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Hysterosalpingography versus hysterscopy in intrauterine pathology research of infertile patients

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Summary

Background: The objective of the present paper is to confirm the validity and reliability of hysterosalpingography (HSG) in intrauterine pathology research of infertile female patients by comparing the hysteroscopy (HC) findings to a "gold standard" test. *Aim: To* analyze HSG and HC findings in infertility patients. *Materials and Methods:* The research was conducted as a prospective study at the Gynecological and Obstetrics Clinic ''Narodni front'' in Belgrade. *Results:* HSG indicated pathological findings in 72.5% of patients whereas HC revealed abnormalities of uterine cavity in 77.5%. In 12.5% of patients, HSG demonstrated a normal uterine cavity, and HC confirmed pathological findings, while in 7.5% of patients with filling defects and irregular shapes on HSG images, HC reported normal findings. In 22.5% of patients normal finding as well as endometrial polyps were reported; congenital malformations (anomalies) were found in 32.5%, submucosal myomas in 12.5% and Asherman's syndrome in 10%. *Conclusion:* HC finding was crucial in final diagnosing.

Key words: Hysterosalpingography; Hysteroscopy; Infertility; Uterine cavity.

Introduction

Congenital abnormalities and inherited uterine diseases may have a negative effect on the complex process of embryo implantation [1]. The abnormalities of the uterine cavity are the cause of infertility in 10% of women, whereas pathological endometrial anomalies were revealed in 45% of patients with unsuccessful conception in *in vitro* fertilisation trials [2]. Such infertility distribution called for investigation of uterine cavity condition as a routine procedure in diagnosing female infertility [3].

As diagnosing methods, hysterosalpingography (HSG) and hysteroscopy (HC) have different approaches in uterine cavity research. The image contrast charging indicated that HSG indirectly provides an insight into the condition of the uterine cavity. According to many clinicians, HSG has been a routine technique so far and the first line intrauterine pathology research of infertile patients [4, 5]. This diagnostic method has been used as a screening procedure in all infertility cases suspected to have intrauterine abnormalities as well as in tubal patency testing.

Due to the direct view of uterine cavity and cervical canal, HC provides accurate and precise diagnosing of intrauteral conditions. The great advantage of this method is definitely its therapeutical application which is considered superior to HSG [6].

The aim of this study is to confirm the validity and reliability of HSG in intrauterine pathology investigation in infertile female patients by comparing the HC findings to a "gold standard'' test.

Materials and Methods

The method was conducted as a prospective study at the Gynaecological and Obstetrics Clinic ''Narodni front'' in Belgrade. It involved 40 women with an average age of 32.79 ± 4.60 years who, due to conjugal infertility, came to the clinic for examinations and treatments. All the patients had a certain examination protocol. In evaluating the HSG validity in comparison to HC findings obtained by viewing the uterine cavity of the examined patients, the time difference between these two diagnostic methods should not have exceeded two or three months. This was the basic criterion for selecting or involving patients in the investigation.

HSG was performed on women following the eighth or tenth day of their menstrual cycle with a short intravenous anaesthesia, radiographic equipment, and iodinated water-soluble contrast medium. HSG findings contained a contrast image of the cervical canal and uterine cavity. The image projection of the uterine cavity was an equilateral inverted triangle in relation to the cervical canal, with sharp edges and homogenous shadow. As a long and narrow homogenous thread, the contrast shadow further spread along oviducts to abdominal cavity. The investigation of the HSG findings, made it possible to observe normal finding and the contrast to observe filling defects and irregularities of uterine cavity.

HC was carried out during the same menstrual period or in the following three to six months, in the early proliferative phase, immediately after the cessation of the menstrual flow

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Table 1. — *Correlation between hysterosalpingography and hysteroscopy.*

Hysterosalpingography	Hysteroscopy				Total	
	Pathological finding		Normal finding			
	N.	%	N.	%	N.	%
Pathological finding	26	65	3	7.5	29	72.5
Normal finding	5	12.5	6	15	11	27.5
Total	31	77.5	9	22.5	40	100

$\kappa = 0.47$; $p > 0.05$

when endometrium was thin, porous, and invulnerable. Diagnostic HC was conducted by introducing a hysteroscope with external shield (sheath) diameter of 5.5mm. The intervention required a dilation of the patient's cervical canal. When the hysteroscope was inserted and cervical canal and uterine cavum visualized, followed the systematic scrutinization of the anterior and posterior cavum wall, both cornual regions, the left and right ostia, as well as the detection of possible abnormalities. As this diagnostic hysteroscope possessed a working channel where hysteroscope instruments could be guided (5 Fr), some minor surgeries were also possible. This referred to the lysis of focal and small intrauteral adhesions, endometrial biopsy, and resection of small pendunculated polyps and myomas.

More extensive cavity surgeries required a resectoscope with an external shield diameter of nine-mm and a large dilation. The resectoscope consisted of a multichannel shield for fluid inflow and outflow. Hysteroscope scissors were mostly used to remove uterine septums, adhesion partitioning, because the septums were most frequently avascular with very little bleeding. They were also removed with resectoscope, a monopolar needle with cutting effect and coagulation, with no bleeding. Pedunculated myomas and polyps were removed with HC monopolar trap. The application of bipolar electrodes required particular attention during the septum resection due to the heat transfer and possible damage of the surrounding healthy endometrium. Ispirol was firstly applied as a distension medium followed by the physiological solution (0.9% NaCl). An automatic pump controlled pressure and fluid flow so that the intrauterine pressure was not higher than 100 mmHg. Both procedures did not cause any serious complications during surgery nor during the recovery period.

Results

HSG indicated normal uterine cavity in 27.5% of patients, whereas 72.5% revealed findings that indicated intrauterine factor as a probable cause of infertility (Table 1). HC finding was crucial in final diagnosing. The frequency of HC diagnosing of uterine cavity reported congenital abnormalities in majority of patients, 13 (32.5%), endometrial polyps was confirmed in nine patients (22.5%), submucosal myomas in five (12.5%) patients, and Asherman's syndrome in four (10%) patients.

HC reported a higher percentage of pathological anomalies in comparison with HSG as well as a lower percentage of normal findings. χ^2-test statistical analysis did not report any significant discrepancy between normal and pathological findings of the two diagnostic methods ($p > 0.05$).

Kappa's quotient was used as a reliability index to measure agreement between two diagnostic methods. The quotient value higher than 0.4 was considered as the evidence of useful correlation between HC and HSG. McNemar's (McN) test analysed discrepancy between results obtained with these methods; it was considered statistically significant at a value $p < 0.05$.

The HSG and HC correlation in diagnosing endometrial polyps/submucosal myomas was quantified by the Kappa's index value ($\kappa = 0.66$) which confirmed positive agreement, as well as uterus subseptus finding ($\kappa = 0.63$), uterus bicornis ($\kappa = 0.5$), uterus arcuatus ($\kappa = 0.67$). Kappa quotient ($\kappa = 0.89$), as a clinical entity, confirmed excellent agreement between HSG and HC in inherited uterus anomalies, and for χ^2 McN there was no statistically significant difference in relation to findings obtained in various conditions of uterine cavity ($p > 0.05$).

In evaluating HSG criterion validity compared to HC as a gold standard in the investigation of uterine cavity, the values for some features of HSG as a diagnostic method are shown in Table 2, whereas the values for each clinical diagnosis are given separately in Table 3. HSG and HC find-

Table 2. — *Hysterosalpingography validity.*

Hysterosalpingography	Dg Acc[1]	Sn[2]	Sp[3]	PPV[4]	NPV[5]	LR+[6]	LR-[7]
	80%	83,87%	66,67%	89,66%	54,55%	2,52	0,24

[1]: diagnostic efficacy, equivalency; [2]: sensitivity; [3]: specifity; [4]: positive predicative value; [5]: negative predicative value; [6]: positive rate veracity; [7]: negative rate veracity.

Table 3. — *Histerosalpingography validity.*

Hysterosalpingography	Dg Acc	Sn	Sp	PPV	NPV	LR+	LR-
Polyps/myomas	75%	71.43%	92.31%	83.33%	85.71%	9,2	0.29
Congenital anomalies	89%	92.31%	96.3%	92.31%	96.3%	24.95	0.08
Uterus subseptus	92.5%	50%	100%	100%	91.89%	0	0.5
Uterus bicornis	95%	100%	94.87%	33.33%	100%	19.49	0
Uterus arcuatus	97.5%	100%	97.43%	50%	100%	38.9	0

Table 4. — *Discrepancies between hysterosalpingography and hysteroscopy findings.*

Hysterosalpingography	Hysteroscopy
Normal finding	Endometrial polyps
Normal finding	Submucosal myoma of the uterus
Normal finding	Uterus subseptus
Arcuate uterus	Normal finding
Filing defects	Normal finding

ings did not agree in all patients in diagnosing intrauterine adhesion, uterus septus, and uterus unicornis unicollis.

HSG findings correlate with HC findings, i.e. the total correlation of normal and pathological findings was 80%. Discrepancies in HSG and HC findings are given in Table 4. In five patients, HSH showed a normal uterine cavity, and HC confirmed pathological findings, endometrial polyps in three patients, uterine myoma, and uterus subseptus in one patient, while in three patients with flaws in contrast charging (filling defects) and irregular shapes on HSG images; HC reported normal findings.

Discussion

In our clinical practice, HSG method has been applied for many years, is still mandatory, and is the first diagnostic method used in the assessment of female infertility. Starting from this assumption, the present study should prove diagnostic accuracy, validity and reliability of the method in 40 female patients compared to HC, the gold standard method in the evaluation of intrauterine pathology.

In this study, HSG was the initial method in investigating conditions of uterine cavity. Pathological anomalies of uterine cavity were visualised as flaws in contrast charging (filling defects) and irregular shapes on HSG images. HSG demonstrated a normal uterus in 11 patients (27.5%) while anomalies on HSG images were reported in 29 (72.5%) patients. In the first group, HC confirmed normal findings in six patients, and pathological cavity abnormalities in five patients, i.e. HSG showed a false negative rate in 12.5% cases. Out of 29 patients with pathological findings on HSG image, HC noted pathological cavity abnormalities in three patients. Hence, HSG in this study showed a false positive rate in 7.5% of patients. Similar rates, both for false positive and false negative findings (11.7% and 13.3%) were shown by Prevedourakis *et al.* in a much larger number of female patients [7].

The results obtained by assessing HSG validity indicated that the this method could ultimately show intrauterine pathology in the patients who, according to diagnostic gold standard method - HC, actually suffered from this disease; the *sensitivity* was 83.87%. In the present investigation HSG *specificity* was not so high, 66.67%, but there was a high correlation between HC and HSG findings; total agreement between pathological and normal finding was 80%. The positive rate veracity (LR+) was 2.52, i.e. abnormal finding on HSG image was three times more likely to be found in patients with pathological findings reported by HC than the patients with normal HC finding. The veracity of the negative rate (LR) was 0.24 and indicates that HSG finding was almost impossible to find in patients with pathological cavity anomalies.

Many authors have demonstrated that HSG has high sensitivity 60-98%, but low specificity 15-81.8%, with somewhat false positive and false negative rates compared to the present study [6, 8-10].

Diagnostic accuracy of HSG compared to HC showed high values in the studies of Roma *et al.* (73%) and Filhoe *et al.* (85.2%), which agreed with the present results (80%) [4, 11].

The agreement of the two diagnostic methods was quantified by Kappa index which in the current study was $\kappa = 0.47$. The κ value indicates regular agreement between HSG and HC results in intrauterine pathology research in infertile patients. In the similar study, the values of κ quotient were interpreted as follows: 0.81-1.0 (excellent); 0.61-0.80 (good); 0.41-0.60 (normal); 0.21- 0.40 (poor), and < 0.20 (very poor) agreement.

The direct sign on hysterosalpingram of the presence of endometrial polyps in the cavity was the defect in contrast charging (filling defect), normal contours but without sharp and regular edges. Due to its soft consistency, they showed tendency to disappear as the contrast instillation in the cavity grew. They could be best observed on the first image when the contrast filled the cavity. The lack of fluoroscopy on the authors' Roentgen apparatus and the magnitude of polyps may have influenced their finding and false negative rate.

HC identified polyps as localized pinkish-grey to white coloured anomalies, covered with mostly smooth and shiny-surfaced endometrium. The localization and the magnitude of polyps varied in patients, most frequently in fundal and isthmic area, magnitude 0.5 to two cm.

All endometrial polyps were removed by hysteroscopic monopolar trap and resectoscope loop. Material was sent on histopathological examination.

Hysterogram showed submucosal myomas as round and regular defects in contrast filling. They most frequently induced partial anomalies, compressions, and reduction of uterine cavity as well as its enlargement.

In direct hysteroscopic visualization, submucosal myomas reported peripheral vascularization through atrophic endometrium and whitish fibrous myoma tissue compared to the surrounding colour of the normal endometrium. Tactile sensation with an inactive electrode provided the sensation of toughness compared to the surrounding soft myometrial tissue. The magnitude of submucosal myomas in patients varied from one to 2.5 cm, all of them being removed with a resectoscope loop in one act.

The HSG image demonstrated similar findings of polyendometrial polyps and submucosal myomas, it was diagnostically difficult to differentiate them without hysteroscopic inspection, so they were marked as one clinical entity in the statistical data procession. HSG indicated the possibility of the polyp/myoma presence in the cavity of ten patients. HC visualized endometrial polyps in nine patients examined and submucosal myomas in five. In two patients, the contrast filling defects on HSG image with a suspected polyp/myoma presence were artifacts, most probably air bubbles and cervical mucus, as HC confirmed normal finding in uterine cavity.

In the evaluation of uterine cavity in women with a large number of miscarriages, Filhoe *et al.* demonstrated a good agreement between HSG and HC (κ =0.79), both for polyps and myomas. Diagnostic accuracy in the investigation of these anomalies was 98% [11]. In the study, Valenzano *et al.* confirmed normal cavity finding in ten patients with HC diagnosis for endometrial polyps and submucosal myoma [12].

According to some studies, HSG is superior to HC for the evaluation of lesions penetrating through myometrium, congenital anomalies as well as the changes in the contour of the uterine wall [13]. Small intrauterine lesions, polyps, submucosal myoma, and intrauterine adhesions that may have a significant influence on the successful implantation, are diagnosed more accurately and precisely by HC than by HSG [14].

HSG image projects intrauterine adhesions as a filling defect with irregular shapes; the result of a constantly present apposition of the anterior and posterior uterine walls and their inability to be distended and separated by contrast. Due to such HSG image finding, the presence of Asherman's syndrome was suspected in three patients. In one patient, while injecting cannula and contrast, only dilated cervical canal was noted, with no further contrast penetration into the cavity.

HC diagnosed uterine synechiae in four patients with positive HSG finding. In two patients, the hysteroscope insertion led to breaking thin filmy adhesions apart. Intrauterine contraceptive device was inserted in one patient and the other patient was recommended HC after three months.

In the current study, HSG and HC showed a perfect correlation in diagnosing intrauterine adhesions (κ = 1) and diagnostic HSG accuracy was 100%.

Other studies did not report such good diagnostic HSG results. In diagnosing synechiae, Filho *et al.* had two false positive rates (3.7%), sensitivity 69.2%, and high specificity 95%. In their study, diagnostic efficacy was relatively elevated 88.9%, as well as the HSG and HC correlation κ = 0.68 [11].

Alborzi *et al.* showed that, due to the intrauterine adhesions confirmed in 17 patients, HSG had sensitivity 70.6% for Asherman's syndrome, specificity 99.4%, PPV 92.3%, and NPV 97.1% [15].

In this study, congenital uterine anomalies are most frequent abnormalities, present in 13 patients. Innate uterine anomalies were similarly present in patients after both diagnostic procedures: HSG 30% and HC 32.5%. Precisely diagnosing congenital disorders is essential because of different surgery treatments and reproductive potential. Various surgery approaches in anomaly therapy require precise diagnosis in order to obtain adequate and optimal therapeutic approach for a patient.

Uterus septus is most commonly found in infertile patients (33.6%) [16]. In the present study, HSG reported cavity septum in three patients. HC diagnosed septums that divided cavum into two cavities, in one act septums were cut with bipolar resectoscope electrode and scissors.

In six patients HC confirmed uterus subseptus, small septums < two cm long, hysteroscopically resected with monopolar needle. In three patients, HSG suspected subseptum. As for other three patients, HSG image was normal in one of them and uterus bicornis was suspected in other two.

Uterus bicornis, is the result of the incomplete infusion of the Müllerian ducts. On HSG image the anomaly varies depending on the defect magnitude, from completely mild fundal depression to a complete separation extending to the inner estuary. On hysterogram, uterus bicornis was suspected in three cases, but HC noted uterus bicornis in only one case, which was confirmed by laparoscopy in one act.

Maleck *et al.* suggested in their study that, due to accurate and precise investigation of the intravaginal anatomy, magnetic resonance was the optional method in detecting uterine irregularities in infertility patients. Laparoscopy and HC were applied in patients expected to have therapeutic treatment [17].

Uterus arcuatus on HSG image demonstrates a fundal saddle shaped depression. Such a finding could be found in two patients. Final diagnosing uterus arcautus was reported in one patient by HC and laparoscopy, whereas in another case the finding was normal.

Today HSG combined with laparoscopy and HC, due to relatively high prevalence of uterine abnormalities, is considered optimal in diagnosing female fertility [18].

Table 3 shows values of HSG validity as compared to all represented clinical entities whose HSG and HC did not match. Such high values of sensitivity, specificity, PPV and NPV, as well as diagnostic accuracy, prove the features of HSG as a diagnostic method in detecting congenital malformations. Similar results in this study were shown by Alborzi *et al.* [15].

In the present study, HSG showed its discrepancy limitations between subsepted and uterus bicornis because of the similar uterine cavity form of the anomalies on the image. Regarding the fact that this study included a small number of patients, with a small number of diagnoses, it is not possible to assess the real diagnostic accuracy of HSG for congenital anomalies.

Finding discrepancies between HSG and HC also referred to the identification of endometrial polyps and submucosal myoma, because HSG did not detect these anomalies, probably due to the fact that lesions were so small to be shown as filling defects on images. HSG is relatively reliable method in diagnosing intrauterine abnormalities. Although HC presents a gold standard method in the evaluation of intrauterine pathology in infertility patients, HSG as a highly sensitive method still remains initial diagnostic method in indirect cavity investigation. In the present study, HSG is, due to the simple performance, low cost, and relatively high reliability, supplement to HC in the investigation of intrauterine pathology.

Nowadays HC is a simple and efficient diagnostic method that enables treatment of cavity pathology and is unique in disclosing small and subtle lesions that other diagnostic methods are not able to detect. If HSG image noted intrauterine abnormality, the final diagnosing should be done by HC inspection of the cavity.

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