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Gel infusion sonography in the evaluation of the uterine cavity

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KEYWORDS: endometrial sampling; gel infusion sonography; GIS; hydrosonography; hysteroscopy; pain scores; SCSH; ultrasound

ABSTRACT

Objectives *To compare gel infusion sonohysterography (GIS) with saline contrast sonohysterography (SCSH) with regard to technical feasibility and procedure-related pain experienced by patients.*

Methods *This prospective observational cohort study included 551 consecutive patients with abnormal bleeding: SCSH was attempted in the first 402 women and GIS was attempted in the following 149. All procedures were performed by the same examiner, in the same clinical setting, using a 2-mm diameter catheter. After contrast sonohysterography, most patients underwent office hysteroscopy (*$n = 502$*) and endometrial sampling (*$n = 323$*). The women were asked to rate the pain experienced during each procedure using a 100-mm visual analog scale (VAS). Patients' characteristics, ultrasound findings, histological diagnosis, technical failures and procedure-related pain were compared between the two procedures.*

Results *The mean ± SD VAS score for contrast sonography, subsequent hysteroscopy and endometrial biopsy were* 22.9 ± 21.7, 38.8 ± 26.6 *and* 50.0 ± 26.3, *respectively, in the SCSH subgroup vs.* 16.5 ± 21.5, 27.6 ± 28 *and* 33.6 ± 30.3, *respectively, in the GIS subgroup (*$P = 0.0051$, $P = 0.0005$ *and* $P = 0.0003$, *respectively). The technical failure rate was 5% in the SCSH subgroup vs. 2% in the GIS subgroup (*$P = 0.1522$*).*

Conclusions *GIS and SCSH showed similar technical feasibility. The procedure-related pain reported by patients during contrast sonohysterography, as well as during subsequent hysteroscopy and endometrial sampling, was less in the GIS group. Copyright © 2009 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Saline contrast sonohysterography (SCSH) is a simple, accurate and cheap technique used in the diagnosis of uterine intracavitary lesions. In a meta-analysis, de Kroon *et al.*[1] reported a sensitivity of 95% for SCSH in the detection of endometrial polyps and intracavitary myomas[1]. The disadvantages of SCSH depend on the catheter used for this procedure. If a simple catheter such as a neonatal suction catheter is used, reflux of saline through the cervix may result in insufficient filling of the uterine cavity or in a transient filling associated with an unstable image. The latter is particularly limiting during three-dimensional (3D) volume acquisition. Improved filling of the cavity may be achieved using larger instillation volumes and/or by increasing the instillation flow. However, this may result in a higher intrauterine pressure causing pain and backflow, and be more uncomfortable for the patient. Moreover, higher instillation rates can cause transtubal flow, with potential seeding of malignant cells into the abdominal cavity[2]. To overcome reflux through the cervix, balloon catheters can be used. Although the use of balloon catheters can achieve improved filling of the uterine cavity, it is associated with a higher risk for excessive intrauterine pressure. Moreover, balloon catheters are much more expensive.

Owing to its physical properties, the substitution of saline by gel could overcome some of the disadvantages of SCSH[3]. The aim of this study was to compare gel infusion sonohysterography (GIS) with saline contrast sonohysterography (SCSH) with regards to technical feasibility and procedure-related pain.

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METHODS

This prospective observational cohort study included 551 consecutive patients who presented at the One Stop Bleeding Clinic of the Department of Obstetrics and Gynecology, University Hospital Gasthuisberg in Leuven, Belgium between October 2004 and October 2007. Those enrolled between October 2004 and November 2006 ($n = 402$) underwent SCSH, and those presenting between December 2006 and October 2007 ($n = 149$) underwent GIS. The study was approved by the local ethics committee and informed consent was obtained from all patients.

All patients underwent a baseline ultrasound examination with color Doppler imaging followed by contrast sonohysterography. All sonographic procedures including contrast sonohysterography were performed by the same examiner (T.V.) in the same clinical setting.

The endometrial thickness was measured before fluid instillation at its thickest part in the sagittal plane. The technique used for SCSH has been described in detail elsewhere[4] but can be briefly summarized as follows: a neonatal suction catheter (2.0 mm in diameter) was inserted through the cervix, after which the transvaginal probe was reinserted. As much sterile saline as required, up to 20 mL, was slowly instilled while ultrasound examination was performed. GIS was performed using the same 2.0-mm neonatal suction catheter through which Endosgel® (Farco-Pharma GmbH, Köln, Germany) ($n = 67$) or Instillagel® (Farco-Pharma GmbH) ($n = 82$) was instilled. Instillagel contains lidocaine hydrochloride 20 mg/g, chlorhexidine digluconate, methyl hydroxybenzoate, propyl hydroxybenzoate, sodium lactate, hydroxyethylcellulose and purified water; Endosgel has the same content, but no lidocaine is added. To facilitate its instillation through the narrow 2.0-mm catheter, the gel was warmed to 37°C to decrease its viscosity. Technical failures were defined as the inability to insert the catheter through the cervix or to obtain sufficient distension of the uterine cavity.

At contrast sonography the sonologist scored the presence or absence of a focal intracavitary lesion as: 'yes' (presence of a focal lesion), 'possible' (a focal lesion is deemed possible, although the sonologist is uncertain about the diagnosis) or 'no' (absence of focal lesion). After ultrasound examination and contrast sonohysterography most patients underwent an office hysteroscopy ($n = 502$) and endometrial sampling ($n = 323$), according to the department's Bleeding Clinic protocol.

Hysteroscopy was performed, without local anesthesia, using a rigid Storz® scope (Storz, Tuttlingen, Germany) with an outer sheath of 3 mm in diameter. Distension of the cavity was achieved by normal saline infusion. The endometrium was sampled immediately after hysteroscopy using a Novak curette in most instances.

After the procedures the patients were asked to fill in a questionnaire including questions about their satisfaction with the Bleeding Clinic's approach and about the pain experienced during the different procedures. Pain was reported using a visual analog scale (VAS); patients were asked to indicate a point on a 100-mm line, with 0 meaning the procedure was not painful at all and 100 meaning that it was the most painful experience one could imagine. Three hundred and eighty-seven patients (70.2%) returned the questionnaire: 95% filled in the VAS scores and 82% the question about general satisfaction with the Bleeding Clinic approach. The patients' characteristics, ultrasound findings, histological diagnosis, technical failures and procedure-related pain were recorded, and compared between the two groups.

Statistical analysis was performed using SAS version 9.1 for Windows (SAS Institute, Cary, NC, USA). The Mann–Whitney *U*-test was used to compare continuous non-normally distributed variables between the two groups, and the chi-square or Fisher's exact test, as appropriate, were used to compare categorical variables. Two-sided *P*-values are reported. A probability level of 0.05 was chosen for statistical significance.

RESULTS

The patients' characteristics are summarized in Table 1; the two subgroups were similar with respect to age,

Table 1 Patient characteristics according to procedure performed: saline contrast sonohysterography (SCSH) or gel infusion sonohysterography (GIS)

	SCSH			*GIS*			
Parameter	n *(%)*	*Mean ± SD*	*Range*	n *(%)*	*Mean ± SD*	*Range*	P*
Age (years)	402	50.7 ± 12.0	21–85	149	50.8 ± 11.8	25–86	0.8412
Weight (kg)	395	69.9 ± 14.2	45–160	149	69.4 ± 13.5	42–125	0.8427
Height (cm)	354	163.8 ± 6.1	149–183	147	164.7 ± 6.8	140–185	0.1874
Parity	402	1.9 ± 1.2	0–7	148	1.8 ± 1.2	0–5	0.4713
ET (mm)	402	9.6 ± 6.8	1.1–49	149	9.4 ± 8.3	0.4–78.5	0.6929
Menopausal status							0.0599
Premenopausal	213 (53.0)			88 (59.1)			
Perimenopausal	32 (8.0)			4 (2.7)			
Postmenopausal	157 (39.1)			57 (38.3)			
Nulliparous	51 (12.7)			23 (15.4)			0.3992

*Mann–Whitney *U*-test for continuous variables and Fisher's exact test for categorical variables. ET, endometrial thickness measured before fluid instillation.

Table 2 Final diagnosis according to procedure performed: saline contrast sonohysterography (SCSH, $n = 402$) or gel infusion sonohysterography (GIS, $n = 149$)

Final diagnosis	*SCSH* (n *(%))*	*GIS* (n *(%))*
Proliferative changes	62 (15.4)	25 (16.8)
Secretory changes	80 (19.9)	30 (20.1)
Atrophy	53 (13.2)	35 (23.5)
Hyperplasia	24 (6.0)	4 (2.7)
Polyp	111 (27.6)	36 (24.2)
Myoma	48 (11.9)	12 (8.1)
Carcinoma*	11 (2.7)	5 (3.4)
Other	13 (3.2)	2 (1.3)

*All patients with carcinoma were postmenopausal. $P = 0.0666$ for differences between SCSH and GIS across all categories (chi-square test).

Table 3 Diagnosis of focal lesions at saline contrast sonohysterography (SCSH) or gel infusion sonohysterography (GIS) compared with the final diagnosis

	Final diagnosis (n *(%))*			
Diagnosis at SCSH or GIS	*No focal lesion*	*Focal lesion**	*Endometrial cancer*	*Total* (n)
SCSH				
Focal lesion	38 (22.9)	121 (72.9)	7 (4.2)	166
Possible focal lesion	12 (66.7)	6 (33.3)	0 (0)	18
No focal lesion	171 (85.9)	27 (13.6)	1 (0.5)	199
Total	221 (57.7)	154 (40.2)	8 (2.1)	383
GIS				
Focal lesion	19 (29.2)	41 (63.1)	5 (7.7)	65
Possible focal lesion	4 (57.1)	3 (42.9)	0 (0)	7
No focal lesion	71 (95.9)	3 (4.1)	0 (0)	74
Total	94 (64.4)	47 (32.2)	5 (3.4)	146

Nineteen SCSH cases and three GIS cases were excluded because the procedure failed. *A 'focal lesion' was defined as an endometrial polyp or an intracavitary myoma. $P = 0.2455$ for differences between SCSH and GIS (Fisher's exact test).

weight, height, parity, menopausal status and endometrial thickness as measured by ultrasound imaging. The final diagnosis was also similar in the two subgroups (Table 2). The final diagnosis was based on ultrasound imaging, hysteroscopy, endometrial biopsy, operative hysteroscopy and hysterectomy findings in 8.0%, 16.2%, 39.8%, 32.6% and 3.5% of patients, respectively, in the SCSH group vs. 13.5%, 12.8%, 42.6%, 21.6% and 9.5% in the GIS group. The detection of focal lesions at contrast sonography was compared with the final diagnosis for each patient (Table 3). There were no significant differences between the SCSH and the GIS groups ($P = 0.2455$, Fisher's exact test).

The technical failure rate of the contrast hysterosonography was 5% in the SCSH subgroup and 2% in the GIS subgroup ($P = 0.1522$). When the patients were asked about their experiences at the Bleeding Clinic, general satisfaction was high in both subgroups

Table 4 Patients' general satisfaction with the Bleeding Clinic approach according to procedure performed: saline contrast sonohysterography (SCSH) or gel infusion sonohysterography (GIS)

Score	*SCSH* (n *(%))*	*GIS* (n *(%))*
Very satisfied	154 (64.7)	56 (69.1)
Satisfied	83 (34.9)	24 (29.6)
Rather unsatisfied	0 (0)	1 (1.2)
Very unsatisfied	1 (0.4)	0 (0)
Total	238 (100)	81 (100)

$P = 0.3086$ for differences between SCSH and GIS (Fisher's exact test).

(Table 4) ($P = 0.3086$). The mean ± SD VAS scores for contrast sonography, subsequent hysteroscopy and endometrial biopsy were 22.9 ± 21.7, 38.8 ± 26.6 and 50.0 ± 26.3, respectively, in the SCSH subgroup vs. 16.5 ± 21.5, 27.6 ± 28 and 33.6 ± 30.3 in the GIS subgroup ($P = 0.0051$, $P = 0.0005$ and $P = 0.0003$, respectively).

DISCUSSION

Our data demonstrate the feasibility of gel infusion sonography; the technical failure rate using a neonatal suction catheter is low and the procedure is better tolerated by the patients than is SCSH. In the authors' experience, the image quality obtained by GIS is at least as good as that with saline infusion (Figure 1).

The gels that we used for GIS are extensively used in male and female bladder catheterization, pediatrics, transurethral and transvaginal surgery, and during laparoscopic sterilization because of their antiseptic, lubricant and anesthetic (Instillagel) properties, and they have been reported to be safe[5–11].

Gel has some useful physical properties; it offers the same negative contrast as saline but its viscosity is much higher than saline resulting in less backflow through the cervix and more stable filling of the uterine cavity, obviating the need for a more expensive balloon catheter. Because of its higher viscosity and the smaller instillation volume required, transtubal spillage is less likely to occur. This may be an additional argument for the use of gel instead of saline, as endometrial malignancy is never completely excluded. Satisfactory filling of the cavity is also particularly important for high quality 3D volume acquisition. The gel's viscosity can be modulated as needed by modifying the temperature; the higher the temperature, the lower the viscosity ($\mu_{(T)} = \mu_0.e^{-b.T}$, where T is the temperature, μ_0 the reference viscosity of the fluid and $\mu_{(T)}$ the viscosity of the fluid at temperature T). In order to be able to instill the gel through a 2-mm thin neonatal suction catheter, the gel's viscosity can be decreased by warming it to 37°C.

The VAS pain scores for contrast sonography, subsequent hysteroscopy and endometrial sampling were significantly lower in the GIS group than the SCSH group. This may be due to the lubricant effect of the

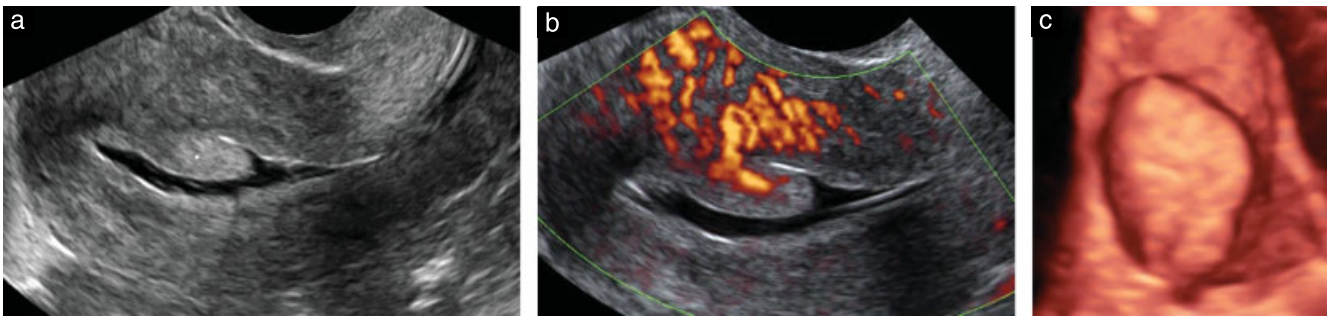

Figure 1 Images obtained on gel infusion sonohysterography showing an endometrial polyp on gray-scale (a), power Doppler (b) and three-dimensional (c) imaging.

gel facilitating the insertion of instruments through the cervix but, because the patients were not randomized, we cannot draw definitive conclusions about this. However, both groups were examined in the same setting and by the same examiner, and the patients' characteristics were not significantly different. A possible beneficial effect of gel on the pain experienced by the patient during contrast sonography and during subsequent intrauterine procedures has to be confirmed in a randomized trial. The question of whether the lidocaine contained in the gel used in more than half of the GIS procedures might have led to lower pain scores has to be considered. However, in a randomized trial comparing gel with and without lidocaine, we could not find any difference in the pain experienced by patients[12]. We demonstrated that GIS is associated with little pain and is therefore very well accepted by the patients. In another series including 100 Pipelle endometrial sampling procedures performed immediately after GIS, the quality of the histology was not affected by the gel[13].

Not all patients answered the questionnaire in this study; some did not return the questionnaire and others did not answer all questions. Although we did not contact these patients to ask them why they did not fully complete the questionnaire, we hypothesize that most of them did so because of lack of time. However, we acknowledge that this may have introduced a bias.

Finally, embryotoxicity is an unresolved issue. In our series one patient became pregnant 3 months after GIS and delivered a healthy baby after an uneventful pregnancy. We feel that it might be prudent in fertile women to advocate contraception in the cycle of the GIS procedure.

In conclusion, GIS seems equal to saline infusion with respect to clinical feasibility, while the procedure-related pain may be less during GIS than during SCSH. The reason for this is unclear and our results need to be confirmed in a randomized trial.

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