*Original Research*

# Intrauterine Lidocaine Instillation and Pain Scores Among Women Undergoing Hysteroscopy-Guided Biopsy

## *A Randomized Controlled Trial*

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**OBJECTIVE:** To compare the visual analog scale (VAS) score for pain and assess patient satisfaction and complications in women receiving intrauterine anesthesia with those receiving placebo during hysteroscopic-guided biopsy.

**METHODS:** The study was conducted in a tertiary care hospital over 17 months, from August 2021 to December 2022. One hundred twenty-six women scheduled for outpatient hysteroscopy-guided biopsy were included in this study and randomized either to the lidocaine (2% 5-mL solution) group or placebo group (63 individuals each). The study adopted a novel approach of vaginoscopic hysteroscopy that employed an intrauterine insemination catheter insertion and administered 2% (5 mL) lidocaine to the lidocaine group or saline (5 mL) to the placebo group. Pain scoring was carried out using the VAS scoring scale at hysteroscope insertion, during hysteroscopic-guided biopsy and after 10 minutes, 30 minutes, and 60 minutes of biopsy. Patient satisfaction level was assessed using the Likert scale. The primary objective was to compare the VAS score for pain between the groups during hysteroscopic-guided biopsy. Power analysis was performed in OpenEpi v3.01 software, using the log-transformed mean difference and standard deviation of the primary outcome (VAS score) of the study groups.

**RESULTS:** The median [interquartile range] VAS pain scores during hysteroscopic-guided biopsy were significantly higher in the placebo group (5 [5–6]) compared with the anesthesia group (4 [3–5]) ($P<.001$). Similar results were noted during insertion of hysteroscope and at 10, 30, and 60 minutes after biopsy. Patients' satisfaction levels were significantly higher in the anesthesia group (30.2% were very satisfied) compared with the placebo group (1.6% were very satisfied) ($P<.001$).

**CONCLUSION:** Intrauterine lidocaine instillation during vaginoscopic hysteroscopy-guided biopsy significantly reduced the pain during and after the procedure. It also improved the satisfaction of the patients after office hysteroscopy. No complications or side effects were associated with intrauterine lidocaine.

**CLINICAL TRIAL REGISTRATION:** Clinical Trials Registry India (CTRI), CTRI/2021/07/034679.

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Office hysteroscopy is a widely used procedure for diagnosing and treating intrauterine pathologies. It plays a major role as the first-line investigation of abnormal uterine bleeding and other benign gynecologic diseases. It is an outpatient procedure, usually done without any analgesia. Causes of unsatisfactory diagnostic hysteroscopy include pain, cervical stenosis, and technical difficulties.[1]

Pain has been stated as the main cause of diagnostic hysteroscopy failure.[2] Patients reported better tolerance when the vaginoscopic approach to diagnostic hysteroscopy is used compared with the

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conventional technique.[3] Several factors have been studied concerning pain during hysteroscopy, such as misoprostol administration for cervical priming, use of analgesia and local anesthesia during the procedure.[1,4] The present study was done to assess the efficacy of intrauterine lidocaine in pain control in women undergoing hysteroscopic-guided endometrial biopsy.

Several studies have evaluated the role of topical anesthetics into the uterine cavity during hysteroscopy for pain control.[5] However, most of these studies have used a tenaculum for holding the cervix during the administration of the drug, which may cause pain. In this study, we used a novel way to introduce topical anesthetic, with the use of an intrauterine insemination (IUI) catheter without holding the cervix with vulsellum.

The current study hypothesized that the participants who receive intrauterine lidocaine instillation will experience significantly lower pain (visual analog scale [VAS]) scores compared with those who receive a placebo (saline instillation) during hysteroscopy-guided biopsy.

## METHODS

This randomized, double-blinded, placebo-controlled study to assess the efficacy and safety of intrauterine lidocaine (2%) instillation in women undergoing outpatient hysteroscopy and endometrial biopsy was conducted at the procedure room in clinic of the department of obstetrics and gynecology in a tertiary care hospital. The Institute Ethics Committee approved the trial and registered it under Clinical Trials Registry India (CTRI/2021/07/034679). The institute funded the study, and it spanned approximately 17 months, from August 2021 to December 2022. In our practice, all women needing endometrial sampling are done with hysteroscopic guidance. Women included in the study were older than 18 years and were in need of a hysteroscopy-guided biopsy. The exclusion criteria were women with pelvic inflammatory diseases, pregnancy, use of cervical priming, hypersensitivity to lidocaine, or prior history of cardiac disease or seizure disorder.

After obtaining the written informed consent, patients were randomized to either the anesthesia group, in which participants received intrauterine anesthesia using 5 mL of 2% lidocaine, or the placebo group, in which participants received 5 mL of normal saline as a placebo. Block randomization with varying block sizes of 4, 6, and 8 generated using a computer was used to randomize the patients in the study arms in the ratio of 1:1. Sequentially Numbered, Opaque, Sealed Envelope allocation was used for concealment.

Before the procedure, a resident physician prepared the study solutions (similar in appearance) in the operation theater. The resident was the only staff unblinded. The solution was given to the surgeon, who was blinded to the allocation. A sterile speculum was introduced into the vagina, and the cervix was visualized. An IUI catheter was gently introduced into the uterine cavity without using the tenaculum. If the instillation with an IUI catheter was found to be difficult, a reusable metallic embryo transfer catheter was used as an alternative. The prepared solution was then instilled into the uterine cavity using this IUI catheter. Care was taken to ensure that the catheter and the speculum were left in place for 3 minutes before they were withdrawn to decrease backflow and allow for an anesthetic effect. Hysteroscopy was carried out after 5 minutes of instillation of the solution. Normal saline was used as the distension medium for hysteroscopy.

The vaginoscopic approach for hysteroscopy was employed for all 126 participants uniformly. In this approach, neither a speculum nor a tenaculum are used; a 30-degree rigid hysteroscope with a 3.8-mm diagnostic sheath (Karl Storz) was introduced into the vagina and then gently into the uterine cavity through the visualized external os. After systematic visualization of the uterine cavity and both tubal ostia, hysteroscopy-guided biopsy was then carried out. A single grasp of tissue from the most abnormal looking area was taken using a 5 French grasper. If no abnormality was visible, a random biopsy was taken using the 5 French grasper. The mean operative time was 6 minutes 30 seconds. The primary outcome was the VAS pain score between the groups during hysteroscopic-guided biopsy. The VAS score was recorded during the insertion of the hysteroscope, during the biopsy, and 10, 30, and 60 minutes after the procedure. Any sign of lidocaine toxicity was recorded. The patients were observed for 60 minutes and assessed for complications and side effects. Additional analgesic requirements, if any, were noted. An injection of ketorolac (60 mg, intramuscular) was given after the procedure for patients who required additional analgesia. The patient's response during the whole procedure was evaluated using the VAS score as a validated measure of pain. The participants were asked to rate their pain level on a 10-cm VAS, where 0 is rated as no pain and 10 as agonizing and unbearable pain. Any associated vasovagal attack symptom was noted. Patient satisfaction was assessed at 60 minutes using a 5-point Likert scale, which is a psychometric measure rated between very satisfied, satisfied, neither satisfied nor dissatisfied, dissatisfied, and very dissatisfied. The operator, participant, and

data collector were blinded to the assignment of participants.

Sample size calculation was determined using a sample size formula to estimate the difference between two independent means. The sample size was calculated to detect 1 unit (1 cm on a 10-cm VAS scale) of the mean difference of pain score between the two groups using the VAS if 2 was the SD within the group. With an alpha error of 5% and the power of the test as 80%, the sample size was calculated to be 126, with 63 patients in each arm. Power analysis was performed in OpenEpi v3.01 software, using the log-transformed mean difference and SD of the study groups' primary outcome (VAS score). With a sample size of 63 participants per study group for an alpha level of 0.05, the study is found to be well-powered (above the 80% threshold) to detect clinically significant differences in pain scores among the study groups. Collected data were analyzed with SPSS 19. The conformity of the measured values to normal distribution was examined using the Kolmogorov-Smirnov test. Continuous variables following normal distribution were represented as mean±SD, and non-normal data were summarized as median (interquartile range). Due to right-skewed distributions of VAS score in the data set, a logarithmic transformation was applied using SPSS v27. To account for the zero values, the transformation used the formula log $(x+1)$. The transformation aimed to stabilize variance and approximate normality. Posttransformation skewness values were within acceptable thresholds. The area under the curve (AUC) value was calculated by the trapezoid rule for the log-transformed VAS scores among the study participants. The average AUC measured pain intensity over time; it was calculated by dividing the total AUC by the time interval from the biopsy to the last pain measurement (60 minutes). Categorical variables were presented as frequencies with percentages, and the $\chi^2$ test was used for comparison. For comparing continuous variables, independent $t$ tests and Mann-Whitney $U$ tests were used depending on the type of distribution. $P<.05$ was considered statistically significant.

## RESULTS

Of 134 women who were assessed for eligibility, eight were excluded; two declined to participate, and six did not meet the eligibility criteria. There was no patient loss to follow-up. The consort diagram is given in Figure 1.

Of the 126 patients who participated in the study, 63 were in the anesthesia arm and 63 in the placebo arm; demographic characteristics showed no significant difference (Table 1). Among the 126 biopsies performed, 84 (66.67%) were for premenopausal abnormal uterine bleeding and 42 (33.33%) were for postmenopausal bleeding.

An IUI catheter or metallic embryo transfer catheter could be inserted in all women in both groups without using a tenaculum. Vaginoscopic hysteroscopy was done in all women in both groups.

The VAS scores consistently showed lower pain scores in the intervention group than in the control group across all timepoints. Median [interquartile range] VAS scores on insertion of the hysteroscope showed a significant difference between the lidocaine group (2 [2–4]) and the placebo group (4 [3–5]). The log transformed data also showed a significant difference, with a mean difference (95% CI) of −0.50 (−0.65 to −0.35). The pain score peaked at time of

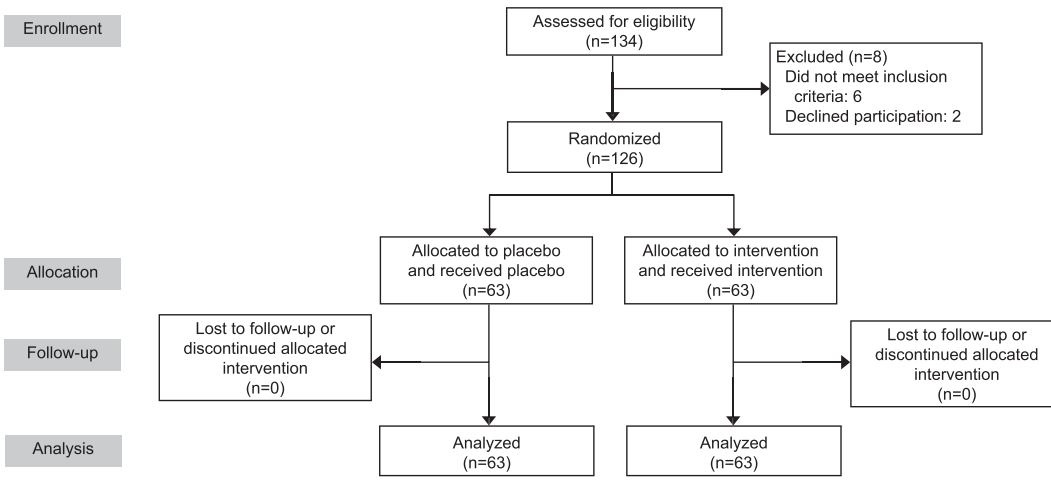


**Fig. 1.** CONSORT (Consolidated Standards of Reporting Trials) flow diagram.
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**Table 1. Sociodemographic Characteristics of the Study Participants (N=126)**

| Characteristic | Lidocaine (n=63) | Saline (n=63) | *P* |
|---|---|---|---|
| Age (y) | 44.0±8.99 | 46.03±12.74 | .303* |
| BMI (kg/m$^2$) | 25.61±4.70 | 26.67±5.14 | .227* |
| Parity | | | |
| Nulliparous | 11 (17.5) | 9 (14.3) | .457† |
| 1 | 12 (19.0) | 6 (9.5) | |
| 2 or more | 48 (76.2) | 40 (63.5) | |
| Previous cesarean delivery | 10 (15.9) | 9 (14.3) | .803† |
| Postmenopausal status | 16 (25.4) | 21 (33.3) | .328† |

BMI, body mass index.
Data are mean±SD or n (%) unless otherwise specified.
* Estimated by independent *t* test.
† Estimated by $\chi^2$ test; $P<.05$ was considered significant.

biopsy in both groups. During hysteroscopic-guided biopsy, the median (interquartile range) VAS score was 4 (3–5) in the lidocaine group and 5 (5–6) in the placebo group, which was statistically significant. The log-transformed data showed a mean difference (95% CI) of −0.36 (−0.46 to −0.26). In the placebo group, pain scores remained approximately the same from insertion to 10 minutes postprocedure but decreased to 1 after 60 minutes.

At later timepoints (30 minutes and 60 minutes after biopsy), the reduction in pain scores became even more evident, with mean differences (95% CI) of −0.76 (−0.91 to −0.60) and −0.63 (−0.79 to −0.47), respectively. All timepoints reported statistically significant differences ($P<.001$), confirming the effectiveness of the lidocaine (Table 2 and Fig. 2). The intervention group had a lower average AUC (0.73) than the control group (1.42), suggesting that the intervention reduced pain scores consistently over time with a 48.6% significant reduction ($P<.001$) in AUC value (Table 3).

Patient satisfaction levels were significantly higher in the anesthesia group compared with the placebo group ($P<.001$) (Table 4). Among the other studied outcomes, only 5 of 126 patients (four in the placebo group and one in the lidocaine group) required additional analgesia in the form of injected ketorolac 60 mg intramuscular; the difference was not significant ($P=.151$). There were no cases of vasovagal symptoms or any lidocaine toxicity in any patient. No complications occurred during or after the procedure.

Biopsy results included normal proliferative endometrium, endometrial hyperplasia with atypia, without atypia, senile atrophy. There were two cases of malignancies (endometrial adenocarcinoma), which required hysterectomy and chemoradiation.

## DISCUSSION

In this study, pain scores during hysteroscopy-guided biopsy were lower with intrauterine lidocaine compared with placebo at all timepoints (insertion of hysteroscope, during the biopsy, and at 10, 30 and 60 minutes after biopsy). Patient satisfaction also was higher in the intrauterine lidocaine group compared with the placebo group.

Pain during hysteroscopy is the main factor affecting patients' tolerance and may result in less

**Table 2. Actual Visual Analogue Scale Scores and Log-Transformed Visual Analogue Scale Scores for Pain at Various Timepoints (N=126)**

| | | | Log Transformed VAS | | | |
|---|---|---|---|---|---|---|
| Timepoint | Lidocaine (n=63) | Saline (n=63) | Lidocaine (n=63) | Saline (n=63) | Mean Difference (95% CI) | *P** |
| At hysteroscope insertion | 2 (2–4) | 4 (3–5) | 1.16±0.53 | 1.67±0.30 | −0.50 (−0.65 to −0.35) | <.001 |
| During biopsy | 4 (3–5) | 5 (5–6) | 1.51±0.34 | 1.87±0.21 | −0.36 (−0.46 to −0.26) | <.001 |
| After 10 min | 2 (1–3) | 4 (3–4) | 0.94±0.56 | 1.54±0.21 | −0.59 (−0.74 to −0.44) | <.001 |
| After 30 min | 1 (0–2) | 3 (2–3) | 0.51±0.54 | 1.26±0.33 | −0.76 (−0.91 to −0.60) | <.001 |
| After 60 min | 0 (0–0) | 1 (1–2) | 0.20±0.37 | 0.82±0.53 | −0.63 (−0.79 to −0.47) | <.001 |

VAS, visual analog scale.
Data are median (interquartile range) or mean±SD unless otherwise specified.
* Estimated by independent *t* test; $P<.05$ was considered significant.

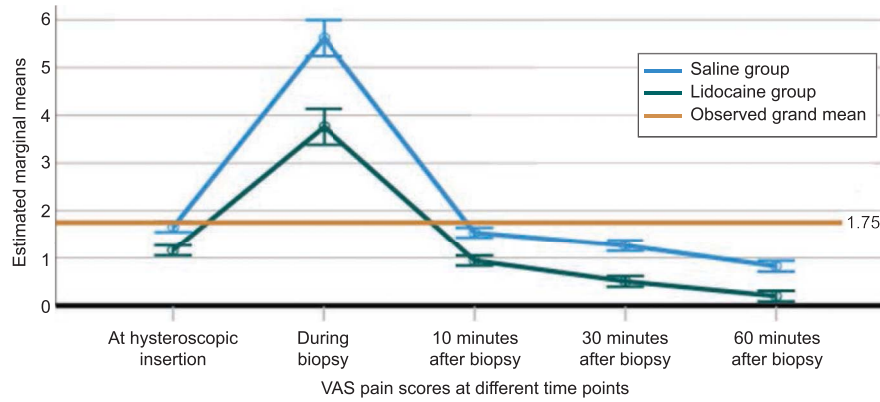


**Fig. 2.** Estimated marginal means of log-transformed visual analog scale (VAS) scores across multiple timepoints, adjusting for the covariate. *Error bars* indicate 95% CI.

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successful hysteroscopy.[6] Although many surgeons use paracervical block for hysteroscopy, paracervical block alone may not alleviate pain during hysteroscopy. It can reduce pain only during the insertion of a hysteroscope, and uterine biopsy still can be the most painful step during hysteroscopy.[6,7] However, there is still a lack of evidence in this regard.[1,3–7] Many randomized controlled trials have studied various methods of analgesia and local anesthesia during hysteroscopy, but the best method of pain management for an outpatient hysteroscopy is not universally agreed on in present practice.[1]

There have been two studies evaluating intrauterine lidocaine during curettage. Benchahong et al[8] concluded that there was significant pain reduction in patients who received intrauterine instillation of lidocaine compared with placebo, during outpatient uterine curettage, 15 minutes and 2 hours after procedure. In a, randomized, placebo-controlled, double-blind study conducted in 84 patients by Arora et al, all patients received either intrauterine 2% lignocaine or normal saline along with oral nonsteroidal anti-inflammatory drugs and paracervical block before the procedure. They concluded that 2% intrauterine lignocaine significantly decreased the pain perception during curettage, immediately postprocedure, and 30 minutes later. This is a simple, effective, inexpensive, and low-risk intervention that can potentially increase the patient acceptability and compliance with such procedures, Aurora[9] suggested in the study.

In a 2015 randomized controlled trial focusing on diagnostic hysteroscopy without biopsy, Senturk et al[10] compared VAS scores in three groups: intrauterine lidocaine, rectal indomethacin, and placebo. They concluded intrauterine Lidocaine was more effective than rectal indomethacin in reducing the pain during hysteroscopy and 10 minutes after the procedure ($P<.05$).

Pain scores were compared in a randomized controlled trial by Mohammadi et al[11] in 2015 with 70 women randomized to two groups: 100 mg of rectal diclofenac or 5 mL of 2% intrauterine lidocaine. The results of their study concluded that no significant difference existed between the two groups in terms of mean pain score during intrauterine visualization ($P=.500$). However, in this study no hysteroscopic-guided biopsies were taken. Lastly, one study found an additional benefit of lidocaine over oral medication in a randomized controlled trial that included 156 menopausal women who received intrauterine lidocaine infusion or oral tramadol (50 mg) or placebo before diagnostic hysteroscopy (52 women/group). They concluded that postmenopausal women reported less discomfort during and after diagnostic hysteroscopy when intrauterine lidocaine and oral tramadol (50 mg) were used compared with placebo. However, passage of the hysteroscope through the cervical canal was made easier by lidocaine than by tramadol.[12]

**Table 3. Area Under the Curve of the Log-Transformed Visual Analogue Scale Score for the Pain at Various Timepoints (N=126)**

| Study Group | Average AUC | % Reduction in Total AUC | 95% CI for Average AUC | *P** |
|---|---|---|---|---|
| Lidocaine | 0.73 | 48.60 | 0.65–0.81 | <.001 |
| Saline | 1.42 | Ref | 1.25–1.59 | — |

AUC, area under the curve.
* Estimated by independent *t* test; $P<.05$ was considered significant.

**Table 4. Postprocedural Efficacy on Patient Satisfaction (N=126)**

| Patient Satisfaction Level | Lidocaine (n=63) | Saline (n=63) | *P** |
|---|---|---|---|
| Very satisfied | 19 (30.2) | 1 (1.6) | <.001 |
| Satisfied | 35 (55.6) | 16 (25.4) | |
| Neither satisfied nor dissatisfied | 8 (12.7) | 31 (49.2) | |
| Somewhat dissatisfied | 1 (1.6) | 15 (23.8) | |

Data are n (%) unless otherwise specified.
* Estimated by $\chi^2$ test.

Strengths of this study are that it includes both premenopausal and postmenopausal women and double-blinding of the intervention. The block randomization procedure employed in this study also helped minimize the selection bias, controlled confounders, and ensured equal number of participants in both groups. A limitation of this study is that it was done in a single center with a fairly homogenous population of multiparous women in which cervical stenosis was not encountered during the hysteroscopies. However, cervical stenosis sometimes may be encountered in real-world practice, which may make administration of an intrauterine drug a challenge. More studies with a more diverse study population are needed to confirm the findings of our study. We conclude that intrauterine lidocaine instillation during hysteroscopy-guided biopsy significantly reduces pain during and after the procedure. It also improves the satisfaction level of the patients.

## REFERENCES


1. Inácio QAS, Troncon JK, Valério FP, Herren H, Nogueira AA, Neto OBP, et al. Misoprostol administration before hysteroscopy procedures–a retrospective analysis. Rev Bras Ginecol Obstet 2022;44:1102–9. doi: 10.1055/s-0042-1755462
2. Hassan A, Haggag H. Role of oral tramadol 50 mg in reducing pain associated with outpatient hysteroscopy: a randomised double-blind placebo-controlled trial. Aust N Z J Obstet Gynaecol 2016;56:102–6. doi: 10.1111/ajo.12431
3. Khoiwal K, Zaman R, Bahurupi Y, Gaurav A, Chaturvedi J. Comparison of vaginoscopic hysteroscopy and traditional hysteroscopy: a systematic review and meta-analysis. Int J Gynaecol Obstet 2024;164:47–55. doi: 10.1002/ijgo.14902
4. Ahmad G, Saluja S, O'Flynn H, Sorrentino A, Leach D, Watson A. Pain relief for outpatient hysteroscopy. The Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD007710. doi: 10.1002/14651858.CD007710.pub3
5. Kosus N, Kosus A, Demircioglu RI, Simavli SA, Derbent A, Keskin EA, et al. Transcervical intrauterine levobupivacaine or lidocaine infusion for pain control during endometrial biopsy. Pain Res Manag 2014;19:82–6. doi: 10.1155/2014/104053
6. Ma T, Readman E, Hicks L, Porter J, Cameron M, Ellett L, et al. Is outpatient hysteroscopy the new gold standard? Results from an 11 year prospective observational study. Aust N Z J Obstet Gynaecol 2017;57:74–80. doi: 10.1111/ajo.12560
7. Asgari Z, Razavi M, Hosseini R, Nataj M, Rezaeinejad M, Sepidarkish M. Evaluation of paracervical block and IV sedation for pain management during hysteroscopic polypectomy: a randomized clinical trial. Pain Res Manag 2017;2017:5309408. doi: 10.1155/2017/5309408
8. Benchahong S, Chanthasenanont A, Pongrojpaw D, Pattaraarchachai J, Bhamarapravatana K, Suwannarurk K. Efficacy of intrauterine lidocaine instillation in reducing pain during endometrial biopsy by Novak. Pain Res Treat 2018;2018:9368298. doi: 10.1155/2018/9368298
9. Arora A, Shukla A, Saha SC. Effectiveness of intrauterine lignocaine in addition to paracervical block for pain relief during dilatation and curettage, and fractional curettage. J Obstet Gynaecol India 2016;66:174–9. doi: 10.1007/s13224-014-0670-9
10. Senturk MB, Guraslan H, Babaoğlu B, Yaşar L, Polat M. The effect of intrauterine lidocaine and rectal indomethacin on pain during office vaginoscopic hysteroscopy: randomized double-blind controlled study. Gynecol Obstet Invest 2016;81:280–4. doi: 10.1159/000441787
11. Mohammadi SS, Abdi M, Movafegh A. Comparing transcervical intrauterine lidocaine instillation with rectal diclofenac for pain relief during outpatient hysteroscopy: a randomized controlled trial. Oman Med J 2015;30:157–61. doi: 10.5001/omj.2015.35
12. Samy A, Nabil H, Abdelhakim AM, Mahy ME, Abdel-Latif AA, Metwally AA. Pain management during diagnostic office hysteroscopy in postmenopausal women: a randomized study. Climacteric 2020; 23:397–403. doi: 10.1080/13697137.2020.1742685


**Authors' Data Sharing Statement**

Will individual participant data be available (including data dictionaries)? *No.*

What data in particular will be shared? *Not available.*

What other documents will be available? *Not available.*

When will data be available (start and end dates)? *Not applicable.*

By what access criteria will data be shared (including with whom, for what types of analyses, and by what mechanism)? *Not applicable.*

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