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Trabajo Original

3D Hysterosalpingo-contrast sonography: Description of the technique and results

Histerosonosalpingografía con contraste 3D: descripción de la técnica y resultados

Virginia Engels Calvo[1], Lucía Serrano González[1], María Martínez-Moya[1], Manuel García-Espantaleón Navas[1], Reyes de la Cuesta Benjumea[1], Luis San Frutos Llorente[1], Ana Royuela Vicente[2], Laura Calles Sastre[1], Palmira Vázquez-Bécquer[1], María del Mar Ríos Vallejo[1] and Tirso Pérez-Medina[1]

[1]Servicio de Ginecología y Obstetricia. Hospital Universitario Puerta de Hierro Majadahonda. Universidad Autónoma. Madrid. [2]Fundación de Investigación Segovia-Arana. Servicio de Estadística Hospital Universitario Puerta de Hierro Majadahonda. Majadahonda, Madrid

Abstract

Objective: To describe the 3-dimensional hysterosalpingo-contrast sonography (3D-HyCoSy) technique and analyze our results with 2 contrast agents: SonoVue® and ExEm Foam®.

Material and methods: Cross-sectional study of 160 infertility patients with unknown tubal patency.

Results: Bilateral tubal patency was diagnosed in 102/153 (66.7%) patients. A similar proportion of bilateral occlusion was observed with both SonoVue® 5/87 (5.7%) and ExEm foam® 4/66 (6.1%) (p = 0.52). Intrauterine disease was suspected in 33/155 (21.3%) patients: 20% (18/90) with SonoVue® and 23.1% (15/65) with ExEm Foam® (p = 0.644). The visual analog scale (VAS) revealed mild pain (VAS ≤ 4: 86.4% [70/81] with SonoVue® vs 86.8% [59/68]) with ExEm Foam® (p = 0.951). A pediatric nasogastric probe was easily used to cannulate the cervical os in 128/159 (80.5%) cases. The volume of ExEm foam® used was lower than that of SonoVue® (median: 3 cc vs 20 cc, p < 0.001).

Conclusion: 3D-HyCoSy is a reliable, well-tolerated, and effortless tool for the sonographic assessment of sterility. The results were similar with both contrast agents.

Key words:

Tubal patency test. Hysterosalpingography. Ultrasound. Infertility. Contrast agent.

Resumen

Objetivo: describir la técnica y analizar nuestros resultados con histerosonosalpingografía con contraste 3D (HyCoSy-3D) utilizando SonoVue® y Exem Foam®.

Material y métodos: estudio retrospectivo de corte transversal en 160 pacientes estériles con permeabilidad tubárica desconocida.

Resultados: el 66,7% (102/153) de las pacientes tuvo permeabilidad tubárica bilateral. El diagnóstico de obstrucción tubárica bilateral fue similar utilizando SonoVue® 5/87 (5,7%) y Exem Foam® 4/66 (6,1%), p = 0,52. Diagnosticamos patología intrauterina en 33/155 (21,3%) de las pacientes, 20% (18/90) con SonoVue® *vs.* 23,1% (15/65) p = 0,644. El dolor percibido resultó leve en la mayoría de los casos (escala visual analógica ≤ 4; 86,4% (70/81) SonoVue® *vs.* 86,8% (59/68), p = 0,951). La canalización cervical fue sencilla con sonda nasogástrica pediátrica en 128/159 (80,5%). Exem Foam® precisó un menor volumen instilado (mediana: 3 cc *vs.* 20 cc, p < 0,001).

Conclusiones: la HyCoSy-3D es una prueba tolerable, sencilla y rentable para el estudio ecográfico en esterilidad. Ambos contrastes mostraron similares resultados.

Palabras clave:

Test de permeabilidad tubárica. Histerosalpingografía. Ultrasonografía. Esterilidad. Medio de contraste.

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Correspondencia:
Virginia Engels Calvo.
Servicio de Ginecología y Obstetricia.
Hospital Universitario Puerta de Hierro.
C/ Manuel de Falla, 1.
28222 Majadahonda, Madrid
e-mail: v_engels_77@hotmail.com

INTRODUCTION

According to the American Society for Reproductive Medicine, ultrasound-based assessment of infertility is the first, essential step in the evaluation of ovarian reserve and associated gynecologic disease (1). In our setting, tubal patency continues to be evaluated mainly using hysterosalpingography (HSG). This approach has clear disadvantages: it is painful, involves complications, uses iodinated contrast medium, and subjects the patient to ionizing radiation (2,3).

In June 2016, we implemented an integral functional and anatomical protocol for the study of the genital-reproductive organs at our center (Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda, Spain). The protocol was based on 3D transvaginal ultrasound with intracavitary contrast, which enables us to evaluate tubal patency. The technique is known as 3D hysterosalpingo-contrast sonography (3D-HyCoSy).

Contrast agents have traditionally included air, saline solution, and, subsequently, more echogenic agents such as SonoVue® (Bracco, Italia). The latter enable enhanced visualization of the tubal lumen but have the disadvantage that they are not specially designed for this purpose, since they are intravenous contrast agents that are generally used for other purposes (eg, evaluation of heart function) (4,5). The contrast agent ExEm Foam® (GynaecologiQ, Delft, The Netherlands) has been on the market since 2007. It contains hydroxyethyl cellulose and glycerol mixed with saline solution to form a foam that enables very clear visualization of the uterine cavity and the Fallopian tubes.

The objective of the present study was to describe 3D-HyCoSy and analyze our results with 2 contrast agents: SonoVue® and ExEm Foam®.

MATERIAL AND METHODS

We performed a cross-sectional retrospective study to evaluate the results obtained with 3D-HyCoSy in all patients who underwent the technique at our center between June 2016 (when the technique was implemented) and October 2017. The inclusion criteria were sterility/infertility in women aged 18-41 years undergoing assisted reproduction who required a tubal patency study and written informed consent to undergo the test. The exclusion criteria were known allergy to the contrast agents (ExEm Foam® or SonoVue®), known tubal obstruction, active pelvic infection, fever of unknown origin, pregnancy, and abnormal vaginal bleeding. Our study was authorized by the Bioethics Committee of Hospital Puerta de Hierro Majadahonda, Madrid, Spain.

Initially, the contrast agent we used was SonoVue®, which is composed of sulphur hexafluoride microbubbles. It is marketed as a powder and solvent for dispersion for injection, and the solution must be prepared immediately before use. We initially used SonoVue® for purely practical reasons: we had decided to apply the technique but did not have an agent that was specially designed for 3D-HyCoSy; therefore we decided to start with an agent that had already been tested elsewhere (6,7,8) and that was available (it is commonly used in the Radiology Department at our center) (Fig. 1).

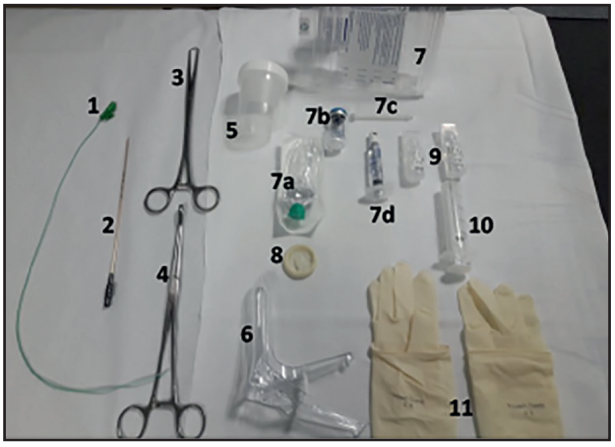

Figure 1. Material used to perform 3D-HyCoSy with SonoVue® contrast. 1. Pediatric nasogastric tube. 2. Kitazato® hard catheter. 3. Pozzi forceps. 4. Foerster clamp. 5. 100-cc sterile container. 6. Vaginal speculum. 7. SonoVue® Kit (a. MiniSpike transfer system, b. Glass vial containing 25 mg of dry lyophilized powder in an atmosphere of sulfur hexafluoride, c. Plunger rod for the syringe containing solvent, d. Glass syringe containing solvent, prefilled with 5 ml of injectable sodium chloride solution 9 mg/mL [0.9%]) 8. Vaginal probe cover. 9. 10-cc vials of saline solution. 10. 10-cc syringe. 11. Sterile gloves.

In May 2017, ExEm Foam® was approved by our Purchasing Department. From this moment onward, we performed 3D-HyCoSy with ExEm Foam®, which was specially developed for the technique. The product comes in 2 x 10-mL syringes, one of which contains 5 mL of ExEm® gel (hydroxyethyl cellulose and glycerol) and the other contains 5 mL of ExEm® water (purified water), as well as a coupling device that makes it possible to create a foam of air microbubbles (9,10) (Fig. 2). The fact that we used 2 different contrast agents over time enabled us to observe and, to the best extent possible (this was not a randomized study), compare the principle characteristics of each (see below).

Before performing 3D-HyCoSy, we used 2D ultrasound to evaluate the pelvic organs. The procedure was subsequently programmed for the immediate postmenstrual phase (days 6 to 12). Once known allergies had been ruled out, patients were premedicated with 1 g of oral azithromycin (taken the night before the test) and 1 tablet of oral Buscapina Compositum® 250 mg/10 mg (taken 1 hour before the test).

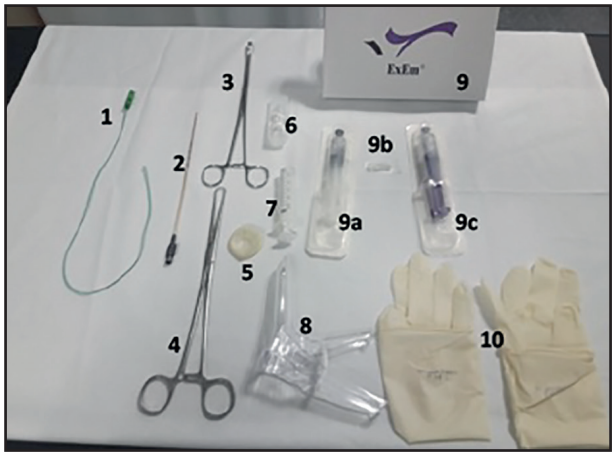

Figure 2. Material used to perform 3D-HyCoSy with ExEm Foam®. 1. Pediatric nasogastric tube. 2. Kitazato® hard catheter. 3. Foerster clamp. 4. Pozzi forceps. 5. Vaginal probe cover. 6. 10-cc syringe of saline solution. 7. 10-cc syringe. 8. Vaginal speculum. 9. ExEm Foam® Kit (a. ExEm-gel, b. ExEm syringe assembly device, c. ExEm-water). 10. Sterile gloves.

3D-HyCoSy was always performed by 2 gynecologists: one to insert the catheter and infuse the contrast and the other to perform the ultrasound. A specialist nurse prepared the material (Figs. 1, 2). The team comprised 3 staff gynecologists and 2 trainees.

Transvaginal ultrasound was performed with a GE Voluson 730 Pro ultrasound device (GE Healthcare, Milwaukee, WI, USA) equipped with a 3D endovaginal transducer (6-12 MHz) and an abdominal 2D transducer (2-7MHz).

In order to simplify the technique and straighten the uterocervical angle, patients came to the test with a full bladder. The internal cervical os was cannulated once the cervix was visualized using a Unidix vaginal speculum. We then introduced a pediatric nasogastric tube (Unomedical CH6, ConvaTec Limited, Deeside, UK) across the cervix with the help of a reusable Foerster clamp and passing the nasogastric tube through one side of the speculum to facilitate subsequent withdrawal. If we were unable to cannulate the internal cervical os, we used a hard Kitazato® catheter and gripped the cervix with reusable Pozzi forceps in the more complicated cases. Once the catheter was inserted into the cavity, we checked its placement using abdominal ultrasound and flushed it with 1-2 cc of 0.9% saline in doubtful cases. If the process was completed successfully, we removed the speculum carefully in order not to move the catheter.

Once the catheter was checked, the first step in carrying out the anatomical-functional study of the internal genital organs was to evaluate the presence of associated gynecologic disease (uterus and adnexal structures) and perform a follicle count for each ovary.

The next step was to infuse the contrast agent and begin the ultrasound study. All images and all 3D ultrasound studies were obtained in the penetration mode in sepia to improve visualization of the contrast agent inside the genital tract. For both contrasts, we first acquired a 3D image of the uterus in the sagittal plane in order to subsequently make a 3D reconstruction of the endometrial cavity in the coronal plane. We did so by adjusting the 3D image to the sagittal plane of the uterus to cover the area from the cervix to the fundus and thus visualize the whole of the endometrial line in relief thanks to the echogenicity of the contrast agent. The sweep angle was the maximum allowed, 120º, with high-quality acquisition. With both the patient and the probe immobile, we performed the automatic volume acquisition, which took a few seconds. The volumes were saved to an external hard disk and evaluated offline in such a way that we were able to classify the morphology of the uterus after 3D reconstruction in the coronal plane according to the 2013 proposal of the European Society of Human Reproduction and Embryology (ESHRE) (11) (Figs. 3, 4).

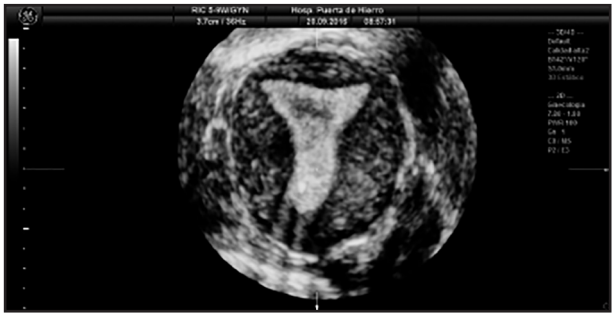

Figure 3. Normal cavity in 3D-HyCoSy.

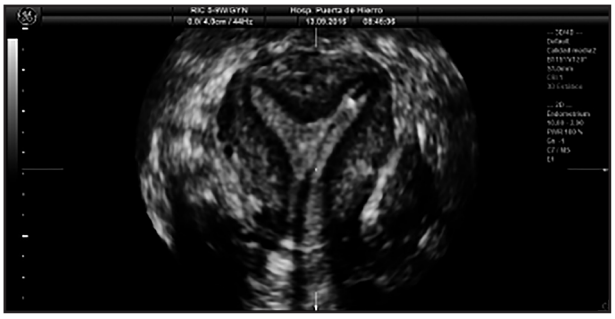

Figure 4. Partial septate uterus (class U2a ESGE) in 3D-HyCoSy.

The technique used to evaluate tubal patency was noticeably different for each contrast. In the case of SonoVue®, infusion of the contrast agent had to be synchronized with the evaluation of the Fallopian tube under study, since this contrast agent is not very dense and only remains in the tube for a short time. This technique requires a certain degree of training and skill using the vaginal probe. In the case of ExEm Foam®, which has a longer half-life inside the

tubes (5-7 minutes, according to ExEm Foam Frequently asked questions (12)), we infused the contrast agent and proceeded to evaluate the tubes. A video and photographs of the flow (or absence of flow) of the contrast agent across the tube were taken (Figures 5 to 9).

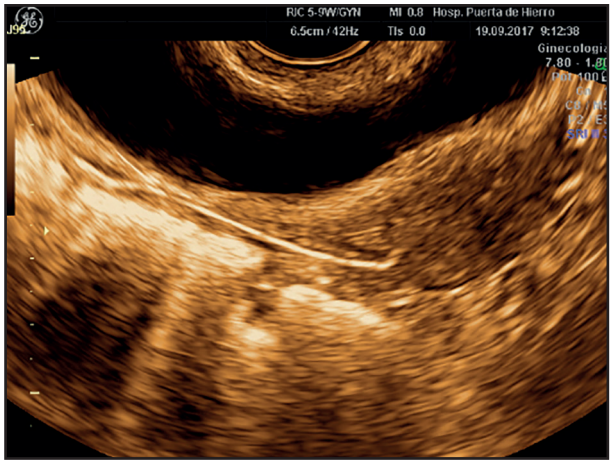

Figure 5. Right tube patent, ExEm Foam®.

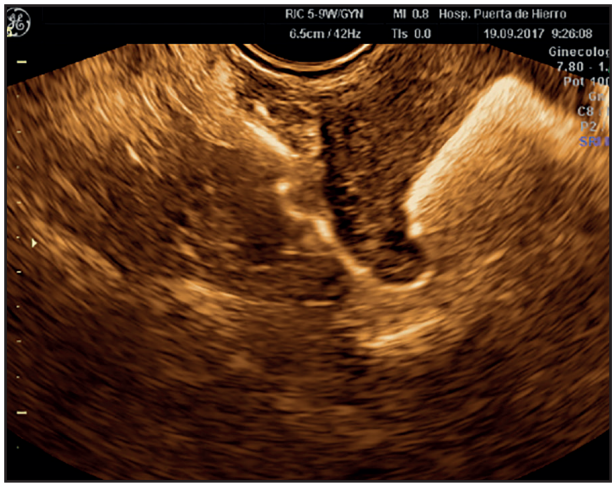

Figure 6. Right tube beaded, ExEm Foam®.

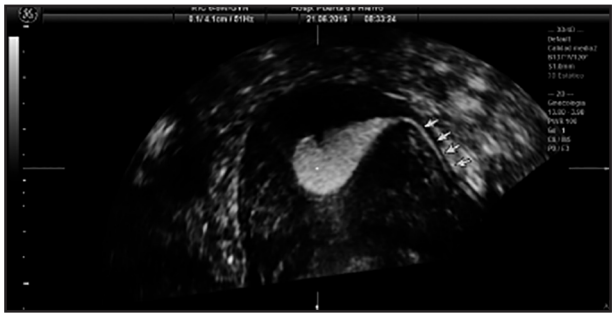

Figure 7. Left tube (arrows) patent, SonoVue®.

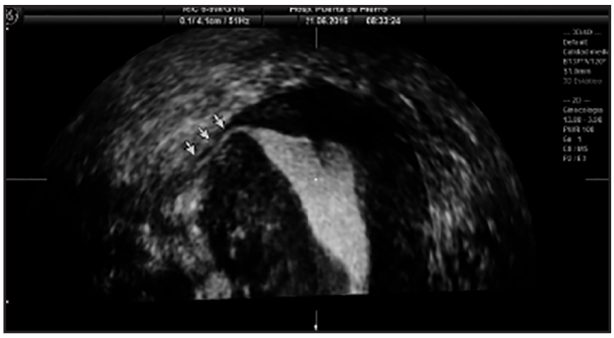

Figure 8. Right tube (arrows) patent, SonoVue®.

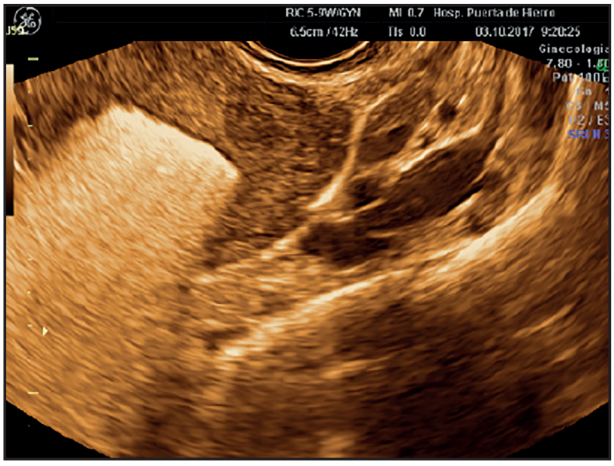

Figure 9. Left tube, ExEm Foam®.

Immediately after the test had finished, the patient was questioned about any pain felt during the procedure with the help of a visual analog scale (VAS).

The patient remained under observation for a few minutes after the test so that immediate complications could be ruled out. The report with the results of the test was provided immediately. Once the process was finished, the patient was given a new appointment during the following weeks to ensure that no complications had arisen, to evaluate the results of other tests, or to start the ovarian stimulation cycle with the following menstrual period.

The parameters recorded for each case were as follows: type of contrast agent, cannulation method (nasogastric tube, Kitazato® catheter, Kitazato® catheter with the aid of Pozzi forceps, or unable to cannulate), volume (cc) of contrast agent used, patency of each tube (visualization of contrast [unilateral, bilateral, or no patency observed]), diseases of the uterine wall, diseases of the uterine cavity, adnexal disease, antral follicle count, and maximum pain felt by the patient according to the VAS (scored from 0 [no pain] to 10 [maximum pain imaginable]). The number of antral follicles was converted into a categorical

variable according to which patients with a mean < 5 follicles between both ovaries were classed as having low ovarian reserve, those with 5-10 follicles were classed as having a normal ovarian reserve, and those with > 10 follicles were classed as having a high ovarian reserve (13). Patients with suspected intracavitary conditions were referred—where possible during the same menstrual cycle—to our Hysteroscopy Unit. Where indicated, patients with at least 1 patent tube initiated a cycle of homologous artificial insemination with ovarian stimulation. In contrast, those with 2 nonpatent tubes were referred to the Radiology Department for HSG, given that this is the gold standard for evaluating tubal patency. All variables were recorded on an Excel spreadsheet, which was subsequently transferred to SPSS®, Version 24, for analysis.

Continuous variables were expressed as mean and standard deviation, maximum, and minimum; categories were expressed as number and percentage. We used the Mann-Whitney test to estimate the differences in the results obtained for quantitative variables. Qualitative variables were analyzed using the chi-square test. All variables with a p value < 0.05 were considered significant.

RESULTS

Between June 2016 and October 2017, we performed 3D-HyCoSy on 160 patients, that is, a total of 319 Fallopian tubes (1 patient had undergone unilateral salpingectomy because of ectopic pregnancy). The mean age of the patients was 34.04 (± 3.413) years (21-41).

Before performing 3D-HyCoSy, we detected intracavitary disease (eg, septa, polyps, myomas) in 12/157 (7.6%) patients who underwent 2D ultrasound at the first visit to assess sterility. We found that the cavity was normal in 145/157 cases (92.4%).

In total, 56/143 patients (39.2%) had a low ovarian reserve, 73/143 (51%) had a normal reserve, and 14/143 (9.8%) had a high reserve.

We detected an associated gynecologic condition that did not affect the cavity (ovarian cysts or fibroids that did not deform the cavity) in 21.3% of cases (34/160).

Data on tubal patency were available for 153 of the 160 patients who underwent 3D-HyCoSy (95.625%). In 6 cases we did not record data for at least 1 of the tubes. The seventh case was that of a patient in whom the internal cervical os could not be cannulated, thus preventing us from performing the technique. In total, we observed bilateral patency in 102/153 patients (66.7%) and unilateral patency in 42/153 patients (27.5%). Obstruction was bilateral in only 9/153 patients (5.9%) (Table I). Of the 153 patients in whom tubal patency could be evaluated, 87 (56.9%) underwent the test with SonoVue® and 66 (43.1%) with ExEm Foam®. We found no statistically significant differences with respect to the diagnosis of tubal patency between the groups: 47/66 cases of bilateral patency (71.2%) with ExEm Foam® vs 55/87 (63.2%) with SonoVue®. Similarly, no statistically significant differences were found for the diagnosis of bilateral tubal obstruction: 4/66 (6.1%) vs 5/87 (5.7%); p = 0.52 (Table I). When each tube was evaluated separately, we saw that the right tube was patent in 67/90 patients (74.4%) with SonoVue® and in 59/70 (84.3%) with ExEm Foam®; in the case of the left tube, the values were 70/90 (77.8%) vs 52/70 (74.3%), respectively.

Table I.
Evaluation of tubal patency using 3D-HyCoSy

Contrast	Bilateral patency	Unilateral patency	Bilateral occlusion	p-value
SonoVue®	55/87 (63.2%)	27/87 (31.0%)	5/87 (5.7%)	0.52 [(a)]
Exem Foam®	47/66 (71.2%)	15/66 (22.7%)	4/66 (6.1%)	
Total	102/ 153 (66.7%)	42/153 (27.5%)	9/153 (5.9%)	

[(a)] *Pearson chi-square.*

Of the 9 bilateral obstructions detected using 3D-HyCoSy, 1 corresponded to septate uterus with a large ovarian teratoma that considerably distorted the location of the tubes in the pelvis. HSG revealed that both tubes were in fact patent. In another case, the patient had undergone unilateral laparoscopic salpingectomy owing to ectopic pregnancy, and the contralateral tube was seen to be have a beaded appearance. Two patients refused to undergo HSG and were directly scheduled for in vitro fertilization, and a further 2 patients did not undergo HSG for other reasons. In 3 patients, HSG revealed unilateral tubal patency, albeit with stasis of the contrast agent at the level of the tube.

3D reconstruction of the uterine cavity in the coronal plane revealed intracavitary involvement in 21.3% of patients (33/155), although no statistically significant differences were observed between the 2 contrast agents (Table II) (Figs. 8 and 9). It is noteworthy that 2D ultrasound revealed intracavitary involvement in 7.6% of patients (see above).

We initially tried to cannulate the internal cervical os using a pediatric nasogastric tube (see above). When the contrast agent could not be delivered to the cavity, we inserted a rigid insemination catheter (Kitazato® hard). Only in very difficult cases did we straighten the uterocervical angle with Pozzi forceps to ease the passage of

the catheter. We managed to insert contrast medium into the cavity using a nasogastric tube in 128/159 patients (80.5%), inserted a hard catheter in 24/159 (15.1%), and used Pozzi forceps in only 7/159 (4.4%). In this case, we did observe statistically significant differences between the 2 contrast agents in terms of being able to cannulate the cervix with the nasogastric tube alone: 78/89 (87.6%) patients in the SonoVue® group vs 50/70 (71.4%) in the ExEm Foam® group; p = 0.034 (Table III).

Table II.
Evaluation of the endometrial cavity using 3D-HyCoSy

Contrast agent	Cavity normal	Cavity affected	p-value
SonoVue®	72/90 (80%)	18/90 (20%)	0.644[(a)]
Exem Foam®	50/65 (76.9%)	15/65 (23.1%)	
Total	122/155 (78.7%)	33/155 (21.3%)	

[(a)] Pearson chi-square.

Table III.
Type of cervical cannulation

Contrast agent	Nasogastric tube	Hard catheter	Pozzi forceps	p-value
SonoVue®	78/89 (87.6%)	8/89 (9.0%)	3/89 (3.4%)	0.034 [(a)]
Exem Foam®	50/70 (71.4%)	16/70 (22.9%)	4/70 (5.7%)	
Total	128/159 (80.5%)	24/159 (15.1%)	7/159 (4.4%)	

[(a)] Pearson chi-square.

The volume of contrast agent instilled was also significantly different in each group: median of 20 cc in the SonoVue® group vs 3 cc in the ExEm Foam® group; p < 0.001 (Table IV).

Finally, we decided to evaluate pain resulting from the test using a VAS. A total of 129/149 patients (86.6%) reported pain of ≤ 4 on the VAS; in other words, most patients considered pain associated with the procedure as absent or mild (14). We found no significant differences in the pain perceived according to the contrast agent used (Table V). We then evaluated whether pain could be due to the technique used to cannulate the cervix. Table VI shows that the percentage of patients cannulated using the nasogastric tube and who felt pain ≤ 4 on the VAS was significantly higher (109/119 [91.6%]) than those in whom contrast was introduced using a hard catheter

Table IV.
Volume of contrast agent injected in 3D-HyCoSy

Contrast agent	Median cc	Mean cc (SD)	p-value
SonoVue®	20.0 cc	23.36 cc (±10.10)	0.000 [(b)]
Exem Foam®	3.0 cc	3.62 cc (±1.29)	

[(b)] Mann-Whitney.

Table V.
Pain perceived during 3D-HyCoSy

Contrast agent	VAS*£ 4	VAS* > 5	p-value
SonoVue®	70/81 (86.4%)	11/81 (13.6%)	0,951[(a)]
Exem Foam®	59/68 (86.8%)	9/68 (13.2%)	
Total	129/149 (86.6%)	20/149 (13.4%)	

[(a)] Pearson chi-square.
** VAS, visual analog scale.*

Table VI.
Pain according to difficulty cannulating the cervix (without taking into account the type of contrast agent)

Cannulation	VAS*£ 4	VAS* > 4	p-value
Nasogastric tube	109/119 (91.6%)	10/119 (8.4%)	0.001[(a)]
Hard catheter	15/23 (65.2%)	8/23 (34.8%)	
Pozzi forceps	4/6 (66.7%)	2/6 (33.3%)	
Total	128/148 (86.5%)	20/148 (13.5%)	

[(a)] Pearson chi-square.
** VAS, visual analog scale.*

(15/23 [65.2%]) or a hard catheter with Pozzi forceps (4/6 [66.7%]) (p < 0.001) (Table VI). Lastly, we asked whether the pain reported varied with the type of cannulation in each group and learned that the pain perceived with SonoVue® increases with the degree of difficulty involved in cannulation (p < 0.001), whereas with ExEm Foam®, the most intense pain does not seem to be associated with the cannulation procedure (Table VII). Among patients whose cervix was cannulated using a nasogastric tube, those in the ExEm Foam® group reported more intense pain than those in the SonoVue® group. The opposite was observed for those in whom cannulation was moderately difficult (hard catheter) or very difficult (hard catheter with Pozzi forceps), namely, women in the SonoVue® group reported

Table VII.
Pain according to contrast medium and type of cervical cannulation

Cervical cannulation	SonoVue®			Exem Foam®		
	VAS*£ 4	VAS* > 4	p-value	VAS*£ 4	VAS* > 4	p-value
Nasogastric tube	65/70 (92.9%)	5/70 (7.1%)	0.000[(a)]	44/49 (89.8%)	5/49 (10.2%)	0.479[(a)]
Hard catheter	3/8 (37.5%)	5/8 (62.5%)		12/15 (80%)	3/15 (20%)	
Pozzi forceps	1/2 (50%)	1/2 (50%)		3/4 (75%)	1/4 (25%)	
Total	69/80 (86.3%)	11/80 (13.8%)		59/68 (86.8%)	9/68 (13.2%)	

[(a)] Pearson chi-square.
** VAS, visual analog scale.*

more intense pain than those in the ExEm Foam® group. The level of pain was very disperse, especially in patients cannulated with a hard catheter and assessed with SonoVue® (Fig. 10).

We observed no severe complications in patients undergoing 3D-HyCoSy, at least in the short and medium terms.

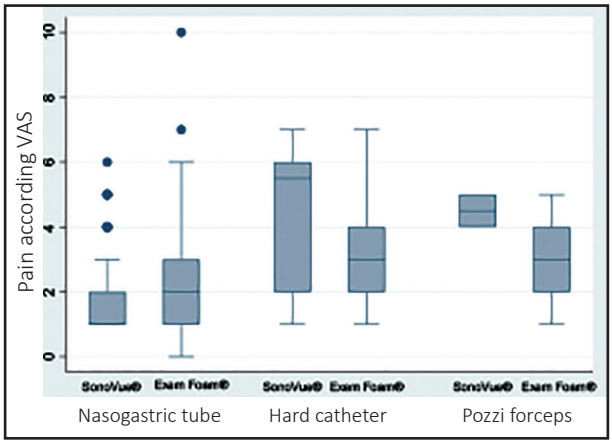

Figure 10. Pain according to contrast medium and type of cervical cannulation. In the group of patients where cannulation was successful with the nasogastric tube, those in whom ExEm Foam® was used reported more intense pain than those in whom SonoVue® was used. In contrast, in patients whose cannulation was moderately difficult (hard catheter) or very difficult (hard catheter and Pozzi forceps), the opposite occurred, namely, women in the SonoVue® group reported more intense pain than those in the ExEm Foam® group. Levels of pain vary widely, especially in patients in the SonoVue® group cannulated using the hard catheter.

DISCUSSION

Starting in June 2016, we referred all patients from our Reproduction Unit who were candidates for ovarian stimulation, homologous artificial insemination, or in vitro fertilization to undergo 3D-HyCoSy. Until then, HSG was only provided to those patients in whom the patency of at least 1 tube was an essential condition for insemination. The technique was not applied in women undergoing in vitro fertilization. Nevertheless, when the 3D-HyCoSy was implemented, we decided to offer the technique to all those patients who wished to undergo it, since it provides information on many more parameters than tubal patency (see below); in addition, the test is easy to perform and has a low complication rate (15). In fact, saline infusion sonography has been proposed as an essential procedure when screening for intracavitary disease (submucosal fibroids, polyps, and uterine adhesions/abnormalities) before assisted reproduction techniques (16).

We recorded an overall bilateral tubal patency rate of 66.7%; the contrast agent could not be observed in either tube in 5.9% of cases. Other authors have reported bilateral tubal patency in 81.8% of cases and bilateral occlusion in 1.5% of cases with HyCoSy (15). If we compare these findings with those considered gold standard such as chromopertubation and HSG, the results of a meta-analysis published in 2016 by Alcázar et al (17) show that, compared with chromopertubation and HSG, HyCoSy has a sensitivity for the detection of tubal occlusion of 98% and a specificity of 90%.

Of note, the prevalence of intracavitary disease in our study was 21.3% with 3D ultrasound compared with 7.6% with 2D ultrasound. In this respect, our group previously demonstrated that findings of endometrial disease with 3D-HyCoSy correlated with hysteroscopy findings (18). Therefore, it seems that 3D-HyCoSy provides very important information with respect to intracavitary diseases that are highly prevalent in sterile patients and that can lead to a poor prognosis of pregnancy.

We found that assessment of tubal patency with 3D-HyCoSy required greater expertise and speed with

SonoVue®, since the window for visualizing the passage of the contrast agent through the tube is small, in contrast with ExEm Foam®, which remains in the uterine cavity and tubes for longer (12). Therefore, it was occasionally necessary to extend the length of the test and instill a greater quantity of the agent, since we had to administer various boluses to be able to visualize the tubes correctly in some cases. Nevertheless, these nuances are difficult to evaluate with the variables we collected. For this reason, and given that ExEm Foam® is specifically designed for evaluation of the female internal genital tract and has proven not to be embryotoxic (19), we prefer to use ExEm Foam®. In fact, we currently perform all our tests only with hydroxyethyl cellulose foam (9). In addition, it is worth noting that the volume of contrast instilled is much lower with ExEm Foam®.

We draw attention to 2 factors for which other authors report different findings (10). First, we did not detect problems with respect to reflux of the contrast medium across the cervix. In fact, we did not even have to use balloon devices to instill the contrast medium, probably because most of the patients in the present study were nulliparous and the likelihood of reflux was lower. Second, it is noteworthy that the technique completely failed in only 1 case, since we were unable to cannulate the cervix.

Also noteworthy is the fact that the cervix was cannulated more often with the nasogastric tube in the SonoVue® group (78/89 [87.6%] vs 50/70 [71.4%]; p = 0.034). In fact, the cervix is cannulated before the contrast agent is introduced; therefore, the results should be similar for both groups. We believe that the difference arose because, as ExEm Foam® is denser, it is more difficult for it to reach the uterus, with the result that it requires better cannulation of the cervix than with SonoVue®, which is a more fluid agent.

Finally, we would like to stress that one of the main advantages of 3D-HyCoSy is the fact that we do not have to depend on another department, thus enabling us to obtain all the data in a single session. 3D-HyCoSy provides information not only on tubal patency, but also on associated gynecologic conditions, through accurate evaluation of the uterine cavity and an ultrasound study of the ovarian reserve simultaneously. Therefore, we believe that 3D-HyCoSy is the ideal tool for the anatomical-functional study of the genital-reproductive organs. Furthermore, in contrast with patients undergoing HSG, those undergoing 3D-HyCoSy do not receive ionizing radiation, and no severe adverse reactions to the contrast agents used have been reported (9).

In conclusion, 3D-HyCoSy has a high diagnostic yield and enables comprehensive assessment of the internal genital organs. In addition, the technique is simple to perform and leaves the gynecologist completely free to carry out a full ultrasound study of the patient's reproductive health.

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