Hysterosonography using saline solution with atmospheric air to evaluate tubal permeability in women in propaedeutic for infertility

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ABSTRACT

Introduction: Tubal pathologies correspond to about 35% of infertility cases. Several methods are used for their investigation, the gold standard test being videolaparoscopy (VLP) with chromopertubation. Hysterosalpingography (HSG) is the method most widely used, however, it only indirectly analyses the endometrial cavity, without providing information on other pathologies. On the other hand, Hysterosonosalpingography (HSNSG) utilizes non-ionizing contrast media and allows for a detailed analysis of the endometrial cavity, uterine tube permeability, and other pathologies of the uterus, ovaries, and adnexa. This is achieved through the use of Endovaginal Ultrasonography (USEV), which demonstrates comparable accuracy to other methods. Objectives: To evaluate tubal permeability through HSNSG, using saline solution with atmospheric air as contrast, and compare with those of HSG. Methods: Observational cross-sectional study with 28 patients with infertility: HSNSG results were compared with HSG, using Kappa’s method to calculate the level of agreement. Questionnaires were also taken to assess the level of pain and discomfort of the examination. Results: The analysis of the right tube had 75% agreement with the HSG with p=0.05 Kappa=0.364 (fair agreement), and 84.7% for the left tube, with p=0.0003 and Kappa=0.674 (substantial agreement). There were 18 (38.9%) cases of tube obstruction at HSG with normal tubes at HSNSG. Regarding the level of discomfort, 64.2% reported mild discomfort, 28.6% moderate and 7.2% intense discomfort. Conclusion: HSNSG has good correlation to HSG and may be the first-line test for investigating tubal permeability in the evaluation of infertile couples.

Keywords: Hysterosonosalpingography; Endovaginal ultrasound; Infertility.

INTRODUCTION

Tubal pathologies are the most common cause of infertility, responsible for up to 35% of cases of female infertility. The uterine tubes are mobile structures, lined with ciliated epithelium, whose peristaltic movements help transport sperm and fertilized eggs. The anatomical and functional integrity of the tubes is crucial for the fertilization process¹.
Several methods are used to investigate the functional and anatomical state of the fallopian tubes, and the ideal method has not been found yet. Hysterosalpingography (HSG) is a widely used method, but it has certain disadvantages. It involves the use of ionizing radiation and can only identify the cavity of the uterus and tubes. Furthermore, it indirectly analyzes the myometrium and tubal walls.

A meta-analysis study showed that HSG has low sensitivity: 0.65 (Confidence interval–95%CI: 0.50-0.78), and specificity: 0.83 (95% CI: 0.77-0.88) for diagnosis of tubal obstruction when compared to laparoscopy, and presents a high prevalence of complications, with 0.3% of pelvic inflammatory disease (PID), with a worsening of the prognosis of infertility.

Endovaginal Ultrasonography (USEV) identifies only gross changes in the fallopian tubes, such as inflammatory processes and hydrosalpinges, and tubal patency is assessed by HSG, HSNSG, or the gold standard, which is laparoscopy with chromotubing.

Hysterosonosalpingography (HSNSG), a procedure used since the 1980s, provides a quick and reliable screening of tubal patency, and consists of the use of contrast of various types, such as saline solution, saline solution with atmospheric air, and ultrasonic contrasts of microbubbles, which are more effective than HSG, in addition to not using ionizing radiation. Moreover, it evaluates physiological changes (such as polycystic ovaries), endometriomas, structural changes in the uterine cavity (such as synechiae, polyps and submucosal fibroids), and Mullerian anomalies, which may be involved in the context of infertility and are not detected or diagnosed with lower accuracy by HSG.

The high cost and lack of availability of microbubble ultrasound contrasts, some of which are not available in Brazil, may make this method unfeasible in most infertility investigation centers, however, the use of saline solution with atmospheric air as contrast makes the viable and lower-cost procedure.

Although it is not a complementary initial investigation exam, diagnostic laparoscopy is the gold standard in the evaluation of the tube-peritoneal factor, and constitutes an exam that provides a view of the pelvic anatomy, allowing the identification of the degrees of tubal obstruction and of adhesions or endometriosis, in addition to identifying pathological findings in 21 to 68% of cases of unexplained infertility.

Despite being the most commonly used method for the initial assessment, HSG still has limitations of tubal patency, more studies are needed to evaluate the feasibility of HSNSG and compare it with HSG. Therefore, this work aimed to evaluate tubal permeability using HSNSG, saline solution with atmospheric air as a contrast and compare its results with those of HSG.

**METHODS**

This is a cross-sectional observational study, with the objective of evaluating tubal patency through HSNSG. The patients were selected through a convenience sample, attended at two outpatient clinics of the public infertility service in the city of Belo Horizonte.

The exclusion criteria included patients with clinically evident signs of cervicitis, patients with suspected pregnancy, and patients in whom the examination could not be performed. All women underwent HSG, the initial method for investigating tubal patency. The HSGs were performed in different private radiology services in Belo Horizonte, which provide services for the Sistema Único de Saúde (SUS), which could be a possible bias factor for this study.

The volunteers went through conventional endovaginal ultrasound (USEV) and Three-Dimensional Ultrasonography (3D US) to evaluate possible uterine anomalies, followed by HSNSG. To perform HSNSG,
pediatric Foley catheter number 8, sterile saline solution, three-way device for mixing saline and air, two sterile 20 ml syringes, and a 1 ml syringe for inflating the Foley catheter balloon were used.

**Exam technique:**
1. Conventional **USEV** involves assessing the uterus and endometrial cavity in all longitudinal and transverse sections, identifying the ovaries and evaluating their mobility, as well as assessing the adnexal regions.
2. 3D US to evaluate possible uterine anomalies.
3. Speculum examination with asepsis of the cervix with topical povidone or chlorhexidine.
4. Placement of a pediatric Foley catheter with balloon inflation with 1-2 ml of saline solution to fix it in the cavity and prevent contrast reflux.
5. Verification, through **USEV**, of the positioning of the catheter balloon above the internal orifice of the uterine cervix.
6. Injection of saline solution (1-5 ml) to evaluate the endometrial cavity.
7. Use of two 20 ml syringes coupled using a three-way device, one with atmospheric air and the other with saline solution (10 ml each).
8. Vigorous mixing of air and saline and injection of contrast.
9. Identification of the uterine tubes by passing echogenic contrast, evaluating one side at a time, with the injection of up to 40 ml of the mixture.

All **USEV** and **HSNSG** exams were performed by the same researcher. An Aplio CUS-AA000 device (Canon) was used, with a multifrequency volumetric convex and endocavitary probe. The average exam time was around thirty minutes.

**Interpretation of the exam:**
1. The tube is considered patent when there is contrast flow through the tube, or with air identified in the cavity close to the ovaries.
2. An occluded tube is considered when there is no observed passage of contrast through the tube or when there is dilation of the lumen with contrast in the isthmic or intramural portions of the tube.
3. An exam is considered invalid when it cannot be completed due to technical reasons or medical complications. At the end of the procedure, patients answered a pain questionnaire, in order to check the tolerability of the method.
4. Considered invalid result when the exam is not completed for technical reasons or medical complications.

At the end of the procedure, patients answered a pain questionnaire, in order to check the tolerability of the method.

**Chart 1- Questionnaire to analyze pain level**

<table>
<thead>
<tr>
<th>Pain level</th>
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</thead>
<tbody>
<tr>
<td>Easily acceptable (very mild discomfort with the exam)</td>
</tr>
<tr>
<td>Acceptable (tolerable but easily acceptable discomfort)</td>
</tr>
<tr>
<td>Tolerable (equivalent to menstrual cramps)</td>
</tr>
<tr>
<td>Barely tolerable (bearable only for a short period)</td>
</tr>
<tr>
<td>Intolerable (pain enough to stop the exam)</td>
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The main outcome assessed was the agreement between **HSG** and **HSNSG** in evaluating tubal patency. Additionally, an analysis of the level of pain and discomfort experienced after the **HSNSG** procedure was conducted. Categorical variables were presented as absolute and relative frequencies and numerical variables as mean (standard deviation–SD). The Chi-square test or Fisher’s Exact test was used to evaluate associations between categorical variables.
Categorical variables were presented as absolute and relative frequencies and numerical variables as mean (standard deviation–SD). To evaluate associations between categorical variables, the Chi-square test or Fisher’s Exact test was used.

The agreement between the methods in analyzing the endometrial cavity and tubal permeability was assessed using the Kappa Agreement Coefficient with linear weights. A result of 1 indicates perfect agreement, while a result of 0 indicates no agreement beyond chance. The analyzes were carried out using Software R and a significance level of 5% was considered.

The study was approved by the Research Ethics Committee (CAAE: 38388720.0.0000.5134). Informed consent was obtained from all patients before their participation. The principles of ethics were respected and are in accordance with Resolution 466/12, of the National Health Council. This study is free from conflicts of interest.

RESULTS

29 patients were evaluated, with a median age of 35 years. There was only one case of exclusion due to cervical stenosis, totaling 28 patients.

Regarding parity, 16 patients (57.1%) were nulligravida and 12 patients (42.9%) had previous pregnancies (0 to 2 births, 0 to 3 miscarriages and 1 ectopic pregnancy). Regarding the time of infertility, the average time was 7.1 years (SD±3.2).

In the evaluation of the endometrial cavity for pathologies possibly related to infertility, two cases of polyps were found on HSNSG, with only one detected on HSG. Additionally, two cases of uterine synechiae were identified, with one being concordant between the two methods and the other detected solely by HSG. Furthermore, HSG failed to detect one case of uterine septation. The results are explained in Table 1.

In the adnexal evaluation, we found six cases of adhesion process on ultrasound examination, two of which were bilateral (which showed normal tubes on both HSNSG and HSG), and four unilateral cases, with discordant results in only one case, which showed normal tubes on HSNSG and obstructed to HSG. Two cases of hydrosalpinx were diagnosed on HSNSG, one bilateral and one unilateral, with tubal obstruction on HSG being found in all of them. Two cases of ovarian endometriomas and four cases of polycystic ovaries were also detected. An ovarian teratoma was also detected, which is probably unrelated to infertility.

Regarding the assessment of tubal patency by HSNSG in comparison with the results of HSG, in relation to the right uterine tube, there was agreement in 21 of the 27 cases (75%) with a p value = 0.0533, with a Kappa index of 0.364. There were four cases of tubal obstruction by HSG, with the tube identified and normal by HSNSG (probably due to cornual spasm), and three cases of obstruction by HSNSG with normal tubes by HSG, as shown in Table 2.

All patients were submitted to a questionnaire to assess the level of pain after the exam, with the following results: 42.9% easily acceptable (very mild discomfort with the exam), 21.3% acceptable (tolerable discomfort, but easily acceptable), 28.6% tolerable (equivalent to menstrual cramps), 3.6% barely tolerable (endurable only for a short period and 3.6% intolerable (pain enough to interrupt the exam).

When evaluating the left tube, we found agreement in 24 cases (85.7%), with a p value = 0.0003, with a Kappa index of 0.674. There was one case of tubal obstruction by HSNSG with a patent tube at HSG and three cases of tubal obstruction by HSG with normal tubes at HSNSG, according to Table 3.

Table 1. Association between hysterosonography and hysterosalpingography of the endometrial cavity
### Table 2: Association between hysterosonography and hysterosalpingography of the right uterine tube

<table>
<thead>
<tr>
<th>Tuba Pervia</th>
<th>RIGHT TUBA–HSNG</th>
<th>TOTAL</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Tubal Obstruction</td>
<td></td>
</tr>
<tr>
<td>RIGHT TUBA HSG</td>
<td>Tuba Pervia</td>
<td>17 (85%)</td>
</tr>
<tr>
<td></td>
<td>Tubal Obstruction</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>21</td>
</tr>
</tbody>
</table>

**HSNG:** hysterosonography  
**HSG:** hysterosalpingography

### Table 3: Association between hysterosonography and hysterosalpingography of the left uterine tube

<table>
<thead>
<tr>
<th>Tuba Pervia</th>
<th>LEFT TUBA–HSNG</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tubal Obstruction</td>
<td></td>
</tr>
<tr>
<td>LEFT TUBA HSG</td>
<td>Tuba Pervia</td>
<td>17 (94.44%)</td>
</tr>
<tr>
<td></td>
<td>Tubal Obstruction</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>20</td>
</tr>
</tbody>
</table>

**HSNG:** hysterosonography  
**HSG:** hysterosalpingography

**Figure 1:** A: cuffed catheter in the endometrial cavity. B: right tuba with contrast. C: left tuba with contrast.

**USEV** plays a critical role in the evaluation of female infertility as it is a part of the initial investigation and is used to detect myometrial pathologies such as (myomas), endometrial cavity (polyps, synechiae, hyperplasias and others), endometriosis and other ovarian pathologies that can be causes of infertility. It detects gross tubal pathologies, such as hydrosalpinges, salpingitis and rare tumors, but does not adequately evaluate normal tubes and is inadequate for evaluating tubal patency. The gold standard for evaluating tubal patency is **VLP with chromotubing**, however, it is an invasive proce-
in which the pressure for injection is greater than in saline solutions and/or microbubble contrast, causing a greater level of discomfort\textsuperscript{10}.

Studies with the purpose of evaluating tubal patency with USEV were initiated in the 1980s and one of the first was performed by Richman et al (1984)\textsuperscript{12} using trans-abdominal US, Tubal patency is diagnosed by injecting saline solution through the cervix, and the detection of free fluid in the posterior uterine cul-de-sac (FSUP) after the procedure confirms it. Randolph et al (1986)\textsuperscript{9}, used the same procedure, through the instillation of approximately 200ml of saline solution with sensitivity and specificity of 100 and 91\% respectively, compared with HSG which had sensitivity and specificity of 96 and 94\%. Subsequently, Volpi et al (1991)\textsuperscript{13} used the endovaginal route and injection of air followed by saline solution, and found agreement with laparoscopy in 83.3\% of cases. Jeanty et al (2000)\textsuperscript{14} used the instillation of atmospheric air, with sensitivity and specificity levels of 85.7 and 87.5\%, correspondingly. All of these procedures were performed using an insemination catheter, which had a high cost (approximately R$200.00). This high cost could potentially make the procedures difficult or unfeasible to perform. Inki et al (1998)\textsuperscript{15} recommended the use of pediatric Foley catheter number 8, considerably reducing the cost of the exam, performing the instillation of atmospheric air followed by saline solution, finding sensitivity of 88.7\% and specificity of 83.3\% when compared with videolaparoscopy (VLP) with chromotubing. Ahinko-Hakamaa et al (2007)\textsuperscript{8} in a study with 559 infertile women found similar results with the use of contrast with saline solution and air to evaluate tubal patency compared to VLP, recommending HSNSG as the first choice exam to evaluate patency tubal\textsuperscript{8}. Robertshaw et al (2016)\textsuperscript{17} used a device for mixing saline solution with air (Fem Vue) and found accuracy similar to HSG for evaluating tubes that had no changes in VLP.
Other contrasts, such as microbubble contrasts like Echovist, have been recommended for performing HSNSG, whose high cost and non-availability in our country make the procedure unfeasible\textsuperscript{19}. Van Welie et al (2022)\textsuperscript{19}, in a randomized study, found similar results between HSG and HSNSG with echogenic foam (HyFoSY) and recommended HSNSG as a first-line test for investigating permeability Tubaria. Calvo et al (2018)\textsuperscript{20} found no differences in results using two echogenic contrasts, sonovue and ExEN foam.

Emanuel et al (2012)\textsuperscript{21} used hydroxymethylcellulose and glycerol gel (HyFoSy) as contrast, as the first step to evaluate the fallopian tubes and the procedure was performed successfully in 93\% of women. Ludwin et al (2017)\textsuperscript{22}, in a comparative study of HyFoSy with USEV and HSNSG using saline solution and air, found a greater accuracy of HyFoSy: 93.7 \times 85.5\%, highlighting the lower cost of HSNSG.

Systematic review study for the diagnosis of tubal occlusion in infertile women comparing HSG with HSNSG, using VLP as the gold standard, found similar results for both methods (sensitivity of 92 and 94\%, and specificity of 95 and 92\%, respectively, for HSG and HSNSG.) The study demonstrated the greater accuracy of HSNSG in diagnosing endometrial, myometrial, and ovarian pathologies. No additional benefit was found from the use of commercial ultrasound contrasts compared to the use of saline solution\textsuperscript{8}.

In the analysis of the right tube, our results showed agreement with the HSG results of 75\% and disagreement in seven cases: three cases showed obstructed tubes at HSNSG with normal tubes at HSG and four cases of normal tubes at HSNSG with obstructed tubes at HSG, due to probable cornual spasm. The p value = 0.05 is at the upper limit of normality, with a Kappa index of 0.364, with reasonable agreement with the HSG results.

In the analysis of the left tube, there was agreement in 84.7\%, with disagreement in four cases (15.3\%): one case of obstruction by the HSNSG with a tube normal to the HS, and three cases of tubes normal to the HSNSG with tubes obstructed by the HSG, due to probable cornual spasm. The p value = 0.0003 showed statistical significance, with a Kappa index of 0.674, indicating strong agreement.

Out of the 18 cases of tubal obstruction identified on HSG, seven cases (38.9\%), four on the right and three on the left, were attributed to probable cornual spasm, which we consider as normal based on the HSNSG results.Robertshaw et al (2016)\textsuperscript{17} found significant agreement between HSG and HSNSG when the tubes were patent, however, when the tubes were found to be obstructed, indicating HSNG as the primary diagnostic test, other procedures were deemed necessary.

US is the first-line exam for evaluating tubal pathologies, with HSG only used to evaluate infertility\textsuperscript{23}. Zajicek et al (2022)\textsuperscript{24} suggest incorporating conventional US and 3D US with HSNSG into routine infertility assessment.

When evaluating the levels of pain and discomfort experienced during the exam, we observed that 7.1\% of the responses indicated barely tolerable or intolerable levels. The majority, 71.5\%, reported acceptable or easily acceptable levels, demonstrating the method’s good overall acceptability. Our results were similar to those of Bohiltea et al (2022)\textsuperscript{25}, who found tolerable or absent pain in 75\% of cases, with 8\% of cases of extreme pain. The fact that no oily contrast is used and the lower pressure for the injection makes this procedure less uncomfortable than HSG\textsuperscript{26}. We do not use painkillers prior to the exam. Riva et al (2022)\textsuperscript{27}, in a systematic review study, did not find sufficient data to evaluate the effectiveness of using analgesics or other strategies for pain relief in these procedures.
The study has certain limitations, including the performance of HSG by different professionals in various locations and the incomplete use of VLP with chromotubation in all patients. Additionally, the absence of a gold standard limits the interpretation of these results solely to the comparison between these two methods.

**CONCLUSION**

The HSNSG proved to be a test that presents a good correlation with the HSG findings in the sample evaluated. Due to its low cost, lack of ionizing radiation, good tolerability, and ability to provide additional information compared to HSG, it is recommended to consider this test in the evaluation of tubal patency for women undergoing infertility workup. Although, other studies, with a more appropriate methodological design, need to confirm these findings.

**REFERÊNCIAS**


The authors declare that there is no conflict of interests in relation to this article.