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Lidocaine Infusion on Hysteroscopic Media versus Oral Diclofenac for Pain Relief during Outpatient Hysteroscopy: A Randomized Controlled Trial

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ABSTRACT

Aim of the work: this work aimed to assess the analgesic efficacy of lidocaine dissolved in the distension medium compared to oral diclofenac before outpatient diagnostic hysteroscopy

Patients and methods: this randomized controlled trial included 44 nulliparous women schedules to undergo diagnostic office hysteroscopy.

The participants were randomly categorized into two groups; **group D** (n=22) received diclofenac 100 mg oral tablets and **group L** (n=22) received 10 ml of lidocaine 2% dissolved in saline (The distension medium). Pain was evaluated during hysteroscope insertion and 5, 10, 15 and 30 minutes after using visual analog scale (VAS). The patient was considered in pain if the VAS score was ≥ 4. **Results:** hysteroscope insertion was associated with pain in 35 patients (79.5%); more frequently in **group L** ($p = 0.021$). Severe pain was reported by 13 patients (29.5%); more in **group L** ($p = 0.099$). All patients were pain-free 15 minutes after procedure start. **Group L** showed significantly higher pain scores with hysteroscopic insertion ($p = 0.017$). The two groups had comparable pain scores 5, 10 and 15 minutes from the procedure start. Few adverse reactions were recorded. The two drugs were hemodynamically stable.

Conclusion: oral treatment with 100 mg diclofenac one hour before office hysteroscopy was a safe and more effective in pain control during the procedure compared to lidocaine dissolved in saline used as the distension medium.

Keywords: Lidocaine, Hysteroscopic, Diclofenac, Pain Relief.

INTRODUCTION

Office hysteroscopy is preferred by most gynecologists for diagnosis and frequently for management of intrauterine pathology. It has the advantage of saving time and costs of hospital admission and escaping anesthesia when compared to operative procedures [(1)]. However, many reports highlighted more or less high frequency of pain and discomfort in association with anesthesia-free diagnostic hysteroscopy. Moderate to severe pain was reported in 30% and 70% of cases [(2,3)]. Pain and low patient acceptance are the main constraints of widespread use of office hysteroscopy. It has been suggested that in experienced hands, analgesics are only needed in the selected cases as in women with previous cesarean section, anxiety and history of chronic pelvic pain [(4)]. Several analgesic methods have been reported in literature for outpatient hysteroscopy. These include nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics, administered orally or intravenously in addition local anesthetics through intrauterine, paracervical, transcervical, or uterosacral routes and topically as a spray, gel or cream[(5)].This randomized controlled trial aimed to assess the analgesic efficacy of lidocaine dissolved in the distension medium compared to oral diclofenac before outpatient diagnostic hysteroscopy.

PATIENTS AND METHODS

This randomized controlled trial was carried out in the Early Cancer Detection Unit in Ain Shams University Maternity Hospital during the period from April 2016 to January 2017. This study included nulliparous women schedules to undergo diagnostic office hysteroscopy for various indications. This study was approved by the Council of Obstetrics and Gynecology Department and the Ethics Research Committee, of Faculty of Medicine, Ain Shams University. All participants have provided written informed consents.

Inclusion criteria were: age between 18 and 35 years and body mass index (BMI) raging between 18.5 and 30 kg\m^2. **Exclusion criteria included:** any contraindication to hysteroscopy, cervical stenosis, polyps and ulcers, patients receiving any form of analgesia and history of previous cervical surgery. This study comprised 44 nulliparous women randomly categorized into two groups: **group D** (n=22)was received oral diclofenac and **group L** (n=22) was received lidocaine. Randomization was performed using computer generated codes. The codes were kept in sealed envelopes to be open 30 minutes before the

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procedure. All members of the procedure team, nursing staff, patients and the anesthetist were unaware of the allocation. All patients had complete clinical examination and detailed medical history was obtained.

Study Procedure

One hour before starting the procedure, patients in the diclofenac group were received 100 mg diclofenac (Voltaren SR tablets, NOVARTIS) by the oral route. Patients of Lidocaine group were received intrauterine 10 ml of lidocaine 2% (20 mg/ml) dissolved into a bag of 500 ml normal saline that was used as the distension medium. The procedure was done in the lithotomy position. Hysteroscopic equipment (Karl Storz, Tuttlingen, Germany) telescope was rigid, 30° Hamou II hysteroscope, model 26157 BT, with a Hopkins II lens system. Distention medium was normal saline at infusion rate of 50 mL/min with 80 mmHg pressure. Pain was evaluated by an independent nursing staff blinded to the type of analgesia on separate occasions during hysteroscope insertion, during and after the procedure at 5, 10, 15 and 30 minutes using a 10-cm visual analog scale (VAS) ; 0 means no pain and 10 meand the worst pain. The patient was considered in pain of the VAS score was ≥ 4.

Sample Size Justification

A previous study found that the pain score on insertion of the hysteroscope was 2.1±1.2 with the use of lidocaine compared to 0.8±1.1 with the use of diclofenac[6]. Based on these results, a sample size of 22 cases in each group was required to elicit the difference at an alpha level of 0.05 and a power of the study of 95%.

Statistical analysis

Statistical analysis was done using IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY, USA). The sample size was estimated using the G*Power© software (Institutfür Experimentelle Psychologie, Heinrich Heine Universität, Düsseldorf, Germany) version 3.1.9.2. Numerical data were expressed as mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage. For quantitative data, comparison between the two groups was done using independent sample t-test or Mann-Whitney test. Chi-square test (Fisher's exact test) was used to examine the relation between qualitative variables. All tests were two-tailed. p-value < 0.05 was considered significant.

RESULTS

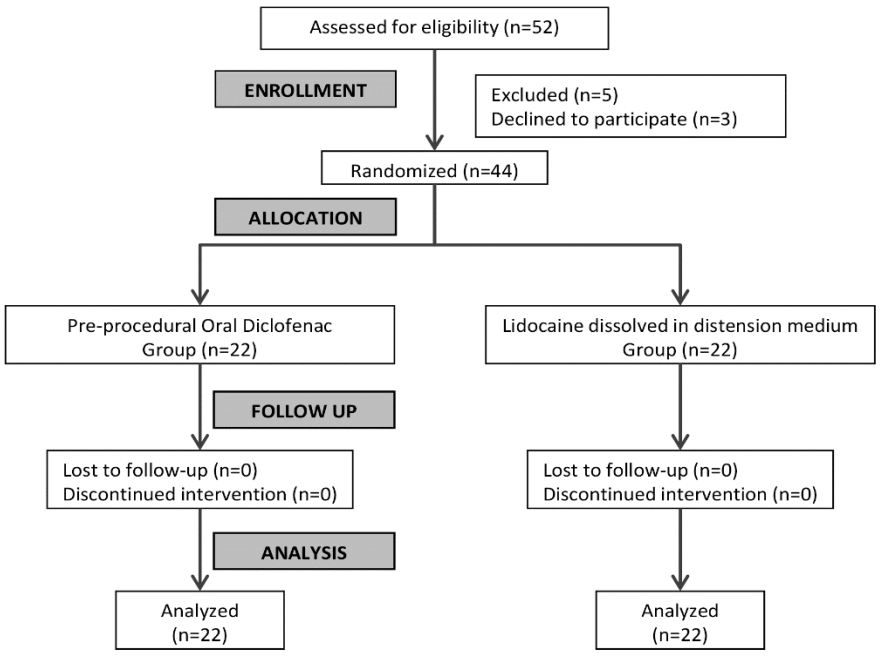

Figure 1: consort flow diagram

Table 1 showed demographic and clinical characteristics of the two studied groups. There was no significant difference between the two groups regarding age, BMI and procedure duration. Indications of hysteroscopy were shown in table 1.

Table 1: age, body mass index, duration of the procedure and indications for hysteroscopy of the three studied groups

	Group D n=22	Group L n=22	p value
Age (years)	28.4±4.5	29.0±3.7	0.595
Body mass index (kg/m^2)	24.4±3.7	24.7±3.1	0.742
Duration procedure (min.)	4.5±1.1	4.7±0.9	0.509
Indications of hysteroscopy			
Infertility	10 (45.5%)	15 (68.2%)	
Endometrial Polyp	5 (22.7%)	2 (9.1%)	
Septate Uterus	4 (18.2%)	2 (9.1%)	
Endocervical Polyp	0 (0.0%)	3 (13.6%)	
Failed ICSI	1 (4.5%)	0 (0.0%)	
Intrauterine Synechiae	1 (4.5%)	0 (0.0%)	
Irregular Uterine Bleeding	1 (4.5%)	0 (0.0%)	

Data are presented as mean±SD or number (%)

On hysteroscope insertion a large proportion of the patients were in pain (35 patients, 79.5%), however, pain was more frequent in **group L** (p = 0.021). Severe pain was reported by 13 patients (29.5%); more in **group L** (p = 0.099). Fewer patients feel pain after 5 minutes (**Table 2).** All patients were pain-free 15 minutes after procedure start. **Group L** showed significantly higher pain scores with hysteroscopic insertion at the start of the procedure (p = 0.017) and 30 min after its end (p = 0.035). The two groups had comparable pain scores 5, 10 and 15 minutes from the procedure start **(Table 2).**

Table 2: pain score and adverse effects in the two studied groups

	Group D n=22	Group L n=22	p value
Moderate Pain (score ≥ 4)			
At the start	14 (63.6%)	21 (95.5%)	0.021
After 5 min	8 (36.4%)	5 (22.7%)	0.322
After 10 min	1 (4.5%)	0 (0.0%)	1.000
Severe Pain (score ≥ 7)			
At the start	14 (63.6%)	21 (95.5%)	0.099
After 5 min	8 (36.4%)	5 (22.7%)	0.488
VAS score			
At the start	4 (2-8)	6 (3-8)	0.017
After 5 min	3 (1-7)	2.5 (1-5)	0.532
After 10 min	2 (1-4)	1 (1-3)	0.103
After 15 min	1 (1-2)	1 (1-2)	0.155
After 30 min	0 (0-1)	1 (0-1)	0.035
Adverse Effects			
Vomiting	1 (4.5%)	1 (4.5%)	1.000
Drowsiness	5 (22.7%)	3 (13.6%)	0.698

Data are presented as median (range), or number (%)

The procedure was considered difficult in only one patient in each group, but all procedures continued to the end. All patients except two in each group reported satisfaction by the procedure. Adverse reactions were shown in **table 2**. Drowsiness was reported by 5 patients in **group D** and 3 in **group L** (p = 0.698). No cases of respiratory depression, hypotension, allergy, or nausea were reported. Slight changes were detected in MAP, heart rate and respiratory rate during and after the procedure compared to baseline readings in the two groups as shown in figures 2 - 4. All changes were within the clinically accepted ranges.

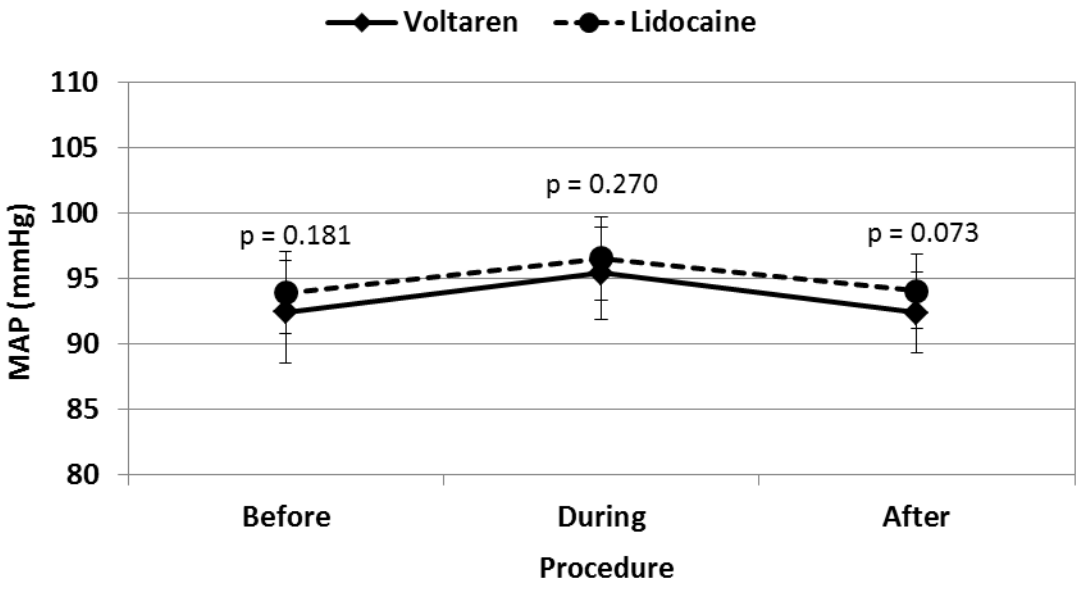

Figure 2: change of mean arterial pressure (MAP) in the two studied groups

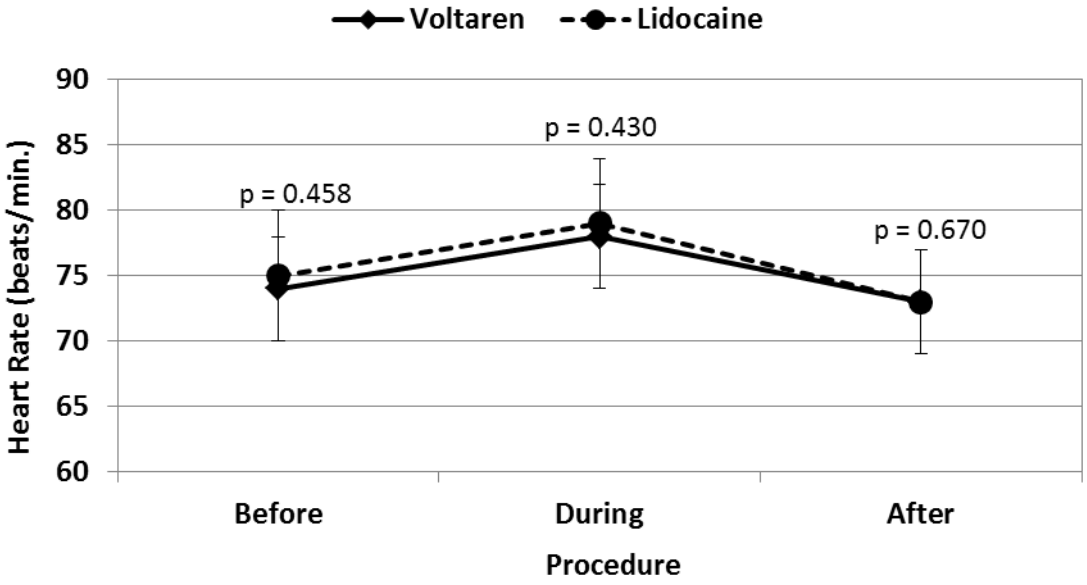

Figure 3: change of heart rate in the two studied groups

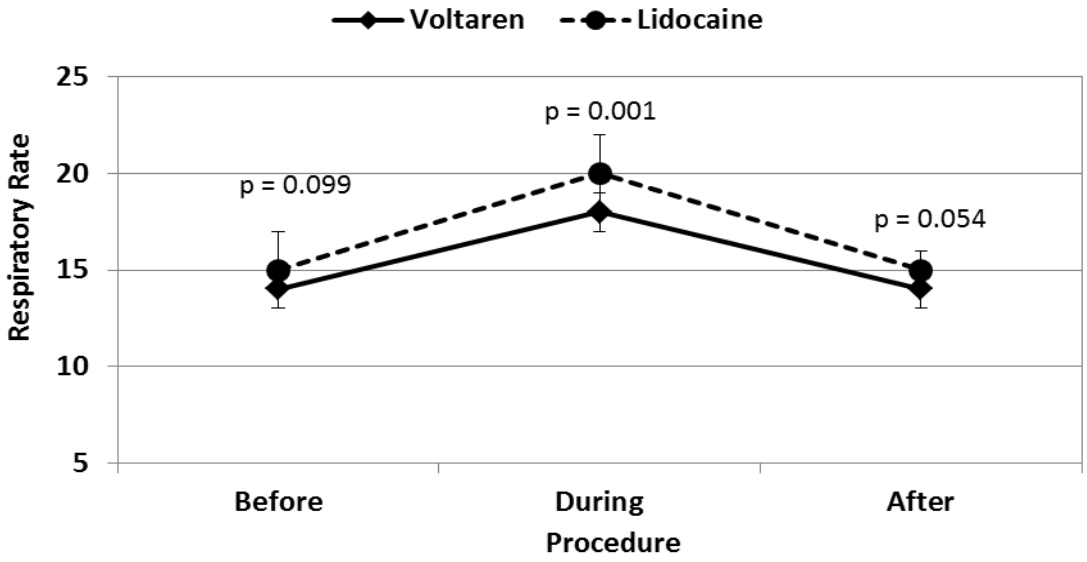

Figure 4: change of the respiratory rate in the two studied groups

DISCUSSION

Office-based gynecologic procedures are currently gaining much interest driven by their advantages over in hospital surgery. These advantages include scheduling convenience, fewer complications, faster recovery and a bridged expense. Nevertheless, patient's satisfaction and procedure safety are still debatable issues. Of these, intra-procedural pain and discomfort gained a voluminous part in recent research. In fact, pain is the principal cause of discontinuing office hysteroscopy[7].

In the current trial, we investigated the analgesic efficacy and safety of two modalities with different route of administration oral diclofenac and intrauterine lidocaine. The rationale for using lidocaine dissolved in the distension medium was it can provide better analgesic effect during and after the procedure. Hysteroscopic insertion was painful in almost 80% of patients and pain was severe in 30%. Pre-procedural oral diclofenac was associated with less frequency of pain at the start compared to lidocaine instillation with distension medium. Thereafter, the two methods were successful in pain control during and after the procedure; all patients were almost pain-free 15 minutes after procedure start in the two studied groups. Both drugs were hemodynamically safe with few minor adverse effects. Pain control during office hysteroscopy starts by small-caliber hysteroscopes[8] and patient information about the duration of the procedure and possibility of discomfort. In the current study, we used a 5 mm outer diameter hysteroscope and normal saline for uterine distention. Normal saline have been reported to produce less discomfort compared to CO_2 and glycine[9]. However, procedural pain has been reported with variable degrees by some investigators. **De Iaco *et al.*** [3] found that about 35% of patients showed severe pain during diagnostic hysteroscopy, while de **Carvalho *et al*.** [1] reported moderate to severe pain in 68.4% of patients. In the current study, 79.5% of patients showed moderate to severe pain on hysteroscope insertion. In the current study, diclofenac in an oral dose of 100 mg one hour before the procedure showed analgesic superiority as the procedure started. Diclofenac belongs to the nonsteroidal anti-inflammatory drugs (NSAIDs) that are known to reduce uterine activity and pain by inhibiting cyclooxygenase and prostaglandins reduction. NSAIDs were effective analgesics by the oral and rectal routes in conventional hysteroscopy and outpatient hysteroscopy[10,11].

However, a meta-analysis did not demonstrate any significant analgesic effect with NSAIDs during or after outpatient hysteroscopy[5] Nevertheless, the Royal College of Obstetricians and Gynaecologists recommended a standard dosage of NSAIDs 1 hour before hysteroscopy to reduce immediate postoperative pain[12]. This agrees with the results of the current study in which diclofenac reduced pain after the procedure compared to lidocaine. In the current study, addition of 10 ml of lidocaine 2% to the distension medium(Saline) reduced pain 5 minutes after starting the procedure. Few studies are available for evaluating intrauterine local anesthesia. In a randomized trial, intrauterine lidocaine was more effective in pain reduction compared to rectal

indomethacin[13]. Another study found that lidocaine spray during outpatient hysteroscopy significantly reduced pain [14]. Transcervical injection of 2 ml of 2% mepivacaine into the uterine cavity before diagnostic hysteroscopy significantly reduced the pain experienced at hysteroscopy and endometrial biopsy [15]. In contrast, a randomized study showed that intrauterine instillation of 5 mL of 2% lignocaine into the uterine cavity before performing office hysteroscopy did not alleviate pain experienced during hysteroscopy [16]. Another study reported that lidocaine diluted in the distension medium was not effective in pain relief [17]. **Mohammadi *et al*.** [6] compared rectal diclofenac with intrauterine lidocaine instillation. The authors reported superior analgesic effectiveness of diclofenac at the start of the procedure and these results are in agreement with the current study. Results of the current study and the previously mentioned reports indicated analgesic effectiveness of intrauterine local anesthetics during the procedure, but not at hysteroscope insertion. Premedication with NSAIDs appeared to be more effective at the procedure starting point. Therefore, we can conclude that using oral diclofenac in a dose of 100 mg one hour before office hysteroscopy is a safe and more effective method for pain reduction during the procedure compared to lidocaine dissolved in saline used as the distension medium. Pre-procedural oral diclofenac has the advantage of superior analgesic effect during insertion of the hysteroscope.

REFERENCES

1. **del Valle C, Solano JA, Rodríguez A and Alonso M(2016):** Pain management in outpatient hysteroscopy. Gynecol. Minim. Invasive Ther.,5:141–147.
2. **de Carvalho S J, Ramos D MM, Ribeiro C A and Albuquerque N LC(2007) :** Pain evaluation in outpatients undergoing diagnostic anesthesia-free hysteroscopy in a teaching hospital: a cohort study. J. Minim. Invasive Gynecol., 14:729–735.
3. **De Iaco P, Marabini A, Stefanetti M, Del Vecchio C and Bovicelli L (2000):** Acceptability and pain of outpatient hysteroscopy. J. Am. Assoc. Gynecol. Laparosc., 7:71–75.
4. **Cicinelli E (2010):** Hysteroscopy without anesthesia: review of recent literature. J. Minim. Invasive Gynecol., 17:703–708.
5. **Ahmad G, O'Flynn H, Attarbashi S, Duffy JM, Watson A(2-10):** Pain relief for outpatient hysteroscopy. Cochrane Database Syst. Rev., (11): 7710-7720.
6. **Mohammadi SS, Abdi M and Movafegh A(2015):** Comparing transcervical intrauterine Lidocaine instillation with rectal diclofenac for pain relief during outpatient hysteroscopy: a randomized controlled trial. Oman. Med. J. ,30:157–161.
7. **Nagele F, Lockwood G and Magos AL(1997):** Randomised placebo controlled trial of mefenamic acid for premedication at outpatient hysteroscopy: a pilot study. Br. J. Obstet. Gynaecol., 104:842–848.
8. **Sagiv R, Sadan O, Boaz M and Dishi M (2006):** A new approach to office hysteroscopy compared with traditional hysteroscopy: a randomized controlled trial. Obstet. Gynecol.,108:387–392.
9. **Shankar M, Davidson A, Taub N and Habiba M(2004):** Randomised comparison of distension media for outpatient hysteroscopy. BJOG Int. J. Obstet. Gynaecol., 111:57–62.
10. **Tam WH and Yuen PM(2001):** Use of diclofenac as an analgesic in outpatient hysteroscopy: a randomized, double-blind, placebo-controlled study. Fertil. Steril. 76:1070–1072.
11. **Hassa H, Aydin Y, Oge T and Cicek K(2013):** Effectiveness of vaginal misoprostol and rectal nonsteroidal anti-inflammatory drug in vaginoscopic diagnostic outpatient hysteroscopy in primarily infertile women: double-blind, randomized, controlled trial. J. Minim. Invasive Gynecol.,20:880–885.
12. **Issat T, Beta J, Nowicka MA, Maciejewski T and Jakimiuk AJ(2014):** A randomized, single blind, placebo-controlled trial for the pain reduction during the outpatient hysteroscopy after ketoprofen or intravaginal misoprostol. J. Minim. Invasive Gynecol.,21:921–927.
13. **Senturk MB, Guraslan H, Babaoğlu B, Yaşar L, Polat M(2016):** The Effect of Intrauterine Lidocaine and Rectal Indomethacin on Pain during Office Vaginoscopic Hysteroscopy: Randomized Double-Blind Controlled Study. Gynecol. Obstet. Invest.,81:280–284.
14. **Soriano D, Ajaj S, Chuong T, Deval B, Fauconnier A and Daraï E (2000):** Lidocaine spray and outpatient hysteroscopy: randomized placebo-controlled trial. Obstet. Gynecol., 96:661–664.
15. **Cicinelli E, Didonna T, Ambrosi G, Schönauer LM, Fiore G, Matteo MG(1997):** Topical anaesthesia for diagnostic hysteroscopy and endometrial biopsy in postmenopausal women: a randomised placebo-controlled double-blind study. Br. J. Obstet. Gynaecol., 104:316–319.
16. **Lau WC, Tam WH, Lo WK, Yuen PM(2000):** A randomised double-blind placebo-controlled trial of transcervical intrauterine local anaesthesia in outpatient hysteroscopy. BJOG Int. J. Obstet. Gynaecol., 107:610–613.
17. **Kabli N and Tulandi T(2008):** A randomized trial of outpatient hysteroscopy with and without intrauterine anesthesia. J. Minim. Invasive Gynecol.,15:308–310.