Use of sublingual buprenorphine for pain relief in office hysteroscopy

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Abstract

STUDY OBJECTIVE: To assess the efficacy of sublingual buprenorphine in the relief of pain associated with office hysteroscopy.

DESIGN: Prospective, randomized study (Canadian Task Force classification I).

SETTING: Tertiary medical center.


INTERVENTION: Before hysteroscopy, 80 women received a tablet of buprenorphine (group A), and 84 women received a placebo (group B). Their pain sensations were evaluated on a 10-cm visual analog scale, and they were asked about the adverse reactions and level of satisfaction on the following day.

MEASUREMENTS AND MAIN RESULTS: The pain score in group A was 3.3 ± 1.1, which was similar to 3.2 ± 1.3 in group B. The pain scores in subgroups of women also were similar within the same group and between the two groups. Thirty-one women (38.8%) in group A reported adverse reactions, including nausea, vomiting, and drowsiness, while none in group B reported any adverse reactions.

CONCLUSION: Office hysteroscopy with a 3.1-mm flexible hysteroscope is a well-tolerated procedure. Sublingual buprenorphine is not helpful in relieving the pain associated with hysteroscopy but is associated with significant adverse reactions.

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KEY WORDS: Buprenorphine; Hysteroscope; Analgesia

Hysteroscopy allows direct visualization of the uterine cavity and directed biopsy, and it is regarded as the gold standard for investigation of intrauterine abnormalities. Although it is generally well tolerated, it is associated with a certain degree of pain and possible vasovagal reaction. Actually, pain is the most common reason for failure to complete the procedure.\(^1\) In 2500 outpatient hysteroscopies reported,\(^1\) 29.8% required local anesthesia, and 3.6% failed, in which 84% were due to excessive discomfort.

Various methods of analgesia have been proposed to suppress the pain associated with hysteroscopy: general anesthesia, paracervical block,\(^2,3\) intracervical injection,\(^4\) lidocaine spray,\(^5,6\) and intrauterine instillation of lignocaine.\(^7\) However, the results are controversial, and there are no established guidelines for the use of analgesia in office hysteroscopy.\(^8\)

Buprenorphine is a potent and safe opioid analgesic with...
partial agonist and antagonist actions. As an analgesic, buprenorphine is used for the relief of moderate to severe pain. Compared with morphine, buprenorphine provides adequate postoperative analgesia of longer duration, and the analgesic potency of parenteral buprenorphine is 25 to 50 times that of parenteral morphine. In a series of 7548 patients receiving buprenorphine in the immediate postoperative period, 90% of patients had good or adequate pain relief.

Buprenorphine also has been used to provide preoperative sedation and analgesia and as an adjunct to surgical anesthesia. Its anxiolytic and sedative properties make it suitable as a preoperative medication. Buprenorphine can be given sublingually as well as parenterally. It is readily absorbed following sublingual administration. Although maximal effect is reached later with sublingual administration, it provides longer duration of action and does not cause discomfort when administered as in parenteral routes. In order to assess the efficacy of sublingual buprenorphine in the relief of pain during hysteroscopy, we conducted a prospective, randomized study under double-blind conditions.

Materials and methods

From September 2003 through March 2004, 179 women referred for office hysteroscopy were included in this study. The study was approved by the medical ethics committee of the hospital. The patients were randomized by computer-generated numbers to receive buprenorphine (Temgesic, Reckitt & Colman, Hull, UK) (group A) or placebo (group B). Every woman put a tablet of buprenorphine (0.2 mg) or a placebo under her tongue 40 minutes before the procedure.

Indications for hysteroscopy included abnormal uterine bleeding, suspected intracavitary lesion (such as uterine synechiae, endometrial hyperplasia, endometrial polyp, or submucosal myoma), and infertility.

All procedures were performed by the same physician (YHL) using a flexible hysteroscope with a 3.1-mm outer diameter and a bending section of 100 degrees both up and down (Olympus HYF Type XP, Tokyo, Japan). The uterine cavity was distended with 5% dextrose solution hung 60 cm above the operating table. Illumination was provided by a 250 W high-intensity cold-light source. No tenaculum or cervical dilatation was used in any procedures.

During the procedure, patients were observed and their pain sensations evaluated by the same nurse using a 10-cm visual analog scale (VAS). For each patient, the worst pain sensations evaluated by the same nurse using a 10-cm visual analog scale (VAS). For each patient, the worst pain score.

On the day after the procedure, the patients were asked to evaluate their level of satisfaction, where 0 = not satisfied, 1 = a little satisfied, and 2 = very satisfied.

All results were expressed as mean ± SD unless otherwise stated. Statistical significance was assessed by independent t-test, Fisher’s exact test, and χ² test when appropriate. SPSS software (Statistical Package for Social Science; Windows version 10.0, SPSS, Inc., Chicago, IL) was used for the statistical analysis. A p value of <.05 was considered as statistically significant.

Results

From September 2003 through March 2004, 179 women underwent office hysteroscopy at our hospital. The procedure failed in 15 women because of cervical stenosis. These women underwent repeat hysteroscopy under general anesthesia. None of the procedures were discontinued because of intolerable pain. Therefore, we enrolled 164 women in the study. Thirty-seven (22.6%) of them were postmenopausal. The indications for hysteroscopy were abnormal uterine bleeding (32.8%), infertility (30.3%), intracavitary tumor lesion (myoma or polyp) (26.2%), and others (10.7%). Among the 164 women, 80 women received buprenorphine (group A), and 84 received placebo (group B). As shown in Table 1, there were no significant differences in patients’ characteristics, including mean age and number of nulliparous, multiparous, and postmenopausal women.

The VAS pain scores are shown in Table 2. The mean pain score in group A was 3.3, which was similar to 3.2 in group B. The pain scores in various subgroups of women, including postmenopausal, nulliparous, and multiparous women, also were similar within the same group and between the two groups. For most patients, the worst discomfort was related to the insertion of the speculum, not the hysteroscopy per se.

In group A, 31 women (38.8%) reported adverse reactions associated with the procedure. Among them, 4 (5.0%) reported only nausea or vomiting, 2 (2.5%) reported only drowsiness, and 25 (31.3%) reported both. None of the women in group B reported any discomfort or adverse effects. No woman experienced vagal reactions.

Table 3 shows the levels of satisfaction. Women in group B were more satisfied with the procedure. Thirty women (37.5%) in group A were not satisfied with the procedure because of adverse effects.

<table>
<thead>
<tr>
<th>Table 1 Patient characteristics</th>
<th>With buprenorphine (n = 80)</th>
<th>Without buprenorphine (n = 84)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yrs)</td>
<td>41.0 ± 12.1</td>
<td>39.6 ± 12.3</td>
<td>NS</td>
</tr>
<tr>
<td>No. (%) premenopausal</td>
<td>61 (76.3)</td>
<td>66 (78.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>30 (37.5)</td>
<td>34 (40.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Multiparous</td>
<td>31 (38.8)</td>
<td>32 (38.1)</td>
<td>NS</td>
</tr>
<tr>
<td>No. (%) postmenopausal</td>
<td>19 (23.8)</td>
<td>18 (21.4)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = not significant by independent t-test and χ² test.
Discussion

Pain associated with hysteroscopy occurs during insertion of the speculum, dilatation of the cervix for insertion of the hysteroscope, distention of the uterine cavity with distention medium, and direct stimulation of the uterine wall by the hysteroscope. Also, the use of tenaculum and biopsy may also cause pain. Office hysteroscopy may be painful, even if it is performed by an experienced surgeon with a nontraumatic technique. In fact, the single most common reason for failure of hysteroscopy is pain.

The effect of local analgesia in office hysteroscopy is inconclusive. Although some studies demonstrated that paracervical block reduced pain, others did not reveal beneficial effect. In addition, paracervical block carries potential complications such as infection, bleeding, toxicity from intravasation or systemic absorption, and sacral plexus trauma. One study showed that intracervical injection was not helpful, and 43% of women found the injection to be the most painful part of the procedure.

The afferent innervations of the upper and lower parts of the uterus differ in the course and source. Afferent fibers conducting pain impulses from the fundus and body follow the sympathetic fibers to T11 and T12; while afferent fibers from the cervix follow the parasympathetic fibers to S2 to S4. Therefore, injection of local analgesic at or around the cervix blocks only pain arising from the cervix, but does not block pain originating from the uterine cavity.

We speculated that systemic administration of analgesics might be more effective than local analgesics in relieving the pain associated with hysteroscopy. Buprenorphine is a narcotic analgesic and can be given by sublingual route, which is easier for patients and physicians, and does not cause the discomfort associated with local injection. In this study, however, we found that buprenorphine had no benefit in reducing the pain associated with hysteroscopy. The mean VAS pain scores were similar between group A and group B. The mean pain scores of the subgroups were also similar within the same group or between groups A and B. This indicates that flexible hysteroscopy is a well-tolerated procedure even without analgesia, so taking buprenorphine beforehand had no beneficial effect. In a study performed by researchers using a 3.5-mm flexible hysteroscope without anesthesia, 94.6% of women experienced little or no pain. A study using a 2.5-mm flexible hysteroscope also found the procedure well tolerated. In that study, mean pain score was higher in postmenopausal women. However, in our study, mean pain scores were similar between premenopausal and postmenopausal women, either with or without buprenorphine.

The adverse effects of buprenorphine are similar to those of morphine and meperidine. In a large series of 7548 Caucasian patients receiving 0.3 to 0.6 mg buprenorphine postoperatively, nausea developed in 8.5% and vomiting developed in 7.3%. However, Chinese patients seem to be very sensitive to buprenorphine. In our study, 27 (36.3%) of 80 women reported nausea or vomiting after taking buprenorphine.

Sedation (including drowsiness) is the most common adverse effect of parenteral buprenorphine, occurring in approximately two-thirds of patients. In our study, 27 (33.8%) of 80 women developed drowsiness. The high incidence of adverse reactions associated with buprenorphine is reflected by the high level of dissatisfaction of patients in group A.

Conclusion

Office hysteroscopy with a 3.1-mm flexible hysteroscope is a well-tolerated procedure. Nearly all patients found this procedure acceptable even without analgesia. Buprenorphine is not beneficial in relieving pain, but is associated with high adverse effects and a lower level of satisfaction.

Table 2

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>With buprenorphine (n = 80)</th>
<th>Without buprenorphine (n = 84)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole group</td>
<td>3.3 ± 1.1</td>
<td>3.2 ± 1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>3.3 ± 1.1</td>
<td>3.2 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>3.3 ± 1.2</td>
<td>3.2 ± 1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Multiparous</td>
<td>3.4 ± 1.1</td>
<td>3.2 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>3.5 ± 1.2</td>
<td>3.1 ± 1.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = not significant by independent t-test; VAS = visual analog scale.

Table 3

<table>
<thead>
<tr>
<th>Level of satisfaction</th>
<th>With buprenorphine No. (%)</th>
<th>Without buprenorphine No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not satisfied</td>
<td>30 (37.5)</td>
<td>0</td>
</tr>
<tr>
<td>A little satisfied</td>
<td>9 (11.3)</td>
<td>15 (17.9)</td>
</tr>
<tr>
<td>Very satisfied</td>
<td>41 (51.3)</td>
<td>69 (82.1)</td>
</tr>
</tbody>
</table>

p <.0001 by Fisher’s exact test.

References


