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# The effect of diluted ropivacaine in distending fluid on cramping pain after hysteroscopic surgeries: a randomized clinical trial study

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## Objective
The effect of ropivacaine on postoperative hysteroscopy has not yet been evaluated; this study investigated the effect of diluted ropivacaine in distending media during hysteroscopy on postoperative cramping pain.

## Methods
This double-blind randomized clinical trial was conducted on 60 women who underwent hysteroscopy at a tertiary hospital. Normal saline was used as the distending fluid in both groups. The intervention group received 10 mL of 2% ropivacaine in only one bottle of 1,000 mL normal saline as a distending fluid, while the control group received 10 mL of normal saline in 1,000 mL normal saline during hysteroscopy. Patients' pain scores were evaluated before hysteroscopy and at 2, 6, 12, 24, and 48 hours after hysteroscopy.

## Results
Based on the results, the pain measured by visual analog scale (VAS) score was significant at 6 and 12 hours after the intervention was significantly lower than that in the ropivacaine group (3.03±1.57 vs. 4±1.49, *P*=0.02 at 6 hours and 1.28±1.36 vs. 2.4±1.43, *P*=0.003 at 12 hours). There were no significant differences in the VAS scores at 2, 24, and 48 hours after the intervention between the two groups.

## Conclusion
Ropivacaine in the distending fluid during hysteroscopy is associated with a significant reduction in pain within a few hours after hysteroscopy with no remarkable adverse effects.

**Keywords:** Ropivacaine; Hystroscopy; Post operative pain

## Introduction

Hysteroscopy is a useful and minimally invasive procedure for the evaluation of uterine cavity and management of some pathologic conditions, including abnormal uterine bleeding. Hysteroscopy is also recommended in infertile patients or recurrent miscarriages in suspected cases of uterine malformations [1,2]. The operative technique allows physicians to evaluate the uterine cavity and simultaneously "see and treat" in one procedure [3]. This method also decreases the duration of the postsurgical recovery period and allows patients to re-

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turn to their daily routine immediately after surgery without additional risks [4].

Some patients develop cramping pain in the lower abdomen after hysteroscopic procedures [5]. Evidence shows that approximately 35% of patients who undergo anesthesia-free diagnostic hysteroscopy experience some degree of pain [6]. There are several methods of minimizing pain after hysteroscopy. Previous studies have shown that normal saline is more comfortable and safer as distension media than glycine and carbon dioxide. Warming the distension fluid to physiological temperature is another method, although its effect on reducing the perceived cramping pain has not yet been proven [7]. The surgeon's experience is another factor that may be associated with reduced postoperative pain [8].

Some patients may use non-pharmacological methods to reduce postoperative pain, such as yoga, transcutaneous electrical nerve stimulation, and music [9-11]. Additionally, nursing education before and after the procedure may be effective in reducing post-operative pain. Moreover, it has been reported that the use of hot water bags is effective in relieving pain in patients who undergo hystrosalpingography [8,9]. Until now, many previous studies have focused on the pharmacological control of cramping pain during hysteroscopy. The results of a meta-analysis study showed that local anesthetics were more effective in controlling pain during the procedure and within 30 minutes after surgery, while their use after 30 minutes of hysteroscopy had no significant effect on reducing pain. Additionally, venous sedatives used more than 30 minutes after hysteroscopy were associated with a greater reduction in cramping pain than para-cervical block [12]. Some of these medications have adverse effects and can increase the risk of surgery in some patients, owing to their side effects [13].

One method used for relieving pain after hysteroscopy is paracervical or intrauterine injection of lidocaine [14]. Lidocaine, ropivacaine, bupivacaine, and a combination of bupivacaine and lidocaine are commonly used as local anesthetics in clinical surgery [15]. The addition of lidocaine to the distending fluid under hysteroscopy has been previously investigated, and contradictory results have been reported regarding its effect. A related study reported that the addition of lidocaine to the distending fluid had no significant effect on relieving pain in patients. However, another study reported that its application had a significant effect on reducing pain in patients [16,17]. Ropivacaine is a local anesthetic with a relatively rapid effect with a long duration compared to lidocaine and is less toxic to the central nervous system and circulatory system in comparison to lidocaine and bupivacaine [18]. To date, the effect of intrauterine use of ropivacaine in relieving pain after hysteroscopy has not been evaluated; therefore, the present study aimed to investigate the effect of diluted ropivacaine in a distending fluid on postoperative cramping pain.

## Materials and methods

### 1. Study design and setting

The present randomized clinical trial study was conducted on women referred to the Rasoul-e-Akram Hospital, a tertiary academic center affiliated with the Iran University of Medical Sciences, who underwent surgical hysteroscopy for treating conditions caused by uterine bleeding, structural disorders, and anatomical abnormalities in 2021.

### 2. Eligibility criteria

This study included women who were candidates for surgical hysteroscopy based on scientific reasons, and provided informed consent to participate in the study. Exclusion criteria included all contraindications for hysteroscopy, including vaginal infections or pelvic inflammatory disease, cervical cancer, and serious medical cases, such as severe heart disease, renal failure, pregnancy, pelvic pain with a visual analog scale (VAS) score of 4 or higher, and sensitivity to ropivacaine.

### 3. Randomization and blinding

To reach two homogeneous groups in terms of number, we used balanced-block randomization (block size: 4) to allocate patients to the intervention or placebo group. Because the researcher and patients were unaware of the allocation to the groups, the study design was double blinded.

### 4. Study procedure

Women who were referred to the gynecology clinic of Rasoul-e-Akram Hospital and candidates for hysteroscopic procedures were included in the study if they met the eligibility criteria. After obtaining signed informed consent, the patients were randomly divided into in-

tervention and control groups. The intervention group received 10 mL of 2% of ropivacaine in 1,000 mL of normal saline in the second bottle, as the distending medium during hysteroscopy. The control group received 10 mL of normal saline in 1,000 mL of normal saline as the distending medium during hysteroscopy. Hysteroscopy in all the patients was performed by the same physician. The patients in both groups underwent diagnostic and therapeutic hysteroscopy, and all procedures were performed without any preoperative analgesia. Anesthesia was performed using the general anesthesia method.

Postoperative pain was evaluated as the main outcome

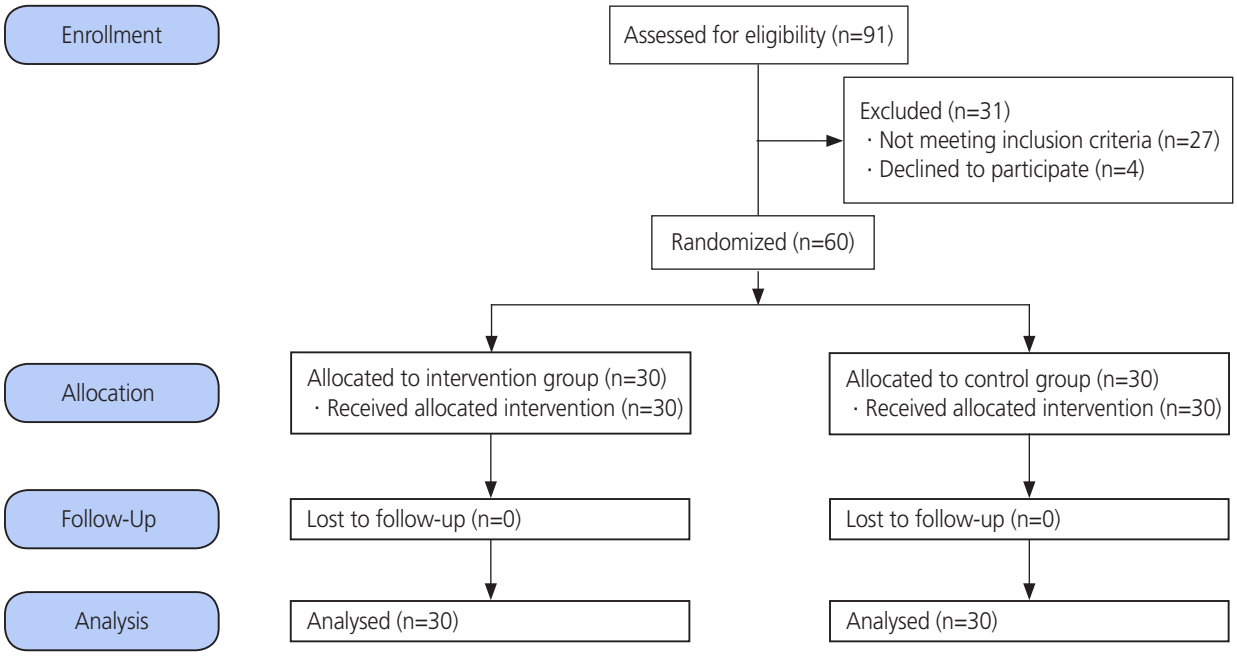


**Fig. 1.** Flowchart of the allocation of patients to the study groups.

**Table 1.** Comparison of continuous demographic and clinical variables between two groups

| Variable | Intervention group | Control group | *t*-statistics | *P*-value[a] |
|---|---|---|---|---|
| Gravidity | 3.10±2.01 | 3.02±1.85 | 0.16 | 0.87 |
| Parity | 0.77±1.10 | 0.70±1.42 | -0.20 | 0.84 |
| Abortion | 0.77±1.33 | 0.30±0.70 | -1.67 | 0.09 |
| Live child | 2.07±1.55 | 1.83±1.49 | -0.59 | 0.56 |
| Dead child | 0.03±0.18 | 0.00±0.00 | -1.00 | 0.32 |
| Cesarean section | 0.77±1.01 | 0.73±1.01 | -0.13 | 0.90 |
| Normal vaginal delivery | 1.60±1.90 | 1.07±1.48 | -1.21 | 0.23 |
| Age (yr) | 41.04±10.92 | 42.48±9.32 | 0.54 | 0.59 |
| Body mass index (kg/m$^2$) | 27.66±4.00 | 29.24±4.68 | 1.33 | 0.19 |
| Duration of operation (mintues) | 20.00±8.85 | 17.83±7.66 | -0.90 | 0.37 |
| Total hospitalization duration (hours) | 18.31±7.56 | 16.46±6.78 | -1.85 | 0.32 |
| Post operation hospitalization time (hours) | 12.07±4.25 | 11.25±3.97 | 1.00 | 0.44 |
| Time to ambulation (hours) | 5.00±1.46 | 5.04±1.48 | 0.09 | 0.93 |

Values are presented as mean±standard deviation.
[a]student *t*-test.

of the study in all patients using VAS and the consumption of analgesics after surgery. This criterion ranges from zero (complete painlessness) to 10 degree (the most severe pain possible). The pain scores of the patients were evaluated at different times, including 2, 6, 12, 24, and 48 hours after hysteroscopy. The side effects of ropivacaine, such as dizziness, blurred vision, and convulsions were assessed using a special questionnaire every time the VAS score was assessed.

### 5. Statistical analysis

We used the parameters of Kucuk et al. [19] for sample size estimation and by considering a power of 80% and significance level of 5%. Thirty patients were considered for each arm of the study. To compare quantitative variables between the two groups, the Kolmogorov-Smirnov and independent *t*-tests were used based on assumption of the normal distribution of variables, and the Mann-Whitney test was used for non-parametric equivalents. The chi-square test was used to compare qualitative variables between the two groups. Data analysis was performed using SPSS software (version 24.0. NY IBM Corp, Armonk, NY, USA). The significance level was set at $P<0.05$.

### 6. Ethics

The Ethics Committee of Iran University of Medical Sciences approved the study (ethics code: IR.IUMS.REC.1400.102), and the study protocol was approved by the Iranian Registry of Clinical Trials (IRCT registration number: IRCT20160527028109N4, registration date: 2021-05-11). All participants provided written informed consent prior to participating in the study.

## Results

A total of 91 patients met the eligibility criteria. Among them, four patients declined participation, while 27 did not meet the inclusion criteria. Finally, 60 eligible patients were randomly allocated into the two groups with 30 patients each. All patients received the allocated intervention and continued the study until the end, and were included in the final analysis (Fig. 1).

Baseline and cycle characteristics of the patients in the two groups are shown in Table 1. The two groups were homogenous in terms of gravity, parity, abortion, live child, dead child, cesarean section, normal vaginal delivery, age, body mass index, duration of operation, blood loss volume during operation, hospitalization time, and time to ambulation

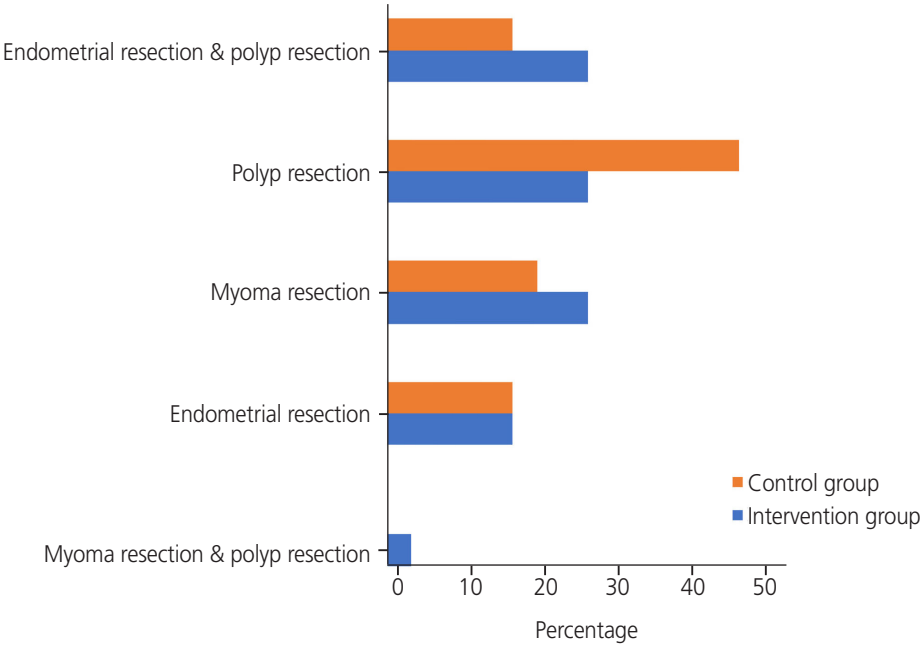


**Fig. 2.** Type of operation comparison between intervention and control group.

(*P*>0.05).

Five patients (16.67%) in the intervention group and three patients (10%) in the control group had regular menstrual cycles (*P*=0.45). Moreover, there was no significant difference between the two groups in terms of irregular menstrual cycles (60% in the intervention group vs. 63.3% in the control group; *P*=0.79). In both groups, abnormal uterine bleeding was the most common diagnosis (51.7% in the control group and 75% in the intervention group). In Fig. 2, we compared the type of operation between the two groups and no significant difference was observed between the two groups (*P*=0.47).

A comparison of the VAS scores between the two groups of patients before and at 6, 12, 24, and 48 hours after the intervention is shown in Table 2 and Fig. 3. There was no significant difference in the mean VAS score between the groups before and at 24 and 48 hours after the intervention (*P*>0.05). At 6 and 12 hours after the intervention, the mean VAS score was significantly higher in the control group than those in the intervention group (3.03±1.57 vs. 4±1.49, *P*=0.02 at 6 hours and 1.28±1.36 vs. 2.4±1.43, *P*=0.003 at 12 hours).

### 1. Side effects of the drugs

In the intervention group, only four patients (13.3%) reported short-term dizziness (lasting less than 2 hours), while in the control group, dizziness was not reported. None of the patients in either group experienced blurred vision or seizures.

**Table 2.** The comparison of visual analog scale score between two groups 2, 6, 12, 24 and 48 hours after intervention

| Variable | Intervention group | Control group | *t*-statistics | *P*-value[a] |
|---|---|---|---|---|
| Hours 2 | 3.10±2.50 | 3.37±2.6 | 0.39 | 0.69 |
| Hours 6 | 3.03±1.57 | 4.00±1.49 | 2.43 | 0.02 |
| Hours 12 | 1.28±1.36 | 2.40±1.43 | 3.09 | <0.01 |
| Hours 24 | 0.48±0.99 | 0.90±1.18 | 1.47 | 0.15 |
| Hours 48 | 0.14±0.52 | 0.57±1.04 | 1.99 | 0.05 |

Values are presented as mean±standard deviation.
[a]student *t*-test.

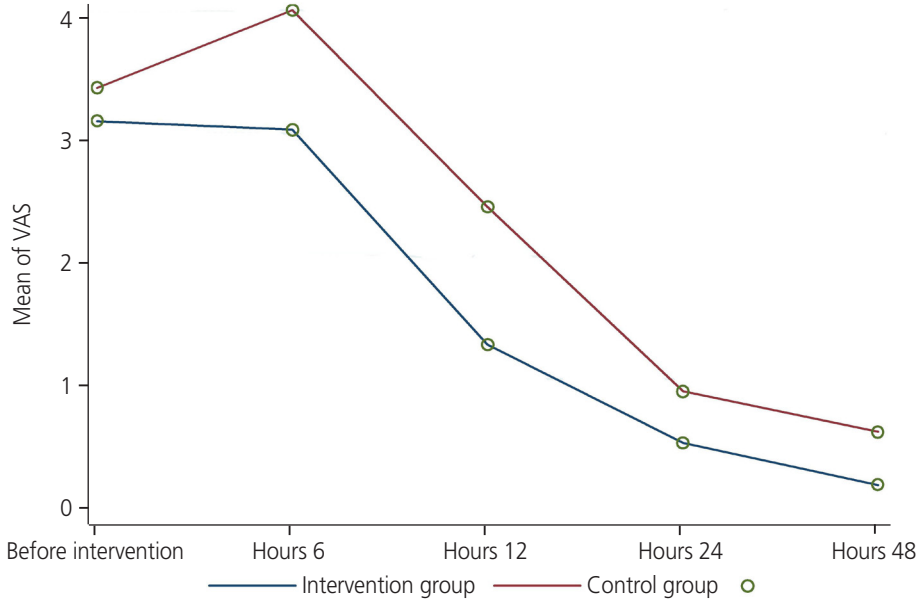


**Fig. 3.** Graphically comparison of visual analog scale (VAS) score between two groups.

## Discussion

In this study, we assessed the effect of diluted ropivacaine in the distending fluid during hysteroscopy on postoperative pain in patients. Diluted ropivacaine at 6 and 12 hours after the intervention was significantly associated with a reduction in cramping pain. Moreover, except for mild short-term dizziness without interference with daily activities in some patients, the use of this drug was not associated with any specific side effects. Therefore, this drug can be used to reduce pain in patients undergoing hysteroscopy immediately after surgery. There was no significant difference in the amount of pain at 24 and 48 hours after the surgery between the intervention and control groups; however, it can be a useful choice to reduce pain in the early hours after the surgery. Ropivacaine causes reversible inhibition of sodium ion influx, thereby blocking impulse conduction in nerve fibers. This action is potentiated by the dose-dependent inhibition of potassium channels. Ropivacaine is less lipophilic than bupivacaine and less likely to penetrate large myelinated motor fibers. The results of this study are consistent with the findings of Barel et al. [16], in which diluted lidocaine was added to the distending fluid during hysteroscopy, resulting in a significant reduction in postoperative pain. Moreover, consistent with our findings, Kucuk et al. [19] found that intraperitoneal instillation of ropivacaine and bupivacaine was significantly effective in reducing post-laparoscopic pain during cholecystectomy. Mahomed et al. [20] reported that the use of local anesthetic drugs in the primary hours after surgery is beneficial forin dropping relieving postoperative pain after hysteroscopy; however, consistent with our findings, there was no significant difference between the two groups regarding the pain score at 24 hours post-procedure. Moreover, in the study by Frawley et al. [21], the administration of intraperitoneal ropivacaine caused a significant reduction in opioid use during recovery compared to the control group.

Regarding the side effects of diluted ropivacaine in distending fluid hysteroscopy, consistent with our findings, the results of a meta-analysis of 12 relevant clinical trials in 2017 showed a low rate of side effects following ropivacaine intraperitoneal injection, and postoperative nausea and vomiting were the major adverse effects [22].

However, the present study has some limitations. First, the study duration was not long enough to assess the long-term effects of the drugs. Second, due to the small sample size of the two groups, are required to.

An important strength of this study was that all surgical procedures were performed by a single surgeon, and this drug was used for the first time in surgical hysteroscopy to relieve postoperative cramping pain, which can be considered as a study novelty. Moreover, the two groups were homogenous in terms of potential confounding variables, and there was no loss to follow-up during the study period, which is another strength of the study.

According to our findings, the use of diluted ropivacaine as distending fluid in surgical hysteroscopy for postoperative cramping pain as a safe drug, is associated with a significant reduction in pain in the first few days after hysteroscopy surgery.

## Conflict of interest

The authors claim no conflict of interest.

## Ethical approval

The ethics committee of Iran University of Medical Sciences approved the study (Ethics code: IR.IUMS.REC.1400.102), and the study protocol was approved by the Iranian Registry of Clinical Trials (IRCT registration number: IRCT20160527028109N4, Registration date: 2021-05-11).

## Patient consent

Written informed consent was obtained from the patients for entering to the study.

## Funding information

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