

# Carbon dioxide versus normal saline as a uterine distension medium for diagnostic vaginoscopic hysteroscopy in infertile patients: a prospective, randomized, multicenter study

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**Objective:** To evaluate the satisfaction rate, efficacy, and complication rate of carbon dioxide (CO<sub>2</sub>) versus normal saline as a uterine distension medium for outpatient diagnostic vaginoscopic hysteroscopy in infertile patients.

**Design:** Prospective, randomized multicenter study.

**Setting:** Hysteroscopy units in two university hospitals and in a private center.

**Patient(s):** One hundred eighty-nine infertile women undergoing outpatient hysteroscopy.

**Intervention(s):** Outpatient hysteroscopy was performed with CO<sub>2</sub> (group A) or normal saline (group B) and with endometrial biopsy when indicated.

**Main Outcome Measure(s):** Quality of the visualization of the uterine cavity, procedure time, complications, patient discomfort, and satisfaction rate.

**Result(s):** Significantly lower abdominal and shoulder tip pain and a lower incidence of vasovagal reactions were observed in group B in comparison with group A. A higher satisfaction rate and a lower operative time were obtained in the normal saline group in comparison with the CO<sub>2</sub> group. Moreover, group A required significantly more analgesics after the procedure than group B.

**Conclusion(s):** Uterine distension with normal saline seems to have less adverse effects and is better tolerated by patients. Moreover, it allows operative procedures to be performed with the new bipolar instruments. (Fertil Steril® 2003;79:418–21. ©2003 by American Society for Reproductive Medicine.)

**Key Words:** Outpatient hysteroscopy, infertile patients, distension medium, carbon dioxide, normal saline, satisfaction rate

In the past few years, hysteroscopy has replaced dilatation and curettage (D&C) for many cases in which investigation of the uterine cavity is required. D&C is considered obsolete because it is a blind method, with a complication rate of 4%–6% and a low sensitivity for local and pedunculated intracavitary lesions (1). Further disadvantages of D&C include the need for hospital admission and general anesthesia. With direct visualization of the uterine cavity, organic lesions are not missed and directed biopsy can be performed.

The ease of the procedure and the reduced discomfort for the patient, thanks to the intro-

duction of the small-diameter hysteroscopes (<3.5 mm), in combination with an atraumatic insertion technique make hysteroscopy a successful outpatient procedure in the vast majority of cases, even in those cases without the need for local anesthesia (2, 3). Moreover, the high patient compliance, the low failure rate, the low frequency of vagal reactions, and the low complication rate (4, 5) observed during hysteroscopy enable us to integrate this technique as the gold-standard diagnostic procedure in daily gynecological practice.

Because the uterine cavity is a virtual space, hysteroscopy requires its distension with a gas-

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eous (CO<sub>2</sub>) or liquid medium at a pressure of 50–150 mmHg to allow complete visualization of the fundus and ostial areas (6). Some authors have previously compared saline solution and CO<sub>2</sub> hysteroscopy in terms of quality of visualization, pain, operative time, and costs during outpatient hysteroscopy with or without local anesthesia (7).

In this study, we evaluated the satisfaction rate, efficacy, and complication rate of CO<sub>2</sub> versus normal saline as a uterine distension medium for outpatient diagnostic gynecoscopic hysteroscopy in infertile patients.

## MATERIALS AND METHODS

Between March 2000 and December 2000, 189 infertile women undergoing outpatient hysteroscopy were referred to the three participating centers. Patients were prospectively randomized and divided into two groups according to a computer-generated random assignment.

In group A (92 patients), gynecoscopic hysteroscopy was performed using CO<sub>2</sub> as a distension medium. In group B (97 patients), gynecoscopic hysteroscopy was performed using normal saline for uterine distension.

Indications for hysteroscopy were abnormal uterine bleeding, increased endometrial thickness at ultrasound, suspicion of endometrial polyp or myoma, endocervical polyp, and repeated spontaneous abortion.

Hysteroscopy was performed using a compact continuous-flow 5-mm hysteroscope (Wolf, Germany). Illumination was provided by a 250-W Xenon light source. The images were viewed on a high-resolution color monitor using a one-chip camera, and unusual lesions were recorded by video. An electronic HAMOU-hysteroinflator adjusted to a flow rate of up to 50 mL/minute and a pressure not exceeding 100 mmHg was used when the uterine cavity was distended with CO<sub>2</sub>. Normal saline was instilled from a flexible 500-mL bag wrapped in a pressure cuff connected to a manometer and pumped up to 80–120 mmHg.

The hysteroscope was gently inserted into the vagina by a new method called vaginoscopy: the scope was introduced into the vagina without a speculum or cervical forceps. The labia minora were closed manually to limit the exit of CO<sub>2</sub> or normal saline, achieving a satisfactory distention of the vagina and visualization of the cervix. The cervix was identified, and the scope was slowly introduced into the endocervical canal. The endometrial surface was inspected systematically, and the tubal ostia were identified. The hysteroscope was then pulled back toward the internal os to obtain a panoramic view of the whole cavity.

If indicated, endometrial biopsy tissue was taken with the biopsy forceps under direct visualization. The endocervical canal was inspected during withdrawal of the hysteroscope. The view quality obtained during hysteroscopy was ranked on a 5-point scale: 0 = very poor, 1 = poor, 2 = adequate,

3 = good, 4 = excellent. The operative time was recorded from the introduction to the extraction of the scope.

Women for whom diagnostic hysteroscopy failed were referred for the exam under analgesia and conscious sedation. Women with an intrauterine pathology were treated using the new bipolar instruments (8) without any additional analgesia or with traditional electrosurgery under general anesthesia.

Women were asked to rate pain during cervical progression, pain during uterine cavity inspection, lower abdominal pain, and shoulder tip pain on a 10-cm visual analog scale (0 = no pain, to 10 = worst imaginable pain) (9). Any other symptom was recorded in the same fashion. Satisfaction rate was evaluated on a 5-point scale: 0 = no satisfaction, 1 = poor satisfaction, 2 = moderate satisfaction, 3 = satisfaction, 4 = high satisfaction.

We determined that 80 patients per group would have >80% power to detect a difference of 0.75 SD in the pain score. The statistical analysis was performed with the use of a commercial software program (Statistica for Windows, Statsoft, Inc., Tulsa, OK). Student's *t*-test was used to compare parametric data between the two groups. Operative time, analgesic requirement, and pain score differences between the two groups were evaluated with the Wilcoxon rank-sum test. Satisfaction rate was analyzed using the  $\chi^2$  test.  $P < .05$  was considered statistically significant.

## RESULTS

There were no differences between groups in terms of age and parity. A total of 189 infertile patients underwent diagnostic gynecoscopic hysteroscopy, 92 of which were performed with the use of CO<sub>2</sub> and 97 with normal saline as the distension medium.

The distribution of intrauterine pathologies was comparable in the two groups. The most frequent hysteroscopic finding was normal endometrium (43 women in group A and 38 in group B). Endometrial polyps were found in 52 patients (23 in group A and 29 in group B); submucosal fibromyomas were present in 16 and 18 cases in groups A and B, respectively (Table 1). In 91.2% of cases, the hysteroscopic findings were comparable to the histopathologic diagnosis.

There were no significant differences in the scores of quality of visualization between the two groups (poor visualization occurred in 12 women in the CO<sub>2</sub> group and in seven women in the normal saline group). However, the total operative time was significantly higher in the CO<sub>2</sub> group compared with the liquid distension group ( $6.9 \pm 3.1$  vs.  $4.9 \pm 3.7$  minutes,  $P < .01$ ). In 17 women (9%), the procedure was complicated by vasovagal reaction. The number of patients with vasovagal reaction was significantly higher in the CO<sub>2</sub> group in comparison with the normal saline group ( $P < .05$ ) (Table 2).

TABLE 1

Hysteroscopic findings during outpatient diagnostic vaginoscopic hysteroscopy using CO<sub>2</sub> or normal saline as a uterine distension medium.

	Group A, CO <sub>2</sub>	Group B, normal saline	Total patients
Normal cavity	43	38	81
Polyp	23	29	52
Myoma	16	18	34
Adhesions	8	9	17
Others	2	3	5
Total	92	97	189

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Postoperative lower abdominal pain and shoulder tip pain scores were significantly higher with the CO<sub>2</sub> distension medium ( $3.6 \pm 1.3$  vs.  $2.2 \pm 1.3$  and  $1.8 \pm 0.8$  vs.  $0.4 \pm 0.2$ , respectively,  $P < .05$ ). Pain scores during cervical progression and inspection of the cavity were similar in the two groups. Satisfaction rate was significantly higher in group B ( $3.3 \pm 0.8$ ) in comparison with group A ( $2.5 \pm 0.9$ ) ( $P < .05$ ). Only six patients needed to stop the procedure (four in group A and two in group B) (Table 3).

## DISCUSSION

Until now, CO<sub>2</sub> hysteroscopy had uncontested value in the diagnosis of uterine bleeding disorders and infertility. Our study clearly shows that, in contrast to the wide experience with CO<sub>2</sub>, normal saline is an equal or better, by some parameters, than distension medium.

The two distension media are similar in terms of viewing quality, although the presence of bubbles is more frequent with the use of the gas and the view could be reduced by the presence of blood. The rate of vasovagal attacks was higher

TABLE 2

Operative data and complications in 189 patients undergoing vaginoscopic hysteroscopy with CO<sub>2</sub> or normal saline.

	CO <sub>2</sub> (n = 92)	Normal saline (n = 97)	P
Operative time (minutes)	$6.9 \pm 3.1$	$4.9 \pm 3.7$	$< .01$
No. of patients with biopsy (%)	21 (22.8)	35 (36.1)	$< .01$
No. of cases with poor visualization (%)	12 (13.0)	7 (7.2)	NS
No. of patients with vasovagal reaction (%)	12 (13.0)	5 (5.1)	$< .05$

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TABLE 3

Pain control and satisfaction rate for 189 women undergoing vaginoscopic hysteroscopy with CO<sub>2</sub> or normal saline.

	Group A, CO <sub>2</sub> (n = 92)	Group B, Normal saline (n = 97)	P
Pain during cervical progression	$1.7 \pm 0.7$	$1.5 \pm 0.4$	NS
Pain during inspection of the uterine cavity	$1.6 \pm 0.8$	$1.7 \pm 0.6$	NS
Postoperative lower abdominal pain	$3.6 \pm 1.3$	$2.2 \pm 1.3$	$< .05$
Postoperative shoulder pain	$1.8 \pm 0.8$	$0.4 \pm 0.2$	$< .05$
Postoperative pain at 2 hours	$0.4 \pm 0.2$	$0.3 \pm 0.2$	NS
Analgesic requirement, n (%)	11 (11.9)	4 (4.1)	$< .05$
Needed to stop procedure, n (%)	4 (4.3)	2 (2.1)	NS
Satisfaction rate	$2.5 \pm 0.9$	$3.3 \pm 0.8$	$< .05$
Failure rate (%)	3.2	2.1	NS

Note: Values are means  $\pm$  SD. NS = not significant.

Pellicano. Diagnostic hysteroscopy: CO<sub>2</sub> or saline? *Fertil Steril* 2003.

in the CO<sub>2</sub> group in comparison with the saline group. These data are different from those reported by Nagele et al. (7).

Normal saline solution reduced procedure time and patient discomfort. We observed a significant reduction both in abdominal pain and shoulder tip pain in group B in comparison with group A, as already reported by other investigators (7). Normal saline is better accepted by women, is highly tolerated, and has a low failure rate.

Moreover, equipment for liquid distension is far simpler and cheaper than that required for CO<sub>2</sub> hysteroscopy, which requires an expensive insufflation system to control flow rate and intrauterine pressure (7). Furthermore, normal saline allows an immediate use of operative devices with or without a bipolar system, with no risks of intravasation. For these reasons, the use of normal saline is more advantageous in comparison with other solutions as a distension medium.

Several studies reported many complications with the use of CO<sub>2</sub> such as severe cardiopulmonary emboli and even death (10), but other studies (11) show that gas emboli occurring during diagnostic CO<sub>2</sub> hysteroscopy are probably not caused by the gas but by inflow of room air. Passive inflow of air is promoted by cervical manipulation, uterine wound surfaces, and head-down position, with the heart lower than the uterus. In this series, we experienced no complications (CO<sub>2</sub> embolism or uterine perforation).

Moreover, the vaginoscopic approach through a direct introduction of the instrument into the vagina has been described both with CO<sub>2</sub> (12) and normal saline (13) hys-

teroscopy. This approach could be very useful in all patients and especially in virgo women. Our data are similar to those reported by Bettocchi and Selvaggi (13) in terms of pain control during the first step of the procedure.

In conclusion, normal saline diagnostic vaginoscopic hysteroscopy offers all the advantages of CO<sub>2</sub> hysteroscopy, is better accepted by patients, and offers the possibility of easily finding and treating in situ many of the lesions observed. Moreover, the safety, efficacy, and low cost make normal saline a good uterine distension medium for outpatient hysteroscopy in infertile patients. All these advantages are especially evident in infertile patients that could better benefit from the rapidity and minimal invasiveness of this approach.

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