COMPARATIVE STUDY OF TRANSVAGINAL ULTRASONOGRAPHY AND SALINE INFUSION SONOHYSTEROGRAPHY IN EVALUATION OF ENDOMETRIAL AND SUBENDOMETRIAL ABNORMALITIES IN PATIENTS WITH ABNORMAL UTERINE BLEEDING.

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Objectives: To determine the superadded diagnostic value of saline infusion sonohysterography (SIS) over the transvaginal ultrasonography (TVS) in detecting endometrial and subendometrial lesions determined by direct visualization of the intrauterine cavity with hysteroscopy.

Patients and Methods: Between October 2002 through August 2004, 58 patients with persistent abnormal uterine bleeding despite at least 3 months of medical treatment were referred for TVS, SIS as well as hysteroscopy and biopsy.

Results: Twenty-three patients were confirmed to have intracavitary uterine abnormality. SIS was able to identify all patients with endometrial and subendometrial abnormalities in comparison to TVS which identified only 15 patients, and SIS was able to identify 31 of the 35 patients reported normally by hysteroscopy in comparison to 32 patients by TVS. SIS yielded a sensitivity of 100%, a specificity of 88.6%, a positive predictive value of 85.2%, and a negative predictive value (NPV) of 100%. Whereas TVS yielded a sensitivity of 65.2%, a specificity of 91.4%, a positive predictive value of 83.3%, and a negative predictive value of 80%.

Conclusion: SIS is simple non-invasive inexpensive procedure that yields additional information over TVS. It allows reliable differentiation between focal and diffuse endometrial and subendometrial lesions. It has equal sensitivity and NPV as hysteroscope and offers substantial advantages over hysteroscopy in terms of time, cost, patient comfort, availability, and risk. Its use could be implemented as a standard test in patients with abnormal uterine bleeding regardless of the results of the transvaginal ultrasonography and before the consideration of hysteroscopy.

Introduction

Abnormal uterine bleeding is the most common reason in both premenopausal and postmenopausal women to undergo an interventional gynecological procedure. In the past 10 years, the treatment of dysfunctional uterine bleeding has evolved considerably and the management differs according to the presence or absence of identifiable uterine abnormalities. The appropriate choice of a test (or tests) to evaluate this abnormality is anything but straightforward and it has become considerably more complex over the last decade, because the range of available tests has expanded.

Office biopsy, dilation and curettage, hysteroscopy, TVS, and SIS are viable procedures to evaluate the cause of the abnormal uterine bleeding and all of these techniques have certain limitation. Decades ago, curettage was the procedure of choice for evaluation of such patients, however, misgivings about the accuracy and reliability as well as the cost and risks of curettage were expressed.5,6 Stoch and Kanbour7 in a study of curettage before hysterectomy found that, in 16% of specimens less than one quarter of the cavity was curetted, in 60% less than one half of the cavity was curetted, and in 84% less than three quarters of the endometrial cavity had been effectively curetted.

In the 1970s, vacuum-suction curettage devices
Vabra and Pipelle) allowed sampling without anesthesia in an office setting, but it has been shown to have severe shortcomings, especially in cases in which the abnormality is focal and not global. Other authors concluded that the undirected sampling, whether through curettage or suction aspiration, will often be fraught with error, especially in cases in which the abnormality is not global but focal (polyps, focal hyperplasia, or carcinoma involving small areas of the uterine cavity).

Hysteroscopy is the gold standard test for the evaluation of abnormal uterine bleeding as it proved to be superior to curettage and biopsy especially in cases where endometrial and subendometrial abnormalities are suspected. However, it is expensive and very operator dependent. It requires specialized equipment and it often requires ambulatory surgery centers and general anesthesia. If hysteroscope is performed as an office procedure with local or no anesthesia, it can potentially result in significant patient discomfort, more over the use of the hysteroscopy is not justified for routine evaluation of all women with abnormal uterine bleeding.

In a series of 962 patients, Emanuel reported that 60% were found to have no endometrial or subendometrial abnormalities during diagnostic hysteroscopy and directed biopsies. In these patients an invasive diagnostic procedure could have been avoided with a reliable noninvasive diagnostic method to exclude these abnormalities.

In the early 1990s, investigators began to use transvaginal ultrasound scanning to determine whether they could predict which patients lacked significant tissue and could thus be spared endometrial sampling. Nevertheless, still there was a debate around the role of ultrasonography in evaluation of pre and postmenopausal women with abnormal uterine bleeding. Many authors reported that until recently patients with postmenopausal bleeding would undergo gynecologic testing only and radiologists are relatively new in their involvement in evaluation of patients with postmenopausal bleeding. More over TVS was believed to be of limited use in premenopausal women with irregular bleeding because it has been associated with high false negative results ranging from 40-50%, and its main benefit was to predict lack of significant abnormality.

Other authors reported that TVS has proved to be safe and noninvasive method for evaluating the endometrial cavity and it become the accepted technique for depicting and differentiating normal from abnormal endometrium.

Recently SIS has become a standard technique in assessment of the uterine cavity in patients with abnormal uterine bleeding as well as in evaluation of endometrial polyps, submucosal fibroids, and adhesions. It helps in selection of the appropriate surgical approach because it allows reliable differentiation between focal and diffuse endometrial and subendometrial lesions.

SIS is a simple, inexpensive and readily learned modality. It yields additional information over TVS of the uterus. Focal abnormalities are beautifully displayed by this technique. This information can then be used to direct the intervention. Biopsy of diffuse abnormalities can be performed with a blind technique, whereas focal abnormalities are best approached with a visually guided biopsy. SIS requires minimal patient preparation, has very few complications, and is well tolerated by patients.

In 1993, a study by Parson and Lense30 termed the technique sonohysterography. This technique has been known by many names, including sono-hysterography, hysterosonography, transvaginal sonography (TVS) with fluid contrast augmentation, and, finally, saline infusion sonohysterography. Several studies reported nearly equal diagnostic accuracy of SIS compared with diagnostic hysteroscopy, therefore, it is well established now that one may refrain from further diagnostic procedures if SIS shows a normal uterine cavity. A recent systematic review and meta-analysis supported this view. Moreover, SIS is less painful compared with diagnostic hysteroscopy, which is advantageous especially for women with a normal uterine cavity because a diagnosis can be achieved with the least possible patient discomfort. Finally, SIS proved to be less expensive compared with diagnostic hysteroscopy. Unfortunately, the positive predictive value of SIS is between 0.75 and 0.95; therefore, a considerable number of women will be scheduled for diagnostic hysteroscopy despite having a normal uterine cavity.
Objectives

To determine the superadded diagnostic value of saline infusion sonohysterography over the transvaginal ultrasonography in detecting endometrial and subendometrial lesions determined by direct visualization of the intrauterine cavity with hysteroscopy.

Patients and methods

From October 2002 through August 2004, 64 women aged 35 to 55 years participated in the study. All patients had persistent abnormal uterine bleeding, despite at least 3 months of medical treatment. Patients were referred for diagnostic transvaginal ultrasonography, SIS, and hysteroscopy. The procedures were explained for all patients included in the study and they were consented according to medical rules.

The exclusion criteria included refusal to undergo endovaginal ultrasonography and/or hysteroscopy, interval pregnancy, suspected current cervical, uterine, or tubal infection, patients suspected as having anovulatory (dysfunctional) bleeding, and active menstrual bleeding. We attempted to schedule patients for examination 2 to 3 days after the completion of menses. All women were given a prescription for doxycycline 100 mg by mouth, to be taken the day before, the day of, and the day after the procedures.

All patients underwent 3 separate studies: transvaginal ultrasonography, saline infusion sonohysterography, and hysteroscopy. They initially performed a transvaginal ultrasonographic examination. This was performed on HDI 5000 SonoCT (Philips) ultrasonography machine with a 5-9 MHz transvaginal probe.

The endometrial cavity contours were studied from the internal os to the fundus in the longitudinal and transverse planes. A normal endometrium and uterine cavity were defined by an echo-dense line in the middle of the uterus with a homogeneous endometrial lining with distinct margins to the myometrium. Any discontinuity was noted, and all other findings, such as deformations of the endometrial lining, any structure with or without well-defined margins or variable echogenicity, were considered to be abnormal. The maximal endometrial thickness was measured in the longitudinal plane. In normal sonograms the endometrial linings were apposed, by definition, and the total double-layer thickness was measured. Normal thickness parameters for the endometrium were set as follows: less than or equal to 12 mm full wall thickness in premenopausal patients, less than or equal to 5 mm full thickness in postmenopausal patients.

Then the SIS procedure was explained to the patient, including the small risk of increased bleeding as well as the even smaller risk of infection. The equipment needed for the examination includes a sterile speculum with an open side, tenaculum, cervical sounds in the event that the catheter does not pass easily through the cervix, 8F Folly’s catheter, 5-mL and 20-mL syringes. The catheter and the balloon must be flushed with sterile saline before insertion to remove as much air as possible. The patient is placed in the lithotomy position. The vaginal speculum was used to visualize the cervix, which was prepared with povidone-iodine (Betadine) before placement of a folly’s catheter. Approximately 2 mL of sterile water was used to inflate the balloon catheter. The speculum was removed, and the transvaginal ultrasound probe was introduced into the vagina. Under direct sonographic visualization, the balloon is gently retracted to occlude the internal cervical os and approximately 5 to 30 mL of warm sterile saline is injected. Complete sonographic evaluation of the endometrial cavity is performed in both the coronal and sagittal planes. Balloon is then deflated and removed.

All patients were scheduled for hysteroscopy and curettage within the following 2-3 days. The procedure was on inpatients basis and were performed under general anesthesia. The cervix was grasped with a single toothed tenaculum and dilated to size 7 H-Hegar. A hysteroscopy was performed with 5.5 mm continuous flow rigid Olympus hysteroscopy (Olympus optical Co. Europe GmbH, Hambra Germany). The uterine cavity was distended with normal saline. After visualization of the endometrial cavity, any detected polyp or small submucous fibroid were removed in the same sitting. If there was no swellings or polyps detected, endometrial biopsy was taken and sent for histopathological examination. The findings of TVS and SIS were described and compared with the hysteroscopic findings. Hys-
teroscopic findings were confirmed by histopathological examinations of the specimen obtained by curettage or resection.

A sensitivity, specificity, positive predictive value, and negative predictive value were calculated for transvaginal ultrasonography, SIS, and the combination of the two modalities.

Results

Of the 64 patients who enrolled, 58 patients completed the study. Four patients, who were informed of their normal TVS and SIS, refused further hysteroscopic evaluation and the other two patients dropped out of the study because they did not proceed with hysteroscopy.

Of the 58 patients included in our study 49 patients were premenopausal and 9 patients were postmenopausal. None of the postmenopausal patients were on hormone replacement therapy. Twenty three of the 58 patients had endometrial and subendometrial abnormalities that impinged in the uterine cavity as determined by direct cavity visualization at hysteroscopy and biopsy (gold standard). There were a total of 43 distinct lesions in the cavity confirmed by gold standard among the 23 patients.

The data was analyzed according to whether each TVS and SIS was able to correctly identify the presence of intrauterine pathologic condition in a given patient rather than the number of intrauterine lesions present in each uterus (table 1). From the 23 patients with intrauterine abnormality, TVS was able to identify 15 patients and 8 patients had false negative results, and from the 35 patients reported normally by hysteroscopy TVS identified 32 patients devoid of endometrial and subendometrial abnormalities and 3 patients with false positive results.

While SIS identified all the twenty three patients with endometrial and subendometrial lesions and in no case was an intrauterine mass detected at hysteroscopy when nothing was visualized during SIS. In 4 of the 35 patients with no endometrial and subendometrial abnormalities confirmed by hysteroscopy, an intrauterine lesion was erroneously detected by SIS that was not seen on hysteroscopy, compared to 3 patients only by TVS.

Transvaginal ultrasonography discovered 15 patients with intrauterine lesions, with a sensitivity of 65.2%, a specificity of 91.4%, a positive predictive value of 83.3%, and a negative predictive value of 80%. Transvaginal ultrasonography failed to identify one third of patients with intrauterine pathologic conditions and had a relatively lower false-positive rate compared with SIS.

SIS, however, yielded a sensitivity of 100%, a specificity of 88.6%, a positive predictive value of 85.2%, and a negative predictive value of 100% for detection of a patient with intrauterine lesion.

Out of the forty three intrauterine lesions, twenty four were polyps, 12 were liomyomas and 7 were endometrial hyperplasia. The number of lesion in each patient ranged from 1 to 5. The criteria of defining the endometrial and subendometrial abnormalities by SIS were as follows: An endometrial polyp is a well-defined, homogeneous, polypoid lesion that is isoechoic to the endometrium with preservation of the endometrial-myometrial interface. Submucosal fibroid is hypoechoic, well-defined, solid mass with an overlying layer of echogenic endometrium, it often distorts the endometrial-myometrial interface and show acoustic attenuation. Endometrial hyperplasia appears as a diffuse irregular thickening of the echogenic endometrial strip.

When the data were analyzed according to each intrauterine mass (rather than each patient), transvaginal ultrasonography identified 18 of the 43 (41.9%) intrauterine masses and SIS identified 30 of the 43 (69.8%) masses (table 2).

Table 1. The ability of TVS and SIS to detect the patients with intracavitary lesion in comparison with the gold standard hysteroscopy.

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Discussion

Up to 20% of office visits to the gynecologist are for abnormal vaginal bleeding. The high prevalence of abnormal uterine bleeding makes this problem a common complaint in the outpatient clinical setting. The causes of abnormal uterine bleeding are diverse, and differentiating whether the source is the result of anovulation or anatomic lesions, when conservative measures, such as oral contraceptives and other progestational agents, fail to treat this problem, an anatomic cause for the patient’s abnormal uterine bleeding should be considered. The most common modalities used to assess anatomic causes of abnormal uterine bleeding have been endometrial biopsy, curettage, hysterosalpingography, transvaginal ultrasonography, SIS, and hysteroscopy. Clearly, a premenopausal and postmenopausal patient with abnormal uterine bleeding needs evaluation, the value of a certain procedure to evaluate such patients in a safe, inexpensive, painless convenient manner is obvious.

In our study, routine TVS by itself was less sensitive than SIS and would not have diagnosed uterine cavity lesions in 8 of the 23 patients with confirmed masses on the gold standard examination (Fig.1,2). The sensitivity and specificity of TVS to detect endometrial and subendometrial abnormalities was 65.2% and 91.4% respectively in comparison to 100% and 88.6% by SIS. More over SIS detected endometrial and subendometrial abnormalities in 20% of the normally reported cases by TVS.

Many authors reported that TVS is of limited use in premenopausal and postmenopausal women with irregular bleeding as they discovered endometrial and subendometrial abnormalities in 37% of the patients of Cohen et al series and (14.8%) of the patients of Dijkhuizen et al series with normal endometrial thickness by TVS and concluded that a normal endometrial thickness excludes hyperplasia but does not eliminate other intrauterine abnormalities, and SIS is useful in identifying these abnormalities. This finding reflects the percentage of patients in our study who showed abnormalities on SIS with apparently normal findings on conventional transvaginal sonograms.

The main procedure in competition with SIS in detection of the intracavitary uterine lesion is the hysteroscope, Timmerman et al found that had a higher accuracy rate than hysteroscope. Soares et al reported 100% sensitivity and specificity. In our study, SIS determined a sensitivity of 100%, specificity of 88.6%, PPV of 85.2% and NPV of 100%.

Our results are higher than reported by Mihm et al who reported sensitivity of 97% specificity of 70.2% PPV of 82.1 and NPV of 94.3%, Williams and Marshburn who reported specificity and PPV of 85% and 75% respectively, as well as Widrich et al who reported sensitivity of 96% and specificity of 88%.

The relative higher specificity (91.4% vs 88.6%) of transvaginal ultrasonography indicates relatively fewer false-positive results than with SIS. This was probably because during transvaginal ultrasonography the close apposition of the endometrial surfaces compressed small-contour irregularities of the normal endometrium. During SIS, however, these contour irregularities of the normal endometrial lining were sometimes prominent enough to cause the radiologist to erroneously record a small endometrial and subendometrial abnormality.

SIS was more able to detect higher number of le-
Fig. 1. Endometrial polyp in 37-year-old woman. A, Sagittal sonogram of uterus shows normal-appearing endometrium. B, sagittal and C, transverse SIS show homogeneous echogenic mass projecting from the posterior endometrium (star).

Fig. 2. Endometrial polyp in 35-year-old woman. Sagittal sonogram of uterus shows normal-appearing endometrium of 11 mm thickness (arrowheads). B, sagittal and C, transverse SIS show homogeneous echogenic mass projection from the posterior right–lateral part of the endometrium (P). Interstitial uterine myomas (M) are noted in both TVS and SIS studies.

Fig. 3. Endometrial polyp in 40-year-old woman. A, Sagittal sonogram of uterus shows normal-appearing endometrium with ? fundal endometrial hyperechoic mass lesion (*). B, sagittal and C, transverse SIS show homogeneous echogenic mass projection from the anterior endometrium. Napothian follicle is noted in both TVS and SIS studies.
Comparative study of transvaginal ultrasonography

At analysis of the false-positive cases in our study, we found that two patients with normal proliferative endometrium were reported endometrial hyperplasia due to thick endometrium in TVS, and SIS. One case with an endometrial blood clot was mistaken for a polyp in SIS, and one case endometrial blood clot and separated endometrial strip was mistaken for a pedunculated myoma in TVS and polyp with intrauterine adhesion by SIS (Fig. 8).

In our study, SIS didn’t fail to indicate that pathologic conditions existed in a given patient. If SIS did not show an endometrial and subendometrial abnormality, then no pathologic condition was seen by the gold standard examination. Depending on our results and in agreement with o’connell5, golstin6, willams21, mihm38, data if SIS had been used to triage our patients to determine whether hysteroscopy was indicated, 35 of the 58 women included in our study would not have needed hysteroscopic examination.

This study has confirmed that saline infusion sonohysterography is a simple technique that yields additional information over transvaginal ultrasonography in comparison to TVS as they detected 69.8% and 41.9% respectively. Therefore, SIS sometimes underestimated the number of lesions present in a given patient but not to the degree of transvaginal ultrasonography. When multiple lesions were present in a given patient, those not detected by SIS were on less than 5 mm in size. SIS was more sensitive in detection of endometrial polyps compared with TVS (25% compared to 62.5%), submucous liomyomas (75% compared to 91.7% respectively) and endometrial hyperplasia (42.9% compared to 47.1% respectively). SIS was able to better delineation of each abnormality and to further characterize it in terms of nature, size, shape, location and number (Fig. 3-5). It can also determine the degree of projection of a subendometrial lesion within the endometrial cavity which help to determine the way of resection (Fig. 6,7).

On the other hand, all patients with intrauterine pathologic conditions as confirmed by hysteroscope were identified by SIS, and all patients with a normal SIS study had a normal intrauterine cavity by hysteroscope.

Fig. 4. Endometrial polyps with cysts in 65-year-old woman A, sagittal TVS shows thickened endometrium with cystic changes. B, Sagittal SIS shows two focal polypoid masses with cystic changes. C, transverse SIS through the lower polyp with obvious cystic changes

Fig. 5. Endometrial hyperplasia in 44-years-old woman. A, sagittal TVS shows 17-mm-thick endometrium. B, sagittal SIS shows thickened endometrium with lobular contours.
Fig 6. Pedunculated submucous myoma in 42-years-old woman. A, sagittal TVS sonogram showing a central, predominantly hypoechoic mass within the uterine cavity. B, Sagittal and C, transverse SIS showing a submucous myoma (arrowheads) with more than 50% of its volume projecting into the uterine cavity. Thin rim of echogenic endometrium is noted covering the submucous myoma. Localized endometrial thickening is also noted (arrows).

Fig 7. Submucous myoma in 39-years-old woman. A, Sagittal transvaginal sonogram showing an ill-defined hypoechoic fundal mass lesion projecting in the uterine cavity (M). B, Sagittal and C, transverse SIS showing a well defined, broad bases hypoechoic submucous myoma (M) with more than 50% of its volume projecting into the uterine cavity. Thin echogenic rim of endometrium is seen partially covering the intrauterine contour of the myoma.

Fig 8. Blood clot mimicking a mass in a 54-years-old woman. A, TVS showed hypoechoic mass within the endometrium (calipers). B, SIS shows heterogeneous mass within in the endometrial cavity (calipers), thin bands are seen crossing the endometrial cavity (arrows) reported as uterine adhesions, underlying thin endometrium is noted (arrowheads). Hysteroscopic examination (not shown) revealed intrauterine blood clot and separated endometrial strip.
Comparative study of transvaginal ultrasonography in evaluation of endometrial and subendometrial conditions in the patient with abnormal vaginal bleeding. It is well tolerated by patients and has very few complications. It helped in detection of all patients with the endometrial and subendometrial lesions including those not detected by TVS. Therefore, because no patient with intrauterine lesions was missed and normal study always indicated normal intrauterine anatomy, we recommended saline infusion sonohysterography as a valuable tool in the diagnosis of women with abnormal uterine bleeding before consideration for hysteroscopy.

In conclusion, SIS is a simple and elegant examination that yields additional information over TVS of the uterus. It allows reliable differentiation between focal and diffuse endometrial and subendometrial lesions. It has equal sensitivity and NPV as hysteroscope and offers substantial advantages over hysteroscopy in terms of time, cost, patient comfort, availability, and risk. Because of the comparable nature of diagnostic findings between SIS and hysteroscope, SIS should be warranted as a first-line study in assessment of abnormal uterine bleeding in premenopausal and postmenopausal patients regardless of the results of the TVS, if the SIS study is positive, a definitive therapeutic procedure selected on basis of SIS results, can be performed. If the SIS study is negative, the patient can be reassured and treated medically.

References


