



## Analgesics for Pain Relief In Outpatient Hysteroscopy

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### Abstract:

We have performed a review of literature to find evidence on the effectiveness of the different methods used to decrease pain perception during office hysteroscopy and identify risk factors of a painful hysteroscopy.

**Keywords:** analgesia, hysteroscopy, outpatient, pain, paracervical block.

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### Introduction:

Outpatient hysteroscopy in the office setting is a safe and effective procedure for diagnosis of intrauterine pathology and abnormal uterine bleeding, as well as for therapeutic operative treatment and transcervical sterilization<sup>(1)</sup>.

Office hysteroscopy is a diagnostic and operative technique with many advantages compared with operating room-based hysteroscopy: it does not require hospital admission, preoperative tests, and general or regional anesthesia. Importantly, it has a decreased postsurgical recovery period and global cost of the procedure<sup>(1)</sup>.

More ever it helps to minimize rate of complications , although it is generally a well-tolerated procedure .However pain, vagal syndrome and hypotension are

common among patients undergoing hysteroscopy<sup>(1)</sup>.

Pain is still the main cause of office hysteroscopy failure. Factors related to pain experience during hysteroscopy are still not well-known. In addition, there is controversy about anesthesia and analgesia for outpatient hysteroscopy. 84% of failed hysteroscopies are due to excessive discomfort. 34.8% of patients who undergo anesthesia-free diagnostic hysteroscopy report severe pain. Report moderate to severe pain [measured by Visual Analog Scale (VAS) score of 5 or more immediately after examination] in 68.4% of patients<sup>(2)</sup>.

An adequate knowledge of anatomy is essential to understand the physiology of pain in hysteroscopy. Anatomical structures of the female pelvis are innervated by two pathways. The fundus of the uterus is

innervated by sympathetic fibers from T10 to L2 via the inferior hypogastric plexus, which enters the uterus by the uterosacral ligaments and by the infundibulopelvic ligament, forming the ovarian plexuses. The upper vagina, cervix, and lower uterine segment are innervated by parasympathetic fibers from S2 to S4, which form the Frankenhauser or uterovaginal plexus, which enters the uterus following the cardinal ligaments. Myometrium and endometrium are innervated by a plexus at the myometrial–endometrial interface. Only the basal third of the endometrium is innervated. Myometrial innervation can vary with disease processes such as endometriosis or adenomyosis<sup>(3)</sup>.

Considering hysteroscopic techniques, pain is mainly produced when speculum or tenaculum are placed, with cervical dilation, passage of the hysteroscope through the cervical canal, and distension of the uterus with fluid. Operative procedures that damage the endometrial walls, such as endometrial biopsy, polypectomy or myomectomy, ablation or tubal sterilization, are also painful. Due to this complex innervation, successful anesthesia requires simultaneous targeting of more than one site, including paracervical and intracervical anesthesia and topical agents in the cervical canal and endometrial cavity<sup>(4)</sup>.

#### **To avoid pain:**

**1- No touch technique:** performing a ‘no touch’ approach (direct entry with vaginoscopy and hydrodistension of the cervix for dilation, while avoiding the use of speculum and tenaculum) and the use of small caliber instruments. Moreover,

normal saline has been shown to be more comfortable and safer than carbon dioxide and glycine as distension medium. Although it is thought that warming the distension fluid to physiological temperature (37.5°C) to reduce pain perception, it has not been proven<sup>(5)</sup>.

**2- A smaller outer diameter of the hysteroscope** decreases pain perceived by the patients. Technological improvements have enabled minimization of the caliber of hysteroscopes (minihysteroscopes  $\leq 3.5$  mm) and instruments. Reduction in outer diameter by 1 mm or 2 mm as well as reduction in total hysteroscope size reduces the section of area of the instrument by 50–75%. The passage of the minihysteroscope through the cervical canal is consequently smoother, causing less pain. Flexible hysteroscopes have also been developed, making it easier to follow the canal pathway. However, this ‘no-touch’ technique is not always feasible, and even when it is possible, it is still sometimes painful. For this reason, identification of risk factors for a painful procedure has to be done<sup>(6)</sup>.

**3- Procedure-related risk factors for pain during hysteroscopy:** are resection of polyps larger than 2.2 cm, and long procedures (>15 minutes). 30% more risk of pain when procedures exceed 3 minutes. Protective factors against unacceptable pain are a higher degree of hysteroscopist experience (reducing the risk by half),. Patients with high risk factors of suffering a painful procedure may be candidates for anesthesia<sup>(7)</sup>.

**4- Controlling anxiety:** has a role in pain perception. Methods for controlling anxiety have been proposed to reduce pain perception. Reducing waiting time has a statistically significant positive correlation, even if weak, with pain perception during hysteroscopy ( $r=0.45$ ;  $p < 0.01$ ). However, anxiety per se, measured by values of anxiety state (State-Trait Anxiety Inventory scales), was not significantly correlated with pain<sup>(8)</sup>.

A randomized trial using music to reduce anxiety during hysteroscopy has proven that it decreases anxiety and pain perceived during the procedure [VAS score 4.83 (no music group) vs. 2.95 (music group);  $p < 0.001$ ]. It also reduces systolic blood pressure and heart rate and, according to **Angioli et al**, distracts the patient from anxiety-provoking thoughts and makes them focus in more pleasant stimuli<sup>(8)</sup>.

**5- Anesthetic and analgesic methods reported in literature for outpatient hysteroscopy:** include oral and intravenous analgesia; nonopioid analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) or paracetamol; opioid analgesics; intrauterine, paracervical, transcervical, or uterosacral local anesthetics; and spray, gel, and cream topical anesthetics<sup>(9)</sup>.

NSAIDs are systemic analgesics that decrease uterine activity and pain by inhibiting cyclooxygenase and reducing circulating prostaglandins. They include naproxen, diclofenac, ibuprofen, and ketorolac<sup>(5)</sup>.

However, studies throw controversial results regarding the use of NSAIDs in hysteroscopic procedures. No beneficial effects from oral diclofenac given 1–2 hours before the procedure during and after conventional hysteroscopy. unable to demonstrate a benefit in pain reduction with the use of 100-mg rectal diclofenac 60 minutes before outpatient hysteroscopy in a randomized controlled trial in nulliparous infertile women. Ketoprofen has also failed to decrease intraoperative pain, but seemed effective for postoperative pain after hysteroscopy. Ketoprofen VAS scores during and immediately after hysteroscopy were higher than misoprostol VAS scores in a randomized controlled trial<sup>(9)</sup>.

Acetaminophen also inhibits cyclooxygenase, acting in the central nervous system instead of the periphery. It is a good option in cases of allergy or intolerance to NSAIDs. Mefenamic acid, a prostaglandin synthesis inhibitor, also reduces circulating prostaglandins. Controversially, a randomized placebo controlled trial concluded that mefenamic acid (500 mg) given 1 hour before outpatient hysteroscopy is not superior to placebo in reducing discomfort during the procedure but significantly reduced postoperative pain (30 minutes and 60 minutes after the procedure)<sup>(10)</sup>.

A Cochrane Review meta-analysis, Pain relief for outpatient hysteroscopy, did not demonstrate any significant reduction with NSAIDs or opioid analgesics during or after the procedure<sup>(10)</sup>.

Opioids have also been used for pain treatment in hysteroscopy. They produce analgesic effects through interaction with

endogenous opioid mu receptors. They provide analgesic effects and cause euphoria. The most frequently used opioid for gynecologic procedures is fentanyl, which causes moderate sedation with a rapid onset and brief duration. It can be reversed by naloxone. sublingual buprenorphine is not only unhelpful in relieving pain associated with hysteroscopy, but is also associated with significant adverse reactions. It reported 38.8% of adverse reactions, including 5% drowsiness, 2.5% nausea or vomiting, and 31.3% of both. The high incidence of these adverse effects limits the use of opioids in the outpatient setting<sup>(11)</sup>.

Local anesthesia: according to the aforementioned Cochrane Review, only local anesthetics provide a significant reduction in the mean pain scores during and 30 minutes after the procedure. They include paracervical, intracervical, transcervical, or uterosacral block and topical application in spray, cream, or gel form. intracervical and paracervical injections of local anesthetic significantly reduced pain in women undergoing outpatient hysteroscopy, whereas transcervical and topical application did not. Paracervical injection was significantly superior to the other anesthetic methods. They also concluded that local anesthetics did not have a significant effect on the incidence of vasovagal episodes<sup>(10)</sup>.

Munro and Brooks' review of local anesthesia for office hysteroscopy also supports that a consistent positive anesthetic effect is only demonstrated with paracervical anesthesia. Five of the six randomized clinical trials that their review included demonstrated reduced pain in patients who received paracervical

anesthesia compared with placebo. Paracervical anesthesia is also effective in hysteroscopic tubal sterilization, but only for passage of the hysteroscope through the cervical canal and for cervical manipulation, not for tubal insertion of the devices<sup>(10)</sup>.

Although the Cochrane Review of paracervical local anesthesia for uterine intervention does not recommend the use of paracervical injection because it does not reduce intraoperative pain, this does not apply to office hysteroscopy, as the review includes procedures that require cervical dilation. Exclusively local anesthesia is not recommended by the Cochrane Review if cervical dilation is needed. Combined cervical block protocols have been studied for resection of polyps and myomas by hysteroscopy<sup>(9)</sup>.

**Lukes et al's** randomized trial found a statistically significant difference in pain score between a group receiving paracervical and intracervical block and a group only receiving intracervical block (1.3 vs. 2.1, respectively). This is supported by another clinical trial, which demonstrated a significant decrease of pain with combined paracervical/intracervical anesthesia during and after 30 minutes of the procedure<sup>(9)</sup>.

The effect of anesthetics and analgesics for pain control in outpatient hysteroscopy provide controversial results. The lack of uniformity in the published papers makes it difficult to draw conclusions. Although ambitious, this review's aim is probably too wide, attempting to assess the subject of analgesia for hysteroscopy, which presents many alternatives and no clear conclusions<sup>(9)</sup>.

A more focused objective would make research and drawing conclusions easier. Potential biases of this review include language restriction to only English papers and publication bias, as only published papers were included, as well as operator bias and departmental policy bias. Heterogeneity is also present, due to the variety of studies included, which was necessary to not incur in a too strict selection that could limit our search<sup>(9)</sup>.

Observational studies were not included in this analysis, due to their low quality. However, the aim of this paper is to give a wide view of the available methods of analgesia for office hysteroscopy according to literature and the factors that influence it, so that we can take them into account to reduce pain when performing hysteroscopy<sup>(9)</sup>.

Future research should be directed to identifying the best analgesic method for office hysteroscopy, to avoid heterogeneity and the use of ineffective methods that can even cause morbidity, and to unification of doses and techniques that could generate international guidelines for this procedure that has no standards for pain control<sup>(10)</sup>.

Nonpharmacological methods could also be useful in reducing hysteroscopy-related pain, such as a no-touch approach with vaginoscopy and minihysteroscopes, reducing waiting time before hysteroscopy, and the use of music during the procedure to reduce anxiety. Risk and protective factors of suffering pain during outpatient hysteroscopy are important for identifying patients who are susceptible to receiving anesthesia. Risk factors include menopause, nulliparity, dysmenorrhea, and a longer time

of procedure. Experience of the hysteroscopist is a significant protective factor against pain perception during hysteroscopy<sup>(10)</sup>.

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