Eastern Journal of Medicine 17 (2012) 67-71

Original Article

Assessment of endometrial cavity of infertil patients with transvaginal sonography, hysterosalpingography, and hysterescopy

Banu Bingol[a,*], Faruk Abike[b], Herman Isci[a]

[a]*Department of Obstetrics and Gynecology, Istanbul Bilim University, Istanbul, Turkey*
[b]*Department of Obstetrics and Gynecology, Medicana International Ankara Hospital, Ankara, Turkey*

Abstract. To compare the accuracy of transvaginal sonography (TVS), hysterosalpingography (HSG) and hysteroscopy (HS) for uterine pathologies among infertile women. 168 women with diagnosis of infertility were enrolled in this study and assessed with TVS, HSG and HS. TVS, HSG and HS were carried out in all cases, in the 5^{th}-8^{th} days of follicular phase of the cycle. Operative hysteroscopy with directed biopsy was considered as the gold standard. HSG, TVS, and HS were conducted by specialized gynecologists, who were blinded to the results of the other examinations. Endometrial polyp (n=66, 39%), submucous myoma (n=46, 28%), endometrial hyperplasia (n=29, 17%) and suspect of intrauterine synechia (n=27, 16%) were detected with TVS. In the evaluation with HSG results, submucous myoma or polyp (n=42, 25%), irregular uterine contour (n=29, 17%), intrauterine synechia (n=24, 15%) were detected. 73 patients (43%) had normal HSG results. HS (with or without resection) results detected endometrial polyp (n=59, 35%), submucous myoma (n=47, 28%), endometrial hyperplasia (n=35, 21%) and intrauterine synechia (n=27, 16%). Endometrial biopsy revealed no atypical hyperplasia of the endometrium. TVS is the primary investigative method for evaluating every infertile couple by means of uterine cavity and ovaries. TVS seems to be additional and superior to HSG. It is a candidate to be an easy and useful method in the detection of uterine abnormalities among infertile women including polypoid lesions, endometrial hyperplasia and submucosal myoma with respect to hysteroscopy as the gold standard. It can be suggested that HSG should be replaced by the diagnostic hysteroscopy as a first-line investigation for intrauterine pathologies in infertile patients.

Key words: Hysterosalpingography, hysteroscopy, infertility, intrauterine abnormalities, transvaginal sonography

1. Introduction

Uterine cavity abnormalities can be a contributing cause of subfertility and recurrent implantation failure. Uterine cavity assessment has been suggested as a routine investigation in the evaluation of subfertile women (1). Uterine cavity abnormalities have been considered as the underlying etiology among 10%-15% of couples seeking infertility treatment (2).

Traditionally, hysterosalpingography has been the most commonly used technique in the evaluation of infertility (1).

*Correspondence: Banu Bingol
Ali Samiyen Sok. 8/8 Sisli/Istanbul, Turkey
Tel.: +90 212 2666646
E-mail: banubingol1975@yahoo.com
Received: 23.02.2012
Accepted: 17.04.2012

Among the conventional methods available for the evaluation of the uterine cavity, transvaginal sonography (TVS) is a simple and innocuous method with high accuracy for most of the uterine cavity diseases, when compared to hysterosalphingography (HSG) (3-6). Transvaginal ultrasound scan allows visualization of the endometrial lining and cavity, and it has been used as a screening test for the assessment of uterine cavity (1). Hysteroscopy (HS) on the other hand has known to have nearly the same accuracy as histopathologic study of the organ itself (7). Following recurrent IVF failure there is some evidence of benefit from hysteroscopy in increasing the chance of pregnancy in the subsequent IVF cycle, both in those with abnormal and normal hysteroscopic findings (7).

HSG has been the most commonly used technique in the evaluation of infertility. They concluded that even though HSG is mainly used

for the assessment of tubal patency, it has a secondary role in the assessment of the uterine cavity. It is also helpful in evaluating uterine cavity abnormalities (8-10). Endometrial polyps or fibroids are shown as filling defects or uterine wall irregularities. HSG can also show intrauterine adhesions and congenital uterine anomalies (8-11). TVS can visualize the endometrial cavity, it has been used as a screening test for the assessment of uterine cavity and it is very well tolerated. TVS has been reported to have positive predictive value as high as 85-95% (12,13). In comparison with hysteroscopy, TVS was reported to have 84.5% sensitivity, 98.7% specificity, 98% positive predictive value and 89.2% negative predictive value (14). Hysteroscopy is the gold standard for the investigation of uterine cavity, particularly when a pathology is suspected. It is a safe test for the direct and accurate diagnosis of intrauterine abnormalities. It permits direct visualization of the uterine cavity, revealing the nature, location, shape, size and vascular pattern of any uterine cavity abnormalities, such as polyps, submucosal fibroids, differences in endometrial thickness and adhesions. It also allows a directed biopsy and therapeutic intervention for the treatment of any pathology. Thus hysteroscopy is performed as a definitive diagnostic tool to evaluate any abnormality suspected on HSG, TVS in routine investigation of infertile patients (13-15). The main disadvantage of traditional hysteroscopy is the need for anesthesia, its relative invasiveness, and the associated cost.

In this study we aimed to compare the accuracy of transvaginal sonography, hysterosalpingography and hysteroscopy for uterine pathologies among infertile women.

2. Material and method

168 women with diagnosis infertility were enrolled in this study and who were assessed with TVS, HSG and hysteroscopy between 2007-2011 in Istanbul Bilim University, Florence Nightingale Hospital. Patients' demographics, complaints, and past medical histories were evaluated. The causes of infertility were established and classified. Patients who had abnormal TVS findings were enrolled in this study. TVS, HSG and HS were carried out in all cases, in 5^{th}-8^{th} days of follicular phase of the cycle. Operative hysteroscopy with directed biopsy was considered as the gold standard. HSG, TVS, and HS were conducted by specialized gynecologists, who were blinded to the results of the other examinations. The results of TVS and HSG were compared with those of HS, and sensitivity and specificity with 95% confidence intervals (CIs) were calculated for each examination. Written informed consent according to Helsinki's Declaration was obtained from each subject following a detailed explanation of the objectives and protocol of the study.

Conventional TVS was performed using a 5.0 MHz transvaginal probe of Voluson Pro (GE Voluson 730, Austria). Uterine position, endometrial thickness and morphology in longitudinal and transverse planes, and ovarian morphology were evaluated. A symmetric double layer endometrium with a thickness of 8 mm or less in the early proliferative phase was considered as normal. In all cases having uterine pathology with TVS methods, hysteroscopy was performed in the same menstrual cycle using a 10-mm operative hysteroscope with 30º optic telescope (Storz, Germany). The uterine cavity was distended with resectosole, with general anesthesia. Electrosurgical resection and correction of abnormalities was performed when needed. HSG was performed in all patients. The speculum was placed into the vagina after vaginal antisepsis, grasping of the anterior lip of the cervix with teneculum forceps, coaptation of the metal cannula into the external cervical orifice for injection of a hydrosoluble iodinated contrast medium (38% meglumine iodamide) with cervical traction. When the contrast medium was given, fluoroscopic assessment was performed.

Statistical analysis was performed using the SPSS 18 package program. Data was expressed as mean ± standard deviation (SD) and percent (%) where appropriate. The sensitivity and specificity of TVS, HSG and HS were calculated by HS with pathology results. The 95% CI for all parameters were also calculated. The diagnostic accuracy was calculated for each uterine disease separately.

3. Results

The patients' most common complaints were detected as menorrhagia (n=42, 25%), hypermenorrhea (n=22, 13%), metrorrhagia (n=14, 8%), hypomenorrhea (n=12, 7%) and menometrorrhagia (n=2, 1%). 46% of patiens (n=76) had no complaints. The mean age of patients were established 35, 1 (23-44) years old (Table 1). The etiology of infertility was detected as unexplained (n=45, 27%), poor responder (n=41, 24%), tubal factor (n=28, 17%), uterine factors (n=22, 13%), male factor (n=21, 12%) and endometriosis (n=12, 7%) (Table 2).

Table 1. Patient demographics and symptoms related to uterine abnormality

Age (years old)	35,1 (23-44)
Hypomenorrhea	12 (7%)
Hypermenorrhea	22 (13%)
Menometrorrhagia	2 (1%)
Menorrhagia	42 (25%)
Metrorrhagia	14 (8%)
No complaints	76 (46%)

Table 2. Etiology of infertility

Unexplained	25 (47%)
Poor response	41 (24%)
Endometriosis	12 (7%)
Male factor	21 (12%)
Tubal factor	28 (17%)
Uterine factor	22 (13%)

All patients were examined with TVS. Endometrial polyp (n=66, 39%), submucous myoma (n= 46, 28%), endometrial hyperplasia (n=29, 17%) and suspect of intrauterine synechia (n=27, 16%) were detected with TVS. In the evaluation with HSG results, submucous myoma or polyp (n=42, 25%), irregulary uterine contour (n=29, 17%), intrauterine synechia (n=24, 15%) were detected. 73 patients (43%) had normal HSG results. HS (with or without resection) results detected endometrial polyp (n=59, 35%), submucous myoma (n=47, 28%), endometrial hyperplasia (n=35, 21%) and intrauterine synechia (n=27, 16%). Endometrial biopsy revealed no atypical hyperplasia of the endometrium (Table 3).

The sensitivity for endometrial hyperplasia was found 0% and 83% for HSG and TVS respectively. HSG sensitivity was 0% for polypoid lesions, but 100% with TVS. For submucosal myomas, sensitivity of HSG and TVS was 89.3% and 97.8%. Concerning gold standard diagnosis of endometrial hyperplasia based on hysteroscopy with directed endometrial biopsy, both TVS and HSG were found to be associated with false negative results missing the diagnosis in 17.1% and 100% of patients and positive predictive value of 83% and 0% respectively. For endometrial polypoid lesions, TVS was determined to be associated with false positive results of 16%, whereas TVS was found to yield false negative results. Concerning diagnostic accuracy for submucosal myoma, false positivity was common for TVS and HSG when compared to the results from operative hysteroscopy. Hysteroscopy was determined to have a sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 100% in detection of overall uterine pathology, respectively. While the rates for sensitivity, specificity, PPV and NPV were equivocal (100%) in the pathological diagnosis for both endometrial hyperplasia and polypoid lesions, specificity and PPV were 100%, respectively in submucosal myomas.

4. Discussion

10%-15% of couples seeking treatment necessiates thorough diagnostic and therapeutic procedures including imaging techniques in the evaluation of infertile women (16,17). Our data regarding classification of abnormalities detected in the endometrial cavity of infertile women were similar to the literature (18) including endometrial polyps (35%), submucous myomas (28%), uterine adhesions (16%) and endometrial hyperplasia (21%) with respect to evaluation by hysteroscopy directed with endometrial biopsy as a gold standard.

TVS allows visualization of the endometrial lining and cavity, and has been used as a

Table 3. Results of HSG, TVS, HS and Pathology

	HSG	TVS	HS	Pathology
Irregulary contour	29 (17%)	N/A	N/A	N/A
Normal	73 (43%)	N/A	N/A	27 (16%)
Endometrial Hyperplasia	N/A	29 (17%)	35 (21%)	35 (20,5%)
Polyp	N/A	66 (39%)	59 (35%)	59 (35%)
Submucous myoma	42 (25%)	46 (28%)	47 (28%)	47 (28%)
Uterin synechia	24 (15%)	27 (16%)	27 (16%)	N/A
Adenomyosis	N/A	N/A	N/A	1 (0,5%)

screening test for the assessment of uterine cavity. TVS is an integral part of IVF treatment and is a procedure with which women have become familiar; furthermore, it is very well tolerated. Baseline periovulatory TVS has been reported to have positive predictive values as high as 85-95% (12,13).

Transvaginal sonography was reported to have an accuracy of 93.8%, PPV and sensitivity of 75%, and NPV and specificity of 96.5% in the diagnosis of benign uterine abnormalities (19). It also allows examination of the ovaries to diagnose any ovarian cyst or polycystic ovaries, adding valuable information required prior to IVF. In comparison with hysteroscopy, TVS was reported to have 84.5% sensitivity, 98.7% specificity, 98% positive predictive value and 89.2% negative predictive value (14). Our results concerning diagnostic accuracy of TVS in detection of uterine abnormalities were comparable to those with an overall sensitivity of 93.8% and a PPV of 83%. TVS misdiagnosed endometrial polyps as endometrial hyperplasia in 6 patients (3.5%) and hyperplasia as polyps in 7 patients (4.2%) in our study. Therefore, the ability of TVS to distinguish between the many causes of a thickened endometrium such as polyp, hyperplasia, endometrial cancer, or even normal thickened endometrium has been questionable.

Traditionally HSG has been the most commonly used technique in the evaluation of infertility. It gives reliable information about the patency and morphology of the fallopian tubes. It is also helpful in evaluating uterine cavity abnormalities (8-10).

HSG results may also be influenced if the procedures are performed at different phases of the menstrual cycle due to the variable trophic changes of the endometrium. False-positive findings can be caused by air bubbles, mucus, and menstrual debris that could mimic filling defects. False-negative findings can result from an excessive amount of contrast media in the uterus obliterating shadows caused by small endometrial lesions (8). As a result, approximately 10–35% of women undergoing fertility investigations, who have a normal cavity at HSG, have been reported to have abnormal hysteroscopic findings (9,10). In addition, HSG does not provide information about trophic, inflammatory, and infectious lesions that may be responsible for poor reproductive outcome in nearly 25% of subfertile women (8). HSG can also show intrauterine adhesions and congenital anomalies as it enables clinicians to visualize the general configuration of the cavity.When compared with hysteroscopy, HSG is considered to have a high sensitivity (60-98%), but a low specificity (15-80%) in detecting uterine abnormalities and is, therefore, associated with relatively high false-positive and false-negative rates (8-11). Another study conducted to assess the diagnostic reliability of hysteroscopy and HSG, demonstrated HSG to have a sensitivity of 79% and a specificity of 82%, with an 18% false positive rate and a 19% false-negative rate (1). In our study, concerning gold standard diagnosis of endometrial hyperplasia based on hysteroscopy with directed endometrial biopsy, HSG was found to be associated with false negative results missing the diagnosis in 100% of patients and positive predictive value 0% respectively. The sensitivity of HSG for endometrial hyperplasia was found 0% and also HSG sensitivity was detected 0% for polypoid lesions. For submucosal myomas, HSG sensitivity was found 89.3%. Similar with the literature, HSG related sensitivity and PPV rates were markedly worse than those of TVS and HS in detection of polypoid lesions and the hyperplasia in our study. It was stated in the literature that HSG and TVS had similar accuracy in detection of intrauterine adhesions, while TVS was associated with a diagnostic failure with sensitivity and PPV of 0% (19). However, in our study the diagnosis made for intrauterine adhesions by TVS was confirmed in 100% of infertile women via saline infusion sonography (SIS) and 89% of HS. TVS has been reported to fail to demonstrate intrauterine adhesions, and to differentiate between submucous myoma, endometrial polyp and proliferative endometrium or endometrial hyperplasia (17,20). However, our data supports the limited number of studies having excellent but difficult to reproduce results (5) on the accuracy of TVS in diagnosis of uterine adhesions. In this regard, current disapproval on TVS as a reliable method in the investigation of intrauterine adhesions due to false negativity as well as false positive results displayed by the method (21,22) may need to be investigated in future studies. Hysteroscopy is the gold standard for the investigation of uterine cavity, particularly when a pathology is suspected. It is a safe test for the direct and accurate diagnosis and treatment of intrauterine abnormalities. It permits direct visualization of the uterine cavity, revealing the nature, location, shape, size, and vascular pattern of any uterine cavity abnormalities, such as polyps, submucosal fibroids, differences in endometrial thickness and adhesions. It also allows a directed biopsy and therapeutic intervention for the treatment of any pathology. Thus, hysteroscopy is performed as a

definitive diagnostic tool to evaluate any abnormality suspected on HSG and TVS in routine investigation of infertile patients (13-15). HS as stated in the literature (23) did provide accurate description of the endometrial cavity since the total agreement was shown between HS and the gold standard in the diagnosis of endometrial hyperplasia and polypoid lesions of the uterine cavity, with 100% accuracy. In conclusion, although TVS is the primary investigative method for evaluating every infertile couple by means of uterine cavity and ovaries. TVS seems to be additional and superior to HSG. It is a candidate to be an easy and useful method in the detection of uterine abnormalities among infertile women including polypoid lesions, endometrial hyperplasia and submucosal myoma with respect to hysteroscopy as the gold standard. Because of the low-positive predictive value and low specificity of the HSG, it will be suggested HSG should be replaced by the diagnostic hysteroscopy as a first-line investigation for intrauterine pathologies in infertile patients.

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