

Routine vaginoscopic office hysteroscopy in modern infertility work-up: a randomized controlled trial

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Abstract This study aims to estimate the safety, efficacy, and patient acceptability of adding vaginoscopic office hysteroscopy (VOH) to the routine infertility diagnostic work-up for evaluation of the endometrial cavity. This study is a prospective comparative diagnostic trial. This study was conducted in a tertiary care referral facility and university hospital. This study comprised a total of 156 infertile patients scheduled for laparoscopy. Seventy-eight patients had VOH on one stop bases in addition to the usual infertility work-up and were assigned as group B while a similar number was examined by the usual diagnostic work-up and assigned as group A. The main outcome measure is the diagnostic accuracy of VOH alone in comparison to hysterosalpingography (HSG) and diagnostic laparoscopy (DL) and assessment of combined VOH and HSG in diagnosing intrauterine abnormalities. There was insignificant difference between both groups regarding socio-demographic and HSG data. Abnormal DL findings were more significant in group A. VOH detected 50 % abnormal endometrial cavity in group B with a significant superiority over HSG. There was a high percentage of agreement in the diagnosis of uterine abnormalities between HSG and VOH (96 %). Generally, VOH was an acceptable procedure with mild pain and feasible in most cases. Adding VOH to the routine diagnostic work-up of infertile couples prior to laparoscopy seems to be a feasible, safe, simple, tolerable, and quick outpatient procedure. It can diagnose intrauterine abnormalities in about a quarter of infertile women with normal HSG. VOH has an additional value to HSG and DL in diagnosing uterine. Nevertheless, whether its use

would increase pregnancy rate among infertile women requires a further longitudinal comparative study.

Keywords Vaginoscopic · Office hysteroscopy · Infertility · Hysterosalpingography · Laparoscopy

Introduction

Diagnosis of infertility causes requires comprehensive testing on both partners. On the female side, infertility testing usually involves hormonal testing to determine the patient's ovarian reserve, diagnostic imaging to see if there are any anatomical problems (such as blocked fallopian tubes or uterine fibroids), and immunological testing to rule out any maternal autoimmunity. Knowing the root cause of a couple's infertility is the first step toward successful fertility treatment.

Unexplained infertility is infertility that is idiopathic in the sense that its cause remains unknown even after an infertility work-up, usually including semen analysis in the man and assessment of ovulation and fallopian tubes in the woman. The available diagnostic tools for intrauterine causes of infertility include transvaginal ultrasonography, hysterosalpingography (HSG), or sonohysterography [1]. Manifest uterine causes may include intrauterine adhesions, polypi, or uterine cavity malformations. Hidden uterine factors may include infections, thin endometrium, poor endometrial receptivity, and immunological incompatibility which have received the most attention in recent years. Most of the uterine causes of infertility can be easily diagnosed using hysteroscopy. Moreover, we frequently predict tubal patency at hysteroscopy by noticing suction of air bubbles by the patent ostium.

Office hysteroscopy is an exciting modern diagnostic tool with expanding popularity all over the world [2]. Adding vaginoscopic approach to office hysteroscopy is an extra simplification of the procedure with elimination of pain during

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examination [3]. Delicate instrumentation of operative office hysteroscopy enabled successful operations even through an intact hymen [4].

Regarding the role of vaginoscopic office hysteroscopy (VOH) in infertility, a lot of the published work on VOH demonstrates the feasibility of the procedure and highlights the possible advantages and the skills of the surgeons. The question is not whether the procedure is feasible or not, but whether VOH is superior to and beneficial to a particular patient as well as cost effective for the community at large. This study aims to estimate the safety, efficacy, and patient acceptability of adding VOH to the routine infertility diagnostic work-up for evaluation of the endometrial cavity.

Patients and methods

After obtaining the acceptance of the ethics committee of Assiut Faculty of Medicine, this study was conducted in the outpatient hysteroscopy unit of the Woman's Health University Hospital from February 2011 to December 2012. It included infertile women referred for diagnostic/operative laparoscopy. Patients were randomly classified into two groups using a computer-generated numbers in sealed envelopes with 1/1 ratio. Dr. Islam was the one responsible for the process of randomization and patient allocation. Group A included usual infertility work-up in the form of normal hormonal profile, basic transvaginal ultrasonography (TVS), normal husband's semen analysis, and a recent HSG. Group B included the same diagnostic tools in addition to VOH. Sample size was estimated utilizing (PS) computer program. For detecting assumed 15 % difference in the rate of abnormal intrauterine findings between group A (10 %) and group B (25 %) with 80 % power at 5 % significance level, it was found that 78 patients are required in each group. Exclusion criteria included suspected pregnancy, active pelvic infection, severe co-morbidity, e.g., severe cardiac, neurologic, or chest disease, other medical contraindications to pregnancy, male factor, or abnormal hormonal profile of both couples. All patients had clear description of the study and were asked to participate. An informed consent was taken from those who agreed.

The included patients were subjected to complete history taking and meticulous physical examination. VOH was done using a 2.9-mm 30° rigid scope with 4-mm single flow sheath (Promis, Tutlingen, Germany), and the uterus was distended with normal saline at 100 mmHg generated from a pneumatic cuff of sphygmomanometer. We used a 250-W Xenon light source for the video OH. The scope was introduced gently through the vulva, vagina, and then the cervical canal without previous dilatation using the saline to expand the way in front of the scope. The cervical canal was examined for polypi, Nabothian cysts, or micropolypi suggestive of chronic cervicitis. The best view of the entire uterine cavity is obtained when the hysteroscope is placed at the junction of the lower

uterine segment and upper cervical canal. The uterine cavity was examined systematically starting by its anterior and posterior walls, the fundus, and the borders, and examination was considered complete if the both tubal ostia were reached describing any gross pathology, e.g., septum, adhesions, polyp, myoma, growth, etc. The primary outcome measure was the feasibility and ability for the diagnosing intrauterine abnormalities by VOH versus HSG. Secondary measures included the accuracy of combination of methods in diagnosing the cause of infertility and patient acceptance of VOH.

Categorical data were described as percentages and compared with chi square and exact Fischer tests. Continuous data were described as mean±SD or median (according to data distribution) and compared using *t* test, Mann-Whitney test, and ANOVA test with LSD post hoc test when appropriate. Correlation was used when appropriate. Simple agreement was calculated as a percentage of the number of cases agreed by both methods as positive plus those agreed by both methods as negative and divided by the total number of cases. A probability value (*P* value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY, USA) and SPSS 16 (Statistical Package for the Social Science; SPSS Inc., Chicago).

Results

We examined 659 patients referred for diagnostic/operative laparoscopy. Of those, 215 had abnormal semen parameter(s), 201 had an ovulation, 63 had no HSG, and 48 refused to participate (some women had more than one cause for exclusion).

This study comprised 156 infertile women who were divided into two groups (78 each), and all completed all examinations. Group A included patients without VOH, while group B included women with VOH. There was no statistically significant difference between both groups regarding age distribution ($P=0.26$), type and duration of infertility ($P=0.73$), or sociodemographic data ($P=0.32$). The same insignificant difference was applied for HSG findings in both groups (Table 1). However, laparoscopic findings were evidently abnormal in group A than group B with a statistically significant difference as shown in Table 2. VOH detected 50 % abnormal endometrial cavity in group B with a significant superiority over HSG (Table 3). Diagnostic indices of VOH and HSG are shown in Table 4. There was agreement in the diagnosis of uterine abnormalities between HSG and VOH in 80 %. Generally, VOH was an acceptable procedure with mild pain and feasible in all except two cases as shown in Table 5.

Table 1 HSG findings of both groups

	Group A (n=78)		Group B (n=78)		P value
	No.	%	No.	%	
Normal cases	52	66.7	50	64.1	0.736
Abnormal cases:	26	33.3	28	35.9	0.736
Uterine abnormalities					
Unicornuate uterus	1	1.3	0	0.0	
Uterine septum	0	0.0	8	10.3	
Arcuate uterus	0	0.0	1	1.3	
Intrauterine adhesions	0	0.0	1	1.3	
Tubal abnormalities:					
Bilateral tubal block	13	16.7	5	6.4	
Unilateral tubal block	9	11.5	3	3.8	
Filling defect	0	0.0	5	6.4	
Pelvic adhesions	3	3.8	5	6.4	

Discussion

There is a general consensus but not evidence-based agreement that basic tests of infertility work-up should include normal semen analysis, ovulation detection test, tubal patency testing, and hormonal profile. Some authors add postcoital test [5]. Non-universal agreement on the steps and stratification of diagnostic tools can be attributed to wide variations of the infertile population regarding age, duration of marriage, primary or secondary infertility, psychologic status of the couple, and the interest of the infertility team. It has been noticed that some centers interested in ART push patients to try IUI or IVF/ICSI without prior laparoscopy or even HSG. Many subsequent failures can be attributed to abnormal uterine cavity or distended hydrosalpingeal tubes which are unfortunately diagnosed too late in many cases. These alarming data call for more strict infertility work-up that should be supported by big infertility societies.

Table 2 Laparoscopic findings of the studied groups

	Group A (n=78)		Group B (n=78)		P value
	No.	%	No.	%	
Normal cases	34	43.6	57	73.1	<0.0001*
Abnormal cases	44	56.4	21	26.9	<0.0001*
Tubal block	11	14.1	9	11.5	
Ovarian abnormalities	14	17.9	6	7.7	
Uterine abnormalities	6	7.7	2	2.6	
Endometriosis	8	10.3	4	5.1	
Extensive adhesions	5	6.4	0	0.0	

*Means highly significant

Table 3 The appearance of endometrial cavity by HSG and VOH among group B population (78 cases)

	HSG		Office hysteroscopy		P value
	No.	%	No.	%	
Normal cases	60	76.9	38	50.0	0.001*
Abnormal cases	18	23.1	38	50.0	0.001*
Endometrial hyperplasia	0	0.0	5	6.6	
Polyp	5	6.4	11	14.5	
Fibroid	0	0.0	4	5.3	
Adhesions	5	6.4	7	9.2	
Septum	8	10.3	11	14.5	
Total	78	100.0	76 ^a	100.0	

^aTwo cases were invisible by office hysteroscopy

*Means highly significant

Infertility related to uterine cavity abnormalities has been estimated to be the causal factor in as many as 10 to 15 %. Moreover, abnormal uterine findings have been found in 34 to 62 % of infertile women. This had been traditionally carried out using HSG. Hysteroscopy despite being a well-known standard diagnostic tool for intrauterine lesions was not widely used for this purpose due to technical difficulties [6,7]. The concept of office outpatient hysteroscopy is expanding worldwide with a lot of publications. In this study, we carried out an infertility work-up algorithm based on four cornerstone steps: semen analysis, HSG, and laparoscopy±office hysteroscopy in 78 women (group B) to judge the value of the latter method. The prevalence of abnormalities was remarkable (50 %). Of these, 14.5 % were uterine or cervical polypi. Similarly, polypi were diagnosed in 21.96 % [8]. We diagnosed uterine septa, submucous tiny myomata, and adhesions in 14.5, 5.3, and 9.2 % of cases, respectively. These figures are more or less similar to other studies [8]. Finally, we found thickened endometrium in 6.6 % women in this study. Detection of delicate endometrial lesions is a marvelous advantage of OH over other diagnostic tools. In a previous study, this team could diagnose endometrial lesions that could not be seen by other tools [2].

Table 4 Diagnostic accuracy of single versus combined tests for assessment of uterine factor among group B

	HSG Vs VOH ^a	VOH+HSG
Sensitivity	39.47	97.4 %
Specificity	100.00	56.2 %
Positive predictive value	100.0	80.9 %
Negative predictive value	62.3	90 %
Accuracy	69.7	59.2 %
AUC	0.697	0.521

^aAgreement between both tests was 80 %

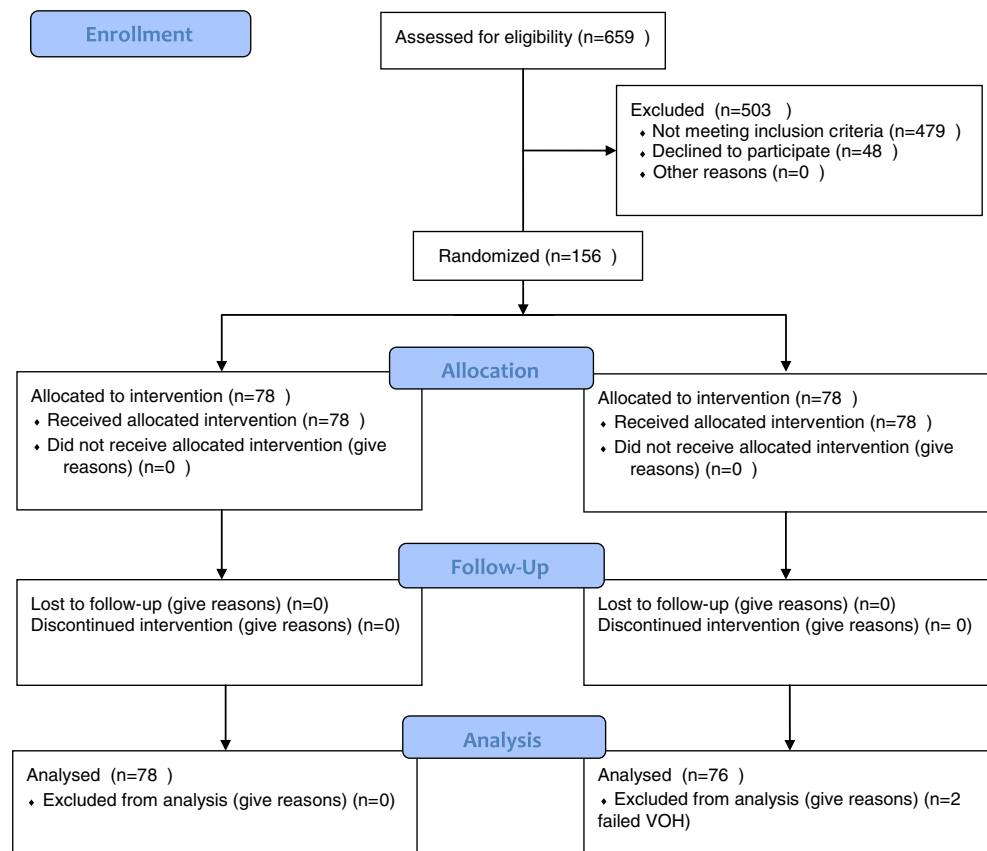
Table 5 Pain grading, acceptability, and feasibility of VOH

	No. (<i>n</i> =78)	Percent
Pain grading		
Mild painful	5	6.4
Moderate painful	3	3.8
Severe painful	1	1.3
Painless	69	88.5
Acceptability		
Tolerable	78	100.0
Not tolerable	0	0.0
Feasibility		
Feasible	76	97.4
Not feasible	2	2.6

In about two third of infertility cases, hysteroscopy findings were not correlated with those found on HSG [9]. Moreover, they reported that 54.3 % of intrauterine adhesions diagnosed on HSG were not found on direct hysteroscopic examination. Diagnosing some missed intrauterine abnormalities with the aid of VOH despite normal HSG would

highlight the central role of this outpatient procedure in eliminating unneeded lengthy induction of ovulation and even IVF/ICSI repeated trials. Furthermore, VOH allows the exact localization of intrauterine lesions and provides a better way than the blunt curettage to ensure complete excision of such lesion. Most importantly, VOH would save money and omit stress for the patient and will improve health care services for the community. Practically, vaginoscopic approach with elimination of speculum insertion and traction on the cervix with a tenaculum had made hysteroscopy as simple as vaginal examination with high patient acceptability of this procedure in this study. Nevertheless, whether adding VOH to the infertility workup prior to DL is better than performing concomitant conventional 4-mm hysteroscopy at the time of DL routinely has not yet been studied. Based on our experience, pre-DL VOH has the advantage of diagnosing any intrauterine abnormalities that would require operative hysteroscopy with proper preparation of the cervix, informing an experienced hysteroscopist, and preparing a suitable operative hysteroscopy set at the time of DL.

In this study, there was 81.6 % of normal laparoscopy that were also normal in HSG and this seems to be logical based on

Fig. 1 CONSORT 2010 flow diagram**CONSORT 2010 Flow Diagram**

the different view they demonstrate (external versus internal). When VOH is combined with HSG, the accuracy is 59.2 %. The degree of agreement was as high as 80 % between VOH and HSG in this conclusion regarding the uterus. Small sample size as well as heterogeneity of infertile women without classification into primary and secondary infertility is a clear drawback of this study. Lack of another group of patients with concomitant conventional hysteroscopy and laparoscopy to be compared with preoperative VOH is an evident disadvantage of this study. From this study, VOH seems to be a feasible, safe, simple, tolerable, and quick outpatient procedure. It can diagnose intrauterine abnormalities in 23.7 % of infertile women with normal HSG. VOH achieves marvelous agreement with HSG in diagnosing uterine abnormalities (96 %). We recommend adding VOH to the routine diagnostic work-up of infertile couples prior to laparoscopy. Nevertheless, whether its use would eventually increase pregnancy rate among infertile women requires a further longitudinal comparative study (Fig. 1).

Conflict of interest Atef M. Darwish, Ahmad I Hassanin, Mahmoud A Abdel Aleem, Ibrahim I Mohammad, and Islam H Aboushama declare that they have no conflict of interest.

Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human

experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 [5]. Informed consent was obtained from all patients for being included in the study.

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