BJOG: an International Journal of Obstetrics and Gynaecology
January 2004, Vol. 111, pp. 57–62
DOI: 10.1046/j.1471-0528.2003.00004.x

Randomised comparison of distension media for outpatient hysteroscopy

Meena Shankar[a], Allan Davidson[a], Nick Taub[b], Marwan Habiba[a,c,*]

Objective To compare saline with and without added lignocaine and carbon dioxide distension for out patient hysteroscopy with regards to patient discomfort and hysteroscopic view.

Design Single blind prospective randomised controlled trial.

Setting Specialist out patient clinics in a large teaching hospital.

Population Women undergoing out patient hysteroscopy and endometrial biopsy for abnormal uterine bleeding.

Method Out patient hysteroscopy using carbon dioxide, saline or saline with lignocaine.

Main outcome measures Visual analogue score (VAS) for pain and present pain intensity (PPI) as assessed by patients and the quality of hysteroscopic view as assessed by the operator.

Results Of the 305 women approached, 300 women were randomised into the study. The mean [SD] VAS for pain in the carbon dioxide group was 2.9 [2.3] and in the saline group was 3.1 [2.6], the difference was not statistically significant ($P = 0.49$). The mean [SD] VAS for pain in the saline plus lignocaine group was 3.2 [2.4]. This was not significantly different from the saline group ($P = 0.72$). There was a statistically significant difference between the confidence rating for the hysteroscopic view for the carbon dioxide compared with the saline group; mean [SD] was 8.3 [2.1] and 9.6 [1.1], respectively ($P = 0.001$).

Conclusion Carbon dioxide and saline as distension media are comparable in terms of overall patient discomfort and satisfaction, but saline provides better views and increases confidence in diagnosis. Adding lignocaine to the saline distension medium does not confer any additional benefit.

INTRODUCTION

Diagnostic hysteroscopy is a common gynaecological procedure, with 68,881 procedures performed in England in 2001/2002.[1] The exact proportion of these procedures done in an out patient setting is difficult to ascertain but is likely to be large. Patient acceptability of out patient hysteroscopy is well documented, but the procedure can be uncomfortable or painful.[2–4] Attempts to make the procedure more acceptable include the use of smaller diameter or flexible hysteroscopes,[4] the use of premedication[5] and the use of local anaesthesia either topically as gel or spray or by injection, but the efficacy of most of these methods remain controversial. There are limited data comparing the two most commonly used distension media for out patient hysteroscopy, carbon dioxide and saline,[6] and conflicting evidence on the efficacy of topical transcervical instillation of local anaesthesia.[7–10] There is also little published evidence from randomised trials of the impact of distension media on the quality of the hysteroscopic view.[5] We set out to compare two distension media: carbon dioxide and saline with regards to patient discomfort and the adequacy of the panoramic view and also to assess whether the addition of lignocaine to saline in the distension medium affects patient discomfort.

METHODS

This study was conducted in the one-stop menstrual clinic and the one-stop post-menopausal bleeding clinic in a large teaching hospital during the period April 2000 to May 2001. Women were eligible to participate if they had an intact uterus and were referred by their general practitioner for abnormal uterine bleeding (pre- or postmenopausal) for which hysteroscopy was indicated (Table 1). The local research ethics committee approved the study, and participants gave written consent. All referred patients were eligible, irrespective of age, parity or general health status. Bleeding at the time of hysteroscopy, the presence of large fibroids, previous cone biopsy and Manchester repair were not considered exclusion criteria. The only exclusion

[a]*Department of Obstetrics and Gynaecology, Leicester Royal Infirmary, UK*
[b]*Department of Epidemiology and Public Health, University of Leicester, UK*
[c]*Department of Obstetrics and Gynaecology, University of Leicester, UK*

* **Correspondence**: Mr M. Habiba, Department of Obstetrics and Gynaecology, University of Leicester, Leicester Royal Infirmary, Robert Kilpatrick Clinical Sciences Building, PO Box 65 Leicester LE2 7LX, UK.

Table 1. The referral criteria for outpatient hysteroscopy for patients recruited into the study.

Indications for hysteroscopy among participants of the study
I. Postmenopausal women (one year of amenorrhoea if <50 and six months amenorrhoea if >50) not on HRT who experience vaginal bleeding (irrespective of amount)
II. Women who experienced recurrent post-menopausal bleeding (except if investigated and confirmed atrophic endometrium within preceding six months)
III. Women who experienced vaginal bleeding while on tamoxifen
IV. Women who experienced abnormal/unscheduled vaginal bleeding on HRT
a. If irregular/acyclical
b. If breakthrough/intermenstrual bleeding
c. If excessively heavy
d. If deviates from previous pattern
e. If continues to bleed after stopping HRT
f. After initial hormone manipulation fails
g. Bleeding after first four months of combined HRT or tibolone
V. Premenopausal women
a. Women with irregular periods
b. Intermenstrual bleeding
c. Women with heavy regular cycles that has not responded to first and second line therapy (tranexamic acid, mefenamic acid, oral contraceptive pill)
d. Women with other risk factors of endometrial carcinoma (PCO, obesity)
e. Women with suspicious findings on ultrasound scan

criterion was if the procedure was not feasible (e.g. the cervix could not be visualised or in the presence of severe cervical stenosis). Randomisation tables were used to generate the randomisation sequence for the three distension media, and the sequence was concealed using serial sealed opaque envelopes in blocks of 15. Randomisation envelopes were drawn after the cervix was visualised, and patients were excluded if the procedure could not be carried out because of severe cervical stenosis. Three study groups of equal size were generated using the distension media: (1) carbon dioxide, (2) saline and (3) saline with the addition of lignocaine.

Hysteroscopy was performed following a standardised procedure in all cases, using a 2.7 mm rigid diagnostic hysteroscope (Wolf Lumina, Richard Wolf GMBH) with a 30° foreoblique lens and a 3.5 mm single flow diagnostic sheath. The procedure involved the use of a bivalve speculum of appropriate size (virginal, small, medium or large) and a three-toothed vulsellum to grasp the anterior lip of the cervix after injecting 0.2–0.5 mL of 4% prilocaine hydrochloride under the mucosa at the site of the vulsellum using a dental syringe. A 4 mm Hegar dilator was passed through the cervix prior to the hysterscope in all cases, if necessary after stepwise dilatation starting with the 1 mm Hegar dilator. Uterine sounding was not used. Carbon dioxide was delivered by Hystero-insufflator (Wisap Semm System, WISAP München Germany) providing a variable flow rate of up to 100 mL/min at a maximum pressure of 100 mmHg. Saline distension was delivered from a 500 mL bag wrapped in a pressure bag connected to a manometer pumped to 150–200 mmHg. Saline with lignocaine was delivered as above with the addition of 40 mL of 2% lignocaine (20 mg/mL) into a bag of 500 mL normal saline. In case of poor image, the operator was allowed to use an alternative distension medium. A standardised endometrial biopsy was performed in all cases using a Pipelle (Laboratoire CCD, Paris, France). No analgesia was used before or after the procedures. All procedures were performed by operators with at least 100 procedures' experience. One of the authors (MH) undertook or directly supervised all procedures where particular difficulties were anticipated (e.g. previous Manchester repair or cone biopsy, $n = 19$). No additional procedures were performed. Following hysteroscopy, patients were asked to fill in a questionnaire to assess pain, shoulder pain, their attitude to having the same procedure again and whether they would prefer a general anaesthetic in the future. The operator was asked to complete a questionnaire addressing whether the patient experienced vasovagal symptoms and his/her subjective assessment of the quality of hysteroscopic view, the reasons for unsatisfactory view or change of distension medium and his/her degree of confidence in the hysteroscopic diagnosis based on the images obtained.

The primary outcome measures were pain or discomfort experienced during the procedure. Pain was assessed using the visual analogue score (VAS) and the present pain intensity (PPI). The PPI derived from the McGill Pain Questionnaire[11] was obtained by grading patients' description of the pain as: 0 = none, 1 = mild, 2 = discomfort, 3 = distressing, 4 = horrible, 5 = excruciating. The quality of hysteroscopic view was ranked by the operator as very satisfactory, satisfactory or unsatisfactory. The operator was also asked to complete a visual analogue scale depicting how confident she/he was of the hysteroscopic diagnosis with 0 as not at all confident and 10 as very confident, on the opposite ends of a 10 cm scale. Secondary outcome measures were the occurrence of shoulder tip pain, nausea, vomiting, dizziness, fainting and patient satisfaction using a visual analogue scale of 0 to 10 (0 = very satisfied, 10 = very dissatisfied).

We assumed that the standard deviation of the 10 cm VAS pain scores in each group would be close to 2.5 cm, from a recent large study involving 1144 patients undergoing out patient hysteroscopy in which the mean pain score on this scale was 4.7 [2.5].[12] It was assumed also that an underlying difference in mean pain score between carbon dioxide and saline distension of 1.0 cm or greater would be of clinical significance. We calculated that a sample size of 100 patients in each group would be needed to detect this difference with 80% statistical power at the 5% level of significance. This same 100 patients per group would be sufficient to detect a similar mean difference (1.0 cm) on the VAS for the confidence rated by the operator for the hysteroscopic view with 80% power at 5% significance, assuming a corresponding 2.5 cm (or less) SD for the VAS for confidence scores in each of the groups.

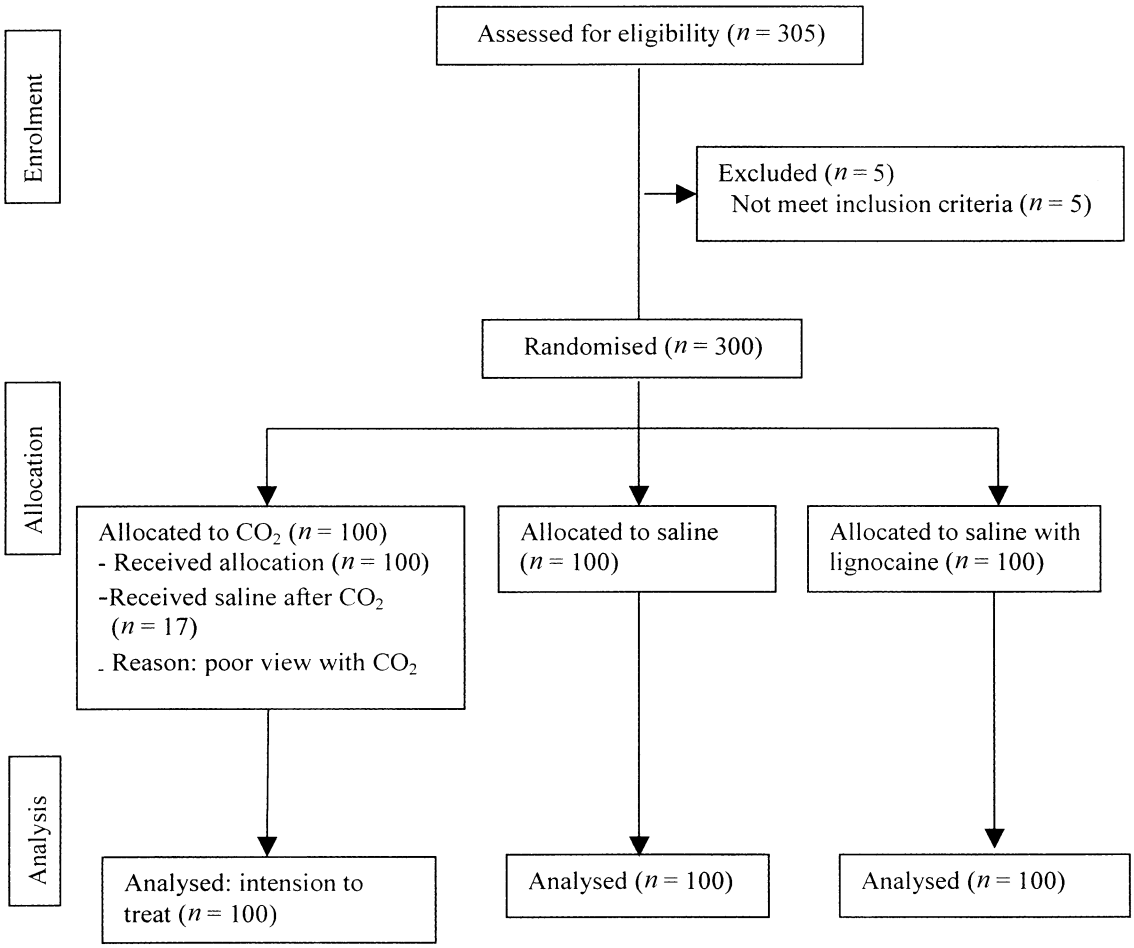

Fig. 1. Flow diagram depicting the outcome of patients recruited into the study.

The mean VAS scores for pain and confidence on hysteroscopic diagnosis for the three groups were compared using the independent sample *t* test assuming equal variances. Relative risks (RR) were calculated for the outcome measures. Dichotomous variables were compared using the χ^2 test with Yates' correction for continuity. A *P* value of <0.05 was considered significant. Patients were categorised as having significant pain using a cutoff point

Table 2. Outcome measures comparing the three groups (carbon dioxide, saline and saline with lignocaine). Values are given as mean [SD], mean {range} or % (95% CI).

Outcome	Carbon dioxide (n = 100)	Saline (n = 100)	Saline with lignocaine (n = 100)
Age (years)	57.8 {40–86}	58.5 {35–91}	57.7 {31–84}
Nulliparous	5 (2, 11)	7 (3, 14)	4 (1, 10)
VAS for pain	2.9 [2.3]	3.1 [2.6]	3.2 [2.4]
VAS for pain >7	8 (3.5, 15.2)	11 (5.6, 18.8)	8 (3.5, 15.2)
PPI >2	9 (4.2, 16.4)	12 (6.4, 20.0)	12 (6.4, 20.0)
Shoulder tip pain	14 (7.9, 22.3)	5 (1.6, 11.2)	2 (0.2, 7.0)
Prefer general anaesthesia	12 (6.4, 20.20)	14 (7.9, 22.3)	21 (13.5, 30.0)
Satisfaction score <3	81 (71.9, 88.2)	90 (82.4, 95.1)	90 (82.4, 95.1)
Nausea/vomiting	2 (0.2, 7.4)	2 (0.2, 7.4)	2 (0.2, 7.4)
Dizziness/fainting	10 (4.9, 17.6)	6 (2.2, 12.6)	4 (1.1, 9.9)
VAS for confidence in diagnosis	8.3 [2.1]	9.6 [1.1]*	
Confidence score >7 for hysteroscopic diagnosis	79 (69.7, 86.5)	95 (88.7, 98.4)*	
Unsatisfactory hysteroscopic view	19 (11.8, 28.1)	4 (1.1, 9.9)*	

Confidence scores and quality of hysteroscopic view are compared only between carbon dioxide and saline.
* Statistically significant ($P < 0.05$) compared with the carbon dioxide group.

Table 3. RR (95% CI) of outcome measures in the three groups — carbon dioxide, saline and saline with lignocaine. Confidence scores and quality of hysteroscopic view were compared only between carbon dioxide and saline.

Outcome	Carbon dioxide *vs* saline	Saline *vs* saline with lignocaine
VAS for pain >7	0.73 (0.28, 1.87)	1.38 (0.86, 2.19)
PPI >2	0.75 (0.3, 1.8)	1.0 (0.44, 2.28)
Shoulder tip pain	2.8 (0.99, 8.7)[a]	2.5 (0.44, 18.5)
Nausea/vomiting	1.0 (0.10, 9.8)	1.0 (0.10, 9.8)
Dizziness/fainting	1.67 (0.58, 5.0)	1.50 (0.39, 6.22)
Patient satisfaction score <3	0.90 (0.81, 1.0)	1.0 (0.74, 1.35)
Confidence score >7 for hysteroscopic view	0.83 (0.77, 0.94)	
Unsatisfactory view	4.75 (1.61, 16.4)	

[a] The difference in VAS for shoulder tip pain was borderline.

of >7 on VAS and >2 on PPI. Similarly, unsatisfactory view on hysteroscopy was analysed as a dichotomous variable. The comparison groups were carbon dioxide *vs* saline and saline *vs* saline and lignocaine. The outcome measures for hysteroscopic view were compared only between the carbon dioxide and the saline groups. An intention-to-treat analysis was used in cases where a change of medium occurred.

RESULTS

Of the 305 patients approached, 5 were not randomised because hysteroscopy was not done, in 1 case, this was because of cervical malignancy, which was biopsied, and in 4 because of severe cervical stenosis that could not be negotiated (Fig. 1). Of the 300 women randomised, 267 (89%) were postmenopausal and 33 (11%) were premenopausal. The characteristics of the women in the three groups and the differences in the outcome measures are given in Table 2. There was no statistically significant difference in the VAS for pain or the number of women experiencing significant pain (VAS for pain >7 or PPI >2) between the three groups. The RR estimate for shoulder tip pain in the carbon dioxide compared with the saline group was 2.8 (95% CI 0.99, 8.72); this was borderline significant at $P = 0.05$ (Table 3). There was a statistically significant increase risk of unsatisfactory view on hysteroscopy (RR = 4.75, 95% CI 1.61, 16.4) with the use of carbon dioxide. The mean [SD] VAS for operator confidence in hysteroscopic diagnosis was 8.3 [2.1] and 9.6 [1.1] for the carbon dioxide and saline groups, respectively. The RR of a high confidence score (>7 on VAS) in the hysteroscopic view was lower for the carbon dioxide compared with the saline group (RR = 0.83, 95% CI 0.77, 0.94). The view was rated as 'very satisfactory' in 84 women in the saline group as compared with 37 in the carbon dioxide group ($P < 0.01$). The reasons for unsatisfactory view in the carbon dioxide group ($n = 19$) were bubbles ($n = 9$), bleeding ($n = 4$), poor distension ($n = 4$), excess mucus ($n = 1$) and reason not stated in one case. In the saline group, the view was unsatisfactory in four cases. In one case each, this was due to bleeding, poor distension or poor light and the reason not stated in one case. The distension medium was changed to saline in 17 of the 19 patients who had an unsatisfactory view using carbon dioxide and the view improved in 11 (64.7%), no further attempt was made in the remaining 2 cases. There were no cases of uterine perforations or excessive bleeding.

DISCUSSION

Out patient hysteroscopy with biopsy has largely replaced traditional in patient dilatation and curettage as an investigation for abnormal uterine bleeding. Distension media have the potential to influence both pain perception and the quality of view and, consequently, the diagnostic accuracy or reliability of the procedure. Our study demonstrates that the overall discomfort experienced by patients was not significantly different between the three distension media. Shoulder tip pain, although more common with carbon dioxide, was only borderline significant; furthermore, it did not alter the mean pain scores. This is at variance with a previously published randomised study, which reported significantly worse lower abdominal and shoulder tip pain with carbon dioxide compared with saline.[5] However, in the study by Nagele *et al.*, more patients in the carbon dioxide group compared with the saline group needed cervical dilatation (35.4% *vs* 17.9% respectively, $P < 0.05$), and the biopsy procedure was not uniform. Both factors could have influenced overall pain perception.

The mean VAS for pain was low in all groups in this study, suggesting good tolerability. Interestingly pain scores were higher than those reported by Nagele *et al.* (mean [SD] for the normal saline group was 0.92 [0.92] and for the carbon dioxide group 1.44 [0.94]), but the number of women experiencing significant pain (>7) in the carbon dioxide group in our study ($n = 8$) was comparable to the number experiencing severe pain ($n = 11/79$) reported by Nagele *et al.* Similar[12] or higher[13] VAS for pain compared with those observed in our study have been reported. The reasons are difficult to ascertain but may be attributable to

different study populations or operative techniques. The mean PPI in our study was 1.6 and 1.7 in the carbon dioxide and saline groups, respectively, which is comparable to the PPI for menstrual pain (mean = 2.4) reported by Melzack.[11] As pain can be experienced at various stages of out patient hysteroscopy, our study has the advantage of standardisation of all interventions including biopsy technique.

Endometrial biopsy has been shown to be the most painful part of the procedure,[10,13–15] but while some of the previous studies used vacuum aspirators or non-standardised biopsy techniques, there remains controversy over the efficacy of transcervical intrauterine anaesthesia. Intrauterine instillation of lignocaine was variably reported to be ineffective[10,14] or effective[8,9] in reducing pain when compared with saline in randomised trials. However, the study by Zupi *et al.*[8] involved only 45 patients, and the differences were not statistically significant. Cicinelli *et al.*[9] studied 80 patients and reported considerably higher (32.5%) incidence of vasovagal reaction in their placebo group compared with our study, and using a 20 cm VAS, their patients experienced relatively high pain scores with a mean and [SD] of 13.45 [5.12] for the group receiving local intrauterine instillation of mepivacaine and 12.05 [4.39] for the group receiving saline as placebo. Davies *et al.*[7] reported local anaesthetic spray to reduce cervical but not uterine pain sensation. The study by Lau *et al.*[10] randomised 90 women to either lignocaine or saline instillation into the uterine cavity prior to hysteroscopy using carbon dioxide insufflation, but there were no statistically significant differences in pain perception or the occurrence of vasovagal episodes. This is in agreement with our study, which involved a larger number of patients.

Carbon dioxide is preferred by many operators as it reduces soiling and is easy to use, but bubbles can cause problems with clarity of view, especially in the presence of bleeding. This has important implications for diagnostic accuracy and may result in missed lesions. In an observational study comparing hysteroscopy with carbon dioxide and with dextrose 5% D5W lactated Ringer's solution in 50 women, Goldfarb[16] reported visualisation and distension to be equally adequate in women without uterine pathology, but that fluid distension was better in women with submucous leiomyomas. This is in agreement with our study, which demonstrated better hysteroscopic view using fluid distension allowing the use of higher manometric pressure than could be safely used with carbon dioxide. The use of fluid distension was associated with a statistically significant higher mean confidence rating for the hysteroscopic view and a lower incidence of unsatisfactory views. This is at variance with the findings of Nagele *et al.*[6] who reported no significant differences between the two distension media, however, in their group there was a higher (13.9%) incidence of poor or very poor vision with the use of carbon dioxide, compared with saline (7.7%). The discrepancy between the two studies could be related to the use of a larger hysteroscope (4 mm) and diagnostic sheath (5.5 mm) in the study by Nagele *et al.* or to their smaller sample size. The most common reason for poor view in our study was the presence of bubbles. The view improved in 11 out of 17 cases following the change to fluid distension, which supports the value of saline distension.

It is interesting to note that despite high acceptance of out patient hysteroscopy, 47/300 (15.7%) of the whole group indicated their preference for a general anaesthetic for a future hysteroscopy. This is comparable to the findings in other studies.[17] In a randomised trial, Kremer *et al.*[17] demonstrated that 83.6% of patients were satisfied with out patient hysteroscopy compared with 77.0% who were satisfied with the same procedure performed as a day case. The extent to which this is influenced by discomfort or pain or by other factors such as embarrassment or anxiety is difficult to ascertain. Passage of the hysteroscope was possible in all but 4 out of the 305 unselected patients approached for enrolment. This contrasts sharply with the initial reported experience with hysteroscopy[18] and reflects accumulated experience, especially the gentle introduction of smaller dilators where necessary.

Because of its nature, this trial could not be double blinded. This creates a potential source of bias, which cannot be eliminated and must be acknowledged. However, operator bias is more likely to have favoured carbon dioxide, the method most widely used at this centre, and possibly nationwide.[6]

CONCLUSION

Out patient hysteroscopy is an acceptable procedure with low levels of pain whatever the distension medium. Carbon dioxide and saline as distension media are comparable in terms of overall patient discomfort and satisfaction but saline provides superior views. No form of local anaesthesia has so far proven effective in reducing the discomfort associated out patient hysteroscopy. We have shown that instilling local anaesthetic in the distension fluid is not beneficial.

Institution

University of Leicester and University Hospitals of Leicester, Leicester, UK.

Conflict of interest and financial support

None.

References

1. Department of Health. *Hospital Episode Statistics 2001/2002*. London: DOH, 2002.
2. de Jong P, Doel F, Falconer A. Outpatient diagnostic hysteroscopy. *Br J Obstet Gynaecol* 1990;**97**(4):299–303.
3. Downes E, Al-Azzawi F. How well do perimenopausal patients accept outpatient hysteroscopy? Visual analogue scoring of acceptability and pain in 100 women. *Eur J Obstet Gynecol Reprod Biol* 1993; **48**(1):37–41.

4. Kremer C, Barik S, Duffy S. Flexible outpatient hysteroscopy without anaesthesia: a safe, successful and well tolerated procedure. *Br J Obstet Gynaecol* 1998;**105**(6):672–676.
5. Nagele F, Lockwood G, Magos A. Randomised placebo controlled trial of mefenamic acid for premedication at outpatient hysteroscopy: a pilot study. *Br J Obstet Gynaecol* 1997;**104**:842–844.
6. Nagele F, Bournas N, O'Connor H, Broadbent M, Richardson R, Magos A. Comparison of carbon dioxide and normal saline for uterine distension in outpatient hysteroscopy. *Fertil Steril* 1996;**65**(2): 305–309.
7. Davies A, Richardson RE, O'Connor H, Baskett TF, Nagele F, Magos AL. Lignocaine aerosol spray in outpatient hysteroscopy: a randomized double-blind placebo-controlled trial. *Fertil Steril* 1997; **67**(6):1019–1023.
8. Zupi E, Luciano AA, Valli E, Marconi D, Maneschi F, Romanini C. The use of topical anesthesia in diagnostic hysteroscopy and endometrial biopsy. *Fertil Steril* 1995;**63**(2):414–416.
9. Cicinelli E, Didonna T, Ambrosi G, Schonauer LM, Fiore G, Matteo MG. Topical anaesthesia for diagnostic hysteroscopy and endometrial biopsy in postmenopausal women: a randomised placebo-controlled double-blind study. *Br J Obstet Gynaecol* 1997;**104**(3):316–319.
10. Lau WC, Tam WH, Lo WK, Yuen PM. A randomised double-blind placebo-controlled trial of transcervical intrauterine local anaesthesia in outpatient hysteroscopy. *Br J Obstet Gynaecol* 2000;**107**(5): 610–613.
11. Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. *Pain* 1975;**1**(3):277–299.
12. De Iaco P, Marabini A, Stefanetti M, Del Vecchio C, Bovicelli L. Acceptability and pain of outpatient hysteroscopy. *J Am Assoc Gynecol Laparosc* 2000;**7**(1):71–75.
13. Vercellini P, Colombo A, Mauro F, Oldani S, Bramante T, Crosignani PG. Paracervical anesthesia for outpatient hysteroscopy. *Fertil Steril* 1994;**62**(5):1083–1085.
14. Broadbent JA, Hill NC, Molnar BG, Rolfe KJ, Magos AL. Randomized placebo controlled trial to assess the role of intracervical lignocaine in outpatient hysteroscopy. *Br J Obstet Gynaecol* 1992;**99**(9): 777–779.
15. Lau WC, Lo WK, Tam WH, Yeun PM. Paracervical anaesthesia in outpatient hysteroscopy: a randomised double blind placebo-controlled trial. *Br J Obstet Gynaecol* 1999;**106**:356–359.
16. Goldfarb HA. Comparison of carbon dioxide with continuous flow technique for office hysteroscopy. *J Am Assoc Gynecol Laparosc* 1996;**3**:571–574.
17. Kremer C, Duffy S, Moroney M. Patient satisfaction with outpatient hysteroscopy versus day case hysteroscopy: randomised controlled trial. *BMJ* 2000;**320**(7230):279–282.
18. Siegler AM, Kemmann E, Gentile GP. Hysteroscopic procedures in 257 patients. *Fertil Steril* 1976;**27**:1267–1273.

Accepted 27 August 2003