Original Article

Assessment of Pain at Different Steps of Diagnostic Hysteroscopy Using Room Temperature Normal Saline versus Warmed Normal Saline Solution as Distension Medium: A Randomized Controlled Trial

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Abstract

Objectives: Compare pain intensity at entry into the cervical os, during uterine distension and 15 min after the procedure, in patients undergoing diagnostic hysteroscopy with room temperature normal saline versus that with saline warmed to 38–40°C, using visual analog scale (VAS) score. Furthermore, compare the time taken and failed procedures between them.
Materials and Methods: This was a randomized controlled, prospective study conducted at a Tertiary Care Center on 100 patients planned for diagnostic hysteroscopy with a 4 mm 30° hysteroscope using vaginoscopy technique. They were divided into two groups of 50 each, with control undergoing the procedure using normal saline at room temperature and the test with saline warmed to 38–40°C as distension medium. Primary outcomes were VAS at the point of entry into the internal os (T0), 1 min later (T1), and 15 min after the procedure (T15). Secondary outcomes were procedural acceptance, time taken, and failed procedures.
Results: The mean VAS in the control group at T0, T1, T15 was 3.31 (1.461;–0.870–0.245), 2.46 (1.398;–0.539–0.498), 0.75 (0.911;–0.379–0.338), respectively, as compared to the test group of 3.62 (1.282;–0.870–0.245), 2.48 (1.148;–0.540–0.498), 0.77 (0.911;–0.379–0.379), respectively. About 73.5% of controls and 68.8% in the test group were willing to undergo the procedure again. About 93.9% of controls would recommend it further as against 93.8% among the test controls. The time taken and number of failed procedures showed no statistical difference.
Conclusion: No significant difference was noted in terms of outcomes measured by warming the distension medium.

Keywords: Hysteroscopy, Likert's, medium, pain, saline, visual analog scale

Introduction

Diagnostic hysteroscopy has emerged as the gold standard for the evaluation of intrauterine pathologies such as abnormal uterine bleeding, postmenopausal bleeding, endometrial hyperplasia, and carcinoma endometrium.[1]

The procedure is well tolerated and cited to cause only mild discomfort in most of the cases. However, pain, vasovagal episodes, and uneasiness are commonly reported. Pain remains the most important reason for procedural failure as also, noted by de Carvalho *et al*. in their study on pain evaluation in outpatients undergoing anesthesia-free diagnostic hysteroscopy.[2] Nagele *et al*. concluded that 84% of failed hysteroscopies were due to patient discomfort while De Iaco *et al*. stated that 34.8% of patients undergoing diagnostic outpatient hysteroscopy report severe pain.[3,4]

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Methods to minimize pain during hysteroscopy have been the focus of research over the past years. The use of liquid distension compared to carbon dioxide has been proven to reduce vasovagal episodes besides providing better image quality although, no significant difference in pain intensity was noted.[5] The "no-touch" vaginoscopy method by Bettocchi and Selvaggi and the use of smaller caliber instruments and optics have been proven to significantly reduce pain perception during hysteroscopy and are now universally endorsed.[6,7] Normal saline used at room temperature as distension medium provokes uterine contractility causing colicky pain. Although it is hypothesized that warming the saline solution to physiological temperature (~38°C) could reduce perceived pain, it has not yet been proven.[8]

We found five studies, to the best of our knowledge, on the use of warm saline for pain relief with one of them using 4 mm hysteroscope, while the rest used 2.9 mm hysteroscope. However, none of the studies could find any significant difference between the groups studied.[8-10] The objective of this study was to compare the pain intensity, procedural difficulty, and patients' acceptance of the procedure when using 4 mm hysteroscope with warm saline versus saline at room temperature as distension medium.

Materials and Methods

This was a randomized, prospective trial conducted at the Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi, from June 2019 to December 2019 after official approval by the Institutional Ethics Committee. Informed written consent was taken from all the patients.

The subjects underwent diagnostic hysteroscopy without any other procedures and in case operative procedures like endometrial sampling were required, they were proceeded with, only after pain scores and other research parameters had been recorded. Any premenopausal woman posted for diagnostic hysteroscopy was included in the study while postmenopausal women, those with suspected pregnancy, history of uterine perforation less than a month prior, previous history of cervical surgeries, genital tract malignancy, active vaginal bleeding, active genital tract infections and those with medical conditions like uncontrolled diabetes and hypertension were excluded from the study.

After a complete history and examination and informed written consent taken by the researcher, patients fulfilling the inclusion criteria were allocated to two groups of 50 subjects each, using a computer-generated randomization table. The test group underwent diagnostic hysteroscopy with normal saline warmed to 40°C while the control group with normal saline at room temperature. Saline was warmed using a Med Mac Fluid warmer available, with the requisite number of saline bottles placed in the warmer set to 40°C on the morning of the procedure. The patient was shifted to the examination table only after the set temperature had been achieved as displayed on the screen of the warmer. The saline bottle was taken out only after the patient was positioned, painted, and draped. The set temperature of 40°C was maintained while the rest of the bottles, required for the remaining procedures, were still inside the warmer. Room temperature determined by the electronic central heating setting was maintained at 25°C.

The primary outcomes measured were the degree of pain experienced by the subjects at the point of hysteroscope entry through the cervical os, during the phase of uterine distension, and 15 min after the procedure. The pain intensity was measured using the visual analog scale (VAS) and noted as "T0" at the time of entry through the cervical os, "T1" at 1 min after the cervical entry, "T15" at 15 min after the procedure completion as marked by the patients from 0 to 10 with 0 indicating no pain to 10 indicating excruciating, unbearable pain. This scale is validated, practical, and universally accepted for pain score measurements.

The secondary outcomes were: (1). Degree of acceptance of the examination measured in terms of patients' readiness to undergo the same procedure again without any analgesia/anesthesia and the likelihood of recommending it further to relatives/friends (2). Failed procedures due to pain or inability to negotiate the os or requiring anesthesia and (3). Time taken to complete the examination in minutes from the vaginal entry to the vaginal exit.

All hysteroscopies were performed by the same gynecologist with rigid continuous flow, 30° view 4 mm hysteroscope assembled in a 5 mm diagnostic sheath using the "no-touch" vaginoscopy technique without the aid of any instruments, with patients in the lithotomy position. Uterine distension was facilitated by normal saline, infusion bags suspended 1.5 m above the patient, administered free-flowing with a hand-pumped pressure bag set to 200 mmHg to maintain the intrauterine pressure between 70 and 100 mmHg. The vaginal wall, cervical canal, lateral, anterior, and posterior walls and the fundus, tubal ostia, and endometrium were observed. In case there was a need of endometrial sampling, it was done only after all the variables of the study had been recorded.

Results

Statistical testing was conducted with the Statistical package for the Social Science System Version SPSS 17.0, Chicago, 2008. Continuous variables are presented as mean ± standard deviation (SD), and categorical variables are presented as absolute numbers and percentages. The comparison of normally distributed continuous variables between the groups

was performed using Student's *t*-test. Nominal categorical data between the groups were compared using the Chi-squared test or Fisher's exact test as appropriate. $P < 0.05$ was considered statistically significant.

Of the 100 procedures undertaken, two patients in the warm saline group and one in the room temperature saline group experienced excessive pain necessitating the usage of analgesics. They were hence, excluded from the study. The final analysis was carried out on 48 patients in the warm group and 49 in the room temperature group [Figure 1]. The control and test groups were matched for age mean (SD; 95% confidence interval) 34.63 (7.93;–2.132–3.772) versus 33.81 (6.64;–2.127–3.768), body mass inde × 26.01 (2.42;–0.464–1.335) versus 25.57 (2.02;–0.463–1.33) and parity of 2.25 versus 2.39, respectively, with no significant difference noted between the groups. The groups were matched in terms of indications of hysteroscopy also [Table 1].

The mean VAS scores at T0, T1, and T15 in the control group was 3.31 (1.461;–0.870–0.245), 2.46 (1.398;–0.539–0.498), and 0.75 (0.911;–0.379–0.338) as compared to that in the test group of 3.62 (1.282;–0.870–0.245), 2.48 (1.148;–0.540–0.498), 0.77 (0.911;–0.379–0.338), respectively, with no statistical difference noted between them [Table 2].

The mean time taken in minutes to complete the procedure was 2.23 (2.195;–0.135–1.573) in the control group as compared to 1.38 (1.196;–0.138–1.571) in the test group showing no statistical difference [Table 3]. The adverse effect of nausea/vomiting was experienced by 4 (8.25%) patients in the control group while no subject in the test group experienced any adverse effects of nausea, vomiting, or vasovagal attacks. Inadvertent cervical trauma occurred in 1 (2%) patient in the control group as compared to 4 (8.3%) in the test group [Table 4].

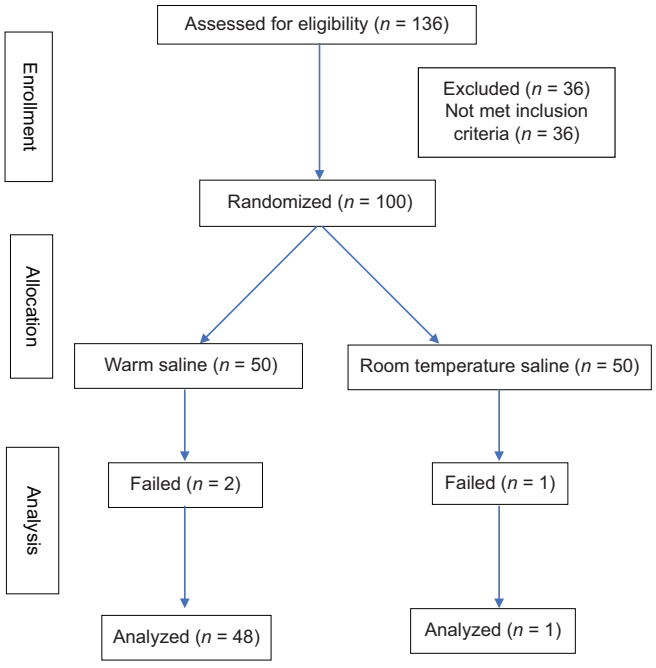

Figure 1: Consort diagram

Of the subjects in the control group, 36 (73.5%) were willing to undergo the procedure again but 13 (26.5%) refused as they were not willing to go through the discomfort or mild pain or the hospital hassle unless absolutely necessary. In the test group, 33 (68.8%) were willing while 15 (31.2%) refused to undergo the same in the future for the same reason that those in the other group cited. However, 46/49 (93.9%) subjects in the control group and 45/48 (93.8%) in the test group would recommend diagnostic hysteroscopy to their relatives or friends [Table 5], considering that it is a quick diagnostic procedure causing just a little discomfort to mild pain.

Discussion

Diagnostic hysteroscopy is the gold standard modality for the diagnosis of intrauterine pathologies.[11] Though it is a generally well-tolerated procedure, pain and uneasiness, commonly reported by patients, are considered to be the most common cause of hysteroscopy failure.[2-4] de Carvalho *et al*. reported moderate to severe pain amounting to a VAS of 5 or more, immediately after examination in 68.4% of patients.[2]

Although the use of miniature instruments has been proven to reduce pain, we used 4 mm hysteroscope with a 5 mm sheath,

Table 1: Comparison of age, body mass index, parity and indications

Variables	Warm (*n*=48) (SD)	Room temperature (*n*=49) (SD)	*P*
Age	33.81 (6.64)	34.63 (7.93)	
BMI	25.57 (2.02)	26.01 (2.42)	
Parity	2.39	2.25	
Indications (*n*)			
Subfertility	20	15	0.257
RPL	7	10	0.451
Menstrual disorders	23	24	0.917
Re-look	4	3	0.675
Placental polyp	1	0	0.310

SD: Standard deviation, BMI: Body mass index, RPL: Recurrent pregnancy loss

Table 2: Comparison of visual analog scale

	NS temperature	*n*	Mean±SD	CI
VAS T0	Warm	48	3.62±1.282	−0.870-0.245
	Room temperature	49	3.31±1.461	−0.870-0.245
VAS T1	Warm	48	2.48±1.148	−0.540-0.498
	Room temperature	49	2.46±1.398	−0.539-0.498
VAS T15	Warm	48	0.77±0.857	−0.379-0.338
	Room temperature	49	0.75±0.911	−0.379-0.338

VAS: Visual analog scale, CI: Confidence interval, SD: Standard deviation, NS: Normal saline

Table 3: Comparison of time taken

Time Taken (min)	n	Mean SD ConfidenceInterval ConfidenceInterval			
		Mean	SD	Confidence Interval	
Warm	48	1.38	1.196	−0.138	1.571
Room temperature	49	2.23	2.195	−0.135	1.573

Table 4: Comparison of adverse effects and complications

	Control, *n* (%)	Test, *n* (%)
Adverse effect (nausea/vomiting)	4 (8.2)	0
Complications (cervical trauma)	1 (2)	4 (8.3)

Table 5: Comparison of readiness to undergo the procedure and chances of recommending it

	Control (room), *n* (%)	Test (warm), *n* (%)
Readiness		
No	13 (26.5)	15 (31.2)
Yes	36 (73.5)	33 (68.8)
Recommendation		
No	3 (6.1)	3 (6.2)
Yes	46 (93.9)	45 (93.8)

because compact hysteroscope was not available at our Institute during the period of this study. Despite the widespread use of 2.9 mm hysteroscope, the same may not be available or affordable to a lot of low-resource countries and limited infrastructure Institutes because of which even today, the 4 mm hysteroscope is the most commonly available as well as the most popularly used endoscope for the purpose of diagnostic hysteroscopy. Our endeavor, through this study, was to find an affordable, easily available, and executable method of reducing pain that did not involve any drugs or pharmaceutical interventions.

Adequate knowledge of the female pelvis and pain physiology is of paramount importance to be able to manage pain well. The uterine fundus is innervated by sympathetic fibers from T10 to L2 via the inferior hypogastric plexus, which enters the uterus by the uterosacral ligaments and by the infundibulopelvic ligament, forming the ovarian plexuses.[12] The upper vagina, cervix, and lower uterine segment are innervated by parasympathetic fibers from S2 to S4, forming the Frankenhauser or uterovaginal plexus, which enters the uterus following the Cardinal ligaments.[12,13] Myometrium and endometrium are innervated by a plexus at the myometrial-endometrial interface. Only the basal third of the endometrium is innervated while myometrial innervation varies with disease processes such as endometriosis or adenomyosis.[14,15] As a result, pain requires management at various levels with no single modality proven to be better than the other.

Considering hysteroscopy, pain is mainly witnessed with the use of speculum or tenaculum, cervical dilation, hysteroscope passage through the cervical canal, and uterine distension with fluid.[16,17] Methods to reduce pain have been the focus of research in the field of hysteroscopy to facilitate shifting the procedure from the operating room to the office, making it cheaper, accessible, and more acceptable to the population. Shankar *et al*. in their study concluded that saline was more comfortable than carbon-dioxide and glycine as distension medium.[5] Almeida *et al.*, on the comparison of warmed saline versus carbon dioxide as distension medium, concluded that warmed saline offered greater degree of satisfaction and caused lesser pain.[9] However, in this study, those subjected to warm saline underwent the procedure by vaginoscopy technique while the gaseous medium underwent the same by conventional method hence, forming a major bias. Most studies on anesthesia or analgesia on pain in hysteroscopy have been inconclusive.[18-20] Some studies have assessed the role of misoprostol, a prostaglandin E1analog for cervical ripening in-office hysteroscopy hypothesizing that it may facilitate the procedure and lower the risk of cervical laceration by dilating and softening the cervix. Although, Sordia-Hernández *et al*. in their study did conclude that there was a considerable decrease of pain and time of the procedure with the use of misoprostol but, this was an unblinded study with high risk of observational bias[21] Nevertheless, there is no consensus in literature on the effect of misoprostol in hysteroscopy.

The "no-touch" vaginoscopy approach, popularized by Bettocchi, using hydro-distension without the use of instruments and also, the use of small caliber instruments are linked with pain reduction of approximately 1.5 on the VAS score during and after hysteroscopy.[22] Although miniature instruments have been proven to reduce pain during hysteroscopy, being relatively expensive, their procurement may not be feasible in all hospitals or Institutes especially in low-resource settings. As a result of widespread availability, even today, 4 mm hysteroscopes are more commonly used for diagnostic procedures the world over. We, in our study also, used 4 mm hysteroscope with a 5 mm outer sheath. Though we had apprehension about how subfertility patients would respond to the same but since vaginoscopy method was utilized in all patients, the procedure was well tolerated by them with mean VAS at T0, T1, and T15 in the room temperature being 3.313, 2.44, and 0.81, respectively, while that in the warm group was 3.94, 2.69, and 0.94, respectively, with no difference noted between the two. All the patients were counseled well regarding the procedure in detail and what to expect from it besides their gentle handling and the "no touch" technique which could be the reason for the low recorded VAS scores.

We compared warm normal saline versus room temperature normal saline for pain relief based on the hypothesis that

warming the distension medium may reduce uterine contractility by means of reduced myometrial response. Evangelista *et al.* in their study on effects of warming the distension medium, found no difference in the pain scores at T1, T2, T15 as well as the time taken between subjects undergoing diagnostic hysteroscopy with warmed normal saline versus that with room temperature normal saline. Although, a greater feeling of comfort was reported among patients with the saline solution warmed to 37.5°C, it that was not proven through the variables evaluated.[8] We designed this study to see if something as simple and as doable as warming the distension medium could, in anyway, make the cervical os yield to the hysteroscope easily and hence, make the hysteroscope passage through the os less painful for the patient. Furthermore, to see if warm saline solution could aid in reducing the pain of uterine distension. Although we found no statistical difference between the outcome measures studied between the two groups, but similar to the conclusion by Evangelista, we also observed that patients who underwent diagnostic hysteroscopy with warm saline solution were more comfortable throughout the procedure. Although, the mean recorded VAS was <4, almost one-third of patients refused to undergo the same procedure again. This can be explained by the fact that despite the low average VAS sore, 29 patients had a VAS of 5 or more. These were the patients who refused to undergo the same procedure again. Besides, a few patients with a VAS score of 4 also, refused to undergo the same unless absolutely necessary not as much because of the pain as for the hassle involved.

Issat *et al*. similarly, conducted a prospective randomized case-controlled study on pain assessment during outpatient hysteroscopy using room temperature versus warm normal saline solution as distension medium and concluded that there was no difference between the two groups either in terms of VAS scores or procedure times.[23] Another stratified randomized trial on patients undergoing operative hysteroscopy by Salazar *et al*. concluded that warming the distension medium neither affected the core body temperature nor the postoperative pain scores.[24]

We also, as projected by the mentioned studies, found no statistical difference in the VAS scores, time taken, complications or failed procedures, and procedural acceptance between the two groups.

Conclusion

Although there are studies in literature suggesting that the use of warm saline as distension medium could reduce pain during hysteroscopy, we found no difference in terms of pain intensity measured by VAS score, procedural difficulty as measured by Likert's scale, or patients' acceptance of the procedure whether using normal saline at room temperature or warming it to 38–40°C.

Procedures utilizing 4 mm hysteroscopes are well tolerated when using gentle approach and vaginoscopy technique. Hence, it is too early to discard them, especially in settings where access to smaller instruments may be a concern.

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Conflicts of interest

There are no conflicts of interest.

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