A Simplified Ultrasound Based Infertility Investigation Protocol and Its Implications for Patient Management

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Purpose: To evaluate whether a simplified infertility investigation protocol, focusing on the use of hysterocontrast sonography (HyCoSy), one blood test, and a semen analysis, would be sufficient as an initial screening test to select couples for specific treatment.

Methods: The infertile couples underwent gynaecological examination, cervical sampling for cytology and Chlamydia trachomatis culture, B-mode transvaginal ultrasonography and basic hormonal analyses followed by a HyCoSy, and a semen analysis. A preliminary diagnosis was made for all patients. A management plan for treatment was suggested when possible; otherwise further examinations were recommended. The data were stored for later analysis and the routine investigation protocol was then adhered to and a final diagnosis and treatment were decided upon.

Results: Agreement between the diagnosis based on HyCoSy and our routine protocol was present in 74% of cases ($N = 73$). In 13% ($N = 13$) there was partial agreement. In 36% the HyCoSy based protocol was considered sufficient to suggest treatment.

Conclusions: A simplified approach may lead to a significant reduction in both the time and cost of investigating an infertile couple.

KEY WORDS: hysterosalpingo contrast sonography; hysterosalpingography; infertility; laparoscopy; simplification.

INTRODUCTION

Traditionally, couples suffering from infertility of at least one year have been offered investigations to find a cause for their problem. In addition to a basic gynaecological examination, in a majority of cases these have included either x-ray hysterosalpingography (HSG) or laparoscopy with dye intubation and in many cases both. The time taken to carry out these procedures often lasts for several months or even longer. The aim of the present study was to evaluate if it may be possible to make the investigation of an infertile couple less invasive, less expensive, and less time consuming.

Accordingly, we designed a simplified infertility investigation protocol based on the use of hystero-contrast-sonography (HyCoSy), a blood test, and a semen analysis, to see if this approach could be a sufficiently accurate initial screen to find the cause of infertility for most couples. Several previous studies have compared transvaginal contrast sonography with both HSG, laparoscopy, and hysteroscopy (1–3). These investigations have suggested that HyCoSy may offer more diagnostic information than an HSG and that HyCoSy may replace HSG in many cases. To our knowledge our study is the first report to test this hypothesis.

The aim of the present study was to compare the management plan made using the simplified HyCoSy based investigation protocol (simplified protocol) with that derived from the full protocol routinely used in our clinic (routine protocol).

MATERIAL AND METHODS

Couples suffering from at least one year of infertility attending the Unit of Reproductive Medicine at the Department of Obstetrics and Gynecology, Sahlgrenska University hospital, Göteborg, Sweden were recruited consecutively from November 1995 to October 1996. A total of 99 women with infertility were recruited to the study. Their mean age was 31.7 years (18–41 years) and their mean duration of infertility was 2.5 years (1–7 years). Primary infertility was present in 60% and 80% of the women were nulliparous. For the

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simplified protocol, infertility investigations included hepatitis and HIV serology for both partners. For the male partner a semen analysis was included, and for the woman culture for *Chlamydia trachomatis* from the cervix, pap smear, rubella serology, serum prolactin, and hystero-contrast-salpingography (HyCoSy). Further endocrine tests were performed in suitable cases. HyCoSy examination included a B-mode scan of the uterus and the ovaries, installation of saline for evaluation of the uterine cavity, and Echovist® (Schering AG, Germany) for evaluation of tubal patency. A 1.2 mm balloon catheter (Schering) was inserted to the level of the internal os of the cervix and the cuff slowly inflated with 0.5–2 ml air. An average of 6 ml of sterile saline (range 2–15) was injected into the endometrial cavity in order to achieve distension of the cavity walls. The presence or absence of polyps, submucous fibroids, and synechiae was noted. Ultrasound contrast media (Echovist) was then injected to evaluate tubal patency. This contrast agent consists of galactose monosaccharide microparticles ($50\% < 2 \mu\text{m}$) in a 20% (weight/volume) solution of galactose. A mean volume of 9 ml of contrast was used for each examination (range 2.5–25 ml). The results were recorded for each tube separately, including the presence or absence of contrast flow in three different segments of the tube (isthmic, ampullary, and fimbrial). Fallopian tube patency was defined as being the visualization of a steady flow of contrast agent within the Fallopian tube lasting at least 5 s in one imaged tubal section. In addition it was noted if contrast became visible in the pouch of Douglas. Based on data from these investigations, a preliminary diagnosis and management plan was formulated in all 99 cases by two clinicians working within the fertility unit. In cases where there was doubt of treatment, the management plan proposed further investigations. The data including the preliminary diagnosis and management plan were stored for later analysis. The couples then entered the routine infertility investigation protocol used in our clinic (routine protocol). This usually included a hysterosalpingography (HSG), post-coital test, and laparoscopy.

Hysteroscopy and immunological investigations were performed when suitable.

After completing the routine protocol a definitive final diagnosis and management plan was made by specialists. They were blind to the results obtained using the simplified protocol. The study design and the distribution of patients are illustrated in Fig. 1. If the final diagnosis and management plan was in agreement with that from the simplified protocol, but

offered further diagnostic information or refined the management plan, then the agreement was considered to be partial.

Statistics

The concordance between the diagnosis and management plans from the simplified and routine protocols was evaluated. Fischer's exact test or χ^2 test were used to compare differences in proportions between groups. A *P* value less than 0.05 was considered significant.

RESULTS

The outcome from the simplified and routine protocols was compared. In 73 cases (74%) the diagnosis derived from the two different protocols were in agreement. In 13 cases (13%) there was partial agreement between the protocols and in 13 cases (13%) there was disagreement (Table I).

After completion of both protocols, the simplified protocol was considered sufficient to give a diagnosis and suggestion of treatment in 36 couples. The most common diagnosis in this group were male and hormonal factors. In the remaining 63 couples, the simplified protocol failed to provide a definitive diagnosis and suggestion of treatment, although a preliminary diagnosis was still made. The main preliminary diagnosis in this group were unexplained infertility and tubal factor. In these cases any further investigations that were thought necessary to clarify the situation were specified. The distribution of the preliminary diagnosis in the two groups are shown in Table II.

Of the 26 cases without complete agreement between diagnosis, 24 originated from those 63 couples where the short protocol was considered insufficient and further investigations were felt necessary to clarify the situation. The proposed investigations were distributed as follows: HSG ($N = 2$); hysteroscopy (5); laparoscopy (56); and immunological analyses (4). The major investigation, laparoscopy, was performed in 49 of the 56 proposed patients. The reasons for the seven patients not undergoing laparoscopy were spontaneous pregnancies and different personal reasons to cancel the infertility work-up. Pathology was detected in 32 of the 49 performed laparoscopies. No major complications were seen after the laparoscopic procedures. Infections related to HyCoSy or HSG, which were performed on the same day, were seen in two cases.

Fig. 1. Study design and distribution of patients.

Among the 36 patients where the short protocol was considered sufficient; all preliminary treatment suggestions were in agreement with the final treatment proposals. Among the 63 patients where the short protocol was considered insufficient, two women became

spontaneously pregnant and four couples were divorced or did not complete the work-up for other reasons. In the remaining 57 cases, where no preliminary treatment was considered possible to give, the final treatment suggestions were mainly IVF, insemi-

Table I. Frequency Distribution of Preliminary and Final Diagnosis in 99 Infertile Couples. More than One Diagnosis May Be Applicable for Each Couple.

Diagnosis	Total	No. preliminary diagnoses			No. final diagnoses
		In 73 couples with agreement	In 13 couples with partial agreement	In 13 couples with disagreement	
		Between preliminary and final diagnosis			Total
Unexplained	30	19	3	8	22
Male	27	22	4	1	28 ^a
Hormonal	21	17	2	2	19
Myomas/uterine	9	8	0	1	10
Minor endometriosis	1	1	0	0	13
Major endometriosis	4	2	2	0	6
Tubal	19	15	3	1	23
Adhesions	1	1	0	0	8
Recurrent abortions	7	7	0	0	7
Ovarian cyst	1	1	0	0	1

^a The addition of one male factor infertility in the final diagnosis is explained by a progressive impairment of sperm quality, which was not evident when the preliminary diagnosis was made.

Table II. The Distribution of Preliminary Diagnosis in 36 Couples Where the Simplified Protocol was Considered Sufficient, Compared with 63 Couples Recommended a More Extensive Work-Up. More than One Diagnosis May Be Applicable for Each Couple.

Preliminary diagnosis	Short protocol sufficient for management plan 36 couples N (%)	Short protocol insufficient for management plan 63 couples N (%)	P value
Unexplained	1 (2.8)	29 (46.0)	0.000
Male	20 (55.6)	7 (11.1)	0.000
Hormonal	12 (33.3)	9 (14.3)	0.040
Myomas/uterine	3 (8.3)	6 (9.5)	1.000
Minor endometriosis	0	1 (1.6)	1.000
Major endometriosis	1 (2.8)	3 (4.8)	1.000
Tubal	5 (13.9)	14 (22.2)	0.428
Adhesions	1 (2.8)	0	0.364
Recurrent abortions	2 (0.05)	5 (7.9)	0.208
Ovarian cyst	1 (0.03)	0	

nation with husbands' semen, and fertility surgery (Table III). A summary of the results are presented in Fig. 2. The time period for completing the investigation using the routine protocol was extended by a mean 83 days (SD 55.8, median 77 days, range 23–287), compared with the simplified protocol, considering the time lapse between HyCoSy and laparoscopy.

DISCUSSION

The use of HyCoSy and its implications on diagnosis and treatment constitute the main difference in the studied infertility work-up, compared with a traditional investigation. Contrast sonography has shown to be equivalent to HSG in detecting tubal pathology (1,4–6) and even more accurate in finding uterine pathology (7–8). In comparison with laparoscopy, the HyCoSy has a lower sensitivity, although some authors claim that the method could replace laparoscopy to a considerable extent (1). However, it has to be pointed out that the method requires a lot of training and experience regarding the ability to diagnose tubal pathology (9). In our setting with referral to a radiologist for HSG, it is an advantage for the gynecologist to perform the HyCoSy personally and for the patient to stay with the same doctor.

The main important questions are, however: 1) is it possible to identify couples that need no further investigation; and 2) is there a risk for misdiagnosing and proposal of incorrect treatment when a simplified work-up is used? If the final diagnosis was considered to be the gold standard, 73 of 99 patients were diagnosed by the simplified protocol and would thus be

unnecessarily delayed by the more extensive protocol. However, only in 36 of those 73 patients was the simplified protocol considered sufficient to suggest treatment and to spare superfluous invasive diagnostics. Our study showed a high overall concordance between preliminary and final diagnosis and a complete concordance between preliminary and final treatment for those who were suggested a simplified work-up. There was no case in which an improper treatment was suggested, which probably reflects the high tolerance of further investigations, applied in the study design. There was still a high pathology detection rate in the performed laparoscopies (32/49), which indicates that the model is appropriate for selecting patients for further investigations. One could argue that IVF could have been advised in all 63 cases where further investigation was suggested. In our opinion, that would have been "over-treatment" incurring a higher cost than necessary. The completed work-up gave the suggestions of IVF in only 14 cases. Other common treatments were insemination with husbands' semen, surgery, and hormonal stimulations, pointing at the effect of the work-up to advise for cheaper alternatives as first line treatments.

To calculate the complete effectiveness of the work-up, the outcomes of treatments in terms of pregnancies should have been considered as well, but the study did

Table III. Frequency Distribution of Preliminary and Final Treatment Suggestions in 93 Subfertile Couples

Treatment options	No. preliminary treatments (36 couples)	No. final treatments (93 couples)
Clomiphene citrate	6	12
Ovulation induction with gonadotrophins	4	6
Prolactinemia treatment	0	1
Other hormonal treatment	0	1
Medical endometriosis treatment	0	2
Surgical endometriosis treatment	0	1
Fertility surgery ^a	1	8
IVF/ICSI	21	35
Insemination with husbands semen	1	15
Insemination with donor semen	1	1
Andrology treatment	1	1
Expectancy	0	6
Treatment for recurrent abortions	2	5

^a Includes surgery on tubes, ovaries, uterus and adhesions. One patient was suggested two treatments (cystoperation + IVF).

Fig. 2. Comparative results of simplified and routine protocol in 99 subfertile women.

not provide any information as to what extent the treatments were successful. Other possible investigations that can be considered as alternative in the simplified work-up is chlamydial serology, which has shown to be even more accurate than HSG in predicting tubal infertility (10). If more invasive investigations are considered necessary, the future work-up could possibly replace conventional laparoscopy with minimally invasive endoscopic procedures like microlaparoscopy and transvaginal pelvicoscopy.

We have during the study period adopted a more restrictive policy towards performing laparoscopy in all subfertility cases. There is obviously an economical benefit from the simplified work-up, which besides costs for hospital stay and surgery, also includes a benefit for the patient in terms of fewer visits and absence of sick leave. The other obvious advantage for the patient is the shorter time period for the work-up to be completed, which implies psychological relief.

We conclude from this study that the simplified protocol can be applied in nearly half of the couples attending an infertility clinic and is particularly suitable in couples with male or hormonal factors as the sole reason for infertility. On the other hand, unexplained infertility after a simplified work-up or suspicion of tubal factor still requires a traditional investigation.

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