) in patients scheduled for assisted reproductive technologies (ART).

Materials and Methods: This study was conducted at the In Vitro Fertilization (IVF) Unit of Fırat University Hospital, between March 2010- January 2012. The 219 patients with no OH within the previous 6 months were enrolled the study with rigid hysteroscope (continuous flow; 30-degree forward-oblique view) assembled in a 4-mm diameter diagnostic sheath with an atraumatic tip. After OH investigation, endometrial sampling was performed with biopsy catheter. The patients in whom the findings were normal proceeded to an IVF cycle within 1 month.

Results: The procedure was successful in 219 patients, with mean (\pm SD) age of 31.9 (\pm 5.2) years, duration of infertility of 6.2 (\pm 4.5) years and number of previous ART trials 1.6 (\pm 1.1). The type of infertility were as follows: 150 primary (68.5%) and 69 secondary infertility (31.5%). Endometrial polyp and uterine subseptum were the major intracavitary abnormalities. Chronic endometritis and endometrial polyp were the major histopathologic abnormalities. Chronic endometritis, uterine subseptum and endometrial hyperplasia were higher in patients \geq 35 years ($p < 0.01$). There was a decrease in the pregnancy rate (40% vs 46%), implantation rate (51% vs 56%) and fertilization rate (69% vs 74%) in the patients with hysteroscopic abnormality compared to patients without abnormality respectively.

Conclusion: To improve the outcome of ART cycles, OH could be performed as a routine procedure for the patients who will experience IVF treatment.

Key Words: *Office hysteroscopy, IVF failure, endometrial pathology*

ÖZET

IVF Ön Hazırlığı Yapılan Hastalardaki Diagnostik Histeroskopi Sonuçlarımız

Amaç: Çalışmamızda invitro fertilizasyon (IVF) tedavisi programına alınmış hastalarda ofis histeroskopi (OH) ile saptanacak intrauterin patolojileri ortaya çıkarmayı amaçladık.

Gereç ve Yöntem: Bu retrospektif çalışmaya Fırat Üniversitesi Hastanesi IVF Ünitesi'nde Mart 2010- Ocak 2012 tarihleri arasında tüp bebek programına alınan ve OH yapılan 219 hasta dahil edildi. Rijid, 30 derece ileri oblik görüşlü-sürekli akımlı, 4mm çaplı, diagnostik histeroskop son 6 ayda ve daha önce OH yapılmamış hastalara uygulandı. OH takiben biyopsi kateteri ile endometrial örnekleme yapıldı. Bulguları normal olan hastalar takip eden 1 ay içinde IVF siklusuna alındı.

Bulgular: Hastaların ortalama yaşı 31.9 (\pm 5.2) yıl, infertilite süresi 6.2 (\pm 4.5) yıl ve daha önceki IVF deneme sayısı 1.6 (\pm 1.1) adet idi. Hastaların %68.5'i primer infertil, %31.5'i sekonder infertil idi. İntrakaviter major anomaliler uterin subseptum ve endometrial polip idi. Histopatolojik major bulgular kronik endometrit ve endometrial hiperplazi idi. Kronik endometrit, uterin subseptum ve endometrial hiperplazi patolojileri 35 yaş üstü hastalarda daha fazla idi ($p < 0.01$). Histeroskopik patoloji saptanan hastalarda gebelik oranı (%40 vs %46), implantasyon oranı (%51 vs %56) ve fertilizasyon oranı (%69 vs %74) histeroskopik patoloji saptanmayanlara göre daha düşük gözlemlendi.

Sonuç: IVF siklusuna alınacak hastalarda tedavi başarısını artırabilmek için OH rutin bir prosedür olarak uygulanabilir.

Anahtar Kelimeler: *Ofis histeroskopi, IVF başarısızlığı, Endometrial patoloji*

Uterine cavity pathologies such as fibroids, polyps, Mullerian anomalies and others have an important role in causing infertility. The evaluation of the uterine cavity could be performed either indirectly by hysterosalpingography (HSG), transvaginal ultrasonography (TVU) and sonohysterography (SH) or directly by hysteroscopy (1-3). Hysteroscopy offers a three dimensional direct visual examination of the uterine cavity. It gives the opportunity to identify the nature of endometrial abnormalities in terms of polyps, submucous fibroids, differences in endometrial thickness (4). Hysteroscopy is an easy, fast and well tolerated diagnostic procedure that can be performed on an outpatient basis. It is known that submucosal or

intramural fibroids that distort the endometrial cavity and are therefore visible at hysteroscopy adversely affect in vitro fertilization (IVF) outcome (5-7). Endometrial polyps might also affect embryo implantation, and thus hysteroscopic polypectomy performed prior to an assisted reproductive technique should be considered (8). A condition that is easily diagnosed by hysteroscopy and is known to affect embryo implantation is septate uterus and it can be corrected by hysteroscopic metroplasty (9, 10). The hysteroscopic evaluation for repeated implantation failures in IVF- embryo transfer cycles has also been advised (11).

Hysteroscopy is feasible in an office setting, that

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employs thinner instruments and saline solution infusion distension, becoming minimally invasive and effective in the detection of intra-uterine pathologies (12). In this study we reported our results about the uterine cavity pathologies that were detected during pre-IVF evaluation.

MATERIALS AND METHODS

This study was conducted at the IVF Unit of Firat University Hospital, between March 2010- January 2012. The women attending the infertility outpatient clinic were subjected to history taking, gynecological examination and routine infertility investigations (if not previously done), including transvaginal sonography, hormonal profile and hysterosalpingography. Among the women attended infertility unit during two years period, 219 patients with decision of IVF treatment but no OH within the previous 6 months were enrolled the study. Rigid hysteroscope (continuous flow; 30-degree forward-oblique view) assembled in a 4-mm diameter diagnostic sheath with an atraumatic tip. The distension medium was normal saline. Vaginal douche and antibiotic prophylaxis with azitromicin (1 g, 3 h before the examination) were prescribed to all patients. Analgesic and anaesthetic premedication were not prescribed to all patients. Misoprostol medication were used to 4 patients in the situation of cervical stenosis. The patients in which the findings were normal proceeded to an IVF cycle within 1 month.

Endometrial polyps were defined as smooth margined masses with a homogeneous texture of variable size and shape, bulging from the endometrium. Submucosal myomas were defined as solid, round structures protruding into the uterine cavity, covered by intact epithelium. Endocavitary polyps and submucosal myomas were distinguished, their location, number and size were noted. Septum or subseptum resection, polypectomy and adhesiolysis were performed with operative hysteroscopy. Only endometrial polyps which were extirped during OH were not exceeded to operative intervention. Endometrial injury was performed after office or operative hysteroscopy with biopsy catheter. The collected endometrial samplings were analysed by histopathologic evaluation.

Data were analyzed using SPSS Version 12.0 (SPSS, Chicago, IL, USA). Results were reported as

mean \pm standard deviation. Ki-square statistics were used to compare discontinuous data and student's t-test were used to compare continuous data. A p value of <0.05 was considered as statistically significant.

RESULTS

The procedure was successful in 219 patients, with mean (\pm SD) age of 31.9 (\pm 5.2) years, duration of infertility of 6.2 (\pm 4.5) years and number of previous ART trials 1.6 (\pm 1.1). The type and the etiology of infertility were as presented in Table 1. Hysteroscopic abnormalities were classified as uterine septum, uterine subseptum, endometrial polyp, unicorn cavity, intrauterine adhesions. Histopathologic findings were as follows: chronic endometritis, endometrial hyperplasia with or without atypia, endometrial polyp and normal (proliferative or secretory) endometrium. Doxycycline with ornidazole antibiotherapy were prescribed to patients with the result of chronic endometritis.

Table 1. Characteristics of all patients in the study

Characteristic	Values (n=219)
Age (years)	31.9 \pm 5.2
Type of infertility	
Primary infertility	150 (68.5%)
Secondary infertility	69 (31.5%)
Duration of infertility (years)	6.2 \pm 4.5
Etiology of infertility	
Male factor	82 (37.5%)
Ovarian factor	45 (20.5%)
Tubal/peritoneal factor	40 (18.3%)
Combined factors	7 (3.1%)
Unexplained	45 (20.5%)
Mean no. of previous ART trials	1.6 \pm 1.1

Note: Values are presented as mean \pm SD and number (%)

The frequency of office and operative hysteroscopy findings were presented in Table 2. The major OH findings were endometrial polyp and uterine subseptum. After histopathologic evaluation, the major abnormality was chronic endometritis and than endometrial polyp was reported. Among 219 women, 31 intrauterine abnormality was observed and 15 operative intervention was performed. In the ROC analysis to determine the possibility of OH abnormality according to age, the area under curve was 0.73 and the highest LR+ value was 6,02 in the point of 35 years. The comparison of histopathologic abnormalities according to cut off value of 35 years revealed out increment in the

Table 2. Office H/S findings and histopathologic evaluation of all women in the study

Office H/S finding	n (%)	Histopathologic finding	n (%)	Operative H/S intervention	n
E. polyp	11 (5)	Chronic endometritis	35 (16)	Polypectomy	8
Uterine subseptus	11 (5)	E. polyp	11 (5.1)	Septum resection	3
Uterine septus	3 (1.5)	E. hyperplasia without atypia	9 (4.1)	Subseptum resection	1
Unicorn cavity	3 (1.5)	E. hyperplasia with atypia	3 (1.4)	Adhesiolysis	3
Intrauterine adhesions	3 (1.5)	Normal	161 (73.4)		
Normal	188 (85.5)	Total	219 (100)		
Total	219 (100)				

Note: Values are presented as number and percentage; E: endometrial.

percentage of chronic endometritis and endometrial hyperplasia over 35 years ($p=0.002$). And also endometrial polyp, uterine septum/ subseptum and intrauterine adhesion were significantly high in the women over 35 years ($p=0.035$).

During IVF procedure, 19 women did not experience embryo transfer. Among 200 women, 92 women came pregnant and the comparison of OH abnormalities between pregnant and nonpregnant women revealed no significant difference (Table 3). Although the differences were not significant, the pregnancy rate (46.9 % vs 40%), implantation rate (56% vs 51%) and fertilization rate (74% vs 69%) of women without OH abnormality were higher than that women with OH abnormality.

Table 3. Comparison of H/S results according to IVF outcome

Characteristic	Pregnancy (-) n (%)	Pregnancy (+) n (%)	P
H/S abnormality			
absence	93 (86.1)	82 (89.1)	
presence	15 (13.9)	10 (10.9)	0.66
Histopathologic findings			
Chronic endometritis	17 (15.8)	15 (16.3)	0.75
E. Polyp	4 (3.7)	3 (3.3)	0.83
E. Hyperplasia	5 (4.6)	2 (2.2)	0.24
E. Hyperplasia with atypia	1 (0.9)	2 (2.2)	0.38
Normal	81 (75)	70 (76)	0.65
Total	108 (100)	92 (100)	

Note: Values are presented as number and percentage; E: endometrial.

DISCUSSION

Office hysteroscopy (OH) is a minimally invasive and well tolerated procedure that allows accurate visual assessment of uterine cavity with the ability to treat uterine pathology in infertile patients. OH was found to strongly reduce the amount of pain compared with the use of traditional hysteroscopes, significantly improving the patients' compliance (13). When routinely performed in a diagnostic work-up of an IVF unit, a significant percentage of patients has been found to carry uterine pathology that may impair the success of fertility treatment (14). We aimed to understand the incidence of uterine pathology among infertile women, and the role that hysteroscopy could play in ruling out infertility causes and improving the way they can be treated.

In particular, a very high incidence of chronic endometritis and endometrial polyp were observed in our study, but the real influence of these pathologies on the outcome of infertility and IVF techniques is still a matter of debate (8, 15, 16). An investigator reported

endometrial polyps in 41% of 82 infertile patients with no dysfunctional uterine bleeding (17). In another study, endometrial polyps were detected in 46.7% infertile patients with endometriosis and in 15% infertile controls (18). The higher incidence of uterine septum/subseptum among infertile patients, which has already been reported by other authors seems to be confirmed in our study population, too (19, 20). However, no clear evidence showing potential impairment of reproduction because of this pathology has been reported (21-23).

OH is applicable at any time of the menstrual cycle (1). However, endometrial polyps are best visualized during the follicular phase, and submucosal myomas during the secretory phase with SH (3). Suboptimal timing during the menstrual cycle may give false results by SH. This limitation makes the SH second choice in infertility practice. There is little risk for intracavitary infection during fluid instillation of procedure (24). This could be excluded with antibiotherapy before (patients with signs of infection)/after the procedure. We concurrently performed endometrial sampling for histopathologic evaluation. This procedure was a kind of endometrial injury and it was suggested that endometrial injury before ART cycle improves the outcome by the way of increased endometrial receptivity (25- 29). In this study we did not have the ability of comparing the effect of endometrial injury on IVF outcome because of the absence of control group and heterogenous IVF population. For our study population, comparison of the incidence of intracavitary pathologies between women according to becoming pregnant, revealed out no significant difference. On the other hand when the pregnancy rate compared according to the presence of intracavitary pathology, the pregnancy rate was high in the absence of intrauterine pathology.

Flushing of malignant cells from the uterine cavity to the peritoneal cavity during hysteroscopy and SH may also happen (30). However, the slower and low-pressure infusion of saline should be expected to carry a lower risk of cell transportation. Moreover, this risk does not appear to be greater than that involved in HSG.

In conclusion, we suggested that OH is an easy, fast, well tolerated evaluation procedure before the ART cycles to improve the IVF outcome.

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