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# Could antispasmodic drug reduce pain during hysterosalpingo-contrast sonography (HyCoSy) in infertile patients? A randomized double-blind clinical trial

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**KEYWORDS:** Fallopian tube; hyoscine-N-butylbromide; infertility; pain; sonosalpingohysterography; SSHG; tubes

## ABSTRACT

***Objective*** *To assess the effectiveness of an antispasmodic drug, hyoscine-N-butylbromide, in reducing pain during hysterosalpingo-contrast sonography (HyCoSy).*

***Methods*** *Eight hundred and sixteen patients undergoing HyCoSy were randomized to receive 10 mg hyoscine-N-butylbromide (n = 408) or placebo (n = 408) per os, 30 min before the procedure, in a double-blind randomized controlled trial. Immediately after the procedure, the patient was asked to describe any pain experienced in comparison with pain usually suffered during the menstrual cycle, and the operator assigned a pain score between 0 and 4 as follows: 0 (no reaction or discomfort), 1 (slight pain, less than menstrual pain), 2 (moderate pain, exceeding menstrual cramps but no vasovagal reaction), 3 (vasovagal reaction or pain requiring observation in a hospital) and 4 (vasovagal reaction or pain requiring resuscitation). The primary aim was to estimate the difference in pain score, considered as a categorical value, between the active arm of the trial and the control group. The secondary aim was to evaluate if pain is related to tubal patency.*

***Results*** *There was no difference in pain score between the hyoscine-N-butylbromide group and the placebo group ($P = 0.807$). There was a negative correlation between pain and tubal patency, regardless of treatment group ($P < 0.0001$).*

***Conclusions*** *Administration of 10 mg antispasmodic drug hyoscine-N-butylbromide does not reduce pain in patients undergoing HyCoSy. Copyright © 2012 ISUOG. Published by John Wiley & Sons, Ltd.*

## INTRODUCTION

About 30–35% of cases of infertility are caused by the tubal factor[1–3]. Traditionally, hysterosalpingography (HSG) and laparoscopy with chromopertubation have been used in the diagnosis of Fallopian tubal pathology[2]. However, HSG cannot be used in all women, because it exposes the patient to X-rays and iodinated contrast medium, and sometimes the procedure is painful[4]. Chromopertubation during laparoscopy represents the gold standard for assessing tubal patency, but it should be used only in selected cases because it requires general anesthesia and carries the risk of severe adverse effects, including injury of the pelvic blood vessels, intestinal loops and urinary bladder.

Another recent method for evaluation of tubal patency is hysterosalpingo-contrast sonography (HyCoSy), a transvaginal ultrasound procedure that uses air and saline solution as the contrast medium. With its high sensitivity and specificity in studying both tubal patency and the uterine cavity, and its high concordance with hysteroscopy, laparoscopy and HSG, it has been used increasingly in recent years[1,2,4–12]. Unlike HSG, HyCoSy also gives information regarding ovarian morphology. It is usually performed in an outpatient setting and it seems to be less painful than is HSG[4,13]. However, while many randomized studies have evaluated how to reduce pain during HSG, few studies have investigated the extent of pain experienced during HyCoSy and possible methods of pain relief[4,6,13–25].

The pain experienced during HyCoSy is related to the uterine distension with saline solution, which may release local prostaglandins, resulting in uterine cramps[6]. Additionally, cervical distension with saline solution may

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cause a vasovagal reaction[6]. Since antispasmodic drugs are commonly used for relief of muscle spasms, our hypothesis was that an antispasmodic drug such as hyoscine-N-butylbromide, a muscarinic receptor antagonist with anticholinergic effects, could decrease pain during HyCoSy by affecting uterine contractions.

Thus, our study aimed to evaluate the efficacy of hyoscine-N-butylbromide in reducing patient discomfort during HyCoSy.

## METHODS

### Study population

The study population consisted of women undergoing infertility investigation at the Institute of Physiopathology of Human Reproduction of the Policlinico Gemelli, Rome between January 2003 and September 2010. A woman was considered eligible if: 1) the couple had been infertile (absence of conception after a period of 12 months without using any contraception) for less than 3 years and 2) her age was between 20 and 41 years. Patients were excluded: 1) if they had a history of hypersensitivity to hyoscine-N-butylbromide, 2) in the presence of, or if there was a history of, abnormal uterine bleeding, 3) if they suffered from acute sexually transmitted disease or pelvic inflammatory disease, 4) in the presence of a concurrent severe male factor or known or suspected pregnancy and 5) if they were undergoing treatment with estroprogestinic drugs.

In total, 856 women were assessed for eligibility; 40 were excluded from the study, 22 because they declined to participate or were uncooperative patients and 18 for stenosis of the internal uterine orifice (Figure 1).

The HyCoSy procedure as well as the study design and objectives were explained orally to all eligible women. Written informed consent was then obtained from all participants. The protocol was approved by the Institutional Board of the Department of Obstetrics and Gynecology.

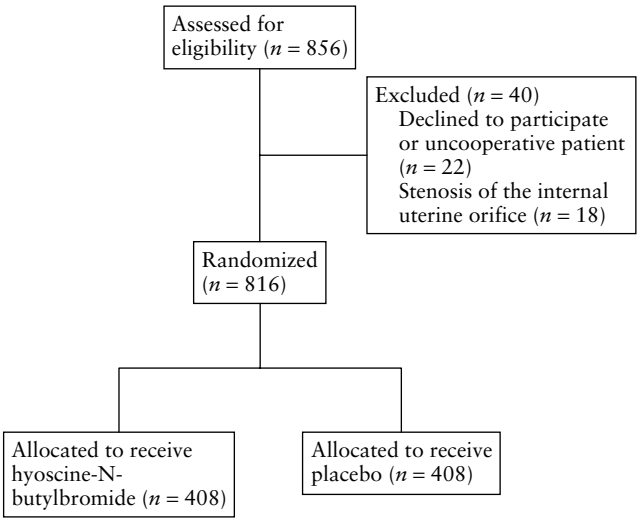


**Figure 1** Flow diagram describing the randomization of patients in the two study groups in this double-blind randomized controlled trial evaluating the efficacy of hyoscine-N-butylbromide in reducing patient discomfort during hysterosalpingo-contrast sonography.

### Study design

This study was a randomized, double-blind, controlled trial comparing the efficacy of an antispasmodic drug with placebo for pain relief during HyCoSy. Before the procedure, each consenting woman was assigned a predetermined computer-generated randomization code to receive either hyoscine-N-butylbromide (active arm) or placebo (control arm). To guarantee the concealment of allocation, the randomization list of study subjects was kept by a staff member who was not directly involved in the study plan.

Both the HyCoSy operator and the patient were blinded to the randomization.

### Interventions

All patients underwent vaginal swabs performed within 3 months before the HyCoSy examination. HyCoSy was performed during the late follicular phase before ovulation. Thirty min before starting the procedure, patients in the active arm received 10 mg hyoscine-N-butylbromide (Buscopan tablets, Boehringer Ingelheim Italia SpA, Milan, Italy) and those in the control arm received the placebo. The placebo tablets looked and tasted identical to the active treatment tablets and contained all of the same non-medicinal ingredients used for color, flavor, sweetening. Both were administered *per os*.

All patients were initially examined by transvaginal pelvic ultrasound with an Esaote Technos scanner (Esaote Technos, Genova, Italy) equipped with a 9.0–5.0-MHz multifrequency endovaginal probe, in order to evaluate uterus and ovaries, as well as to confirm the initial absence of fluid in the pouch of Douglas. A sterile speculum was then inserted and the cervix was visualized and disinfected. A Foley catheter 6 Fr in diameter (Porges, Coloplast A/S, Humlebaek, Denmark) was inserted into the uterine cavity and the balloon of the catheter was inflated with 1.5–2 mL sterile saline to secure the catheter in the uterine cavity. The speculum was then removed and the balloon's position was confirmed by ultrasound.

The operator could then begin the examination. To evaluate tubal patency bilaterally, air and sterile saline (15 mL of each) were instilled through the Foley catheter using a 50 mL syringe under transvaginal ultrasound guidance. If the air and the saline solution produced hyperechogenic spots around the ovary and fluid appeared in the pouch of Douglas, the tubes were considered patent. Conversely, absence of hyperechogenic spots around the ovary and absence of fluid in the retrouterine space after instillation of air and saline was interpreted as tubal obstruction.

At the end of the procedure, fluid accumulation in the peritoneal cavity was observed using ultrasound. The balloon was deflated and the catheter removed, with simultaneous injection of saline solution (about 1.0 mL)

into the uterine cavity to extend it, allowing evaluation of its morphology and detection of any abnormalities. If necessary, the procedure was repeated to exclude tubal spasm.

A mean time period of 10 min was sufficient for complete investigation of the pelvis and uterine cavity.

### Pain scoring

Immediately after the procedure, the operator asked the patient to describe any pain experienced during the procedure, comparing it with pain usually suffered during the menstrual cycle. The pain level was then assessed by the operator using the Stacey score[26] (Table 1).

### Outcomes

The primary aim was to estimate the difference in pain scoring between the patients in the active arm of the trial, treated with hyoscine-N-butylbromide, and those in the control group, who received the placebo. The secondary aim was to evaluate if pain scoring was related to tubal patency.

### Statistical analysis

The $\chi^2$ test or Fisher's exact test were used as appropriate to compare frequencies between categorical variables. Comparison of averages for continuous variables was carried out by Student's *t*-test or Mann–Whitney *U*-test when the distribution of data was not normal, and values are presented as mean ± SD. Statistical significance was defined as a two-sided *P*-value $< 0.05$ for all analyses, which were carried out using the STATA software package v.10.1 (Stata Corporation, College Station, TX, USA).

## RESULTS

A total of 816 women were selected randomly (1 : 1) to receive either hyoscine-N-butylbromide ($n = 408$, Group A) or placebo ($n = 408$, Group B) before undergoing HyCoSy. As shown in Table 2, there were no statistically significant differences between groups in age or past obstetric history (full term pregnancy, spontaneous miscarriage, voluntary termination of pregnancy, primary infertility and extrauterine pregnancy). There was no statistically significant difference in pain score between the hyoscine-N-butylbromide group and the placebo group ($P = 0.807$). Fallopian tubal patency assessed as unilateral or bilateral stenosis was similar among the two groups.

There were statistically significant differences in pain scoring according to Fallopian tubal patency, regardless of treatment group ($P < 0.0001$, Table 3). Tubal patency appeared to be closely related to pain perception during HyCoSy, since women with bilateral tubal stenosis were more likely to experience severe discomfort, pain and/or vagal effects compared with patients with patent tubes in both studied groups. Accordingly, the great majority of patients with physiologic tubal anatomy reported lower pain scores during HyCoSy: 84.7% of patients in the placebo group and 79% of those in the hyoscine-N-butylbromide group suffered no discomfort or had only slight pain.

**Table 1** Standard scale used to score pain in a double-blind randomized controlled trial evaluating the efficacy of hyoscine-N-butylbromide in reducing patient discomfort during hysterosalpingo-contrast sonography

| *Score* | *Description* |
|---|---|
| 0 | No discomfort/reaction |
| 1 | Mild pain, less or equivalent to period pain |
| 2 | Moderate pain, more severe than period pain but no vasovagal reaction |
| 3 | Vasovagal reaction/pain requiring observation in hospital |
| 4 | Vasovagal reaction/pain requiring resuscitation |

Adapted from Stacey *et al.*[26]. Vasovagal reaction was defined as a limited episode of systemic hypotension, characterized by bradycardia and peripheral vasodilatation[43,44].

## DISCUSSION

This double-blind, randomized, controlled trial was designed to evaluate the efficacy of an antispasmodic drug (hyoscine-N-butylbromide) in reducing pain during HyCoSy.

The HyCoSy method is an acceptable, time-efficient and well-tolerated alternative to HSG; it has been found to have comparable accuracy in the assessment of the uterine cavity and tubal patency[4,5,27,28]. It is the most efficient first-line diagnostic tool for evaluation of the Fallopian tubes on the basis of availability, accessibility, associated risks and cost[1]. However, besides cervical stenosis, in some patients severe pain (with or without vasovagal reaction) may limit its success[1,29].

Most investigations of HyCoSy have focused on its sensitivity and specificity, with few evaluating possible methods of pain relief and pain score during the procedure[4,6,11,13,24,25,30–32]. Some authors showed that the HyCoSy technique is equivalent to hysteroscopy and HSG for evaluation of the uterine cavity, but it is less painful and invasive[4].

Guney *et al.*[6] performed the first study to compare the effects of administration of a local anesthetic and a placebo during HyCoSy; they found a statistically significant difference in terms of pain reduction with the use of intrauterine topical local anesthetic during, immediately after and 20 min after the procedure. However, this result was not confirmed in other uterine procedures, such as HSG and hysteroscopy[33,34].

Some authors have attributed the pain during sonohysterography to the location of the catheter used. In particular, in a randomized trial, Spieldoch *et al.*[35] found that intracervical catheter placement caused significantly less pain than did uterine catheter placement. Pain experienced during HyCoSy is generally caused by uterine contractions, induced by the air and saline solution

**Table 2** Main characteristics including pain scores among the two groups in a double-blind randomized controlled trial evaluating the efficacy of hyoscine-N-butylbromide in reducing patient discomfort during hysterosalpingo-contrast sonography

| *Characteristic* | *Hyoscine-N-butylbromide group* (n = *408*) | *Placebo group* (n = *408*) | P |
|---|---|---|---|
| Age (years) | 34.2 ± 4.2 | 34.6 ± 4.2 | 0.178‡ |
| Past obstetric history | | | 0.942§ |
| Full-term pregnancy | 35 (8.6) | 33 (8.1) | |
| Spontaneous miscarriage | 54 (13.2) | 52 (12.7) | |
| Termination of pregnancy | 17 (4.2) | 12 (2.9) | |
| Primary infertility | 294 (72.1) | 304 (74.5) | |
| Extrauterine pregnancy | 8 (2.0) | 7 (1.7) | |
| Pain score* | | | 0.807† |
| No discomfort/reaction (Score 0) | 135 (33.1) | 140 (34.3) | |
| Mild pain, less or equivalent to period pain (Score 1) | 174 (42.6) | 165 (40.4) | |
| Moderate pain, more severe than period pain (Score 2) | 83 (20.3) | 82 (20.1) | |
| Vasovagal reaction/pain requiring observation (Score 3) | 13 (3.2) | 19 (4.7) | |
| Vasovagal reaction/pain requiring resuscitation (Score 4) | 3 (0.7) | 2 (0.5) | |
| Fallopian tubal patency | | | |
| Bilateral tubal patency | 300 (73.5) | 282 (69.1) | 0.378§ |
| Unilateral tubal stenosis | 86 (21.1) | 100 (24.5) | |
| Bilateral tubal stenosis | 22 (5.4) | 26 (6.4) | |

Data given as mean ± SD or *n* (%). *Adapted from Stacey *et al.*[26]. †$\chi^2$ test. ‡Student's t-test. §Fisher's exact test.

**Table 3** Frequency distribution for pain score according to Fallopian tubal patency among the two groups in a double-blind randomized controlled trial evaluating the efficacy of hyoscine-N-butylbromide in reducing patient discomfort during hysterosalpingo-contrast sonography

| *Fallopian tube patency* | *No discomfort (Score 0)* | *Mild pain (Score 1)* | *Moderate pain (Score 2)* | *Vasovagal reaction or pain requiring observation in a hospital/resuscitation (Score 3–4)* | P* |
|---|---|---|---|---|---|
| Placebo group | | | | | < 0.0001 |
| Bilateral tubal patency (*n* = 282) | 119 (42.2) | 120 (42.5) | 36 (12.8) | 7 (2.5) | |
| Unilateral tubal stenosis (*n* = 100) | 15 (15.0) | 40 (40.0) | 36 (36.0) | 9 (9.0) | |
| Bilateral tubal stenosis (*n* = 26) | 6 (23.1) | 5 (19.2) | 10 (38.5) | 5 (19.2) | |
| Hyoscine-N-butylbromide group | | | | | < 0.0001 |
| Bilateral tubal patency (*n* = 300) | 119 (39.7) | 118 (39.3) | 39 (13.0) | 24 (8.0) | |
| Unilateral tubal stenosis (*n* = 86) | 16 (18.6) | 21 (24.4) | 34 (39.5) | 15 (17.4) | |
| Bilateral tubal stenosis (*n* = 22) | 0 (0.0) | 7 (31.8) | 6 (27.3) | 9 (40.9) | |

Data given as *n* (%). *Fisher's exact test.

injected for uterine distension and for the study of tubal patency[36]. Inflation of the catheter's balloon stimulates the nerve fibers of the uterine cervix, causing pelvic pain and vasovagal reaction. Moreover, the uterine dilation causes the release of local prostaglandins and initiates uterine cramps and pain during the procedure. To minimize possible bias, even though pain intensity during HyCoSy has been reported to be independent of the volume of solution injected[25], we used the same amount of contrast medium for each patient.

In this study, we tested whether the antispasmodic drug hyoscine-N-butylbromide, commonly used for muscle spasm relief, could reduce the pain caused by uterine cramps during HyCoSy. Hyoscine-N-butylbromide, which obtained trade mark registration in the USA in 1951, is known for its antispasmodic action. It acts by inhibiting cholinergic transmission in the abdominopelvic parasympathetic ganglia, thus relieving spasm in the smooth muscles of gastrointestinal, biliary and urinary tracts and female genital organs, especially the cervicouterine plexus, and aiding cervical dilatation[37]. Previous studies have attempted to use it to relieve abdominal cramping during various procedures, such as endoscopy and labor analgesia, as well as in cases of renal colic. Whether its use provides benefits is still controversial and only one study has investigated its possible benefit for pain relief during sonohysterography for evaluation of the uterine cavity: in their double-blind, randomized, controlled trial, Jareethum *et al.*[38] observed no statistically significant differences in pain reduction by using hyoscine-N-butylbromide, mefenamic or placebo. Similarly, in our study, hyoscine-N-butylbromide did not significantly reduce pain in patients undergoing HyCoSy for tubal patency evaluation.

Our finding that hyoscine-N-butylbromide did not provide pain relief could be due to several factors,

one possibility being the low dose (10 mg) and/or the route of administration (*per os*). In fact, in urology, gastroenterology and obstetrics clinics the analgesic effect of hyoscine-N-butylbromide has been observed following intravenous or intramuscular administration, and sometimes the effect is seen at doses of 20 or 40 mg[37,39,40]; doses of 10 mg, however, are commonly used in clinical practice in gynecology and obstetrics.

Our results confirm a close relationship between pain perception during HyCoSy and tubal obstruction, as described in other studies[41,42]. In patients with tubal obstruction, the intrauterine pressure reached during the procedure may induce overdistension of the uterine muscular fibers, resulting in higher uterine contractility.

In conclusion, our study suggests that there is no benefit in administering 10 mg *per os* hyoscine-N-butylbromide for the prevention of pain, prior to HyCoSy in infertile women.

## REFERENCES


1. Hajishafiha M, Zobairi T, Zanjani VR, Ghasemi-Rad M, Yekta Z, Mladkova N. Diagnostic value of sonohysterography in the determination of fallopian tube patency as an initial step of routine infertility assessment. *J Ultrasound Med* 2009; **28**: 1671–1677.
2. Ahinko-Hakamaa K, Huhtala H, Tinkanen H. The validity of air and saline hysterosalpingo-contrast sonography in tubal patency investigation before insemination treatment. *Eur J Obstet Gynecol Reprod Biol* 2007; **132**: 83–87.
3. Kupesic S, Plavsic BM. 2D and 3D hysterosalpingo-contrast-sonography in the assessment of uterine cavity and tubal patency. *Eur J Obstet Gynecol Reprod Biol* 2007; **133**: 64–69.
4. Brown SE, Coddington CC, Schnorr J, Toner JP, Gibbons W, Oehninger S. Evaluation of outpatient hysteroscopy, saline infusion hysterosonography, and hysterosalpingography in infertile women: a prospective, randomized study. *Fertil Steril* 2000; **74**: 1029–1034.
5. Lindheim SR, Adsuar N, Kushner DM, Pritts EA, Olive DL. Sonohysterography: a valuable tool in evaluating the female pelvis. *Obstet Gynecol Surv* 2003; **58**: 770–784.
6. Guney M, Oral B, Bayhan G, Mungan T. Intrauterine lidocaine infusion for pain relief during saline solution infusion sonohysterography: a randomized, controlled trial. *J Minim Invasive Gynecol* 2007; **14**: 304–310.
7. Fleischer AC, Vasquez JM, Cullinan JA, Eisenberg E. Sonohysterography combined with sonosalpingography: correlation with endoscopic findings in infertility patients. *J Ultrasound Med* 1997; **16**: 381–384.
8. Heikkinen H, Tekay A, Volpi E, Martikainen H, Jouppila P. Transvaginal salpingosonography for the assessment of tubal patency in infertile women: methodological and clinical experiences. *Fertil Steril* 1995; **64**: 293–298.
9. Soares SR, Barbosa dos Reis MM, Camargos AF. Diagnostic accuracy of sonohysterography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases. *Fertil Steril* 2000; **73**: 406–411.
10. Rudigoz RC, Salle B, Piacenza JM, de Saint-Hilaire P, Gaucherand P. Hysterosonographic study of the uterine cavity. *J Gynecol Obstet Biol Reprod* 1995; **24**: 697–704.
11. Killick SR. Hysterosalpingo contrast sonography as a screening test for tubal patency in infertile women. *J R Soc Med* 1999; **92**: 628–631.
12. Helpman L, Wolman I. Hysterosalpingo contrast sonography for the evaluation of the tubal factor in infertility investigation: review of literature. *Rev Gynaecol Perinatal Pract* 2003; **3**: 171–176.
13. Hamed HO, Shahin AY, Elsamman AM. Hysterosalpingo-contrast sonography versus radiographic hysterosalpingography in the evaluation of tubal patency. *Int J Gynaecol Obstet* 2009; **105**: 215–217.
14. Anserini P, Delfino F, Ferraiolo A, Remorgida V, Menoni S, De Caro G. Strategies to minimize discomfort during diagnostic hysterosalpingography with disposable balloon catheters: a randomized placebo-controlled study with oral nonsteroidal premedication. *Fertil Steril* 2008; **90**: 844–848.
15. Owens OM, Schiff I, Kaul AF, Cramer DC, Burt RAP. Reduction of pain following hysterosalpingogram by prior analgesic administration. *Fertil Steril* 1985; **43**: 146–148.
16. Peters AAW, Witte EH, Damen ACH, Holm JP, Drogendijk AC, Velde EA, Trimbos JB. Pain relief during and following outpatient curettage and hysterosalpingography. A double blind study to compare the efficacy and safety of tramadol versus naproxen. *Eur J Obstet Gynecol Reprod Biol* 1996; **66**: 51–56.
17. Elson EM, Ridley NTF. Paracetamol as a prophylactic analgesic for hysterosalpingography: a double blind randomized controlled trial. *Clin Radiol* 2000; **55**: 675–678.
18. Costello MF, Horrowitz S, Steigrad S, Saif N, Bennett M, Ekangaki A. Transcervical intrauterine topical local anesthetic at hysterosalpingography: a prospective, randomized, double blind, placebo-controlled trial. *Fertil Steril* 2002; **78**: 1116–1122.
19. Kafali H, Cengiz M, Demir N. Intrauterine lidocaine gel application for pain relief during and after hysterosalpingography. *Int J Gynecol Obstet* 2003; **83**: 65–67.
20. Frishman GN, Spencer PK, Weitzen S, Plosker S, Shafi F. The use of intrauterine lidocaine to minimize pain during hysterosalpingography; a randomized trial. *Obstet Gynecol* 2004; **103**: 1261–1266.
21. De Mello JF Sr, Abrao MS, Cerri GG, de Barros N. Evaluation of pain in three hysterosalpingography techniques: metal cannula with and without paracervical blockage and balloon catheter. *AJR Am J Roentgenol* 2006; **187**: 86–89.
22. Tur-Kaspa I, Seidman DS, Soriano D, Greenberg I, Dor J, Bider D. Hysterosalpingography with a balloon catheter versus a metal cannula: a prospective, randomized, blinded comparative study. *Hum Reprod* 1998; **13**: 75–77.
23. Costello MF, Steigrad S, Collet A. A prospective, randomised, single blinded, controlled trial comparing two topical anaesthetic modalities for the application of a tenaculum to the cervix. *J Obstet Gynaecol* 2005; **25**: 781–785.
24. Rogerson L, Bates J, Weston M, Duffy S. A comparison of outpatient hysteroscopy with saline infusion hysterosonography. *BJOG* 2002; **109**: 800–804.
25. Socolov D, Boian I, Boiculese L, Tamba B, Anghelache-Lupascu I, Socolov R. Comparison of the pain experienced by infertile women undergoing hysterosalpingo contrast sonography or radiographic hysterosalpingography. *Int J Gynaecol Obstet* 2010; **111**: 256–259.
26. Stacey C, Bown C, Manhire A, Rose D. HyCoSy–as good as claimed? *Br J Radiol* 2000; **73**: 133–136.
27. Saunders RD, Shwayder JM, Nakajima ST. Current methods of tubal patency assessment. *Fertil Steril* 2011; **95**: 2171–2179.
28. Tur-Kaspa I, Gal M, Hartman M, Hartman J, Hartman A. A prospective evaluation of uterine abnormalities by saline infusion sonohysterography (SIS) in 1009 women with infertility or abnormal uterine bleeding. *Fertil Steril* 2006; **86**: 1731–1735.
29. Elsayes KM, Pandya A, Platt JF, Bude RO. Technique and diagnostic utility of saline infusion sonohysterography. [Review] *Int J Gynaecol Obstet* 2009; **105**: 5–9.
30. Goodman MP. Rapid Lidocaine Infusion Sonohysterography and Biopsy. *J Am Assoc Gynecol Laparosc* 1996; **3** (Suppl): S16.
31. Dijkman AB, Mol BW, van der Veen F, Bossuyt PM, Hogerzeil HV. Can hysterosalpingocontrast-sonography replace hysterosalpingography in the assessment of tubal subfertility? *Eur J Radiol* 2000; **35**: 44–8.
32. Ayida G, Kennedy S, Barlow D, Chamberlain P. A comparison of patient tolerance of hysterosalpingo-contrast sonography (HyCoSy) with Echovist-200 and X-ray hysterosalpingography

for outpatient investigation of infertile women. *Ultrasound Obstet Gynecol* 1996; **7**: 201–204.
33. Costello MF, Horrowitz S, Steigrad S, Saif N, Bennett M, Ekangaki A. Transcervical intrauterine topical local anesthetic at hysterosalpingography: a prospective, randomized, double-blind, placebo-controlled trial. *Fertil Steril* 2002; **78**: 1116–1122.
34. Lau WC, Tam WH, Lo WK, Yuen PM. A randomised double-blind placebo-controlled trial of transcervical intrauterine local anaesthesia in outpatient hysteroscopy. *BJOG* 2000; **107**: 610–613.
35. Spieldoch RL, Winter TC, Schouweiler C, Ansay S, Evans MD, Lindheim Sr. Optimal catheter placement during sonohysterography: a randomized controlled trial comparing cervical to uterine placement. *Obstet Gynecol* 2008; **111**: 15–21.
36. Widrich T, Bradley LD, Mitchinson AR, Collins RL. Comparison of saline infusion sonography with office hysteroscopy for the evaluation of the endometrium. *Am J Obstet Gynecol* 1996; **174**: 1327–1334.
37. Aggarwal P, Zutshi V, Batra S. Role of hyoscine N-butyl bromide (HBB, buscopan) as labor analgesic. *Indian J Med Sci* 2008; **62**: 179–184.
38. Jareethum R, Suksompong S, Petyim S, Prechapanich J, Laokirkkiat P, Choavaratana R. Efficacy of mefenamic acid and hyoscine for pain relief during saline infusion sonohysterography in infertile women: a double blind randomized controlled trial. *Eur J Obstet Gynecol Reprod Biol* 2011; **155**: 193–198.
39. Gomaa N, Uhlig A, Schusser GF. Effect of Buscopan compositum on the motility of the duodenum, cecum and left ventral colon in healthy conscious horses. *Berl Munch Tierarztl Wochenschr* 2011; **124**: 168–174.
40. Tytgat GN. Hyoscine butylbromide – a review on its parenteral use in acute abdominal spasm and as an aid in abdominal diagnostic and therapeutic procedures. *Curr Med Res Opin* 2008; **24**: 3159–3173.
41. Korell M, Seehaus D, Strowitzki T, Hepp H. Radiologic versus ultrasound Fallopian tube imaging. Painfulness of the examination and diagnostic reliability of hysterosalpingography and hysterosalpingo-contrast-ultrasonography with echovist 200. *Ultraschall Med* 1997; **18**: 3–7.
42. Holz K, Becker R, Schürmann R. Ultrasound in the investigation of tubal patency. A meta-analysis of three comparative studies of Echovist-200 including 1007 women. *Zentralbl Gynakol* 1997; **119**: 366–373.
43. Benditt DG, Ferguson DW, Grubb BP, Kapoor WN, Kugler J, Lerman BB, Maloney JD, Raviele A, Ross B, Sutton R, Wolk MJ, Wood DL. Tilt table testing for assessing syncope. *J Am Coll Cardiol* 1996; **28**: 263–275.
44. Chen-Scarabelli C, Scarabelli TM. Neurocardiogenic syncope. *BMJ* 2004; **329**: 336–341.