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ORIGINAL ARTICLE

To Evaluate the Accuracy of Saline Infusion Sonohysterography (SIS) for Evaluation of Uterine Cavity Abnormalities in Patients with Abnormal Uterine Bleeding

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Abstract
Objective To evaluate the accuracy of transvaginal sonography (TVS) and saline infusion sonohysterography (SIS) for detection of uterine cavity abnormalities in patients with abnormal uterine bleeding (AUB) taking hysteroscopy as the gold standard.
Methods This was a prospective study done in the department of Obstetrics and Gynecology of a tertiary care academic hospital. Sixty premenopausal and postmenopausal women who presented with AUB underwent TVS, SIS, and hysteroscopy. The presence of focal abnormality and the type of abnormality, i.e., polyp, submucous myoma, and endometrial hyperplasia, were noted. The results of TVS and SIS were compared with hysteroscopy.
Results On hysteroscopy, 76.67 % ($n = 46$) patients were diagnosed with intra cavity abnormalities. SIS showed sensitivity, specificity, PPV, and NPV of 89.1, 100, 100, and 73.7 %, respectively. In comparison, TVS showed sensitivity, specificity, PPV, and NPV of 43.48, 78.57, 86.96, and 29.73 %, respectively.
Conclusions SIS was found to be more sensitive and specific than TVS in detection of intra cavity abnormalities.

Keywords SIS · Hysteroscopy · AUB · TVS · Endometrial polyps

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Introduction

Abnormal uterine bleeding (AUB) is the single most common reason for gynecological referrals in premenopausal and postmenopausal patients [1]. In premenopausal women, AUB is diagnosed when there is a substantial change in frequency, duration, or amount of bleeding during or between periods. In postmenopausal women, any vaginal bleeding 1 year after cessation of menses is considered abnormal and requires evaluation. It can be caused by a variety of uterine abnormalities such as polyp, submucous myoma, endometrial hyperplasia, and endometrial cancer and these account for more than 40 % of cases [2]. Cases of AUB require a systematic diagnostic and therapeutic approach to rule out these abnormalities. A variety of tools are available for diagnosis of uterine cavity abnormalities that lead to AUB. Transvaginal sonography (TVS), saline infusion sonohysterography (SIS), and hysteroscopy have been used commonly. TVS plays an important role as the initial modality, but suffers from the drawback that it has a high false-negative rate in

diagnosing focal intrauterine pathology [3]. SIS which involves instillation of saline into the uterine cavity during scanning improves the accuracy. SIS distinguishes between focal lesions which require a directed biopsy for diagnosis and removal and global thickening which can reliably be sampled with an office biopsy approach [3].

Hysteroscopy helps in direct visualization of the whole uterine cavity and when combined with guided biopsy allows accurate identification of endometrial pathology. It has been accepted as the "gold standard" for evaluation of the uterine cavity [4]. Concerns have been raised about hysteroscopy being not only an expensive and invasive procedure but also unnecessary in 50 % of patients who have a normal uterine cavity [5].

The purpose of our study was to evaluate the accuracy of SIS for detection of uterine cavity pathology, using hysteroscopy as the "gold standard."

Materials and Methods

This prospective study was conducted in the Department of Obstetrics and Gynecology, PGIMER, Dr. RML Hospital, New Delhi, from November 2010 to January 2012. Premenopausal (>40 years) and postmenopausal patients presenting with AUB were subjected to detailed clinical history and examination. Patients with active pelvic inflammatory diseases, known genital tract malignancies, adnexal masses, pregnancy, and cervical pathology were not included in the study. Patients thus selected underwent TVS and SIS followed by hysteroscopy.

In premenopausal women, SIS was performed after cessation of menses in the proliferative phase no later than day 10. In postmenopausal women, the procedure was performed at any time. TVS was performed with Siemens Sonoline Adara (7.5 MHz) by an ultrasonologist and endometrial thickness was measured and any focal pathology noted. Patients with endometrial thickness <4 mm were not included in the study. SIS was performed in the same sitting with the help of a gynecologist. Under all aseptic precautions, a sterile Sims speculum was introduced in the posterior vaginal wall and anterior lip of the cervix held with a valsellum. Foley's catheter no. 8 was advanced through external os into the endometrial cavity and the balloon was inflated. The speculum was carefully removed and the endovaginal probe was inserted beside the catheter. Under direct sonographic visualization, the balloon was gently retracted to occlude the internal cervical os and 15–20 ml saline was injected in the endometrial cavity, pushing the opposed walls of the endometrium apart. The anechoic fluid was then juxtaposed against the echogenic endometrium, giving exquisite details of the uterine lining. Complete sonographic evaluation of the endometrial cavity was performed in both the coronal and sagittal planes. Endometrial thickness was measured by adding the anterior and posterior endometrial thickness excluding the anechoic fluid part. The balloon was then deflated and evaluation of the lower uterine segment and the endocervical region was performed. The catheter was then removed. Results of the TVS and SIS were expressed using the following criteria: endometrial hypertrophy (single-layer endometrial thickness >6 mm for premenopausal women and >3 mm for postmenopausal women); endometrial polyp (hyperechogenic lesion with a pedunculated attachment to the endometrium); and submucosal myoma (lesion of mixed echogenicity disrupting the endometrial continuity) [6].

Hysteroscopy was performed with Hopkins II straight forward 5 mm, 0 degree/30 degree telescope (Karl Storz, Germany) under paracervical anesthesia within 6 weeks of SIS. The distension medium used was normal saline 40–50 ml/min, at the pressure of 50–100 mm of Hg. Three hours prior to the procedure, tablet Misoprost 400 microgram was inserted per vaginally.

With insertion of the hysteroscope, the endocervical canal was visualized followed by the uterine cavity. The observations were categorized as normal uterine cavity, endometrial hyperplasia, polyp, and submucous fibroid. The hysteroscope was rotated to view the anterior, posterior, and lateral walls and a guided biopsy was taken. Polypectomy was done for endometrial polyp. If no focal endometrial pathology was found, curettage was done. Tissue samples were sent for histopathology. During the procedure, the pulse rate and blood pressure were monitored. The patients were kept under observation ~4–6 h after the procedure. Patients who did not complete all three, TVS, SIS, and hysteroscopy, were excluded from the study.

Data were analyzed by SPSS 16.

Sensitivity, specificity, PPV, and NPV for SIS and TVS were calculated.

Results

Out of 60 patients, 48.3 % ($n = 29$) were premenopausal and 51.7 % ($n = 31$) postmenopausal. Out of 31 postmenopausal patients, 45.77 % (13/31) were menopausal for more than 5 years. Among postmenopausal women, the duration of the complaint was <6 months in 87.6 % (27/31). In the premenopausal age group, 20.68 % (6/29) had a duration of complaints of <6 months.

Seventy-five percent of patients had mean BMI more than 25. The mean age was 53.71 years. Sixty-five percent of patients had either hypertension or diabetes or both.

On TVS, 61.66 % ($n = 37$) patients had normal uterine cavity and 38.34 % ($n = 23$) were diagnosed with uterine cavity abnormalities, viz., 15 % ($n = 9$) had polyp, 6.66 %

Table 1 Findings at TVS, SIS, and hysteroscopy in patients with AUB ($n = 60$)

Findings	TVS (%)	SIS (%)	Hysteroscopy (%)
Normal cavity	61.66	31.7	23.33
Uterine cavity abnormalities	38.34	69.3	76.67
Endometrial polyp	15	41.7	51.67
Submucous myoma	6.66	21.7	20.0
Endometrial hyperplasia	16.66	5.0	5.0

($n = 4$) had submucous myoma, and 16.66 % ($n = 10$) had hyperplasia (Table 1).

At SIS, 31.7 % ($n = 19$) had normal endometrial cavity and 69.3 % ($n = 41$) were diagnosed with intra cavity abnormalities. Endometrial polyp was the most frequent lesion found in 41.7 % ($n = 25$). Thirteen patients (21.7 %) had submucous myoma and three patients (5 %) had endometrial hyperplasia (Table 1).

On hysteroscopy, 23.33 % ($n = 14$) had normal endometrial cavity and 76.67 % ($n = 46$) patients were diagnosed with intra cavity abnormalities. Endometrial polyp was the most frequent lesion found in 51.7 % ($n = 31$) followed by submucous myoma in 20 % ($n = 12$) patients and endometrial hyperplasia in 5 % ($n = 3$) (Table 1).

TVS allowed detection of 20 of 46 patients with abnormal findings (sensitivity = 43.48 %).Twenty-three patients were found to have abnormal findings on TVS and hysteroscopy confirmed the findings in 20 patients (specificity 78.57 %) (Tables 2, 3). There were 3 false-positive and 26 false-negative findings, thus giving a PPV of 86.96 % and NPV of 29.73 %.

SIS allowed the detection of 41 out of 46 patients with intra cavity abnormalities indicating sensitivity of (89.1 %). Forty-one patients were found to have abnormal findings on SIS and hysteroscopy confirmed the findings in all (specificity 100 %). There were five false-negative and no false-positive results, indicating NPV of 73.7 % and PPV of 100 %, taking hysteroscopy as the gold standard (Tables 2, 3).

Table 2 Comparison of findings at TVS, SIS, and hysteroscopy

Hysteroscopy findings			
	Abnormal	Normal	Total
TVS			
Abnormal[a]	20	3	23
Normal	26	11	37
SIS			
Abnormal	41	0	41
Normal	5	14	19
	46	14	60

[a] Includes endometrial polyp, submucous fibroid, hyperplasia

Table 3 Comparison of diagnostic parameters of TVS and SIS (hysteroscopy as "gold" standard)

Diagnostic parameters	TVS (%)	SIS (%)
Sensitivity	43.48	89.1
Specificity	78.57	100
Positive predictive value	86.96	100
Negative predictive value	29.73	73.7

Table 4 Comparison of SIS results with hysteroscopy

SIS result	Hysteroscopic findings			
	Normal cavity	Hyperplasia	Submucous myoma	Endometrial polyp
Normal cavity (19)	14	0	3	2
Hyperplasia (3)	0	3	0	0
Submucous myoma (13)	0	0	9	4
Endometrial polyp (25)	0	0	0	25
Total (60)	14	3	12	31

The accuracy of SIS for diagnosis of individual abnormality was calculated. Polyp was the most common finding on hysteroscopy ($n = 31$). On SIS, 25 patients had endometrial polyp; hysteroscopy confirmed the diagnosis of endometrial polyp in all cases (specificity 100 %) (Table 4). SIS missed the diagnosis of polyp in 6 out of 31 patients (sensitivity 80.64 %). Submucous myoma was diagnosed in 12 patients on hysteroscopy and 9 (75 %) could be picked correctly on SIS (sensitivity 75 %). Out of 13 patients diagnosed with submucous myoma on SIS, 9 were confirmed and other 4 were polyps (specificity 69.23 %). Three patients had endometrial hyperplasia on SIS. On hysteroscopy, all three patients were found to have endometrial hyperplasia (sensitivity and specificity 100 %). On hysteroscopy, normal endometrial cavity was found in 14 patients; SIS picked up all of these patients as having a normal endometrial cavity (sensitivity 100 %). However, on SIS, 19 patients were found to have a normal endometrial cavity; hysteroscopy confirmed the diagnosis in 14 patients, 3 had submucous myoma, and two patients had endometrial polyp. SIS missed the focal pathology in five women, which was picked up by the hysteroscopy (Table 4).

TVS detected only 9 out of 31 polyps (sensitivity 29.03 %). All 9 polyps diagnosed on TVS were confirmed by hysteroscopy (specificity 100 %). Sensitivity of TVS for submucous myoma and hyperplasia was nil and 66.66 %,

Table 5 Comparison of TVS result with hysteroscopy

TVS result	Hysteroscopic findings			
	Normal	Endometrial polyp	Submucous fibroid	Hyperplasia
Normal Cavity (37)	11	15	10	1
Endometrial polyp (9)	0	9	0	0
Submucous fibroid (4)	1	3	0	0
Hyperplasia (10)	2	4	2	2
Total (60)	14	31	12	3

respectively. The diagnosis of endometrial hyperplasia was false positive in 80 % of cases on TVS as 4 cases of polyps and 2 cases of fibroid were interpreted as hyperplasia (Table 5).

Discussion

The present study evaluated the diagnostic accuracy of TVS and SIS for detection of intra cavity abnormalities taking hysteroscopy as the gold standard. Hysteroscopy was taken as the gold standard as its sensitivity and specificity in the detection of uterine cavity abnormalities have already been proven [4]. A single investigator (PV) performed TVS and SIS to eliminate interobserver variation. One person performed (IC) all hysteroscopies and the results of SIS were not known to her.

In the present study, on hysteroscopy, 76.67 % ($n = 46$) of women were found to have intra cavity abnormalities. Schwarzler et al. [7] and Dueholm et al. [8] found the incidence of uterine cavity abnormality to be 53 and 35 %, respectively, in patients of AUB.

In the present study, sensitivity, specificity, PPV, and NPV of TVS in detecting uterine cavity abnormalities in patients of AUB were 43.47, 78.5, 86.96, and 29.73 %, respectively. This was low compared to other studies. Feitosa et al. [9] reported the sensitivity and specificity of TVS in diagnosis of abnormal findings in patients of AUB as 83.3 and 83.3 %, respectively. SIS combined with TVS showed more accuracy in detection of lesions in uterine cavity in the present study. Sensitivity, specificity, PPV, and NPV of SIS in detecting abnormal lesion were 89.1, 100, 100, and 73.7 %, respectively. Erdem et al. [10] analyzed 122 women with AUB and found that SIS had sensitivity of 97.7 % and specificity of 82.45 %, while TVS demonstrated sensitivity of 83.5 % and specificity of 70.6 %. Karsidag et al. [11] in a study on postmenopausal women demonstrated that TVS had sensitivity of 63 %, specificity 78 %, PPV 89 %, and NPV of 41 %. They found the sensitivity, specificity, PPV, and NPV to be 93, 56, 86, and 71 %, respectively, for SIS. Thus, most other studies have also found SIS to be a better test.

In the present study, polyp was the most common finding (51.7 %). Polyps were the most prevalent lesion in studies by Feitosa et al. [9] and El-khayat et al. [12] (33.3 and 26 %, respectively). In the present study, sensitivity and specificity of SIS were 80.64 and 100 % for polyps compared to 29.35 and 100 % for TVS, respectively, implying that the detection rate of polyp increased significantly on addition of SIS to TVS. In a similar study by Schwarzler et al. [7] on 104 patients, the detection rate of polyp went up from 56 to 84 % on SIS. They also observed that SIS decreased the number of false-negative results from 11 to 4 without increasing the number of false-positive results. Specificity of both TVS and SIS was found to be 100 % in detection of endometrial polyp in the present study. In a study by Yildizhan et al. [13], the sensitivity and specificity of TVS in detecting endometrial polyp were 65.2 and 87.9 %, respectively, compared with 91.3 and 93.1 % for SIS.

The sensitivity of SIS was 75 % for submucous myoma, while the specificity was 69.23 %, and no case of myoma was diagnosed accurately on TVS. Riko et al. [14] in a study concluded that SIS findings were consistent with hysteroscopy in 97.5 % of patients with submucous myoma.

Both SIS and TVS have been found to have high sensitivity (100 and 66.6 %, respectively) for endometrial hyperplasia; however, SIS was more specific than TVS (100 vs 20 %, respectively). The reason for the very low specificity is that TVS fails to discriminate between hyperplasia and submucous myoma. Mohammad et al. [15] reported sensitivity of 73.35, 71.4, and 91.95 % for polyp, hyperplasia, and submucous myoma, respectively, whereas the specificity was 96 % for polyps, 82.3 % for hyperplasia, and 90.7 % for submucous myoma on SIS.

Conclusions

The addition of SIS to TVS significantly improved the sensitivity and specificity for detecting focal endometrial pathology. Considering the excellent correlation between SIS and the hysteroscopy, it can be used as an alternative procedure whenever hysteroscopy is not available. Hysteroscopy can be reserved for cases when an intrauterine

lesion has already been diagnosed on SIS or when SIS is inconclusive.

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