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Comparison of hysterosalpingography diagnostic value with laparoscopy and hysteroscopy findings in infertility research

Muradiye Yildirim[a,*], Ali Yanik[b]

[a] *Ankara City Hospital, Department of Obstetrics and Gynecology, Ankara, Türkiye*
[b] *Cumhuriyet University, Faculty of Medicine, Department of Obstetrics and Gynecology, Sivas, Türkiye*

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Abstract

Aim: To compare hysterosalpingography (HSG) findings with laparoscopy (LS) and hysteroscopy (HS) findings in infertile patients and evaluate their adequacy in diagnosis

Materials and Methods: The presented retrospective study was conducted on 106 patients diagnosed with primary and secondary infertility. LS-HS procedure was applied to the cases who could not get pregnant at the end of six months after HSG. Sociodemographic data and tubal, uterine, endometrial, and pelvic findings were compared. Sensitivity, specificity, and positive and negative predictive values were calculated.

Results: Primary infertility was observed at a higher rate. (n=68, 64.2%). Most of the patients were in the 24-29 age group. The maximum duration of infertility has been observed in the range of 1-4 years. Compared with LS in tubal patency, the sensitivity of HSG was 85%, specificity 65%, positive predictivity 88.3%, and negative predictivity 58.6%. Compared with HS in detecting uterine pathologies, the sensitivity of HSG was 94.9%, specificity 53.3%, positive predictivity 72.7%, and negative predictivity 89.7%.

Conclusion: In evaluating infertile patients, HSG is reliable in detecting tubal blockage. Due to its low specificity, invasive methods can be applied, especially in unexplained infertility whose pathology is not seen in HSG. These methods are complementary rather than the alternative.

Introduction

Infertility is the clinical inability to conceive despite regular unprotected vaginal intercourse for 12 months before age 35 and six months after that. The term subfertility is also used synonymously with infertility [1]. It is a psychosocial and medical problem affecting 8-12% of couples of reproductive age worldwide [2]. In recent years, interest in infertility clinics has increased due to the age of conception due to working life and the developments in assisted reproductive techniques. Among the women who meet the definition of infertility, those who have never been pregnant are called primary, and those who have been pregnant at least once are called secondary infertility [3]. Secondary infertility is more common than primary infertility due to acquired pathologies and sexually transmitted diseases [4]. Infertility can result from male components to female components or a combination thereof. Male infertility alone is seen at a rate of 20-30%, which is the factor in 50% of the total cases [5]. The causes of female infertility are ovarian, tubal, endometrial, uterine, and cervical factors. The tubal factor is one of the most common causes of female infertility, with a rate of 25-40%. Up to 10 percent of cases are unexplained infertility [6].

After the infertility diagnosis, detailed hormonal and organic pathology examinations are performed. One year may not be expected in patients over 35, with irregular menstrual cycles, endometriosis (EM), pelvic inflammatory disease, or reproductive system anomalies [4]. Methods such as HSG, hysteroscopy, and laparoscopy evaluate infertility's tubal, uterine, or pelvic factors. Although laparoscopy is considered the gold standard for assessing the tubes and pelvis, it is not routinely applied because it is invasive and requires anesthesia. Non-invasive, economical, and easy to use, HSG is the traditional approach for imaging gynecological pathologies. It gives information about the size and shape of the uterine cavity and the structure and opening of the tuba [7]. Hysteroscopy is a specialized endoscopy that allows direct visualization, diagnosis, and treatment of intrauterine pathologies that adversely affect fertility. Laparoscopy is an invasive procedure that evaluates tubal factors and a systematic evaluation of the pelvis. It requires anesthesia and has risks of surgical complications such as infection and organ injury [5]. All three

*Corresponding author:
Email address: my48523@gmail.com (Muradiye Yildirim)

methods can be applied diagnostically or operatively and have a wide range of use in gynecology. In our study, we hypothesized that the diagnostic value of HSG is as good as LS and HS. For this purpose, we compared HSG findings with HS and LS findings regarding tubal patency and uterine and pelvic pathologies in infertile patients.

Materials and Methods

Study design and participants

This retrospective case-control study was performed at Cumhuriyet University Faculty of Medicine, Department of Obstetrics and Gynecology. One hundred six patients diagnosed as primary or secondary infertile were included in the study. Patient information was obtained from hospital records. Ethics committee approval was obtained for the study (Cumhuriyet University Clinical Research Ethics Committee, Decision no: 2011-07/07). An informed consent form was obtained from all participants. The rules of the Declaration of Helsinki were complied with in the study.

Those who had a recent pelvic infection, who were suspected of pregnancy, and who had morphological abnormalities (cervical stenosis, vaginal septum) detected during the examination, those with unexplained vaginal bleeding, hypersensitivity to the contrast agent used in HSG, and those who refused to receive anesthesia were excluded from the study. In addition, general contraindications of laparoscopy such as acute peritonitis, acute abdomen, advanced pelvic cancer, obesity, hiatus hernia, severe pelvic inflammatory disease, intestinal obstruction, cardiopulmonary diseases, coronary artery disease, bleeding diathesis were also excluded from the study.

Procedures

After taking prophylactic antibiotic treatment (200 mg oral doxycycline) 30 minutes before the procedure, between the 7th and 10th days of the menstrual cycle, a speculum was inserted into the vagina under sterile conditions. The vagina and cervix were cleaned with an antiseptic solution. A tenaculum holds the cervix at 11 o'clock, and the funnel-shaped end of the metal cannula is inserted into the external os to prevent backflow of contrast medium. Water-based contrast material was used for the procedure. While maximum traction was applied to the uterus during extraction, sequential spot X-ray images were obtained by injecting 4cc into the uterine cavity until the tube and the transition to the abdomen. After the procedure, 2x100 mg/day of doxycycline was given for five days. In addition, patients were advised to take nonsteroidal anti-inflammatory drugs when necessary. It was noted whether there was a passage through one or two tubes, deformities, hydrosalpinx or pelvic adhesions (Figure 1a). Smooth-surfaced, rounded, permanent, and nondisplaced filling defects on consecutive films were evaluated as polyps or submucous fibroids (Figure 1b). Suspicious lesions with a more hypoechoic appearance and changed shape, size, and displacement on sequential films were considered air bubbles. Irregularity of the cavity contours or filling defects sharp enough to angulate the contours were classified as uterine adhesions.

Figure 1. a: Bilateral hydrosalpinx in HSG, b: Filling defect in HSG due to submucous fibroid.

In our clinic, the LS-HS procedure is applied to patients who still cannot conceive six months after HSG. In laparoscopy (Karl-Storz Endoscope, Germany), Again, between 7-10 days of the cycle, under general anesthesia, after insufflation, the inspection was performed by entering a 10 mm trocar under the umbilicus. The upper abdomen, intestines, omentum, uterus, ovaries, fallopian tubes, pelvic wall, ligaments, and pouch of Douglas were observed. For a clear image, the atraumatic holder was advanced to the abdomen with the aid of a second trocar (5 mm). A third trocar (5 mm) was applied when intervention was required. Whether the tube was open or not was investigated with 0.25% methylene blue given with a uterine manipulator [8]. Adnexal adhesions and endometriosis (EM) detected were graded according to the American Fertility Society (AFS) classification [9, 10]. When the laparoscopic examination was completed, appropriate interventions were applied to the patients with organic pathology. Then, before the patient was awakened from general anesthesia, the cervical canal was dilated up to 7 Hegar bougies, and the cavity was entered. Diagnostic hysteroscopy was performed with a hysteroscope (Karl-Storz Endoscope). Isotonic was used as the distention medium. Cavity contours and tubal ostia were examined [11]. Necessary surgical intervention was performed in cases with intrauterine pathology. After checking the uterus and abdomen with the laparoscope again at the end of the operation, the laparoscope and hysteroscope were removed. The procedure was terminated by suturing the incision area.

Statistical analysis

We calculated the sample size using G Power software (version 3.1; Franz Foul, Universitat Kiel) [12]. The noncentrality parameter λ=17.25, critical χ^2=7.8147279, and effect size= 0.5 (large) were determined for the sample size, with a p-value (two tails) of 0.05 and a power of 95%. It was found that there should be at least 69 cases. We used the simple random sampling method from probability sampling methods for study sampling. By comparing HSG findings with LS-HS findings in detecting intrauterine pathologies, sensitivity, specificity, and positive and negative predictive values were calculated to detect tubal, endometrial, and pelvic pathologies. Data were analyzed using the Statistical Package for the Social Sciences version 14.0 program. Chi-square and Mc Nemar's test were used to compare the data between groups, and $p<0.05$ was con-

sidered significant. The chi-square test was used to find the validity (sensitivity, specificity, positive predictivity, and negative predictivity values) of the HSG method.

Results

Primary infertile group 64.2% (n=68); the secondary infertile group was 35.8% (n=38). Body mass index (BMI) of 55.7% (n=59) of the cases was in the range of 25-29 kg/m^2. Minimum body weight was 45, maximum 86 kg.

Most primary infertility is between the ages of 24-29; it is seen that secondary infertility is mainly observed in the age range of 30-35 years. The menstrual cycle duration of the patients was between 19 and 42 days. The mean age of the patients was 28.8±5.6 years (Table 1). The duration of infertility in the cases ranged from 1 to 20 years. It is summarized in Table 2. No significant difference was observed in the distribution of infertility duration of the cases. When the HSG results of the cases were evaluated, 45.3% (n=48) were found to be normal. The tubal factor was responsible for 27.4% (n=29) of the cases. Of these 29 tubal pathologies, 23 were unilateral, and 6 were bilateral tubal obstructions. Six cases were evaluated as bilateral hydrosalpinx. The uterine factor was seen in 27.4% of the cases (n=29). 14 uterine septum, seven arcuate uteri, one uterus didelphys, and seven filling defects were detected. The distribution of the cases according to the HSG findings is shown in Table 3. Twenty-seven (25.5%) cases who underwent laparoscopy were evaluated as normal. Tubal pathology in 18.9% (n=20), uterine pathology in 10.4% (n=11), ovarian pathology in 19.8% (n=21), EM in 25.5% (n=27) was detected. The distribution of laparoscopy findings is given in Table 4.

Adhesion was detected laparoscopically in 33% (n=35) of the cases. Adnexial adhesions accompanied 2 of 3 bilateral obstructions and 6 of 20 unilateral blocks. There was EM detected laparoscopically in 25.5% (n=27) of the cases. Most cases, 70.4% (n=19), were diagnosed as mild EM. The distribution of adhesions and endometriosis detected in laparoscopy is shown in Table 5. Adhesion and endometriosis were classified according to the American Fertility Society (AFS) classification [9, 10].

Compared with laparoscopy, the sensitivity of HSG in tubal pathologies was 85%, specificity 65%, positive predictivity 88.3%, and negative predictivity 58.6%. When HSG and hysteroscopy findings were compared, the sensitivity of HSG in detecting uterine pathologies was 94.9%, specificity was 53.3%, positive predictivity was 72.7%, and negative predictivity was 89.7%. Findings are shown in Table 6.

Discussion

We showed that HSG is a reliable method for detecting tubal occlusion, has high sensitivity, but has low specificity in the evaluation of uterine pathologies. Especially in unexplained infertility and unsuccessful treatment at-

Table 1. Classification of cases according to age groups.

Age group	Primary infertility		Secondary infertility		Total	
	n	Percent (%)	n	Percent (%)	n	Percent (%)
18-23	17	16.03	3	2.83	20	18.86
24-29	32	30.18	11	10.37	43	40.56
30-35	12	11.32	17	16.04	29	27.35
36-41	7	6.6	4	3.77	11	10.37
42-	0	0	3	3	3	2.83
Total	68	64.15	38	35.85	106	100

Table 2. Classification of cases according to the duration of infertility.

Duration of infertility	Primary infertility		Secondary infertility		Total	
	n	Percent (%)	n	Percent (%)	n	Percent (%)
1-4 year	27	25.47	15	14.15	42	39.62
5-8 year	24	22.64	15	14.15	39	36.79
9-12 year	8	7.54	7	6.6	15	14.15
13-16 year	7	6.6	0	0	7	6.6
16-20 year	2	1.88	1	0.94	3	2.83
Total	68	64.15	38	35.84	106	100

Table 3. Classification according to hysterosalpingography findings.

Diagnosis	n	Percent (%)
Normal	48	45.28
Tubal pathology	29	27.35
Uterine pathology	29	27.35
Total	106	100

Table 4. Cases according to laparoscopic pelvic findings.

Diagnosis	n	Percent (%)
Normal	27	25.5
Tubal pathology	20	18.9
Ovarian pathology	21	19.8
Uterine factor	11	10.4
Endometriosis	27	25.5
Total	106	100

Table 5. Adhesion and endometriosis groups according to American Fertility Society criteria.

Classification of adhesion	Case (n)	Percent (%)
Mild	23	65.7
Moderate	7	20
Severe	5	14.3
Total	35	100
Stage of endometriosis		
Mild	19	70.4
Moderate	5	18.5
Severe	3	11.1
Total	27	100

Table 6. Comparison of hysterosalpingography with laparoscopy and hysteroscopy findings.

HSG		Laparoscopy			Hysteroscopy		
		Normal	Pathology	Total	Normal	Pathology	Total
Normal	Case (n)	68	9	77	56	21	77
	Percent (%)	88.3	11.7	100	72.7	27.3	100
Pathology	Case (n)	12	17	29	3	26	29
	Percent (%)	41.4	58.6	100	10.3	89.7	100
Total	Case (n)	80	26	106	59	47	106
	Percent (%)	75.5	24.5	100	55.7	44.3	100

tempts, methods that will allow invasive and therapeutic approach can be preferred.

The mean age of our patients was 28.8±5.6 years, and the age range was 19-42. In the last century, the age of fertility desire and the age of first birth has been increasing. However, female age is one factor that comes to the fore in the etiology of infertility [13]. The study group consisted of 64.2% primary infertile patients. Secondary infertility is more common nowadays due to the increase in the incidence of sexually transmitted diseases and genital tract infections with age [14]. Other possible causes are unsafe abortion methods and postpartum endometritis. The majority of the patients in this study (55.7%) had a BMI range of 25-29 kg/m^2, that is, overweight. Being heavy in women, and obesity; are among the causes of infertility and affects the duration of conception [15]. In present study patient population, 25.5% of the primary infertile group and 14.2% of the secondary infertile group had an infertility period of 1-4 years. The group with infertility between 16-20 years constituted the smallest group of infertile patients. As the duration of infertility increases, the cost of treatment and invasive approaches increase, and the live birth rate decreases [16].

The most crucial step in evaluating an infertility patient is visualizing the genital tract. HSG is a traditional technique used safely for more than a century in gynecology and infertility. Despite their various advantages, it is debatable whether LS and HS can replace a primary method such as HSG. The essential benefits of HSG are that it can be applied in an office environment, does not require anesthesia, and is a simple and inexpensive method. Laparoscopy is an invasive technique accepted as the gold standard in diagnosing tubal patency and pelvic-peritoneal disease [17]. Our comparison with LS found that HSG has high sensitivity and moderate specificity. Some studies have found the reliability of HSG to be questionable in determining tubal patency, but they have concluded that it can be used as a complementary and adjunct method [18-20]. In a retrospective study investigating the safety of HSG, it was concluded that LS should be performed in unilateral or bilateral occlusion. However, HSG was said to be reliable when bilateral was detected [21]. On the other hand, some studies argue that HSG still maintains its primary position in routine evaluation in infertility studies [22-25]. These investigators concluded that LS is unnecessary if HSG findings are specific and peritoneal disease or adhesions are not suspected.

The unilateral occlusion in HSG is mainly due to the contrast medium's tendency to follow the less resistant pathway, so the tube that appears occluded is probably normal. Another explanation for false positives is inadequate cervical cannula placement, insufficient intracavitary pressure, and contrast medium leakage [26]. We thought that this result, which is not compatible with the literature, may be due to the small patient population in our study or the use of water-based contrast material.

In this study, tubo-peritoneal disease was detected in 55.8% of the cases, including adhesion in 29.8%, endometriosis in 9%, mixed pathology in 16.9%, when LS was applied to the cases evaluated as normal in HSG. Laparoscopy is the gold standard in the diagnosis and treatment of tubo-peritoneal factors [6]. In the laparoscopic examination, endometriosis was found in 25.5% of our patients, ovarian pathology in 19.8%, and uterine factor in 10.4%. LS is the standard gold technique in peritoneal disease. If the patient has dysmenorrhea, chronic pelvic pain, sacro-uterine nodularity, previous pelvic disease or abdominal surgery, laparoscopy seems necessary even if the HSG is normal [27].

In the present study, we showed that the sensitivity of HSG compared to HS was 94.91%; the specificity to be 53.31%. These findings are consistent with the literature. HS is a valuable and direct method that provides a safe and rapid evaluation in diagnosing intrauterine anomalies. The localizations of endo-cavitary lesions reveal their structure and guide biopsies for histological evaluation. It also allows for a therapeutic approach. One of the most critical conditions for pregnancy is endometrial receptivity. For this, intrauterine evaluation is essential. HSG and HS are methods applied for this purpose. Recent studies have shown that combining HSG and diagnostic HS will provide further benefits [28].

Limitations

The strength of this study is that it was conducted in a tertiary center, and both primary and secondary patients were evaluated. The limitations are its retrospective nature and the small size of the population. Prospective future studies can be planned, including large participants and pregnancy outcomes.

Conclusion

Investigating the causes of infertility should start with simple and inexpensive methods, and more advanced tech-

niques should be used when necessary. LS and HS allow both diagnosis and treatment. Both ways have the advantage in this aspect. All three methods are complementary rather than alternative to each other.

Disclosure

This article was presented orally on the 3rdInternational Obstetrics and Newborn Days of the University of Health Sciences.

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Ethical approval

Ethics committee approval was obtained for the study (Cumhuriyet University Clinical Research Ethics Committee, Decision no: 2011-07/07).

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