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Echovist-200 as an Ultrasound Contrast Medium for Hysterosalpingocontrast Sonography

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ABSTRACT

Objective To assess image quality and tolerance of Echovist-200 as a hysterosalpingocontrast medium.

Design Open clinical trial

Setting Chiang Mai University Hospital

Subjects Infertile women who required evaluation of tubal or uterine abnormalities.

Intervention The uterus and fallopian tubes were assessed by both plain ultrasound and hysterosalpingocontrast sonography using Echovist-200.

Main outcome measures The primary outcome variable was the image quality of the internal genitals after the use of Echovist-200. Secondary variables included the presence or absence of uterine and tubal abnormalities, pain and other adverse events.

Results Fifty patients were enrolled into the study. The mean age was 32.7 ± 4.2 years, the mean volume of Echovist-200 used was 10.9 ± 3.9 ml and the mean duration of examination was 6.8 ± 3.0 minutes (mean ± standard deviation). Seven insertions of catheter were problematic and one had balloon rupture. Image quality after instillation of Echovists-200 was rated as good in all cases. Both tubes were patent in 34 patients (68%), patent on one side in 13 (26%), occluded bilaterally in 2 (4%) and 1 tube was not assessable (2%). Forty eight patients (96%) experienced a total of 58 adverse events. Pelvic pain was present in 24 of 50 (48%).

Conclusion The use of Echovist-200 in HyCoSy enhances image quality for the evaluation of the internal genitals. HyCoSy showed good diagnostic performance in the evaluation of the tubes and uterus. The procedure was safe with minor adverse events.

Key words: Echovist-200, hysterosalpingo contrast sonography, HyCoSy, ultrasound

Abnormalities of the fallopian tubes and uterus are common causes of female infertility. Assessment of tubal patency is an essential step in the investigation of infertile couples.[1]

Conventional methods include X-ray hysterosalpingography (HSG) and chromolaparoscopy. HSG involves radiation exposure while laparoscopy needs surgical intervention that must be done in an operating room under regional or general anesthesia. Hysterosalpingocontrast sonography (HyCoSy) is an attractive alternative as it involves no radiation or surgery, and it can be done in an office setting without the use of anesthesia.

Dextran and saline solutions were previously used as contrast media in HyCoSy. However, they produced less intense contrast effects and made it difficult to evaluate tubal patency and uterine morphology. Echovist-200 (Schering AG, Berlin) is a suspension of soluble galactose microparticles in an aqueous galactose solution (20% weight by volume). It acts as a strong acoustic scatter medium and thus allows better visualization of the uterine cavity and tubal status at ultrasound examination. The objectives of this study were to further assess the diagnostic efficacy, safety and tolerance of Echovist-200 in HyCoSy for the diagnosis of fallopian tube patency and uterine abnormalities among Thai women in our center.

Materials and Methods

The Ethical Committee of the Faculty of Medicine, Chiang Mai University, approved the study. Detail of the study was explained to eligible subjects and written informed consent was obtained prior to entry into the study.

Women were invited to participate if they: 1) had congenital uterine anomalies; 2) had other suspected uterine abnormalities such as synechiae or benign tumors involving endometrial contour; 3) required evaluation of tubal patency. They were excluded from the study if they: 1) had known or suspected acute or chronic pelvic inflammatory disease; 2) had galactosemia; 3) were under 18 years of age; 4) had known or suspected intact pregnancy; 5) were in lactation period; 6) were critically ill or medically unstable; 6) had received any contrast material within the past 48 hours prior to the study; 7) had abnormal vaginal bleeding; 8) had a risk of spreading infections or malignant cells from the genital tract; 9) had mental retardation; 10) had language or geographic barrier that precluded follow-up by visit or telephone call 24 hours after the procedure.

Demographic data, medical history and indications for HyCoSy were recorded on standardized forms. General physical examination and pelvic examination were then performed. All HyCoSy procedures were done in the first half of the menstrual cycle. Before administration of Echovist-200, a plain sonographic examination was carried out by a single observer (O.S.) to assess the image quality of the uterus and fallopian tube. The results were recorded as “good”, “sufficient”, “poor” or “no imaging”. Sonographic images were obtained using Aloka SSD 620, equipped with a 5 Mhz electronic sector-scanning transvaginal probe.

An assessment was also given as to whether the uterus was normal, abnormal or not assessable. After the plain scan was completed, the cervix and the vagina were cleaned with antiseptic solution. An intrauterine balloon catheter was inserted into the uterine cavity and the balloon was inflated carefully with 2 ml of sterile saline. The vaginal ultrasound transducer covered with a sterile glove was then inserted into the vagina. Echovist-200 was injected slowly into the uterine cavity and fallopian tubes. Video recording was done during the operation. Images were rated again as “good”, “sufficient”, “poor” and “no imaging”. This rating was to be compared with rating of images before contrast perturbation.

Echovist-200 was supplied by Schering AG, Germany in 2 components: a vial containing D-galactose microparticles (3 g) and a vial containing 20% D-galactose carrier solution (13.5 ml). Echovist-200 suspension (200 mg/ml) was prepared by transferring galactose solution into the vial containing the microparticles. The vial was then immediately shaken vigorously for about 5 seconds and the homogenous, milky-white suspension was

used within 5 minutes in order to obtain reproducible contrast effects.

After the procedure, the patients were allowed to go home and were contacted 24 hours later by telephone, asking about any adverse effects.

For quantitative variables, descriptive statistics (N, mean, median, standard deviation, minimum and maximum) were to be calculated and used to generate appropriate tables. Frequency tables would be constructed for qualitative variables.

Results

The study was completed in all 50 enrolled cases. Mean patients' age (± S.D.) was 32.7 ± 4.2 years (range 23-44 years). Infertility, with or without tubal obstruction was the reason for the examination in 46 patients (92%). Four (8%) were evaluated for suspected uterine abnormality. Twenty-nine women (58%) were nulligravida. Of the 21 women (42%) with previous pregnancies, 13 had delivered at least one live birth, 6 had spontaneous miscarriages and 2 had ectopic pregnancies.

Each woman in this study required only one vial of Echovist-200 for the procedure. The mean volume (± S.D.) used was 10.9 ± 3.9 ml of Echovist-200 (range 4 - 15 ml, mode = 15 ml). On the average, examination took 6.8 ± 3 minutes (range 4 - 18 minutes, mode = 5 minutes).

Catheter insertion was without problems in 42 women (84%). Seven cases had difficult catheter insertion and one had balloon rupture. During pertubation all cases except two had mild to moderate discomfort.

Image quality was rated as good in all cases both before and after instillation of Echovist-200. Forty-five patients (90%) had normal uteri and 5 (10%) had abnormal findings on both plain and HyCoSy examination: 4 myoma uteri and 1 bicornuate uterus. HyCoSy revealed that 39 of 50 (78%) tubes on the left side and 43 of 50 (86%) on the right were patent, while one tube (2%) on the right side was not assessable because the catheter was inserted into the left uterine horn. (Table 1)

Forty eight patients (96%) experienced a total of 58 adverse events. The most common event was pelvic pain reported by 24 patients. The majority (37 of 58 or 63.8%) of adverse events were of mild intensity. (Table 2)

Four patients later underwent laparoscopic dye injection. Concordant tubal patency was demonstrated in 6 tubes (75%). There was one false positive and one false negative diagnosis. Eight (16%) patients became pregnant during the 3-month follow up period.

Table 1. Tubal evaluation by HyCoSy

Tubal findings	Frequency	Percentage
Both tubes patent	34	68
One tube patent	13	26
One tube patent/one tube not assessable	1	2
Both tubes occluded	2	4

Table 2. Adverse events and their intensities

Events	Intensity			
	Mild	Moderate	Severe	Total
Pelvic pain	14	8	2	24
Discomfort during insertion	14	5	2	21
Abdominal pain	4	1	0	5
Pelvic discomfort	3	0	0	3
Abdominal discomfort	1	0	0	1
Fainting	0	1	0	1
Nausea	0	1	0	1
Vomiting	0	1	0	1
Discomfort during dye injection	1	0	0	1
Total	37	17	4	58

Discussion

HyCoSy is a simple procedure that can be performed as an out patient procedure. As such it may be performed early in the investigation of infertile couples to give important information on the uterus and fallopian tubes.

Abnormality of the uterus was demonstrated in 10% and obstruction of one or both tubes in 30% of the cases in this study. Our findings agreed with Ayida et al,[2] who reported apparently normal uterus in 82% and tubal patency in 71% of the cases.

Tubal patency investigated by HyCoSy compares favorably with conventional hysterosalpingography (HSG) and laparoscopy with dye injection. In a study on 76 women by Deichert et al,[3] concordance rate between HyCoSy and HSG/chromolaparoscopy was found to be 87.5%. A similar study on 77 women by Degenhardt et al[4] showed a concordance of 85% between results of HyCoSy and HSG/chromolaparoscopy. In this study the concordance of tubal patency between HyCoSy and chromolaparoscopy was only 75%, which was lower than other reports which ranged from 84-87.5%.[2-5] This could be due to the small number of cases who had both HyCoSy and laparoscopy The effect of çlearning curveé before the achievement of technical competence could also be another contributory factor. Data from over 600 patients showed that HyCoSy had a sensitivity 71.4%-100%,[6] a specificity of 82.2%-87%,[5,6] a positive predictive value of 63.2-80%,[6,7] and a negative predictive value of 87-100%[6,7] when compared with HSG/chromolaparoscopy. Misdiagnosis of tubal occlusion could result from tubal spasm as seen with HSG. In case of sactosalpinx, tubal flow could give false impression of tubal patency.[6]

In this series 8 patients (16%) became pregnant within 3 months after HyCoSy. In a large study on 3,631 HSG using different contrast media, Acton et al[8] reported pregnancy rates between 20-40%. The pregnancy promoting property of oil-based contrast media in HSG over that of water-soluble media has been demonstrated in many controlled studies.[1,9] The low pregnancy rate in this study may be due to a short follow-up period and the use of Echovist-200 which is a water-soluble medium.

An important adverse effect of HyCoSy is the occurrence of pain, which occurred in about half of the patients in this study. However, the

majority were of mild intensity and the procedure could be completed in all cases. Adverse events other than pain were recorded in less than 10% of the cases. Most of the adverse effects were related to the procedure rather than the trial substance itself. Other researchers[2-7] also reported a similar experience.

In conclusion, the use of Echovist-200 in HyCoSy is a valuable outpatient procedure for the investigation of uterine and tubal infertility. The test is safe with relatively minor adverse effects.

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