Role of Hysterosonography in Assessment of Uterine Causes of Pre- and Postmenopausal Bleeding


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Abstract

Objective: To measure the diagnostic values of Saline Infusion sonohysterography (SIS) in diagnosis of uterine causes of pre- and postmenopausal bleeding.

Design: Descriptive study.

Patients: A total of fourteen patients sixteen of which were post-menopausal and the remaining twenty four were premenopausal.

Settings: Suez Canal University Hospital, radiology department.

Results: Saline infusion Sonohysterography (SIS) was found to be highly sensitive and specific in diagnosis of endometrial polyps, endometrial carcinoma, endometrial hyperplasia and submucous fibroids as compared to that of transvaginal sonography. Although (SIS) had similar accuracy in diagnosis of endometrial carcinoma, submucous or intramural fibroid as well as endometrial atrophy to that of (TVS) with respect to being slightly lower, it represents a considerably higher values of accuracy in the diagnosis of either endometrial hyperplasia or endometrial polyps.

SIS found to have almost negligible complication.

Conclusion: With its higher sensitivities, specificities, positive and negative predictive values, SIS can be better used than TVS in evaluating those patients with abnormal uterine bleeding, as TVS often does not provide the physician with sufficient diagnostic information.

Key Words: Hysterosonography – Saline infusion sonohysterography – SIS.

Introduction

ABNORMAL uterine bleeding is a common gynaecological problem among the female population. In an international study done by the World Health Organization, it was found to affect 1011 out of 5322 women surveyed (19%) from 14 different countries. It does not only affect the physical condition of the female, but also affects her psychological status as well, with much interruption of her life style [1].

Postmenopausal bleeding may be defined as bleeding that occurs after 12 months of amenorrhea in a middle aged woman [2].

Patients who present with postmenopausal bleeding should be carefully examined to uncover the source of bleeding, a common rule of thumb is that postmenopausal uterine bleeding should be considered endometrial carcinoma until proven otherwise [1].

Regarding the work up for abnormal uterine bleeding, after careful history and physical examination followed by laboratory analysis to exclude systemic and extra-uterine causes of bleeding, the search for uterine causes starts, usually with ultrasound imaging of the uterus and pelvic structures either trans-abdominally or trans-vaginally [3].

Transvaginal ultrasound is the primary tool of investigation in women having abnormal bleeding, assessing the uterine size and endometrial thickness (according to each phase of the menstrual cycle and its normal measurements in postmenopausal period) [3].

Because Saline Infusion Sonohysterography (SIS) allows distinction between diffuse and focal abnormalities, moreover, hysterosonography can provide a relatively non-invasive, less painful, more easy and reliable procedure, as well as being nearly of the same accuracy of other invasive techniques, so it will help much more in reducing the burden of such gynaecological problem as it provides physicians with a cost-effective way to plan the next step in case management [3].
The purpose of this study was to measure the diagnostic values of Saline Infusion sonohysterography (SIS) in diagnosis of uterine causes of pre- and postmenopausal bleeding.

Patients and Methods

Study population:

We studied 40 female patients complained of either pre- or post-menopausal bleeding and referred to our diagnostic radiology department in Suez Canal University Hospital, Ismailia, to be investigated for a uterine cause, after applying the criteria had been recruited for the study.

Timing of the examination:

In premenopausal women with regular cycles, the procedure was performed between days 6 to 10 of the menstrual cycle to avoid the possibility of disrupting an early pregnancy. For women with irregular cycles, the procedure was performed after the cessation of bleeding. In postmenopausal women, the procedure was performed at any time.

Technique of examination: Hysterosonography involved the instillation of sterile saline under continuous sonographic visualization.

In most cases, there was no special patient preparation.

a- A baseline transvaginal ultrasound was performed prior to SIS to assess:

Endometrial thickness; to be considered abnormal, it should be >5mm in postmenopausal females and >8mm. in premenopausal females at the 6th to 10th day of menstrual cycle.

Uterine size, uterine wall texture, adnexal structures.

b- Technique of hysterosonography:

The patient was placed in lithotomy position, then a sterile speculum was inserted into the vagina, cervix was cleansed by an antiseptic solution (povidone-iodine 10% solution). The catheter that used was prefilled with saline prior to insertion to minimize artefacts, and then inserted into the uterine cavity to the level of the uterine fundus, the speculum was then removed and transvaginal transducer was inserted into the vagina, the catheter then identified and repositioned in the endometrial cavity if necessary. Sterile saline was then injected slowly through the catheter under continuous sonographic control.

The uterus was scanned systematically in sagittal and coronal planes to delineate the entire endometrial cavity and appropriate images were recorded.

Images were analyzed without awareness of the pathologic diagnoses of the patients.

The endometrium was considered as abnormal if it was equal to or thicker than 8mm in the premenopausal period and in a postmenopausal patient on hormone replacement therapy. In a postmenopausal patient who was not on hormone replacement therapy The SIS examination was regarded as abnormal if the endometrium was equal to or thicker than 5mm (both layers).

The size of the focal abnormality was also measured. On SIS examination, endometrial lesions were classified as diffuse thickening, focal thickening suggestive of endometrial polyp, endometrial cancer, uterine synechia and submucosal leiomyoma.

The sensitivities, specificities and positive and negative predictive values of TVS and SIS examinations were calculated.

Abnormal sonohysterographic findings:

Endometrial atrophy, endometrial hyperplasia, intra-cavitary polyp, submucosal leiomyoma and endometrial carcinoma.

To confirm sonographic data, histopathological assessment was done to the diagnosed abnormal endometria and correlated the results obtained by hysterosonography with that of histopathology.

Statistical values used in the study:

Data sheet was interpreted on SPSS computer program to obtain different statistical relations which are represented in the results.

Statistical values such as sensitivity, specificity, positive and negative predictive values as well as accuracy of both transvaginal sonography (TVS) and saline infusion sonohysterography (SIS) were calculated.

Test between two proportions is the test used for the comparison between the accuracy of the two tests used in the study (TVS & SIS), using a specific equation with standardization of the level of significance.

Results

Saline infusion Sonohysterography (SIS) was found to have higher sensitivity and specificity in diagnosis of endometrial polyps, endometrial carcinoma, endometrial hyperplasia and submucous
fibroids as compared to that of transvaginal sonography as shown in Table (1).

Regarding accuracy, (SIS) was found to have approximately similar percentage of accuracy in diagnosis of endometrial carcinoma, submucous or intramural fibroid as well as endometrial atrophy to that of (TVS) with respect to being slightly lower, however, it represents a considerably higher values of accuracy in the diagnosis of either endometrial hyperplasia or endometrial polyps.

On SIS a complication in the form of cramp-like pain in the supra-pubic region was seen in five patients, one of them suffered severe uterine cramp during instillation of fluid leading to termination of the examination after repulsion of the catheter, but among the rest, pain was tolerated not requiring termination of the procedure and occurred during fluid instillation.

A similar type of pain was experienced by four patients, soon after termination of the procedure and was relieved shortly after taking an antispasmodic and did not recur.

Mild to moderate spotting was seen in most of the patients (twenty-nine) after the procedure and was shortly relieved after a short period of rest.

No significant complications were noted after performing TVS except minimal smearing of the covered transvaginal probe by blood seen in nineteen patients after TVS and in twenty-nine patients after (SIS).

Table (1): A comparison of the sensitivity, specificity, negative and positive predictive values of (TVS) and (SIS) regarding different pathological entities.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial Hyperplasia</td>
<td>72.2</td>
<td>94.1</td>
<td>94.1</td>
<td>94.1</td>
<td>61.9</td>
</tr>
<tr>
<td>Endometrial Polyp</td>
<td>40</td>
<td>92</td>
<td>86.7</td>
<td>50</td>
<td>81.8</td>
</tr>
<tr>
<td>Submucous Fibroids</td>
<td>83.3</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Mural Fibroids</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Superficial Endometrial Carcinoma</td>
<td>33.3</td>
<td>33.3</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Endometrial Atrophy</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Table (2): Demonstrates the complications of (TVS) and (SIS) in the study population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>TVS</th>
<th>SIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain in procedure</td>
<td>Three</td>
<td>Five</td>
</tr>
<tr>
<td>Pain after procedure</td>
<td>None</td>
<td>Four</td>
</tr>
<tr>
<td>Bleeding after procedure</td>
<td>Minimal probe smearing in 19 patients</td>
<td>Mild to moderate spotting in 29 patients.</td>
</tr>
<tr>
<td>Post procedure evidences of (PID)</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Fig. (1-A): Sagittal TVS of a postmenopausal female showing diffuse endometrial thickening with multiple cystic changes, note the intramural fibroid.

Fig. (1-B): Sagittal SIS of the same patient irregular endometrial thickening with cystic changes and normal endometrial-myometrial junction.
Perform SIS with trial SIS 3D US

Fig. (2-A): Sagittal TVS demonstrated marked thickening of the endometrium measuring 3.7cm.

Fig. (2-B): SIS revealed large submucous echogenic mass, which extended transmurally within the myometrium. The endometrial stripe thickness was normal.

Fig. (3): Sagittal SIS showing diffuse asymmetrical thickening, note the sonographic diagnosis of small polyp (P) as well as the diffuse endometrial thickening of the posterior uterine wall (arrow heads).

Fig. (4): Sagittal SIS showing diffuse symmetrical and homogeneous thickening, better seen with uterine distention, no polyps are seen, but noted transverse band representing synaechia (arrow).

Discussion

Common sonographic indications for SIS, as mentioned by Cullinan et al. [4], are to evaluate the cause of focal or generalized endometrial thickening and poorly defined endometrium and to differentiate intramural from submucous myomas in the presence of a uterine leiomyoma of intermediate location.

Goldstein RB [5] stated certain contraindications for SIS, including pregnancy and pelvic inflammatory disease (to avoid flourishing of infection in the later) which we followed in our study as exclusion criteria.

Failure rate in our study was 12.5% (i.e. in five out of forty cases). In one patient, the presence of large cervical polyp prevented catheter advancement; another patient suffered a severe form of

Among five patients, hysterosonography was failed due to failure of catheterization, giving a failure rate of 15% (Chart A).

<table>
<thead>
<tr>
<th>TVS trial</th>
<th>Performed SIS</th>
<th>Failed SIS with 3D US</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>100</td>
<td>87.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12.5</td>
</tr>
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<td></td>
<td></td>
<td>2.5</td>
</tr>
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Chart A: Percentage of success and failure rates in SIS.
uterine cramp during the instillation of fluid leading to catheter repulsion and intolerability to complete the examination, while in the other three cases which were postmenopausal, catheter advancement was also blocked by the presence of previously undiagnosed cervical stenosis.

Cullinan et al. [4] and Chung & Parsons [6] reported that cervical polyps and cervical stenosis were the causes of catheter introduction hindrance on SIS.

In other literature, failure rate was 4.6% to 7.0% as Dessole et al. [7] reported.

De Kroon et al. [8] added other two causes for failure of procedure such as severe spill of saline solution that resulted in inadequate distension of the uterine cavity. The other cause is pain, severe uterine cramps and intolerability to complete the examination. In his study the failure rate equals 5.6% most of them were postmenopausal mainly due to cervical stenosis.

From the different pathological entities presented in our study, endometrial hyperplasia formed 45% (eighteen out of forty cases); simple hyperplasia was the commonest form, as proven pathologically. This was emphasized by Cortan et al. [9] who stated that simple (cystic) endometrial hyperplasia was the most common form of all types of hyperplasia.

According to Malpani et al. [10] and Granberg et al. [11], endometrial hyperplasia appeared by transvaginal sonography (TVS) as a well-defined thickened, highly reflective layer occupying the whole endometrial cavity. Dubinsky et al. [12] added that a benign appearance at SIS was defined as a thin endometrium, diffuse smooth endometrial thickening, or a smoothly margined, homogeneously echogenic, pedunculated endoluminal mass. A suspicious appearance was defined as either irregular thickening of the endometrium or an inhomogeneous, irregular endoluminal mass.

Regarding endometrial hyperplasia in our study, SIS was more sensitive, more specific and more accurate than TVS in its diagnosis (94.1% and 72.2% sensitivity, 94.1% and 63.6% specificity and 91.4% and 67.5% respectively), that SIS diagnosed endometrial hyperplasia in sixteen out of eighteen cases, however TVS diagnosed only thirteen cases. This does not mean that TVS failed in diagnosing global endometrial thickening in these cases, but it depicted this in many cases having multiple small polyps, that gave a false impression of asymmetrical thickening in some of them, so they were misinterpreted as endometrial hyperplasia.

Dubinsky et al. [13], reported that despite its sensitivity, SIS could not reliably differentiate between hyperplasia and malignancy. This was because cases of carcinoma might be seen on SIS to have symmetrical homogenous endometrial thickening that may be misinterpreted as endometrial hyperplasia.

Ryu et al. [14] reported that TVS has its limitations in depicting small nodular lesions, which are isoechoic within the endometrium and even a normal thickness endometrium may be seen to represent endometrial hyperplasia. In his study, small endometrial polyps or submucosal leiomyomas (usually less than 15mm sized) could not be correctly detected with TVS, even large adenomyoma and synechia could not be diagnosed either.

In some cases, the differentiation between endometrial polyp and polypoid adenomatoid hyperplasia was difficult. However, SIS had successfully detected these lesions that could not be found in TVS in sixteen cases of his study, including an atypical adenomyoma and the uterine synechia.

Regarding endometrial polyps, in our study, it was diagnosed if focal endometrial thickening and increased echogenicity or if a positive hyperechoic line sign (+/-cystic areas) on TVS and if a polypoid mass on SIS, were identified within the endometrial cavity with the echo texture of the mass being hyperechoic compared to that of the normal myometrium.

Fleischer & Kepple, [15] and Hulka et al. [16], stated that polyps were identified with TVS by the presence of a well-defined focal thickening of the endometrium with increased reflectivity.

In our study, TVS succeeded in the diagnosis of only less than half of the cases having endometrial polyps (four cases out of ten) with a sensitivity of 40% and a specificity of 86.7%. This was not through direct visualization of the polyps nor was TVS able to correctly depict the site of attachment, as well as, the size of the polyps and their pedicles as SIS did.

It was through indirect signs that we based our sonographic diagnosis of polyps, namely, hyperechoic line sign and focal endometrial thickening with increased reflectivity, especially in the presence of cystic spaces. On viewing these sonographic signs, we suspected the presence of polyps, but were not 100% sure. Unfortunately, on SIS and
biopsy, our suspicion was not always true, the matter that decreased the sensitivity and specificity of TVS in the diagnosis of polyps, so that the difference between it and SIS was statistically significant.

The hyperechoic line sign was not a specific sign for polyps, as Baldwin et al. [17], mentioned. It was a sign of any intracavitary lesion (i.e. polyps, submucous myomas or focal endometrial malignancy).

Transvaginal sonography (TVS) succeeded in the diagnosis of polyps ranging from 12-35mms. Despite what will be mentioned and as some authors mentioned, sixty percent (six cases out of ten) of the polyps included in this study was seen by TVS as mere endometrial hyperplasia, but were diagnosed by SIS as polyps. TVS failed to depict polyps in six cases were misinterpreted as endometrial hyperplasia, none of these polyps had cystic changes and none elicited a hyperechoic line sign.

A single case was diagnosed as polyp by both TVS and SIS but the D&C biopsy revealed endometrial hyperplasia which confirm that the blind biopsy may lead to false negative results, other two cases had heterogeneous endometrial lining and irregular thickening were also falsely depicted as having multiple small polyps but proven pathologically to be endometrial hyperplasia.

A small submucous lieomyoma surrounded by a hyperechoic line was depicted by TVS as endometrial polyp, but on SIS, it was clearly seen as submucous lieomyoma with a thin overlying endometrial lining.

The last case actually had a well-defined polyp, which was correctly diagnosed on both TVS and SIS but its pathological report yielded a malignant polyp without myometrial invasion.

Many authors stressed out the low specificity of TVS in the diagnosis of polyps, compared to that of SIS. From these authors were Syrop & Sahakian, 1992, who mentioned that for females with uterine polyps, conventional TVS might demonstrate a thickened endometrial interface and biopsy fails to yield sufficient tissue for diagnosis. With SIS an intracavitary polyp will be seen surrounded by anechoic fluid, demonstrating that the endometrial lining was normal and that the thickened endometrial interface was due to the presence of the polyp.

Chung and Parsons [6], also reported that, an abnormally thick, irregular, or indistinct endometrial echo seen on initial TVS entailed a broad differential diagnosis including diffuse and focal processes. With focal processes, a visually directed biopsy might be necessary. However, with diffuse ones, a blind biopsy might be performed on an outpatient basis.

Because SIS allowed distinction between diffuse and focal abnormalities, it provided the gynecologist with an effective way to plan the next step in case management. In addition, Dubinsky et al. [12], said that SIS could provide more specificity in distinguishing between various intracavitary processes than could TVS or even endometrial biopsy. They added that a thickened endometrium at TVS was a reliable predictor of endometrial disease. Although this sign was sensitive, the nonspecific nature of the thickening had led most gynecologists to use tissue-specific techniques, such as blind endometrial biopsy or D & C, as the initial screening methods for endometrial disease.

De Vries et al. [2] also concluded, in their study of the role of TVS, SIS and hysteroscopy in the assessment of abnormal uterine bleeding in premenopausal women, that SIS was more sensitive and specific than TVS in this aspect.

Transvaginal sonography (TVS) could not differentiate cases of hyperplasia from those with carcinoma with a low sensitivity, which when compared in our study to that of SIS, it showed similar values. This is might be attributed to the small number of cases included in the study (40 cases), among which only three patients found to have endometrial carcinoma one of them was correctly diagnosed with both sonographic modalities, another one was misinterpreted as an endometrial polyp by either TVS or SIS, which proved pathologically to be malignant endometrial polyp without myometrial invasion.

The last case was wrongly diagnosed by TVS as endometrial hyperplasia because the endometrium appeared homogenously and symmetrically thickened with no specific signs of malignancy, but SIS was failed due to tight cervical stenois.

This have led to similar sensitivity, specificity, positive predictive values and negative predictive values of both sonographic techniques keeping the slightly higher accuracy preserved to TVS most probably due difficulties in the technique of SIS not due to poor method of assessment.

Concerning focal carcinoma, it was expected to present other sonographic signs of malignancy (e.g. heterogeneity); otherwise, the differentiation
between it and polyp would be extremely difficult, which occurred in one case in our study.

We think that the role of TVS in these cases is to help in staging of known malignancy rather than detection of it (especially in early cases), as mentioned by Fleischer et al. [15] and Goldstein et al. [5].

Lowe, 1999 [18], stated that a very small percentage of polyps might contain malignant foci. Only one (out of twenty-two) of the cases of endometrial polyps present in the study was pathologically proven malignant, which only formed 4.3% of the total number of cases.

Endometrial adenocarcinoma, derived from endometrial glandular cells, is by far the most common malignant tumour arising in the body of the uterus. Endometrial adenocarcinoma was in fact the only form of endometrial malignancy present in our study. It was seen pathologically in all three cases (7.5%).

Regarding submucous leiomyomas, SIS helps to differentiate submucous fibroids from polyps, an issue that might be difficult on TVS [19]. We did not face such a problem, as only one out of the six cases in our study TVS failed to diagnose as submucous fibroid and was diagnosed as an endometrial polyp with a heterogenous echotexture. On SIS, a submucous leiomyoma was discovered and the endometrium was completely normal.

Transvaginal sonography (TVS) could successfully depict submucous leiomyoma and its sub-endometrial location, as will be discussed shortly; however, it failed in detection of the exact location of the fibroids in two cases, which was clearly defined by SIS. This was because of the presence of a poorly defined endometrium.

Ryu et al. [14] TVS also cannot differentiate submucosal from intramural leiomyoma in many instances, which is an important distinction for the physician to consider for the treatment planning.

On the other hand, endometrial atrophy was diagnosed when the endometrium was 4mm or less in thickness. With SIS, since a single layer of the endometrium was seen, it was possible to determine if endometrial atrophy or focal areas of asymmetrical endometrial thickening existed.

Transvaginal sonography (TVS) and saline infusion sonohysterography (SIS) had successfully detected of the case of endometrial atrophy. However, only one case of an endometrial atrophy does not provide a tool for critical judgement on the reliability of the technique.

Regarding the overall sensitivity of TVS and SIS in our study, it was found that (SIS) is more sensitive 100% than TVS, 97.4% and but both were equal in specificity (50%). Also SIS was found to have positive and negative predictive values higher than TVS, as well as higher accuracy.

It was noted that SIS recorded little difference as compared to TVS, being in the higher direction, this might be attributed to the small number of cases and many pathological varieties represented in the study, for which, it may be needed to conduct similar research on a larger sample of population and during longer period of study.

Bree et al. [20] studied the accuracy and outcomes using TVS and SIS in a series of 98 patients with PMB. Using pathology and six months follow-up as proof, the study resulted in a sensitivity of 98%, specificity 88%, positive predictive value of 94% and negative predictive value of 97%.

Ryu et al. [14] had conducted a study to assess the utility of SIS as a screening method in 105 patients with abnormal uterine bleeding; he found that the sensitivity and specificity were 79.0% and 45.8% for TVS and 95.1% and 83.3% for SIS, respectively. The positive and negative predictive values were 83.0% and 39.3% for TVS and 95.1% and 83.3% for SIS, respectively.

He concluded that TVS is a sensitive method to evaluate the uterine cavity lesions but it often does not provide the physician with sufficient diagnostic information. With its higher sensitivities, specificities, positive and negative predictive values, SIS can be better used than TVS in evaluating those patients with abnormal uterine bleeding. A conclusion we agree with.

References