Saline infusion sonography compared to hysteroscopy for uterine cavity evaluation in abnormal uterine bleeding

Gabriela Dimitriu1* and Ibrahim A. Abdelazim2

1Department of Obstetrics and Gynaecology, South Tyneside Hospital, U.K.
2Department of Obstetrics and Gynecology, Ain Shams University, Egypt and Ahmadi Hospital, Kuwait.

ABSTRACT

Background: Evaluation of abnormal uterine bleeding in women ≥40 years or menopausal women is of critical importance to confirm the benign nature of the problem, and to exclude endometrial carcinoma. Aim: This study designed to evaluate the accuracy of the saline infusion sonography compared to hysteroscopy in diagnosing uterine cavity abnormalities in cases of abnormal uterine bleeding.

Subjects and Methods: One hundred and eighty-six (186) women diagnosed as abnormal uterine bleeding were included in this comparative study, and agreed to have a trans-vaginal ultrasound assessment of uterine cavity with the use of saline as the contrast medium beside the hysteroscopic assessment. Both hysteroscopy and saline infusion sonography procedures were done postmenstrual in the early-mid follicular phase of a cycle of the same menstrual cycle. Statistical analysis was done using statistical package for social sciences version 20 (Chicago, IL, USA), and Chi-square test ($X^2$) to compare the accuracy of the saline infusion sonography to hysteroscopy in diagnosis of uterine cavity abnormalities.

Results: The uterine cavity abnormalities diagnosed in 40.3% (75/186) of the women included in this study (17.7% (33/186) endometrial polyps, 10.2% (19/186) sub-mucous fibroid, 4.8% (9/186) uterine septum, 3.2% (6/186) uterine adhesions, 2.8% (5/186) endometrial hyperplasia, and 1.6% (3/186) thin or atrophic endometrium). In this study, the hysteroscopy was more sensitive (98.7% versus 97.4%), more specific (100% versus 99.1%), and more accurate (99.5% versus 98.4%) than saline infusion sonography. In addition, the hysteroscopy had higher predictive values, 100% positive predictive value, and 99.1% negative predictive value compared to 98.7% positive predictive value, and 98.2% negative predictive value for saline infusion sonography in diagnosis of uterine cavity abnormalities (this difference was statistically insignificant, $P > 0.05$).

Conclusion: Saline infusion sonography is a simple, well tolerate procedure can be used in out-patients setting to diagnose uterine cavity anomalies in cases of abnormal uterine bleeding when outpatient hysteroscopy is not available or as complementary tool to confirm the diagnosis detected by hysteroscopy.

Keywords: Saline, sonography, hysteroscopy, uterine, bleeding.

Introduction

Abnormal uterine bleeding is a major gynecological problem, accounting for 33% of outpatient referrals, including 69% of referrals in peri-menopausal, and postmenopausal age group.[1,2] Evaluation of abnormal uterine bleeding in women ≥40 years or menopausal women is of critical importance to confirm the benign nature of the problem, and to exclude endometrial carcinoma, so that medical or conservative treatment can be offered, and unnecessary surgery can be avoided.[2,3]

Uterine cavity evaluation is a basic step in the investigation of abnormal uterine bleeding.[4] Hysteroscopy is known as the gold standard procedure for uterine cavity assessment, it
enables diagnosis, and treatment of intrauterine pathology in the same outpatient setting.\textsuperscript{[5]} Hysteroscopy is an excellent tool for the diagnostic, and therapeutic work-up in women with abnormal uterine bleeding.\textsuperscript{[5-7]} Trans-vaginal ultrasonography (TVS) is the standard method applied to screen for possible endometrium or uterine cavity abnormalities.\textsuperscript{[8]} The uterine cavity lining can be expanded with saline/gel infusion sonography (SIS), hysterosalpingography (SIHS).\textsuperscript{[5]} It has been reported that the expansion of uterine cavity with saline during TVS, improves the delineation of uterine cavity abnormalities.\textsuperscript{[9-12]} This study designed to evaluate the diagnostic accuracy of the SIS compared to diagnostic hysteroscopy in diagnosing uterine cavity abnormalities in abnormal uterine bleeding.

**Subjects and Methods**

One hundred and eighty-six (186) women with abnormal uterine bleeding were randomly enrolled in this comparative study conducted over two years from January 2011 to January 2013. Ethical approval of the study was given by local institute ethical committee of Ahmadi Hospital, Kuwait Oil Company (KOC), Kuwait. After informed consent, we performed a detailed clinical assessment of the participants followed by laboratory investigations (complete blood count (CBC), coagulation profile, prolactin, thyroid and liver function tests). Inclusion criteria were, women ≥40 years presenting with abnormal uterine bleeding, endometrial thickness >4 mm, normal activated partial thromboplastin time (APTT), and normal platelet count. We excluded women with possibility of pregnancy, history of contraception, received hormonal treatment in last 6 months before inclusion in this study, endometrial thickness ≤4 mm, women with endocrine disorders, and abnormal liver function tests. Participants agreed to have a trans-vaginal ultrasound assessment of uterine cavity with the use of saline as the contrast medium (SIS) beside the hysteroscopic assessment. Both hysteroscopy & SIS procedures were done postmenstrual in the early-mid follicular phase of a cycle of the same menstrual cycle. Trans-vaginal ultrasound was done by an expert sonographer, blinded to the patients’ data, using Philips HD9 (Philips Inc., Amsterdam, Netherlands) with 2D convex probe 4-9 MHz. We initially examined the myometrium, and endometrium in longitudinal and transverse planes. Irregularities and any distortion of the endometrial echo were noted. Thereafter we inserted a paediatric Foley’s catheter (No. 5) through the cervix and inflated it with 1-2 ml of saline for the self-retention. Five to fifteen (5-15) ml of physiologic saline solution was slowly infused to distend the uterine cavity during continuous scanning. The uterine cavity was evaluated with attention to its contour, dimensions, regularity, and thickness of the endometrium, and presence of endometrial polyps or fibroids in at least 2 planes during the distension and by the end of it. Office hysteroscopies were carried out in a standardized manner, using a 5-mm outer-diameter continuous flow Bettocchi hysteroscopy with 30° direction of view (Karl
Storz Endoscopy, Utrecht, Netherlands). Normal sterile, an isotonic saline solution was used for distension of the uterine cavity. The uterine cavity was assessed on its shape (normal, arcuate or septate), and the presence or absence of abnormalities (endometrial polyps, myomas, adhesions and septa). Any uterine abnormalities diagnosed in the studied cases were treated using operative hysteroscopy under general anaesthesia, and specimens obtained were sent for histopathological examination. Participants received non-steroidal analgesic 30 minutes before the SIS and hysteroscopy, and prophylactic antibiotics (200 mg of doxycycline before followed by 100 mg twice daily for 10 days after). The diagnosis of endometrial polyps, endometrial hyperplasia and atrophic endometrium was confirmed when the result of histopathological examination of the endometrial biopsies taken during hysteroscopy obtained, while, the diagnosis of sub-mucous myoma, and intrauterine adhesions was confirmed when the recorded findings during hysteroscopy reviewed by senior gynecologist.\[5]\n
**Sample size and Statistics**

The required sample size was calculated using G Power software version 3.17 for sample size calculation (Heinrich Heine Universität; Düsseldorf; Germany), setting \( \alpha \) -error probability at 0.05, power (1- \( \beta \) error probability) at 0.95% and effective sample size (w) at 0.3. The effective sample includes more than 110 women needed to produce a statistically acceptable figure. Statistical analysis was done using statistical package for social sciences version 20 (Chicago, IL, USA). Data presented as number (n) and percentage (%), and chi-square test \((X^2)\) used for statistical analysis. The significance level was set at 0.05.

Sensitivity: is the proportional detection of individuals with the disease of interest in the population.

Specificity: is the proportional detection of individuals without the disease of interest in the population.

Positive predictive value (PPV): is the proportion of all individuals with positive tests, who have the disease.

Negative predictive value (NPV): is the proportion of all individuals with negative tests who are non-diseased.

**Results**

One hundred and ninety women were included in beginning of this study to compare the accuracy of the SIS to hysteroscopy in diagnosis of uterine cavity abnormalities in women presented with abnormal uterine bleeding. Two records and two histopathology reports were lost during patients` follow up and finally statistical analysis done for One hundred and eighty-six (186) women. The uterine cavity abnormalities diagnosed in 40.3% (75/186) of the women included in this study (17.7% (33/186) endometrial polyps, 10.2% (19/186) sub-mucous fibroid, 4.8% (9/186) uterine septum, 3.2% (6/186) uterine adhesions, 2.8% (5/186) endometrial hyperplasia, and 1.6% (3/186) thin or atrophic endometrium). Table 1

During hysteroscopic evaluation of the uterine cavity of the studied cases, one case of small...
sub-mucous fibroid was diagnosed as normal uterine cavity (one case false negative), while during SIS evaluation of the uterine cavity of the studied cases, two cases were diagnosed as normal uterine cavity (one cases of endometrial polyp + one case of Ascherman’s syndrome (two cases false negative)), and one case of endometrial polyp was diagnosed as endometrial hyperplasia (one case false positive).

Table 1 Table 1. Hysteroscopic and SIS findings in the studied population

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hysteroscopic findings (n = 186)</th>
<th>SIS findings (n = 186)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal uterine cavity (111 cases true negative)</td>
<td>112 (111 + 1) (1 case of sub-mucous fibroid was diagnosed as normal cavity = false negative)</td>
<td>113 (111 + 2) (2 cases diagnosed as normal cavity = one cases of endometrial polyp + one case of Ascherman’s = 2 cases false negative)</td>
</tr>
<tr>
<td>Abnormal Uterine cavity (75 cases true positive)</td>
<td>74 (75-1)</td>
<td>73 (75-2)</td>
</tr>
<tr>
<td>Endometrial polyp (n=33)</td>
<td>33</td>
<td>31</td>
</tr>
<tr>
<td>Sub-mucous fibroid (n=19)</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Uterine septum (n=9)</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Intrauterine adhesions (Ascherman’s) (n=6)</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Endometrial hyperplasia (Thick endometrium) (n=5)</td>
<td>5</td>
<td>6 (1 case of endometrial polyp diagnosed as endometrial hyperplasia = false positive)</td>
</tr>
<tr>
<td>Thin (atrophic) endometrium (n=3)</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

n: number. The diagnosis of endometrial polyps, endometrial hyperplasia and thin (atrophic endometrium) were confirmed by the histopathological results, while the diagnosis of intrauterine adhesions and sub-mucous myoma was based on the hysteroscopic findings reviewed by senior gynecologists. SIS = Saline infusion hysterosonography

In this study, the hysteroscopy was more sensitive (98.7% versus 97.4%), more specific (100% versus 99.1%), and more accurate (99.5% versus 98.4%) than SIS. In addition, the hysteroscopy had higher predictive values, 100% PPV & 99.1%NPV versus 98.7% PPV and 98.2% NPV for SIS in diagnosis of uterine cavity abnormalities in cases of abnormal uterine bleeding (this difference was statistically insignificant, P>0.05) using chi-square (X^2) test.

Table 2 Table 2. The sensitivity, specificity, accuracy and the predictive values of the hysteroscopy & SIS

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hysteroscopy</th>
<th>SIS</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity = true positive / true positive + false negative X 100</td>
<td>75/76(75+1)X100 = 98.7%</td>
<td>75/77(50 + 2) X100 = 97.4%</td>
<td>&gt;0.05*</td>
</tr>
<tr>
<td>Specificity = true negative / true negative + false positive X 100</td>
<td>111/111(111+0)X100 = 100%</td>
<td>111/112 (111+1)X100 = 99.1%</td>
<td>&gt;0.05*</td>
</tr>
<tr>
<td>PPV = True positive / (True positive + false positive) X 100</td>
<td>75/75 (75+0)X100 = 100%</td>
<td>75/76 (75 + 1) X100 = 98.7%</td>
<td>&gt;0.05*</td>
</tr>
<tr>
<td>NPV = True negative / (True negative + false negative) X 100</td>
<td>111/111(111+1)X100 = 99.1%</td>
<td>111/113 (111+2)X100 = 98.2%</td>
<td>&gt;0.05*</td>
</tr>
<tr>
<td>Accuracy = True positive + true negative / (True positive + true negative + false positive + false negative) X 100</td>
<td>75+111/(75+111+0+1) = 186/187 = 99.5%</td>
<td>75+111/ (75+111+1+2) = 186/189 = 94.4%</td>
<td>&gt;0.05*</td>
</tr>
</tbody>
</table>

* = Non-significant difference Chi-square test (X^2) used for statistical analysis. Data presented as number and percentage (%).

NPV = Negative predictive value. PPV = Positive predictive value.

SIS = Saline infusion sonography

**Discussion**

Hysteroscopy is known as the gold standard procedure for uterine cavity assessment, it has been reported that the expansion of uterine cavity with saline during trans-vaginal sonography, improves the delineation of
uterine cavity and increases the detection of the uterine cavity abnormalities.\textsuperscript{[9-12]}

One hundred and eighty-six (186) women diagnosed as abnormal uterine bleeding were included in this comparative study, and agreed to have TVS assessment of uterine cavity with the use of saline (SIS) as the contrast medium beside the hysteroscopic assessment.

The uterine cavity abnormalities diagnosed in 40.3\% (75/186) of the women included in this study (17.7\% (33/186) endometrial polyps, 10.2\% (19/186) sub-mucous fibroid, 4.8\% (9/186) uterine septum, 3.2\% (6/186) uterine adhesions, 2.8\% (5/186) endometrial hyperplasia, and 1.6\% (3/186) thin or atrophic endometrium.

\textit{Devleta Balić et al}, found that the most frequent abnormalities during evaluation of uterine cavities were endometrial polyps (60.7\% by TVS and 35.7\% by hysteroscopy), septate uterus (14.3\%), sub-mucosal myoma (12.5\%), endometrial hyperplasia (8.9\% by TVS and 33.9\% by hysteroscopy), and Ascherman's syndrome (3.6\%).\textsuperscript{[13]}

In addition, \textit{Kasius et al}, screened 107 asymptomatic, infertile women for uterine cavity abnormalities before in-vitro fertilization/Intra-cytoplasmic injection (IVF/ICSI), and they found that the most frequent abnormalities during evaluation of uterine cavities were endometrial polyps (11.2\%), septate uterus (1.9\%), and sub-mucosal myoma (1.9\%).\textsuperscript{[14]}

During hysteroscopic evaluation of the uterine cavity of the studied cases, one case of small sub-mucous fibroid was diagnosed as normal uterine cavity (one case false negative), while during SIS evaluation of the uterine cavity of the studied cases, two cases were diagnosed as normal uterine cavity (one cases of endometrial polyp + one case of Ascherman's syndrome (two cases false negative)), and one case of endometrial polyp diagnosed as endometrial hyperplasia (one case false positive). In this study, the hysteroscopy was more sensitive (98.7\% versus 97.4\%), more specific (100\% versus 99.1\%), and more accurate (99.5\% versus 98.4\%) than SIS. In addition, the hysteroscopy had higher predictive values, 100\% PPV \& 99.1\%NPV versus 98.7\% PPV and 98.2\% NPV for SIS in diagnosis of uterine cavity abnormalities (this difference was statistically insignificant).

\textit{Devleta Balić et al}, concluded that the specificity was higher in hysteroscopy than in TVS in the diagnosis of endometrial polyps (92.3\% versus 56.4\%), while the sensitivity was identical (100\%), and the sensitivity of TVS in the diagnosis of endometrial hyperplasia was higher than that of hysteroscopy (86.4\% versus 22.7\%), while specificity was identical (100\%).\textsuperscript{[13]}

In addition, \textit{Devleta Balić et al}, concluded that hysteroscopy is more reliable in diagnosis of uterine cavity abnormalities than TVS and the use of a high frequency ultrasound probe leads to a lack of diagnostic clarity between endometrial polyps and hyperplasia.\textsuperscript{[13]}

\textit{Aydia et al}, screened 44 patients by hysteroscopy, and SCHS (saline contrast hyster-on-sonography) before IVF/ICSI, they diagnosed uterine cavity abnormalities in 16 women by hysteroscopy, and the SCHS was in complete agreement with hysteroscopy in 13...
out of 16 cases.\textsuperscript{[15]} In addition, \textit{Aydia et al}, found that the SCHS had a 87.5% sensitivity, 100% specificity, 100% PPV and 91.6% NPV during evaluation of uterine cavity abnormalities and they concluded that SCHS is a simple, well tolerated procedure that can be performed to avoid expensive diagnostic hysteroscopy, and significant findings can be treated by operative hysteroscopy prior to IVF/ICSI.\textsuperscript{[15]}

\textit{Seshadri et al}, concluded that SIS is commonly used for detailed evaluation of the uterine cavity as part of pre-treatment assessment in infertile women.\textsuperscript{[16]} In addition, \textit{La Sala et al}, concluded that the TVS could be used as first step investigation to exclude uterine pathologies, and could reduce the number of hysteroscopies done in women with normal uterine cavity.\textsuperscript{[17]}

\textit{Seshadri et al}, in a recent systematic review concluded that SIS is sensitive tool and comparable to the gold standard hysteroscopy in the diagnosis of uterine cavity abnormalities in infertile women.\textsuperscript{[18]}

Lost records during follow up was the only limitation faced during this study, and large comparative study needed to confirm the diagnostic accuracy of SIS in diagnosis of uterine cavity abnormalities.

This study concluded that SIS is simple well tolerate procedure can be used in outpatients setting to diagnose uterine cavity anomalies in cases of abnormal uterine bleeding when outpatient hysteroscopy is not available or as complementary tool to confirm the diagnosis detected by hysteroscopy.

\textbf{Acknowledgments}

To women agreed to participate in this study.

\textbf{Conflict of interest}

No conflict of interest related to this study.

\textbf{Financial Disclosure}

Authors themselves funded study.

\textbf{References}


