original article

Warm distension fluid reduces pain severity in office hysteroscopy: a randomized controlled trial

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Citation: Gulucu S, Cakmak B. Warm distension fluid reduces pain severity in office hysteroscopy: a randomized controlled trial. Ann Saudi Med 2021; 41(3): 135-140. DOI: 10.5144/0256-4947.2021.135

Received: January 21, 2021

Accepted: February 20, 2021

Published: June 3, 2021

Funding: None.

BACKGROUND: Abnormal uterine bleeding (AUB) affects approximately 14% to 25% of women of reproductive age. The most common use of office hysteroscopy is to evaluate pathologies related to AUB and reproductive health, but office hysteroscopy can also be used for the diagnosis and treatment of other intrauterine pathologies.

OBJECTIVE: Investigate the effects of the temperature of the distension fluid on pain severity in patients undergoing diagnostic office hysteroscopy due to AUB.

DESIGN: Randomized controlled clinical trial.

SETTING: Tertiary care center in Turkey.

PATIENTS AND METHODS: One hundred perimenopausal patients with AUB were randomly allocated according to the temperature of the distension fluid used in office hysteroscopy (37°C or 25°C). Pain intensity was assessed using a visual analog scale (VAS). Six VAS measurements were compared over the course of the hysteroscopy: pre-treatment (VAS-1), at vaginal entry (VAS-2), at the cervical ostium transition (VAS-3), while in the cavity (VAS-4), at the end of the procedure (VAS-5), and 30 minutes after the end of the procedure (VAS-6).

MAIN OUTCOME MEASURES: VAS

SAMPLE SIZE: Fifty in each group enrolled, one drop out.

RESULTS: The VAS-3, VAS-4, and VAS-5 scores were significantly lower for patients in the warm fluid group than in the room temperature group ($P<.05$), whereas the VAS-1, VAS-2, and VAS-6 scores were similar in both groups.

CONCLUSION: The application of warm distension fluid in office hysteroscopy reduces pain severity compared with the application of an unheated fluid.

LIMITATIONS: The main limitations of the study were that a subgroup analysis could not be performed due to an insufficient number of cases, and we were unable to evaluate vasovagal symptoms.

CONFLICT OF INTEREST: None.

Abnormal uterine bleeding (AUB), a common clinical problem, affects approximately 14% to 25% of women of reproductive age in many ways—physically, emotionally, socially, and financially.[1-3] In women aged >40 years, AUB must be diagnosed as quickly as possible. Patients with AUB should be evaluated to determine whether drug therapy is sufficient or whether organic lesions requiring surgical treatment are present. The most common pathological causes of AUB during the reproductive period are uterine polyps and myomas; common causes in the perimenopausal period are myomas, polyps, hyperplasia, and endometrial cancer.[4] Various methods are used to assess endometrial cavity pathologies. The uterine cavity can be evaluated by transvaginal ultrasound (TVUS), saline infusion sonography (SIS), dilatation and curettage, hysterosalpingography (HSG), hysteroscopy, or magnetic resonance imaging.

The most common use of office hysteroscopy is to evaluate pathologies related to AUB and reproductive health, but it can also be used for the diagnosis and treatment of other intrauterine pathologies. Office hysteroscopy, which involves imaging of the vagina, endocervical canal, and uterine cavity by camera, with the use of distension agents, can be performed in an outpatient examination environment, causes minimal inconvenience, and does not require inpatient monitoring in a hospital. Moreover, it is an important diagnostic tool because it is a safe and effective method that can facilitate immediate diagnosis.[5,6] Due to these properties, the uterine cavity is evaluated by office hysteroscopy for infertility and AUB. In the past, hysteroscopy required analgesia or anesthesia due to the size of the equipment and the technologies and solutions used. The use of hysteroscopes with diameters of up to 3 mm for diagnostic purposes decreased the need for painful cervical dilatation.[7] The primary disadvantage of hysteroscopy is the inconsistency in patient discomfort. Pain continues to be the primary reason for unsuccessful hysteroscopic interventions. Currently, the most important target in hysteroscopic procedures is to increase patient comfort by minimizing pain without increasing costs or the risk of complications. Many different medical treatments, such as nerve stimulation, have been used to reduce pain during office hysteroscopy.[8-10]

Previous studies have shown that laparoscopy with warm air and the use of warm contrast media during HSG and SIS reduces the severity of pain.[11-13] We hypothesized that the use of a warm distension fluid in office hysteroscopy would reduce the severity of pain associated with the procedure. Therefore, the aim of this study was to investigate the effects of distension fluid temperature on pain severity in patients undergoing office hysteroscopy due to AUB.

PATIENTS AND METHODS

A prospective clinical trial was conducted to assess pain in women undergoing office hysteroscopy. The participants were randomly allocated into groups with a warmed saline or room temperature saline as the distension medium. The patients were randomly allocated into two groups by assignment of single- and double-sequence numbers according to the order of treatment. We enrolled 100 perimenopausal patients who received gynecological outpatient services with histories of AUB and diagnosis of focal lesions in the uterine cavity by TVUS between December 2015 and August 2016. A minimum sample size of 94 was calculated by power analysis using Cohen's standard effect size (α=0.05, 1-β=0.80). However, considering the probability of patient loss to follow up, 50 people were included in each group. Criteria for admission were perimenopausal status, AUB, and the detection of suspected intrauterine lesions by TVUS. Exclusion criteria were the presence of pelvic infection, pregnancy and its complications, and suspicion of genital malignancy. The study was approved by the institutional ethics committee (Approval no. 15-KAEK-176) of Gaziosmanpasa University, Tokat, Turkey, and written approval and informed consent were obtained from each participant.

Detailed medical histories were obtained and physical and pelvic examinations were performed in all patients. All patients underwent TVUS (Logiq P5 Premium; GE Healthcare, Chicago, IL, USA) using a vaginal probe (frequency, 4–9 MHz). Based on this evaluation, patients in whom intrauterine focal lesions were detected underwent office hysteroscopy. Age, gravidity, parity, body mass index, last delivery date, previous delivery method, and histories of systemic and surgical diseases were evaluated before conducting office hysteroscopy. Patients were informed about management procedures, interventional stages, possible complications, and use of the visual analog scale (VAS) scores. Office hysteroscopy was performed using the same instruments (Richard Wolf GmbH, Knittlingen, Germany) and the same operator (SG) when bleeding was absent or minimal. No medication (analgesic, prostaglandin, or antibiotic) was administered to the patients before or after the procedure. Normal saline (0.9% isotonic liquid) was used as the distension medium. The distension fluid was prepared in an incubator by heating to 37°C (body temperature) or was unheated (25°C room temperature). The liquid temperatures were confirmed by infra-red thermometer before the procedure. The patients were placed in the

dorsal lithotomy position on a gynecological examination table. The procedure was performed using a 30°-angled office hysteroscope with an internal diameter of 2.7 mm (external diameter, 5 mm). A double-chamber fluid pump that provided a constant intra-cavity pressure of 120–200 mm Hg was used for distension of the uterine cavity. Office hysteroscopy was performed using a vaginoscopic approach ("no-touch" method). No speculum, cervical dilatation, or povidone-iodine lavage was used in any patient. A sterile hysteroscope inserted into the vagina provided vaginal distension and enabled visualization of the cervix. Following detection of the cervix, the hysteroscope was moved forward through the cervical canal. The procedure was terminated after evaluation of the endocervical canal, cavity, and ostia.

Pain assessment was conducted by recording patient VAS scores at six points during the procedure: before the procedure (VAS-1), at vaginal entry (VAS-2), at the cervical ostium transition (VAS-3), while in the cavity (VAS-4), at the end of the procedure (VAS-5), and 30 minutes after the end of the procedure (VAS-6). The researcher who performed the hysteroscopy was asked to record patient VAS scores at the relevant stages of the procedure. Patients were discharged on the same day. Patients with focal lesions were directed to operative hysteroscopy, whereas those without focal lesions were directed to the dilatation and curettage process.

The VAS is a safe, easy, descriptive, well-established, and accepted instrument for pain assessment. It is usually horizontal or vertical and 10 cm in length, depicting a scale ranging from "no pain" to "excruciating pain." The VAS may simply illustrate a straight line, or a line divided into evenly spaced segments, or it may have descriptive words placed along the line to describe pain levels. The VAS has been shown to be more sensitive and reliable in the measurement of pain intensity than other one-dimensional scales, and patients aged > 5 years usually describe this method as easy to understand and perform.[14,15]

Statistical analyses were performed using the IBM SPSS statistical software (version 18.0; Armonk, New York, United States: IBM Corp). For statistical comparisons, the *t* test was used for parametric values, and Pearson's chi-square or Fisher's exact tests were used for categorical variables. Categorical variables were expressed as numbers and percentages and continuous numerical variables were expressed as means and standard deviations. *P* values <.05 were considered to be statistically significant.

RESULTS

Ninety-nine patients completed the study because one patient was unable to comply due to pain and underwent hysteroscopy under general anesthesia. No significant difference in any demographic characteristic (age, gravidity, parity, body mass index, type of delivery, and systemic disease) was detected between the groups (**Table 1**). VAS scores recorded before the procedure (VAS-1) were similar in both groups (*P*=.078). Similarly, VAS scores did not differ significantly between groups when the hysteroscope entered the vagina (VAS-2, during vaginal distension) or 30 minutes after the procedure had been completed (VAS-6). However, the VAS-3 (cervical ostium transition), VAS-4 (in the uterine cavity), and VAS-5 (end of procedure) scores were significantly lower in the group that underwent examination with a warm versus a room temperature distention fluid (**Table 2**). No complication (uterine perforation, genital injury, bleeding, or infection) developed during or after the procedure in any of the 99 patients. Histopathological examination was performed in 88 patients. Hormonal changes, endometrial hyperplasia, endometrial polyps, endometritis and endometrial cancer were recorded in 45.4%, 17%, 27.3%, 8% and 2.3% of patients, respectively.

DISCUSSION

The primary limitation of the office hysteroscopy procedure is the pain experienced by patients. One of the most painful steps of the procedure is the passage of

Table 1. Demographic and clinical characteristics of the patients grouped by the temperature of the distension fluid.

Characteristic	Warm (n=50)	Room temperature (n=49)	*P* value
Age (years)	45.7 (3.2)	45.5 (3.6)	.686
Gravidity	4.2 (1.9)	4.12 (1.9)	.947
Parity	3.0 (1.2)	3.22 (1.5)	.348
Body mass index (kg/m^2)	29.9 (4.9)	30.0 (5.5)	.807
Mode of delivery			
Vaginal delivery	31 (62.0)	33 (67.3)	
Cesarean delivery	4 (8.0)	5 (10.2)	.256
VD and CS	14 (28.0)	10 (20.4)	
Systemic disease	13 (26.0)	16 (32.6)	.509
Hypertension	7 (14.0)	8 (16.3)	.779
Diabetes mellitus	3 (6.0)	6 (12.2)	.295
Thyroid disorders	7 (14.0)	6 (12.2)	.766

Data presented as mean (standard deviation) or n (%).

Table 2. Visual analog scale scores of the patients grouped by the temperature of the distension fluid.

VAS score	Warm (n=50)	Room temperature (n=49)	*P* value
VAS-1	.18 (.43)	.40 (.67)	.078
VAS-2	.94 (.76)	1.02 (.82)	.616
VAS-3	3.74 (1.22)	4.42 (1.41)	.028
VAS-4	2.84 (1.28)	3.46 (1.27)	.020
VAS-5	2.02 (1.11)	2.59 (.97)	.003
VAS-6	.92 (.80)	1.20 (.91)	.138

Data presented as mean (standard deviation). VAS: visual analog scale.

the hysteroscope through the cervical canal, and another painful step occurs during uterine distension. The transition of the hysteroscope through the cervical canal is particularly difficult for nulliparous and postmenopausal women. We found that the use of distension fluid warmed to body temperature (37°C) decreased pain severity during office hysteroscopy. Pain intensity was similar with the use of warmed and unwarmed fluids before the procedure and 30 minutes after the procedure. However, pain intensity (as reflected by VAS scores) was lower during the procedure when warm fluid was used.

Our results contrast with those from several other studies. Evangelista et al[16] conducted a randomized controlled study to compare pain intensity and degree of satisfaction with hysteroscopic examinations using saline solution kept at room temperature (control group) and heated to 37.5°C (test group) in 64 reproductive-aged and postmenopausal women. The authors reported no significant difference between groups in pain, duration of the examination, or degree of patient satisfaction immediately after the examination or at 1 and 15 min after the procedure.[16] In another prospective randomized study that compared pain scores between women having hysteroscopy with warm (36°C) compared with room-temperature (25°C) saline as distension medium, the results again showed that the median VAS scores were not different between the two groups during and after the hysteroscopy.[17] In another prospective study involving 100 women who underwent diagnostic or operative hysteroscopy for indications such as abnormal uterine bleeding, removal of the intrauterine contraceptive device and endometrial polyp resection, the effects of distension fluid temperature on pain/discomfort and patient satisfaction were compared. It was reported that the distension fluid at room temperature (25°C) or body temperature (37°C) did not differ on the ease of operation, clarity of the hysteroscopic view, procedural discomfort/pain, or patient satisfaction.[18] The discrepancy between our study and the other studies may be explained by differences in the participants (reproductive-age and postmenopausal) and types of procedure (diagnostic and operative). These factors were all more homogeneous in our study and a single operator performed all of the procedures.

Considering these differences, the effects of warm liquid on pain during hysteroscopy should be evaluated further in larger populations. In studies of the effects of creams, gels, and sprays containing local anesthetic agents on pain scores during hysteroscopy, these methods were not shown to have any pain-reducing effect, except to reduce the pain associated with tenaculum use.[6,19] In a large-scale study of 2500 cases, Nagele et al20 performed 5-mm rigid hysteroscopy with local anesthesia administered to patients only if they reported experiencing pain. Only 29.8% of the patients required local anesthesia. Upon closer examination, the authors found that patients given local anesthesia were subjected to cervical dilatation for reasons such as nulligravidity and postmenopausal status. In another study of 1144 patients, only 56 (4.6%) patients could not complete the procedure due to pain.[21] In addition, 189 (16.5%) patients complained of pain. Although these patients were not notable in terms of parity or menopause, the pain scores of older and younger patients were higher. These two studies with large samples yielded relatively low rates of detection of patients who had difficulty tolerating pain during office hysteroscopy procedures when anesthesia was not used. The lack of local anesthesia use in these studies also had advantages, such as shortened patient recovery time, lack of anesthesia complications, and lower costs. The use of misoprostol was shown to reduce the severity of pain experienced during cervical transit in office hysteroscopy.[22,23] Due to the effect of misoprostol on cervical ripening, its use was reported to reduce pain caused by passage through the cervical canal during hysteroscopy. The duration of time between misoprostol application and treatment also had an effect on pain management, as less pain was reported when hysteroscopy was performed 12 hours after misoprostol administration.[23]

On the other hand, the reduction of intrauterine pressure during office hysteroscopy to decrease pain due to uterine dystrophy also decreased the severity of pain, but compromised the ability to obtain images.[24] In our study, no local anesthetic agent or systemic analgesic (i.e., non-steroidal anti-inflammatory drug, paracetamol) was used to reduce pain, and misopros-

tol was not used for cervical ripening. Local heat treatment is used for muscle spasms because it increases blood flow, relaxes muscles, and relieves pain, and was reported to provide safe, rapid, and effective pain relief in the treatment of acute pelvic pain.[25] Due to these effects, we hypothesized that warm distension fluid would reduce pain during hysteroscopy, and our results support this hypothesis.

Our vaginoscopic approach ("no-touch" method) was terminated in only one patient due to pain. According to the literature, the rate of non-completion of the office hysteroscopy process is 1.3–5.2%.[26] Thus the rate of failure in our study was acceptable. The "no-touch" technique is considered suitable, based on the number of successful office hysteroscopies in our practice. Uncomplicated uterine scars do not have an impact on pain experienced during or immediately after diagnostic outpatient hysteroscopy.[27]

The main limitations were that a subgroup analysis could not be performed due to the insufficient number of cases; we were unable to evaluate vasovagal symptoms; a high pressure fluid pump was used to distend the uterine cavity; the effect of temperature on image clarity and processing time were not evaluated; and clinical trial registration was not made. However, the strengths of the study were that a homogeneous group was formed by evaluation of patients only in the perimenopausal period, and the study design was prospective.

In conclusion, the application of 37°C distension liquid for office hysteroscopy was beneficial in reducing pain related to the procedure. The application of warm (37°C) distension liquid in office hysteroscopy evaluation can reduce patient pain during the procedure and improve compliance with the procedure compared with the application of room temperature (25°C) distension liquid. Furthermore, patients can be diagnosed rapidly, at low cost and with high accuracy, but without the risk of complications of anesthesia. Ultimately, the patient is able to quickly return to a normal life.

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