



International Journal of Reproductive Medicine & Gynecology

Review Article

Pain Management for Office Hysteroscopy -

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Submitted: 12 March 2018; Approved: 18 April 2018; Published: 23 April 2018

Cite this article: Jose C, Fausto A. Pain Management for Office Hysteroscopy. *Int J Reprod Med Gynecol.* 2018;4(1): 017-021.

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INTRODUCTION

Office hysteroscopy is an indispensable tool in modern gynecology. Diagnostic hysteroscopy is considered the gold standard for the study of intra-uterine pathologies [1].

Diagnostic hysteroscopy is commonly performed in an office setting by inserting the hysteroscope into the external cervical OS and advancing the scope under direct visualization until entering the uterine cavity distending the uterus with the selected distention media, commonly normal saline. Over the last few years, there have been great advancements in surgical instruments for use in gynecological procedures, the creation of smaller hysteroscopes, as well as improvements in operative techniques [2]. These advancements have facilitated the performance of hysteroscopy becoming a popular procedure. In an effort to decrease cost and facilitate patient access, hysteroscopic procedures are increasingly migrating from the operating room to the office [3-5]. One major obstacle to transitioning hysteroscopy to the outpatient settings is pain management as the procedure is largely viewed as painful. Pain along with inability to access the uterus are often cited as the main reasons for failed office hysteroscopy.

There is no consensus in the literature as to the optimal method of pain relief. It is important to establish evidenced-based pain management protocols to decrease pain associated with office hysteroscopy, which will reduce the rate of failed procedures and therefore decrease cost, time, and risk associated with performing the procedure in the operating room with the additional risk of general anesthesia. In this review article, I will outline effective pain control regimens based on the current published literature that could be used as a guide to manage pain when performing in-office diagnostic and operative hysteroscopy.

FACTORS AFFECTING PAIN DURING HYSTEROSCOPIC PROCEDURES

The experience of pain associated with hysteroscopy, as any other pain eliciting procedure, is influenced by many factors related to the patient and the operative technique. Adequate patient selection for in office procedures is extremely important. Some patients will only tolerate the procedure if performed under general anesthesia. Table 1 list risk and protective factors associated with pain perception during in office hysteroscopy. Providers should screen each patient to ensure that the patient is a good candidate for in-office performance of the needed procedure.

Patient related factors

Parity: There is conflicting evidence regarding the influence of prior vaginal delivery and the pain reported during office procedures. Although some research shows that nulliparity does not increase pain during reported during in office hysteroscopy. Masson et al.

[6] published a prospective observational study revealing that the number of spontaneous vaginal deliveries is inversely correlated with pain intensity during hysteroscopy. This is concordant with findings published by Van Dongen et al. [7] who reported that nulliparous women have a 27% higher risk of perceiving pain at Visual Analog Scale (VAS) > 5 during hysteroscopy when compared to women who have had vaginal deliveries. It is speculated that the more dilated multiparous cervix will require less force to introduce the hysteroscope as opposed to a nulliparous cervix that will pose more resistance.

Menopausal status: In an observational study of over 200 patients, Carta et al. [8] described menopause status as a specific risk factor associated with pain > 4 in VAS (OR, 2.81; 95% CI, 1.10-7.40). On the other hand, Torok et al. [9] in a study evaluating pain level during office hysteroscopy according to menopausal status, parity, and size of the instrument, found no correlation between menopausal status and pain during office hysteroscopy.

Cervical canal: Mazzon et al. [6] evaluated the correlation between pain perceived during hysteroscopy and the characteristics of the cervix, specifically the angle and morphology of the cervical canal. They concluded that the anatomy of the cervical canal does not seem to play an important role for pain. However, the presence of cervical adhesions and the resulting force needed to enter the uterine cavity is a major factor generating pain during hysteroscopy. In a recent video-article publication Bettocchi et al. [10] described different techniques to overcome the difficult cervix in over 30,000 in office hysteroscopy procedures, demonstrating that the surgical technique and gynecologist experience is an important factor to reduce pain during in office hysteroscopy.

History of chronic pelvic pain and/or dysmenorrhea: There is solid, consistent evidence that suggests that a history of chronic pelvic pain or dysmenorrhea is associated with increased chance of unacceptable pain during hysteroscopy.

Anxiety: It is reasonable to assume that reducing pre-procedure anxiety has a positive impact on the patient's experience of pain during the procedure. Elevated levels of anxiety in patients waiting for hysteroscopy have been reported. In a large study of over 500 patients interviewed by a physician before undergoing hysteroscopy, 65% reported anxiety. However, to what extent anxiety may affect pain experienced by patients during hysteroscopy remains unclear [11]. Pharmacologic intervention such as use of anxiolytics and sedatives as well as non-pharmacologic interventions to reduce operative anxiety has been suggested.

PROCEDURE/TECHNIQUE FACTORS

Duration of the procedure

Duration of the procedure is considered a limitation when performing in office procedures. Longer procedures and more difficult to tolerate. There is conflicting evidence suggesting that severe or intolerable pain is more frequently reported in procedures lasting longer than 2 minutes. A prospective study including 558 patients reported that the duration of the procedure was significantly longer in patients who reported having experienced severe pain during the procedure. However, based on our personal observation, shorter procedures tend to be better tolerated [12].

Experience of the operator

Hysteroscopist experience has been shown to be associated with patient's perception of pain during hysteroscopy. Experts tend to

Table 1: Risk and protective factors associated with pain perception during in office hysteroscopy.

Increased pain	Decreased pain
Nulliparity	History of vaginal delivery
Postmenopausal status	High volume hysteroscopist
History of chronic pain/Dysmenorrhea	Short procedure
Anxiety	Low distention pressures
High level of anticipated pain	Small diameter hysteroscopes



perform the procedure more quickly and smoothly, thereby causing less discomfort to the patient.

Distension media

Hysteroscopy requires distention of the uterine cavity to allow adequate visualization. It is well accepted that the use of normal saline is associated with less pain than carbon dioxide. An important, frequently neglected, factor that generates pain and discomfort is the filling pressure utilized during the procedure. Higher uterine filling pressures cause excessive pain, which can result in failed procedures. The optimal filling pressure to provide adequate visualization without causing excessive pain is around 50 mmHg.

Hysteroscope size

In the last two decades, a new generation of “mini” hysteroscopes that are 1 to 3 mm smaller than the conventional 5 mm instruments have hit the market. These small scopes have made more feasible to perform in-office hysteroscopy as they require less dilation of the cervical canal, cause less trauma, and thereby decrease the pain experienced during the procedure. A systematic review of 8 studies including 2322 patients who underwent office hysteroscopy without anesthesia concluded that 3.5 mm rigid mini-hysteroscopes are associated with significantly less pain than conventional 5 mm hysteroscopes [13].

Use of flexible hysteroscopes

The incorporation of fiber optic technology has produced flexible hysteroscopes with the ability to accommodate the pathway of the cervical canal. However, there is insufficient evidence at this time to demonstrate the superiority of flexible over rigid instruments.

Vaginoscopic approach

In 1997 Bettocchi and Selvaggi [4] presented a revolutionary approach to hysteroscopy advocating the “vagoscopic approach” for diagnostic hysteroscopy, which avoids the use of a speculum and tenaculum. They presented a series of 1200 hysteroscopy, of which 680 were performed using the vaginoscopic approach and were found to be associated with significantly decreased rates of patient’s discomfort. This technique soon became widespread and is currently the preferred approach of most expert hysteroscopists. A RCT from Sagiv et al. [14] compared the vaginoscopic approach without anesthesia to the traditional approach with intracervical anesthesia. Eighty-three women underwent hysteroscopy without use of a speculum, tenaculum, or anesthesia. Forty-seven women received intracervical anesthesia with 10 ml of 3% mepivacaine hydrochloride solution. Hysteroscopy was performed using 0.9% saline solution as distention media and a rigid 3.7-mm hysteroscope in both groups. Both mean pain scores during the examination and after completion of the procedure were significantly lower in the group without use of a speculum, tenaculum, or anesthesia ($p = 0.008$). We strongly encourage the use of vaginoscopy whenever possible.

PAIN MANAGEMENT OPTIONS

Local anesthesia

The use of local anesthesia is a common practice to decrease pain when performing in office procedures. The administration of local anesthesia in gynecologic procedures can be performed using different modalities: topical, intrauterine, intracervical, and paracervical. Safe use of anesthetic drugs requires a complete understanding of the potency, avoiding toxicity, and early recognition of potential complications [15].

Topical agents

Uterine Cervix: There is conflicting data to evaluate the use of topical anesthetics on the cervix to decrease pain during hysteroscopy. Wong et al. [16] found no benefit using lignocaine gel applied on the cervix before the procedure, whereas Soriano et al. [17] demonstrated substantial reduction in pain associated with the use of lidocaine spray. Anesthetic agents delivered by sprays, gels and creams provide anesthesia to superficial pain receptors. A later published meta-analysis concluded that topical cervical anesthesia was not effective in decreasing pain during hysteroscopy when compared to placebo (20.32; 95% CI, 20.97 to 0.33) [18].

Uterine Corpus: Another commonly used modality is the administration of intrauterine local anesthesia. This technique has been investigated in several trials. A review published by Cooper et al. [17] concluded that intracavitary anesthesia was not effective (20.11; 95% CI, 20.31 to 0.10). Moreover, a systematic review of the use of intrauterine anesthesia for different gynecologic procedures concluded that intrauterine anesthesia is an effective method of pain management for some gynecologic office procedures but not for all [19].

Injectable agents

The most common local anesthetics used in the office are lidocaine and bupivacaine. The maximum dose of lidocaine without epinephrine should not exceed 4.5 mg/kg. A dose of 200 mg of lidocaine (20 ml of 1% lidocaine) is often used for paracervical block and is well below the threshold of toxicity. At low serum levels of lidocaine, patients may experience tinnitus and numbness of the mouth. This is not uncommon when using paracervical blocks. At higher levels of lidocaine, patients may experience visual disturbances, confusion, seizure, or cardio-respiratory arrest. Techniques to lower the risk of lidocaine toxicity include adding vasopressin or epinephrine to reduce systemic absorption and aspirating before injecting to reduce the risk of intravascular instillation.

Paracervical block: Although the paracervical block has been shown to be effective for many gynecologic procedures, performing the block itself causes considerable patient discomfort. There is no consensus on the proper technique to perform a paracervical block with great variability in the location and depth of injection as well as type and dose of anesthetic used. However, regardless of the technique, an extensive systematic review of local anesthesia during gynecologic in-office procedures concluded that there is significant reduction in pain associated with the use of paracervical anesthesia (21.28; 95% Confidence Interval [CI] 22.22 to 20.38) [20].

Systemic medications

Office-based analgesia/anesthesia is typically limited to the provision of moderate sedation or less, but most providers restrict their practice to minimal sedation using a combination of oral anxiolytics and analgesics with local anesthesia. Minimal sedation is defined as a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be somewhat compromised, ventilation and cardio-vascular functions are not affected.

Moderate sedation, also known as conscious sedation, is defined as a drug-induced depression of consciousness during which patients are able to respond to verbal commands, either alone or accompanied by light tactile stimulation.

NSAIDs: Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), such as ibuprofen, are commonly used prior to and after gynecological procedures to reduce pain. Their mechanism of action involves the inhibition of cyclooxygenase, which results in a reduction of the amount of circulating prostaglandins. A recent study found that ibuprofen 600 mg, given 30 minutes preoperatively, improved pain control and decreased postoperative pain when compared to placebo in patients undergoing uterine aspiration for first trimester abortions. NSAIDs have also been combined with misoprostol in an effort to decrease pain [21]. Li et al. [22] compared misoprostol alone versus misoprostol combined with diclofenac for women having abortions between 7 and 12 weeks of gestation. They found a small decrease in pain during the procedure among multiparous subjects only (mean 58 vs 63, $P = .06$, median 51 vs 68). NSAIDs have not been shown to interfere with the action of exogenous prostaglandins such as misoprostol.

Opioids: The use of opioid drugs has been mainly studied during abortions and uterine aspiration procedures. In 2011, a systematic review and meta-analysis of pain management for office gynecologic procedures identified only 1 placebo-controlled RCT evaluating opioid drugs. This study evaluated the use of sublingual buprenorphine for hysteroscopy and concluded that this medication did not decrease pain but substantially increased side effects including nausea, vomiting, and drowsiness [23].

Benzodiazepines: Benzodiazepines are anxiolytic medications that have been shown to be safe for use to decrease pain during first-trimester uterine aspiration. However, there is no data suggesting this type of oral medication decreases procedural pain for other gynecologic procedures [24].

Misoprostol: Misoprostol has been studied for cervical ripening prior to hysteroscopy. One meta-analysis of 10 studies concluded that misoprostol leads to greater preoperative dilation, decreased need for additional dilation, and reduced rates of cervical laceration in premenopausal women. The greatest benefits were seen in nulliparous women and with operative hysteroscopy [25]. However, women treated with misoprostol had higher rates of side effects and minor complications such as transient vaginal bleeding, cramping, and preoperative fever. The optimal dosing regimen for cervical ripening before hysteroscopy is unclear. In premenopausal women, studies have found either 200, 400, or 1000 g of vaginal misoprostol or 400 g of oral misoprostol given at least 9 to 12 hours preoperatively to be superior to placebo. Most of these studies focused on nulliparous women [26]. There are few trials comparing routes of administration, dosage, and interval to procedure. Batukan C et al. [27] compared 400 mcg of oral vs vaginal misoprostol given 10 to 12 hours before operative hysteroscopy in a double-blinded, placebo-control trial. The authors found vaginal misoprostol to be superior in baseline cervical dilation and decreased time required for cervical dilation. Other trials evaluating vaginal misoprostol for shorter intervals, 4 to 6 hours preoperatively, have not shown evidence of any effect. With the current evidence we can conclude that misoprostol has greater effect in pregnant and premenopausal patients. For postmenopausal women the data is conflicting, and most studies do not show a benefit from misoprostol. Misoprostol's actions on the cervix may require endogenous estrogen. It is not known if more intensive dosing regimens would affect the postmenopausal cervix [25].

CONCLUSIONS

In office hysteroscopy plays an important role in modern gynecology. The number of procedures that are being currently

performed in an office setting is growing. Patient comfort directly affects the ability of the hysteroscopist to safely complete a procedure. Adequate patient selection is a fundamental step to achieve a successful office-based practice.

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