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Pain assessment during outpatient hysteroscopy using room temperature versus warm normal saline solution as a distention medium – a prospective randomized study

T. Issat[1,2], J. Beta[1,3], M.A. Nowicka[1], A. Durczyński[1], A.J. Jakimiuk[1,2]

[1] Department of Obstetrics, Women's Diseases and Oncogynecology, Central Clinical Hospital of Ministry of Interior and Administration, Warsaw
[2] Center for Reproductive Health, Institute of Mother and Child, Warsaw (Poland)
[3] Women's Health Directorate, Medway Maritime NHS Foundation Trust, Gillingham (United Kingdom)

Summary

Objective: To assess the efficacy of warm normal saline distention solution versus a standard, room-temperature normal saline as distention medium for pain relief during outpatient hysteroscopy. *Materials and Methods:* A prospective randomized case-placebo controlled study was conducted in tertiary care centre - Central Clinical Hospital of Ministry of Interior and Administration. Study group consisted of 100 women referred for outpatient hysteroscopy between January 2015 and July 2015. Every patient, who was referred for an office hysteroscopy, was offered to participate in the study to receive a sterile, 0.9% normal saline warmed up to 36°C as distention medium. Control group were women receiving sterile, room temperature of 25°C, 0.9% normal saline solution as a distention medium. No pre-medication nor analgesia were used. A visual analogue scale (VAS) was used for one-dimensional pain assessment. Women were asked to mark a VAS score before, during, and five and 15 minutes following the procedure. *Results:* Median VAS scores during and directly after the anaesthesia-free hysteroscopy were no different between two groups. ($p = 0.554$ and $p = 0.121$, respectively). There were also no differences in the procedure time between groups ($p = 0.845$). *Conclusions:* Warm normal saline distention solution does not reduce the pain during and at the end of the outpatient hysteroscopy. The effect does not depend on the age of women, menopausal status, parity or type of outpatient hysteroscopy (operative or diagnostic).

Key words: Office hysteroscopy; Outpatient hysteroscopy; Distention medium.

Introduction

Outpatient hysteroscopy, also known as office hysteroscopy, is an established diagnostic tool [1]. The procedure involves miniaturised endoscopic device to visualise and examine the uterine cavity, without the need for operating room facilities or anaesthesia. It is indicated for the assessment of women with abnormal uterine bleeding [1]. Other common procedures include endometrial polypectomy [2], removal of small submucous fibroids [3], endometrial ablation [4], removal of lost intrauterine devices, and transcervical sterilisation [5] or as a part of sub-fertility evaluation and management.

One of the main causes of procedure failure is patient discomfort and pain. Advocated risk factors include nulliparity, cervical stenosis, chronic pelvic pain, anxiety, and menopause, as well as hysteroscope diameter, operative time, and characteristics of the intrauterine lesion (location, shape and size) [6, 7].

Pain from uterine cavity is driven by visceral afferent fibers with sympathetic fibers through the hypogastric nerves to the T12-L2 spinal ganglia [8]. Pain from the cervix and vagina is conducted by visceral afferent fibers to the S2-S4 spinal ganglia via the pudendal and pelvic splanchnic nerves, along with parasympathetic fibers [9]. Biopsy or destruction of endometrium may cause additional pain as a result of uterus contraction [10]. Some authors suggested that the pain during the procedure might be related to prostaglandin release as a result of the hysteroscope manipulation or uterine distention [11].

There is no consensus on the optimal method of pain reduction during outpatient hysteroscopy [12] with several different approaches being reported, including use of lidocaine gel [13], intravenous tramadol [14], intrauterine and intracervical lidocaine [15, 16], mifepristone [17] or sublingual buprenorphine [18]. Additionally, results of some studies suggested that the outpatient hysteroscopy performed under moderate sedation might increase patient safety and satisfaction [19]. Results from previous studies showed that vaginal misoprostol administrated before the procedure reduced pain during and directly after the hysteroscopy, when compared to placebo or ketoprofen [20].

Recently published guidelines for clinical practice from the French College of Gynaecologists and Obstetricians recommended that office hysteroscopy should be per-

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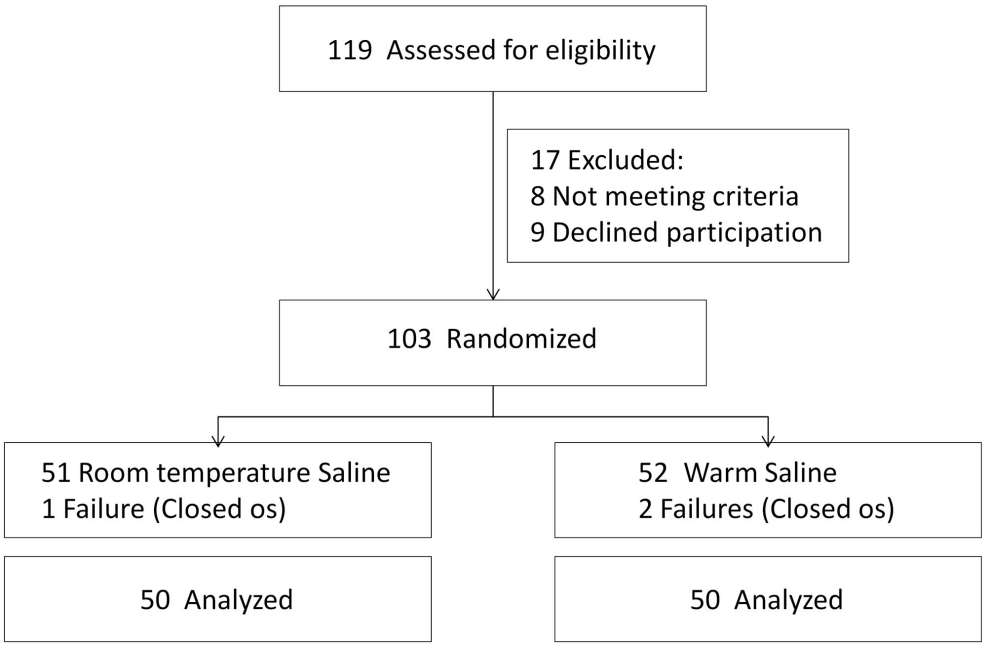

Figure 1. — Flow diagram of the randomization process.

formed without any anesthesia with normal saline as a distention medium [21]. According to Royal College of Obstetricians and Gynaecologists (RCOG) guideline, women without contraindications should be advised to consider taking standard doses of non-steroidal anti-inflammatory agents (NSAIDs) around one hour before their scheduled outpatient hysteroscopy appointment with the aim of reducing pain in the immediate postoperative period [22]. One of the recommendations for further research was to assess the effectiveness of warming fluid distention media on relieving pain in outpatient hysteroscopy.

The aim of this study was to assess the efficacy of a warm normal saline distention solution versus a standard, room-temperature normal saline as distention medium for pain relief during outpatient hysteroscopy. Secondary measures included side effects, complications failure rate, procedure time, and the pain level during each stage of the procedure.

Materials and Methods

A prospective case-placebo controlled study was conducted to assess pain in women undergoing outpatient hysteroscopy. Two groups were defined as study group of women having hysteroscopy with a warmed normal saline distention solution versus women having a standard, room-temperature normal saline as distention medium. The study was approved by the institutional research ethics committee (Decision Letter 73/2012). Between 1st of January 1 and July 1, 2015, 100 women underwent outpatient hysteroscopy in the present Department of Obstetrics, Women's Diseases and Oncogynecology, Central Clinical Hospital of Ministry of Interior, Warsaw. All women agreed to participate in the study and written informed consent was obtained.

All women aged over 18 years referred for hysteroscopy for diagnosis of abnormal endometrium on ultrasound, endometrial polyps, and uterine bleeding were included in the study. All participants had a pelvic ultrasound examination performed confirming the initial diagnosis. Women with endometrial polyps measuring more than 30 mm were excluded and referred for operative hysteroscopy under anesthesia. Women with a possible pregnancy, lower genital tract infections, gestational trophoblastic disease, presence of endocervical polyps visualized on a speculum examination, asthma, acute porphyria, hepatitis, renal failure, lactation, and oversensitivity to one of the agents or their elements, were excluded.

Patients were identified and selected on admission. Randomization to receive a sterile, 0.9% normal saline warmed up to 36°C as distention medium with women receiving room temperature, sterile 0.9% normal saline solution as controls was generated automatically in an allocation ratio of 1:1 (Figure 1). No pre-medication was used as described previously [20]. The randomization envelopes were opaque and were kept in an outpatient hysteroscopy room in a closed study box. After informed consent was obtained, randomisation was performed. Each of the envelopes was taken out of the box according to the number of randomisation.

The procedure of outpatient hysteroscopy was performed according to the Royal College of Obstetricians and Gynaecologists Green-Top Guideline Nr. 59 [22]. Briefly, outpatient hysteroscopy was conducted outside of the formal operating theatre in a treatment room with adjoining private changing facilities and the toilet. The 3.2-mm versascope hysteroscope was used with normal saline solution as a distention medium. When appropriate, a versapoint was used to cut the polyps or fibroids, and to facilitate extraction of fragments, 5F forceps were used. For the simple biopsy of endometrium, only 5F forceps were used. A 300-W xenon lamp and video camera were used. Distention fluid pressure was generated using an automated flow-meter pump set for 120 mmH_2O of intrauterine pressure. All procedures involved vaginoscopy and there were no dilators used. In all study cases the temperature of the solution was confirmed with the automated fluid warmer.

For one-dimensional assessment of pain, a visual analog scale (VAS) was used. A VAS scale consists of a ten-cm line ranging

Table 1. — *Women' characteristics and results. U-Mann Whitney test for continuous variables and exact Fisher and χ^2 for categorical variables.*

		Warm saline (n=50)	Control (n=50)	*p* *
Age (years); median (IQR)		43.00 (32.00 - 53.00)	46.50 (37.00 - 57.25)	NS
Weight (kg); median (IQR)		68.50 (57.00 - 79.00)	67.00 (60.00 - 77.00)	NS
Height (cm); median (IQR)		165.50 (161.00 - 175.00)	162.00 (154.50 - 171.00)	NS
Parity; n (%)	Nulliparous	24 (48.00)	21 (42.00)	NS
	Multiparous	26 (52.00)	29 (58.00)	
Postmenopausal; n (%)		34 (68.00)	27 (54.00)	NS
Concomitant diseases; n (%)	Chronic arterial hypertension	12 (24.00)	14 (28.00)	NS
	Diabetes	3 (6.00)	2 (8.00)	NS
	Asthma	0	0	
Referral diagnosis	Abnormal endometrium on US	15 (30.00)	15 (30.00)	NS
	Endometrial polyps	19 (38.00)	16 (32.00)	
	Infertility	0	3 (6.00)	
	Uterine bleeding	15 (30.00)	16 (32.00)	
	Other	0	1 (2.00)	
Procedure type; n (%)	Operative hysteroscopy	23 (46.00)	22 (44.00)	NS
	Diagnostic hysteroscopy	27 (54.00)	28 (56.00)	
Procedure time (s); median (IQR)		210.50 (150.00 - 295.00)	197.50 (135.00 - 305.00)	NS
Pain assessment	VAS score before the procedure	0	0	
	VAS score during the procedure	4.00 (2.00 - 7.00)	3.00 (2.00 - 6.00)	NS
	VAS score at the end of the procedure	2.00 (0 - 4.00)	1.00 (0 - 2.00)	NS
	VAS score 15 min. after the procedure	0	0	
Need for additional painkillers; n (%)		2 (4.00)	2 (4.00)	NS

*Significance reported at $p < 0.05$.

from ''no pain'' to ''worst pain experienced''. Results are expressed in ordinal numbers on a scale ranging from zero to ten. The women were asked to mark VAS scale before, during, and five and 15 minutes after the procedure. Postoperative pain assessment and management included an optional dose of 100-mg oral ketoprofen if requested.

Vaginal bleeding, nausea, vomiting, diarrhea, and fever were also assessed as side effects. The following complications were investigated: uterine perforation, false cervical passage, cervical laceration, and infection. A failure rate and the time of the procedure were recorded. Additionally, the subjective patient's worst pain experience was noted for the following stages of the procedure: passage through the cervical canal, distention of the uterine cavity, biopsy, excision of the lesion or removing tissue from the uterus.

Patient characteristics were compared, using the Chi square test and Fisher exact test for categorical variables and U-Mann Whitney for the continuous variables. The statistical software package SPSS 17.0 was used for data analyses.

Results

No adverse effects or complications were reported in either group. Median age, weight, height, menopause status, parity, gravidity, and indication for outpatient hysteroscopy were similar in both groups. The women' characteristics are presented in Table 1.

The results of this study showed that the median VAS score during the outpatient hysteroscopy and directly after the procedure (five minutes) was similar regardless of the distention solution temperature ($p = 0.545$ and $p = 0.121$, respectively). There were no differences in procedure time between the groups ($p = 0.845$). Median procedure time for placebo group was 211 seconds compared to 198 seconds for warm saline group. There were no differences between both groups regarding the need of additional analgesia after the procedure (two and two women, respectively, $p = 1.000$).

Discussion

Pain is still the most common reason for failure of office hysteroscopy. The aim of this study was to assess potential effect of increasing the temperature of the medium in regard to pain sensation during outpatient hysteroscopy. A VAS was selected because it has been found to correlate well with patient's verbal pain assessment [23].

The main results of this study showed that the median VAS scores during hysteroscopy and directly after the procedure (five minutes) were not significantly different in women who received warm normal saline distention solution when compared with a room-temperature normal saline as distention medium during the outpatient hysteroscopy ($p = 0.319$ and $p = 0.06$, respectively). There were no statistical differences between three groups in the median VAS score assessed 15 minutes after the procedure. This effect was not related to the patient's age, hormonal status, parity or type of the procedure (operative or diagnostic) (Table 1). The present study did not show any statistical differences between the groups regarding procedure

time (p = 0.414).

There is limited number of studies reporting use of warmed saline solution as distention medium - both from different centers but in the same country [24, 25]. Results of the first study showed no significant differences between a warmed normal saline solution group (37.5°C) compared with controls [24]. Number of patients were smaller, however (n=30 and n=34, respectively). Authors of the second study reported less patient discomfort and greater satisfaction in a warmed saline solution group compared with gaseous distention medium group. It is worth mentioning that two study groups were not homogenous as women from the gaseous medium group had additional speculum and clamping of the cervix with Pozzi forceps [25]. Standard infusion fluids are stored in room temperature and some authors suggested that temperature of the distention solution itself may trigger uterine contraction and pain during hysteroscopy as it is much lower than the body temperature [22]. Anatomical studies showed that under normal conditions, endometrium is lacking terminal innervation [26]. As such patients should not experience pain during the biopsy, which is contrary to everyday practice. Interestingly, recently published data suggested that nerve fibers are also expressed at the level of functional layer of the endometrium and may contribute to pain during office hysteroscopy. Additionally, authors of the study found that women suffering from endometriosis or adenomyosis are more likely to experience such pain [26]. Other critical moments of the procedure include passing through cervical canal, myometrial contractile activity caused by distention medium or direct but accidental stimulation of the myometrium with the grasper [26]. Cervical and uterine cavity dilatation may also lead to vasovagal reactions like dizziness, vomiting or even shock [27]. The present authors did not find any differences with regards to vasovagal reactions between two groups.

Several studies confirmed that distention using normal saline solution is more acceptable to patient, because the procedure is smoother, faster, and also easier to perform when compared to carbon dioxide (CO_2) as a medium [28]. Some authors suggested that intrauterine anesthesia during the office hysteroscopy might be of benefit. Recently published results of randomized trial and systematic review however do not support the hypothesis. Transcervical/intrauterine anesthetic did not significantly reduce the amount of pain experienced during the procedure [29]. Moreover, three other studies reported significant reduction in pain score during hysteroscopy while using intrauterine anesthesia, but only one, which was included to analysis, was of good quality [30]. Author of the latter reported that there was no differences between placebo and lignocaine groups [31].

Strengths of the present study include prospective case-placebo controlled study design, number of patient randomized in each arm, and the fact, that a single, experienced operator performed all of the procedures.

Conclusion

Numerous studies addressed the problem of effective pain relief during outpatient hysteroscopy, but the results are not robust nor equivocal [12-20]. It seems that there is still space for improvement to make this procedure painless and fully acceptable for every patient who would then benefit from minimally invasive approach. Unfortunately, the results of the study showed that a warm normal saline distention solution does not give pain relief during and directly after office hysteroscopy and therefore it is unlikely to be useful in everyday setting.

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Corresponding Author:
A.J. JAKIMIUK, M.D.
Department of Obstetrics
Women's Diseases and Oncogynecology
Central Clinical Hospital of Ministry of Interior
Woloska Street 137
02-507 Warsaw (Poland)
e-mail: jakimiuk@yahoo.com