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Evaluation of Hysteroscopy in Infertile Patients

Şerife Eskalen[1], Burcu Dinçgez Çakmak[2], Nigar Sofiyeva[1], Kutsiye Pelin Berberoğlugil Öçal[1]

[1]İstanbul University Cerrahpaşa Faculty of Medicine, Department of Obstetrics and Gynecology, İstanbul, Turkey
[2]University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Clinic of Obstetrics and Gynecology, Bursa, Turkey

Abstract

Objective: The aim of this study was to evaluate the hysteroscopy results in infertile patients and to compare the clinical pregnancy, live birth and abortion rates between patients with uterine cavity abnormalities treated with operative hysteroscopy and patients with normal uterine cavity.

Methods: Three hundred and nineteen patients who underwent hysteroscopy for infertility between January 2010 and December 2015 were included in the study. The patients were divided into two main groups: diagnostic and operative. The patients who had normal uterine cavity in exploration and who did not require surgical intervention were referred as diagnostic hysteroscopy group. Patients who underwent surgical intervention during the procedure were named as operative hysteroscopy group. The operative hysteroscopy group was divided into groups as endometrial polyp, submucous myoma, septum, adhesions and T-shaped uterus. Demographic data, laboratory parameters and pregnancy outcomes after hysteroscopy were recorded. Clinical pregnancy, live birth and abortion rates were compared between the groups.

Results: The demographic and laboratory characteristics of the diagnostic (n=74) and operative hysteroscopy (n=245) groups were similar. After operative hysteroscopy, 53.9% of the patients had clinical pregnancy and 41.3% of them had live birth. In the diagnostic hysteroscopy group, the clinical pregnancy rate was 55.2% and the live birth rate was 41.7%. There was no significant difference between the two groups in terms of clinical pregnancy and live birth rates. In addition, there was no difference between the two groups in terms of pregnancy acquisition methods and mean duration of conception. In the operative hysteroscopy subgroups, the highest rates of clinical pregnancy and live birth were in patients undergoing endometrial polyp and septum resection, and abortion rates were highest in T-shaped uterus and septum resection groups.

Conclusion: We concluded that treatment of uterine cavity pathologies with operative hysteroscopy in infertile patients provided similar clinical pregnancy and live birth rates to patients who have normal uterine cavity.

Keywords: Hysteroscopy, infertility, pregnancy outcomes

INTRODUCTION

Infertility is the condition in which a couple in reproductive ages cannot achieve pregnancy despite regular unprotected sexual intercourse for one year below the age of 35 and for more than 6 months above the age of 35 (1). Appropriate selection of the tests to be performed in this case, which affects approximately 10-15% of all reproductive couples, is extremely important in both diagnosis and treatment (2). Infertility is a process that demolishes families socioeconomically and psychologically. The main causes of infertility are ovulatory dysfunction (20-40%), tubal and peritoneal pathology (30-40%), male factor (30-40%), unexplained infertility (10%) and uterine pathologies (10-15%), and intrauterine pathologies are one of the reasons that can be treated surgically (3). It is known that the frequency of intrauterine pathologies increases in infertile patients. The presence of intrauterine pathologies negatively affects fertility by decreasing the receptivity and implantation success (4). The methods used to detect these pathologies are ultrasonography (US), saline infusion sonography (SIS), hysterosalpingography (HSG) and hysteroscopy (HS). HS is a widely used method in the diagnosis and treatment of intracavitary pathologies in gynecology practice. In addition to providing direct observation of the cervical canal and uterine cavity, HS is a preferred technical method in the evaluation of infertile patients in

Address for Correspondence: Burcu Dinçgez Çakmak, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Clinic of Obstetrics and Gynecology, Bursa, Turkey
E-mail: burcumavis@gmail.com Phone: +90 530 544 88 28 ORCID ID: orcid.org/0000-0002-5034-3285

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recent years because it is a minimally invasive procedure, has low complication rate, allows for diagnostic and therapeutic interventions, and has high sensitivity and specificity (5). The aim of this study was to evaluate the results of HS applied to infertile patients and to compare the clinical pregnancy, live birth and abortion rates of patients treated with operative HS for intrauterine pathologies with patients with normal cavities.

METHODS

Ethics committee approval was received for this study from the Ethics Committee of İstanbul University Cerrahpasa Faculty of Medicine (approval number: 135378). Patient files were reviewed retrospectively. The study included 319 infertile patients who underwent diagnostic HS for indications such as polyps, submucous myoma, suspicion of septum, adhesion, uterine deformity, recurrent implantation failure (two or more failed embryo transfer cycles) and infertility treatment between January 2010 and December 2015 in İstanbul University Cerrahpaşa Faculty of Medicine, Department of Obstetrics and Gynecology. Age, obstetric history (pregnancy, birth, abortion and optional curettage count), height, weight, body mass index (BMI), duration of infertility, etiology of infertility, previous treatment for infertility, US findings, SIS and HSG findings if performed, HS indications, HS findings, pregnancy acquisition method (spontaneous or assisted reproductive techniques), presence of systemic or gynecological diseases, history of previous gynecological intervention, drug use, and smoking and alcohol use were recorded. In addition, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol, prolactin, thyroid stimulating hormone (TSH) and anti-mullerian hormone (AMH) levels measured between the 3rd and 5th days of menstrual cycle were recorded. The visualization of endocervical canal, uterine cavity and both tubal ostium was determined as a criterion for a HS to be accepted as sufficient. Patients over 40 years of age, with a history of recurrent pregnancy loss, who were reported to have malignancy as a result of pathological examination and patients who could not be operated due to insufficient cervical dilatation during HS were excluded. In our clinic, HS procedure is performed on the 8th-11th days of the menstrual cycle after menstrual bleeding under general anesthesia in the operating room. The instruments required for HS include a) 30°, size 4 mm, 30 cm long Olympus (Storz®) hysteroscope, b) metal sheath, size 5.5 mm, with working channels for distension, irrigation and semirigid operating instruments, c) computer with 37 inch Sony® (Japan) monitor, camera and DV studio AVIO program with special recording for each patient, d) cuff infusion pump system with 5% Mannitol fluid bag, e) Olympus (Storz®) 250 Watt halogen light source, and f) hysteroscopic scissors, unipolar electrocautery, and resectoscope for surgical intervention. After the speculum is placed in the dorsolithotomy position on the gynecological table, the vagina is cleaned with povidone iodine solution and the cervix is held with a tenaculum and dilated using Hegar cervical dilators up to number 8-9. The procedure starts with the evaluation of the cervix and cervical canal, and then the internal os is passed and mannitol solution is used to provide 80 mmHg intrauterine pressure for distension of uterine cavity. Both tubal ostia and uterine cavity walls, appearance of endometrium, compatibility with menstrual phase, presence of space-occupying pathology in the cavity and presence of uterine anomaly are evaluated. The structures with or without pedicle that are covered with endometrium and have a smooth surface are defined as polyps. Submucous myomas are defined as vascularized structures protruding into the uterine cavity. Uterine septum is a fibrous tissue that divides the cavity into two and that has various lengths extending from fundus to the internal cervical canal. Regarding intrauterine pathologies detected during HS, the surgeries performed are polypectomy for endometrial polyps, myomectomy for submucous myomas, septum resection in patients with uterine septum and adhesiolysis in patients with adhesion. According to the procedure performed during HS, patients included in the study were divided into two main groups as diagnostic and operative HS. Patients with normal uterine cavity in exploration, who did not require surgical intervention and who did not undergo any additional procedure were referred to as diagnostic HS group, and patients who underwent surgical intervention during the procedure were referred to as operative HS group. Operative HS group was divided into subgroups as endometrial polyp, submucous myoma, septum, adhesion and T-shaped uterus. The data regarding the treatment methods used for pregnancy after HS, whether pregnancy could be achieved and pregnancy outcomes were recorded. Clinical pregnancy, live birth and abortion rates after HS were compared between the groups. Clinical pregnancy was defined as detection of intrauterine embryo heartbeats by US. Abortion was defined as fetal loss of less than 500 grams and/or until 22nd gestational week.

Statistical Analysis

STATA14 (Stata Corp LP, TX, USA) program was used for statistical analysis of the study. The inpopulation distributions of demographic and clinical data of the patients included in the study were evaluated by Shapiro-Wilk test. In the study, Independent Samples t-test Mann-Whitney U test were used to compare the demographic and clinical characteristics of the main groups of operative and diagnostic HS. Chi-square test

was used to compare the reproductive results between the two groups. Mann-Whitney U test was used for the evaluation of laboratory parameters, as they were non-normally distributed. One-way ANOVA and Kruskal Wallis test were used for the evaluation of demographic and clinical parameters among operative HS subgroups, and Kruskal Wallis test was used for the comparison of laboratory parameters. P<0.05 was considered statistically significant at 95% confidence interval, and numerical data were expressed as mean and standard deviation.

RESULTS

Of the 319 patients included in the study, 74 (23.2%) underwent diagnostic HS and 245 (76.8%) underwent operative HS. The results of HS applied to the patients are shown in Table 1. Patients were divided into two groups as diagnostic HS and operative HS. Demographic and clinical characteristics of both groups are shown in Table 2. There was no statistically significant difference between two groups in terms of age, height, weight, BMI and duration of infertility (p>0.05). When the laboratory parameters of the patients who underwent operative and diagnostic HS were examined, no significant difference was found between the two groups in terms of FSH, LH, estradiol, prolactin, TSH and AMH levels (Table 3). While the clinical pregnancy, birth and abortion rates of 213 out of 245 patients who underwent operative HS could be obtained; reproductive results were obtained in 67 of 74 patients who underwent diagnostic HS. The clinical pregnancy, live birth and abortion rates of the operative and diagnostic HS groups were calculated and shown in Table 4. There was no statistically significant difference between the two groups in terms of these parameters (p>0.05). There was no statistically significant difference between the two groups in terms of contraception methods [(in vitro fertilization (IVF), insemination and spontaneous pregnancy] (p=0.260 for diagnostic group and p=0.968 for operative group). The mean time to pregnancy after HS was 9.54 (±9.6) months for the patients in the diagnostic HS group, and 9.96 (±10) months for the patients in the operative HS group. There was no significant difference between the two groups in terms of time to pregnancy after HS (p=0.837). Operative HS patients were divided into polyp, myoma, uterine septum, uterine adhesion and T-shaped uterine subgroups according to HS findings. There was no significant difference between the groups in terms of age, height, weight, BMI and duration of infertility (p=0.585, 0.391, 0.292, 0.544 and 0.971, respectively). Similarly, no statistically significant difference was found between operative HS subgroups in terms of FSH, LH, estradiol, prolactin, TSH and AMH levels (p>0.05). In addition, when the fertility results were evaluated according to the subgroups, the highest clinical pregnancy and live birth rates were seen in the patient group who underwent endometrial polyp and uterine septum resection. The abortion rate was

Table 1. Hysteroscopy findings

Findings	n (%)
Endometrial polyp	146 (45.7%)
Uterine septum	49 (15.4%)
Uterine adhesion	28 (8.8%)
Submucous myoma	12 (3.8%)
T-shaped uterus	10 (3.1%)
Normal uterine cavity	74 (23.2%)

Table 2. Demographic and clinical characteristics of operative and diagnostic hysteroscopy groups

	Operative hysteroscopy (n=245)	Diagnostic hysteroscopy (n=74)	p
Age (years)	32.43±0.32	32.2±0.55	0.549[a]
Height (cm)	161.02±2.35	159.68±1.17	0.114[b]
Weight (kg)	68.73±1.26	67.21±1.96	0.523[b]
BMI (kg/m^2)	26.22±0.44	26.3±0.71	0.878[b]
Infertility period (ay)	53.10±3.53	54.86±5.60	0.641[a]

[a]Mann-Whitney U test; [b]independent-samples t-test, BMI: Body mass index

Table 3. Laboratory parameters of operative and diagnostic hysteroscopy groups

	Operative hysteroscopy (n=245)	Diagnostic hysteroscopy (n=74)	p*
FSH (mIU/mL)	7.39±0.30	7.26±0.50	0.659
LH (mIU/mL)	5.75±0.27	6.07±0.51	0.532
Estradiol (mIU/mL)	52.56±3.73	62.37±9.49	0.731
Prolactin (ng/mL)	15.89±0.67	19.22±2.22	0.539
TSH (µg/mL)	2.35±0.19	1.84±0.20	0.115
AMH (ng/mL)	3.07±0.33	2.88±0.57	0.542

AMH: Anti-mullerian hormone, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, TSH: Thyroid stimulating hormone, *Mann-Whitney U test was used for statistical analysis

Table 4. Reproductive outcomes of operative and diagnostic hysteroscopy groups

	Diagnostic hysteroscopy (n=67) n (%)	Operative hysteroscopy (n=213) n (%)	p*
Clinical pregnancy	37 (55.22%)	115 (53.99%)	0.860
Live birth	28 (41.7%)	88 (41.3%)	0.945
Abortion	4 (5.9%)	16 (7.5%)	0.669

*Chi-square test was used for statistical analysis

found to be highest in the patient group with T-shaped uterus (Table 5). In addition to these findings, patients included in the study were evaluated for complications. Uterine perforation was observed in one patient during HS and one patient developed endometritis after the procedure. Both complications were seen in the operative HS group.

Table 5. Reproductive results of operative hysteroscopy subgroups

	Clinical pregnancy rate (%)	Live birth rate (%)	Abortion rate (%)
Endometrial polyp	69/130 (53%)	58/130 (44.6%)	6/130 (4.6%)
Submucosal myoma	4/10 (40%)	3/10 (30%)	1/10 (10%)
Uterine septum	28/43 (65.1%)	18/43 (41.8%)	6/43 (13.9%)
Uterine adhesion	11/24 (45.8%)	8/24 (33.3%)	1/24 (4.1%)
T-shaped uterus	3/6 (50%)	1/6 (16.6%)	2/6 (33.3%)

DISCUSSION

According to the results of our study, there is no significant difference between the operative and diagnostic HS groups and the operative HS subgroups in terms of clinical pregnancy and live birth rates, which are described as reproductive outcomes. Routine use of HS is controversial if no intrauterine pathology is suspected in infertile patients. European Society for Human Reproduction and Embryology and the Royal College of Obstetricians and Gynaecologists do not recommend HS in initial evaluation in patients without indication (6,7). In the National Institute for Health and Care Excellence guideline, HS is not recommended if there is no clinical indication in the initial investigation and treatment of fertility, i.e. if there is no suspicion of uterine anomaly or intrauterine pathology detected by imaging methods such as US, HSG, SIS, since HS does not improve reproductive outcomes when no uterine pathology is detected (8). In a multicenter randomized controlled Trial of Preventing Hypertension study, 702 patients under 38 years of age with recurrent IVF failure and normal uterine cavity were evaluated. Live birth rates between groups with and without performed HS were compared and it was shown that HS before IVF did not increase the live birth rate (9). Similarly, in the Intervention Nurses Start Infants Growing on Healthy Trajectories study, it was reported that routine HS before the first IVF treatment did not change the clinical pregnancy and live birth rates (10). In contrast to these studies, in a randomized prospective study by Rama Raju et al. (11), it reported that the rate of clinical pregnancy and live birth were significantly higher in patients who underwent HS among 520 infertile patients with recurrent IVF failure and normal HSG findings. In the literature, the effect of operative HS on clinical pregnancy acquisition and live birth rates in patients with intracavitary pathology detected by US, HSG and SIS is still unclear. When the operative and diagnostic HS group was compared in patients with uterine cavity pathology, Di Spiezio Sardo et al. (12) did not obtain sufficient evidence showing that clinical pregnancy rates increased. Varasteh et al. (13) evaluated 78 infertile patients who underwent HS, and found that 19 patients had normal cavities, 23 had polyps, and 36 had submucous myomas. It was reported that clinical pregnancy and live birth rates were 42.1% (n=8) and 36.8% (n=7) in the diagnostic HS group, 78.3% (n=18) and 65.2% (n=15) in the polypectomy group, and 52.8% (n=19) and 36.1% (n=13) in the myomectomy group. While clinical pregnancy and live birth rates were found to be significantly different between diagnostic HS and polypectomy groups, no difference was found between diagnostic HS and myomectomy groups. In their study with 215 infertile cases with polyps, Perez-Mediha et al. (14) found that clinical pregnancy rate was 63% and 28% in patients who underwent polypectomy before and without insemination, respectively. In our study, the clinical pregnancy rate was 55.2% and live birth rate was 41.7% in patients without intrauterine pathology in the diagnostic HS group. In the operative HS group, these rates were 53.9% and 41.3%, respectively. In addition, clinical pregnancy rate was 53% and live birth rate was 44.6% in 130 patients who underwent polypectomy. In other words, contrary to the findings of Varasteh et al., (13) there was no statistically significant difference between the diagnostic HS group and the polypectomy subgroup. Another result from the subgroup analysis of the operative HS group was that there was no difference between the diagnostic HS group and the patient group undergoing myomectomy in terms of clinical pregnancy and live birth rates. In our study, the clinical pregnancy rate was 40% and the live birth rate was 30% in the myomectomy group. Ahdad-Yata et al. (15) reported a 33.8% pregnancy rate after hysteroscopic myomectomy, which is similar to our study. However, contrary to our study, Pritts et al. (16) and Shokeir (17) reported increased clinical pregnancy rates with myomectomy. Intrauterine adhesions may prevent sperm migration from the cervical canal or uterine cavity and implantation of the embryo by causing full or partial tubal occlusion. They may cause implantation failure by severe endometrial damage (18). Bhandari et al. (19) found that pregnancy rate after hysteroscopic adhesiolysis was 52.2% and live birth rate was 43.4%. Zikopoulos et al. (20) reported the cumulative live birth rate as 64.7% after the operation. Roy et al. (21) reported that the pregnancy rate after hysteroscopic adhesiolysis was 40.4% and 86.1% of these

cases resulted in live birth. In our study, the clinical pregnancy rate in patients with adhesiolysis was 45.8% and was consistent with the literature. However, in our study, no difference was found in the clinical pregnancy rate between the diagnostic HS group and the adhesiolysis group. Uterine septum is the most common mullerian anomaly seen in 35% of women in the reproductive period (22). Poor blood supply to the septum and cervical insufficiency lead to impaired implantation and poor embryo development (23). In a study by Bendifallah et al. (24), the pregnancy rate after septum resection was 60.9% and the live birth rate was 54.7%. In a review by Nouri et al. (25) which included 18 trials, the clinical pregnancy rate was 60% and the live birth rate was 45% according to the reproductive results of 1501 women. In our study, the rate of clinical pregnancy after septum resection was 65.1% and the live birth rate was 41.8%.

CONCLUSION

As a result, it was concluded that the rate of clinical pregnancy was similar between the patients with corrected intracavitary pathology in the operative HS group and the patients with no evidence of intracavitary pathology in the diagnostic HS group. The results show that hysteroscopic correction of intracavitary pathology increases the rate of clinical pregnancy equivalent to the patients with normal cavity.

Ethics

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of İstanbul University Cerrahpaşa Faculty of Medicine (approval number: 135378).

Informed Consent: Retrospective study.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ş.E., K.P.B.Ö., Concept: Ş.E., K.P.B.Ö., Design: N.S., K.P.B.Ö., Data Collection or Processing: N.S., Ş.E., Analysis or Interpretation: B.D.Ç., K.P.B.Ö., Literature Search: B.D.Ç., Ş.E., Writing: B.D.Ç., Ş.E.,

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