INTRODUCTION

Postmenopausal bleeding (PMB) constitutes a significant proportion of gynaecological referrals and occurs in nearly 3% of menopausal women. Post-menopausal bleeding is always a cause for concern due to increased incidence of endometrial carcinoma in this age group. Only about 10% of patients with post-menopausal bleeding have endometrial carcinoma, others have diffuse and focal etiologies like endometrial atrophy, polyps and sub-mucosal fibroids. Diagnostic hysteroscopy along with endometrial biopsy is considered the gold standard in the diagnosis of intrauterine pathology.

ABSTRACT

Objective: To validate the diagnostic efficacy of saline infusion sonohysterography (SIS) in the evaluation of uterine cavity, in women with postmenopausal bleeding and endometrial thickness ≥ 5 mm.

Study Design: Cross-sectional study.

Place and Duration of Study: Military Hospital, Rawalpindi, from March 2005 to July 2008 and Combined Military Hospital, Multan, from September 2008 to June 2009.

Methodology: Seventy seven eligible participants included women complaining of postmenopausal bleeding were included; out of whom 69 completed the procedure satisfactorily. Pain scores during procedure were assessed to determine patient acceptability. Following saline infusion sonohysterography all patients also underwent an out door pipeelle endometrial biopsy in a one-stop postmenopausal bleed clinic. Findings of sonohysterography were compared with hysteroscopy/ hysterectomy specimen.

Results: Majority of the patients 34 (49.2%) experienced no pain during the procedure, 51 (74%) women had a positive SIS and the findings were negative in 18 (26%) patients. The commonest abnormal finding on SIS was focal thickening in 23 (32%) and endometrial polyp in 12 (17%) cases. Saline infusion hysterosonography picked up 3 cases of false positive polyps (5.8%) and missed a case of submucous fibroid near cervix (1.8%). Upon comparison of findings of hysteroscopy and hysterectomy in 53 cases, there was complete agreement in a total of 43 (88%) cases. The sensitivity of sonohysterography was 92% and specificity was 78%. All the ladies with abnormal SIS had diagnostic or therapeutic procedures and finally only 24 (35%) were managed on conservative follow-up. Normal SIS led to conservative management in 16 (88%).

Conclusion: Sonohysterography in combination with endometrial biopsy is a useful technique useful for the evaluation of postmenopausal bleeding. Patient acceptability and diagnostic capability is high and it reduces demand for hysteroscopy.

Key words: Postmenopausal bleeding. Saline infusion sonohysterography. Hysteroscopy.
through the thickest area from outermost border of endometrium from one side to the other. Women with cervical carcinoma, pyometra or hematometra were excluded. Eligible participants included 77 women with postmenopausal bleeding and endometrium thickness $\geq$ 5 mm. Those with immeasurable endometrium were also included as these often harbour a malignancy. Therefore, immesurable endometrium was assumed to be $\geq$ 5 mm. Patients on HRT (hormone replacement therapy) or Tamoxifen were also included and the same cut off of $\geq$ 5 mm endometrial thickness was used.

All patients had a cervical smear and pelvic examination. The SIS was performed directly under TVS. Monitoring with standard preparation, precautions and technique. When endometrium was seen on the screen, saline infusion was started. Failed examinations were dealt with by sounding the cervical os, using Tenaculum and Sim's speculum or using 50 ml syringe in patulous cervix. Failed cervical cannulation was defined as failed procedure. Poor filling or non-distensible cavity was labeled as abnormal SIS and not failed procedure.

Examination was considered normal if the sonogram showed a regular hypoechoic line with a distinct margin at endo/myometrial interface.

Abnormal findings included ill defined thickening or irregular echogenicity of endometrium. Endometrial polyp was described as a homogenous mass emerging from endometrium without disruption of endo-myometrial interface. Movement upon injecting saline helped to differentiate them from blood clots which can be displaced anywhere in the cavity, whereas polyp had limited mobility. A sub-mucous fibroid was defined as solid structure of mixed echogenicity arising from myometrium after disrupting myometrium and bulging into cavity. Adenomyosis was defined as presence of myometrial cysts and heterogenous echogenicity of myometrium. Poorly distensible cavity was also recorded as abnormal.

At the end of the procedure pain was assessed using present pain intensity scale (PPI) as described by McGill Pain Questionaire. It was graded on a scale of 0-6: 0=no pain, 1=mild, 2=moderate, 3=distressing, 4=horrible and 5=excruciating.

Before removing the tube all saline was aspirated from the cavity of uterus. This was followed in all cases by a pipelle endometrial sampling. Those patients with endometrial carcinoma/complex or some with simple endometrial hyperplasia (with high risk features) were straight away booked for hysterectomy. Hysteroscopy was performed in cases of inadequate endometrial biopsy, inadequate cavity distension at SIS and focal lesion with normal biopsy or simple endometrial hyperplasia.

If focal lesion removed at hysteroscopy was found to be benign endometrial polyp, the hysterectomy was deferred. Those in whom lesion could not be removed hysteroscopically and where directed biopsy was abnormal, were once again managed by hysterectomy. In patients where only hysteroscopy was done this was considered gold standard. Where both procedures were performed sequentially findings of hysterectomy specimen (opened in theatre to view cavity) were considered gold standard. Figure 1 gives the algorithm that we followed for management of PMB.

After assessing concordance between SIS and findings of hysteroscopy/hysterectomy specimens, positive and negative predictive value of SIS was calculated. Agreement or disagreement between SIS and gold standard were calculated to assess the validity of SIS.

**RESULTS**

Majority of the patients belonged to age group 56-65 years. The mean BMI was 26±2.9. Eight (10%) patients had failed procedure. There were 3 patients on Tamoxifen and 4 on hormone replacement therapy (HRT, Table I). Majority of patients experienced no pain on PPI scale (50%), whereas pain score of 1,2 and 3 was observed in 22, 8 and 5 patient respectively. Pain score of 4 or 5 was not observed in any patient (Table I).

Hydrosonography only added an extra 75 rupees and an additional 5-7 minutes to the TVS.

**Table I**: Patient demography and clinical characters: n=77.

<table>
<thead>
<tr>
<th>Clinical characters</th>
<th>Number</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-55 years</td>
<td>27</td>
<td>35%</td>
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<tr>
<td>56-65 years</td>
<td>31</td>
<td>40%</td>
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<tr>
<td>66-75 years</td>
<td>19</td>
<td>25%</td>
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<tr>
<td><strong>BMI</strong></td>
<td>26±4.25(mean)</td>
<td></td>
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<tr>
<td>On HRT</td>
<td>4</td>
<td>5%</td>
</tr>
<tr>
<td>On Tamoxifen</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Endometrial thickness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immeasurable</td>
<td>3</td>
<td>4.34%</td>
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<tr>
<td>5-10</td>
<td>26</td>
<td>37.8%</td>
</tr>
<tr>
<td>11-13</td>
<td>18</td>
<td>26%</td>
</tr>
<tr>
<td>$\geq$ 14</td>
<td>19</td>
<td>27%</td>
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<tr>
<td><strong>Pain score n=69</strong></td>
<td></td>
<td></td>
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<tr>
<td>0</td>
<td>34</td>
<td>49%</td>
</tr>
<tr>
<td>Present pain Intensity (PPI) score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>22</td>
<td>31%</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>12%</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>8%</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Abnormality n=69</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal thickening</td>
<td>16</td>
<td>23%</td>
</tr>
<tr>
<td>Polyp</td>
<td>12</td>
<td>17%</td>
</tr>
<tr>
<td>Submucous fibroid</td>
<td>5</td>
<td>7%</td>
</tr>
<tr>
<td>Adenomyosis</td>
<td>4</td>
<td>6%</td>
</tr>
<tr>
<td>Combination of above</td>
<td>12</td>
<td>17%</td>
</tr>
<tr>
<td>Non-distensible cavity</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td>No abnormality</td>
<td>18</td>
<td>26%</td>
</tr>
</tbody>
</table>

Percentages have been rounded off.
Endometrial focal thickening was observed to be the commonest (23%) abnormality followed by polyps, (17%) on SIS (Table I). Comparison between SIS and histopathology showed that SIS was abnormal in 100% of the cases with carcinoma/complex hyperplasia (Table I), nine (13%) cases of carcinoma endometrium and 5 (7%) cases of complex endometrial hyperplasia. Some ladies with simple endometrial hyperplasia were also subjected to hysterectomy in view of associated high risk features like obesity, hypertension diabetes and fear of loss to follow-up. Figure 1 shows the algorithm used to manage postmenopausal bleeding in the present study.

In case where there was more than one pathology, like endometrial hyperplasia with polyp/sub-mucous fibroids, SIS missed one abnormality in some cases. Diagnostic accuracy of SIS is shown in Table II, by comparing findings hysteroscopy in 8 cases and hysterectomy specimen in 43 cases. SIS picked-up 3 cases of false positive polyps (probably blood clots) and missed a case of sub-mucous fibroid near cervix. There was complete agreement in the remaining 43 (84%) cases. The sensitivity of SIS was 92% and specificity was 78%.

The evaluation and management of postmenopausal bleeding is evolving continuously with the advent of newer imaging modalities. Endometrium is more difficult to measure in postmenopausal patients due to diffuse endomyometrial border. The purpose of this study was to establish the patient’s acceptability and diagnostic accuracy of SIS in postmenopausal patients. As patients with immeasurable endometrium often harbour a cancer so these patients were included in the study. In this study 5 mm cut-off for women on HRT was used as described earlier. Some authorities recommend a higher cut-off point like 7 mm for patients on Tamoxifen but we used the same cut-off.

Soft paediatric catheter that is pliable and has better toleration, was used in this study. Balloon catheter leads to more pain and is also more expensive. The procedure failed in 8 (10.3%) of the cases in present series as compared to 25 (17.4%) in a study by Meng et al. The group used a 5F catheter with an inflatable balloon. The study by Meng et al. did not use the 5 mm cut-off as in this study so the frequency of genital tract atrophy must have been higher. This could be the reason for variations in results. The failure rate reported in previous studies is 13.5% and 7%, and same was observed in this series. All the ladies with abnormal SIS had diagnostic or therapeutic procedures and finally only 8 (15%) were managed on conservative follow-up in this study. The impact of normal SIS was conservative management in 16 (88%) cases.

In the present study 34(49%) of the patients felt no pain and same was observed earlier in a study at Netherland. The learning curve of SIS is considered to be very short for those familiar with gynaecological ultrasound. Failure is almost always due to cervical
stensosis. Pisal et al. used size 20 spinal needle to
overcome cervical stenosis.9 Inconclusiveness may
occur due to back-flow in 10% of procedures. In present
series poor cavity distension was found in cases of
endometrial cancer and endometrial tuberculosis, which
in this age group was rather unusual and same was
observed earlier.9 Both ladies with endometrial
tuberculosis were recently menopausal and rather
young aged, < 52 years. Distension difficulties in SIS
raise the suspicion of carcinoma. In these cases even
the clinical value of, spectral Doppler ultrasound,
examination of the uterine, sub-endometrial and
endometrial vessels using Doppler ultrasound is
uncertain.10 Endometrial vascularity may be useful in
predicting focal lesions in women with postmenopausal
bleeding, but not for making a specific diagnosis.
State-of-the-art Doppler ultrasound for endometrial vascularity
is not widely available. False positive cases are very
high (52%), while determining the value of endometrial
vascularity in the prediction of focal lesions.11 The
detection rate of Doppler ultrasound is slightly lower
than that for saline infusion, whereas the false-positive
rate of Doppler is around five times higher. The clinical
value of 3D ultrasound is a matter of current debate.12

de Kroon et al. did a meta-analysis of diagnostic
accuracy of SIS in women reporting with abnormal
uterine bleeding.12 In the 24 studies evaluated three
studies reported on efficacy exclusively in postmeno-
pausal women with hysterectomy and or hysterec
tomy as a reference test.4,13,14 Two studies used > 5 mm cut-
off and one used > 6 mm cut-off, all at variance with this
study with a cut-off of ≥ 5 mm. The sensitivity and
specificity in these studies were 96/92%, 100/95% and
89/50% respectively. The present results of 92% sensitivity
and 78% specificity are close to the pooled
result of de Kroon’s meta-analysis -95% for sensitivity
but less for specificity-88%.6 Hydrosonography is a
useful procedure in screening for intracavitary pathologies
and allows differentiation of intracavitary, endometrial,
and sub-mucosal abnormalities. SIS was abnormal in all
cases of endometrial carcinoma/complex hyperplasia in
the current study. There was good comparison between
hysteroscopy and SIS where the former was the gold
standard. The accuracy of hysteroscopy and SIS was
almost equal though SIS is less expensive and better
tolerated.15 These results have been further refined by
3-D SIS.16 Also in our unit only indoor hysteroscopy is
available. Many studies have confirmed that SIS is as
good as hysteroscopy under general anaesthesia at
detecting/excluding focal lesions. Hydrosonography is
less painful and cost effective than hysteroscopy.17 In
many units in Pakistan hysteroscopy is not available.
Hence the latter can be replaced in the local setting by
SIS. SIS greatly reduces the number of unnecessary
hysteroscopy as it is only indicated where focal lesions
need further evaluation/removal. SIS also gives information
about myometrium in addition to cavity as adenomyosis
was diagnosed correctly in this study. Because D and C
fails to diagnose about 10% of endometrial cancers and
50% of polyps and hyperplasias, the presence of a focal
lesion dictates an operative hysteroscopy.18

The examination of hysterectomy specimen is the
ultimate gold standard. As for hysterectomy there was
agreement between 37 (86%) and disagreement in 6
(14%) cases. Great majority of women with
pathological cavities were defined by SIS. Two studies
compared SIS and hysteroscopy to hysterectomy
showed comparable diagnostic value of the two.18 While
many comparative studies on efficacy of SIS versus
hysterectomy/hysteroscopy are blinded this study was
only partially blinded.4,14,17 Often the same operator
performed SIS and the gold standard procedure.
However, SIS could not differentiate benign from
malignant lesions. But SIS helps in choosing the patient
where operative hysteroscopy is required. Two recent
studies19,20 have shown the promising feasibility of
ultrasound guided biopsy of endometrial pathology. Wei
et al. used a curette during SIS and removed lesions
< 20 mm.19 Lee et al.20 removed polyps under SIS
guidance. This study showed a very high frequency of
endometrial carcinoma/complex hyperplasia (20%) in
the population under study, unlike the study by Meng
et al. where there were no cases of carcinoma
endometrium.5 Other studies have reported finding of
endometrial carcinoma in approximately 4-5% and other
complex hyperplasias in an additional similar number.
Population included in this study was at high risk with
endometrial thickness of ≥ 5 mm leading to high pick-up
of abnormalities. In the study by Meng et al. majority of
patients were on HRT and SIS helped in HRT
adjustment.5 In this study only 4 (5%) patients were on
HRT. A question of concern is –does SIS facilitate
dissemination of malignant cells? Most studies have
found no association with hysteroscopy. In a retro-
spective study of endometrial carcinoma with similar
stage I disease, there was no difference in survival at 5
years between patients who had undergone hyster-
scopy before definitive surgery.21 SIS is assumed to be
equally safe.

CONCLUSION

Feasibility of saline contrast hysterosonography is
approximately similar to diagnostic hysteroscopy in an
outpatient setting. SIS in the evaluation of PMB is more
economical and less painful. It helps in decision making,
segregates high risk patients for further work-up and
definitive surgery. In addition to being acceptable and
accurate, it can greatly reduce the demand for
hysteroscopy. In view of high accuracy of SIS, it can be
recommended, along with endometrial biopsy as the
standard procedure for the evaluation of women with
postmenopausal bleeding.

REFERENCES


