

Does intravenous lidocaine added to nonsteroidal anti-inflammatory drugs reduce pain during colposcopy? A prospective randomized double-blind study

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ABSTRACT

Objectives: In recent years, lidocaine infusion for pain management during long operations is becoming more widespread in anesthesiology practice. However, only a limited number of studies have reported the intravenous use of lidocaine for short-term interventions. The aim of this study was to investigate the effectiveness of intravenous lidocaine use in pain management during colposcopic cervical biopsy and endocervical curettage (ECC).

Material and methods: Patients between the ages of 18 and 65 years with abnormal cytological findings or who were determined to be human papillomavirus (HPV)-positive were included in this randomized double-blind study. The lidocaine group (Group L, n = 30) was intravenously administered 50 mg dexketoprofen + 1.5 mg/kg lidocaine in 10 mL saline for 3 min 30 min before the procedure. The control group (Group C, n = 30) was intravenously administered 50 mg dexketoprofen in 10 mL saline for 3 min, 30 min before the procedure. During the procedure, pain scores were assessed using the visual analogue scale (VAS). In addition, patients, operator satisfaction and duration of procedure were assessed.

Results: There were no differences in the demographic data of the groups. Pain scores during biopsy and ECC were significantly lower in Group L than in Group C ($p < 0.001$). The duration of the procedure was significantly shorter in Group L than in Group C (5.00 ± 0.78 vs 6.12 ± 1.16 , respectively; $p < 0.001$). Patient and operator satisfaction were significantly higher in Group L than in Group C ($p < 0.001$).

Conclusions: Intravenous lidocaine administration can be used as an alternative approach to reduce pain and increase operator and patient satisfaction during colposcopy-directed biopsy and ECC procedures in office settings.

Key words: pain; colposcopy; lidocaine

Ginekologia Polska 2021; 92, 12: 844–849

INTRODUCTION

Cervical cancer is prevalent worldwide and ranks second after colon and breast cancers in terms of frequency [1]. It has been shown that owing to the screening programs launched in underdeveloped countries, the cervical cancer ranking in terms of frequency has decreased to the 10th position. Because it has a long precancerous period, various screening methods that have been developed can help prevent cervical cancer [2]. The Papanicolaou (Pap) smear method used for screening purposes allows the early-stage detection of cancers and their precursors [3].

Using colposcopy, which is a more advanced examination technique, to shed further light on an abnormal cytological diagnosis is nowadays a frequently used approach in treatment management [4]. Colposcopy is a complementary method that is used to shed light on abnormal cytological findings. Biopsies are taken from sites that are suspected during visualization, and the actual aim of the examination is to exclude invasive cervical cancer [4, 5].

Colposcopy-directed cervical biopsy is a procedure that is performed on women identified as having an abnormal Pap smear or abnormal human papillomavirus (HPV) test result [6].

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Received: 12.12.2020 Accepted: 15.02.2021 Early publication date: 14.04.2021

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This procedure, which causes varying degrees of pain — from mild to severe — is typically performed in office settings without the requirement for anesthesia [7–10]. However, the pain caused during the procedure adversely affects patient compliance and decreases the effectiveness of the practitioner. For this reason, many studies in the literature have investigated the effectiveness of various types of anesthesia and analgesia, including the administration of benzocaine gel and topical or submucosal injection of lidocaine [11].

In recent years, intravenous lidocaine (IVL) has been used as a postoperative analgesic [12]. There is currently no study assessing the effect of IVL on pain during such a short procedure as colposcopy.

The aim of our study was to investigate the effect of the administration of IVL primarily on the pain score and secondarily on the satisfaction level of patients and operator during colposcopic biopsy, which causes discomfort and pain in patients despite being a short procedure.

MATERIAL AND METHODS

This double-blind, prospective, randomized study was conducted at the gynecologic oncology department of our gynecology and obstetrics clinic. The study was initiated after the approval of the Local Ethical Committee of Ataturk University Medical Faculty was obtained. The patients were informed in detail about the anesthetic procedures, pain scores, and colposcopic procedures, and their informed consents were obtained.

Patients between the ages of 18 to 65 years who could self-evaluate their pain score and who either had an abnormal cytology that required advanced examination or who had been identified as HPV-positive were included in the study. Patients with known liver, kidney, and advanced-stage cardiac diseases and malignancies; those under the age of 18 years; those known to be allergic to the medication used in the study; those using chronic pain killers; those identified as being pregnant; those with whom communication could not be established; and those with no indication for endocervical curettage (ECC) were excluded from the study.

Patients were divided into two groups in a randomized manner using a computer software. Study groups and double-blind design are summarized at Table 1.

The lidocaine group (Group L, n = 30) was administered 50 mg dexketoprofen trometamol IV 30 min before the procedure. Anesthesia induction was performed with the infusion of 1 mg midazolam (IV) and IV 1.5 mg/kg lidocaine in 10 mL saline in 3 min.

Similarly, the control group (Group C) was administered 50 mg dexketoprofen trometamol IV 30 min before the procedure. Anesthesia induction was performed via infusion of 1 mg midazolam (IV) and IV 10 mL saline in 3 min.

The operators and patients were blinded to information regarding group-specific drug infusion. Office settings were arranged in a manner that would meet the requirements for administration of anesthetics. Monitoring and resuscitation equipment were made available, and it was ensured that the referral system was adequate for any case of emergency. All procedures were performed with an anesthetist experienced in office settings.

Binocular colposcopic examinations were performed by same colposcopist using punch biopsy and ECC forceps.

Study outcomes

The pain levels of the patients were assessed using visual analogue scale (VAS) scores (0: no pain, 10: the worst pain imaginable) at the time of speculum placement, cervical biopsy, ECC, and the 10th minute following the procedure. Patient and practitioner satisfaction were assessed based on a scale of 1 to 4 (1: poor, 2: moderate, 3: good and 4: excellent). The duration of the procedure and demographical data of the patients were recorded.

Statistical analysis

Statistical analysis was performed using SPSS software version 21.0 (IBM Corp., Armonk, New York, USA). The distribution of variables was evaluated for normality using the histogram test and Kolmogorov–Smirnov test. Descriptive data were expressed as mean ± standard deviation. Normally distributed data consisting of continuous variables were analyzed using the Student's t test. Data without normal distribution were analyzed using the Mann–Whitney U test. Categorical variables were analyzed using the χ^2 or Fisher's exact test. A value of $p < 0.05$ was considered statistically significant.

Table 1. Study groups

	Group Control	Group Lidocaine
Sedatives	1 mg midazolam	1 mg midazolam
NSAID's (30 minutes before procedure)	100 mL normal saline + 50 mg dexketoprofen trometamol	100 mL normal saline + 50 mg dexketoprofen trometamol
Intravenous solution (3 minutes before procedure)	10 mL normal saline	10 mL (normal saline + 1.5 mg/kg lidocaine)

NSAID — nonsteroidal anti-inflammatory drugs

RESULTS

Seventy-six patients were included in the study. Two patients who were examined routinely and were found to have a positive B-HCG test, three patients for whom saturation was performed on the cervix due to bleeding that occurred after the procedure, and 11 patients with no indication of ECC were excluded from the study. Data for a total number of 60 patients were analyzed.

Demographic and cytological characteristics of the groups are shown in Table 1. Comparisons between patient data for age, height, weight, cytological anomalies, and HPV positivity revealed no significant differences (Tab. 2). When compared in terms of cytological abnormalities, L-SIL was found to be the most frequent abnormality in both groups. Colposcopy indications were observed to be similar

for both the groups. All procedures were successfully completed without any serious side effects, such as complications, severe bleeding, or allergic reaction to lidocaine.

Paresthesia of the tongue was observed for a short period of time in two patients in the lidocaine group, and it resolved on its own within five minutes following the procedure and without any additional medication being administered.

Pain scores of the groups are shown in Table 3. VAS scores during cervical biopsy and ECC were significantly lower in Group L compared with Group C ($p < 0.001$). The duration of the procedure was significantly shorter in Group L than in Group C (5.00 ± 0.78 vs 6.12 ± 1.16 , respectively; $p < 0.001$). Patient and operator satisfaction were significantly higher in Group L than in Group K ($p < 0.001$).

Table 2. Demographic data of study

		Group Control (n = 30)	Group Lidocaine (n = 30)	p
Age [year]		37.10 ± 7.37	36.53 ± 6.93	0.760 ^a
Weight [kg]		65.80 ± 11.74	68.53 ± 10.03	0.066 ^a
Height [cm]		158.47 ± 5.83	161.10 ± 5.03	0.336 ^a
Procedure time [min]		6.12 ± 1.16	5.00 ± 0.78	< 0.001 ^b
HPV (yes/no)		10/20	14/16	0.292 ^c
Cervical Cytology	ASC-US	10	8	0.878 ^c
	H-SIL	2	4	
	L-SIL	11	11	
	ASC-H	2	3	
	Normal	5	4	

Values are presented as mean ± standard deviation or number; HPV — human papilloma virus; ASC-US — undetermined significance; H-SIL — high grade squamous intraepithelial lesion; L-SIL — low grade squamous intraepithelial lesion; ASC-H — can not exclude high grade lesion; ^aIndependent Sample t test; ^bMann-Whitney-U test; ^cChi-square test

Table 3. Pain scores, patient and operator satisfaction

		Group Control (n = 30)	Group Lidocaine (n = 30)	p
VAS	Speculum Placement	0 (0–1)	0 (0–1)	0.421 ^a
	During Biopsy	4 (3–4)	2 (1–3)	< 0.001 ^b
	Endocervical curettage	5 (4–6)	2.5 (2–3)	< 0.001 ^b
	After Procedure	0 (0–0)	0 (0–0)	1.000 ^a
Patient Satisfaction	Poor	17	2	< 0.001 ^c
	Moderate	11	8	
	Good	2	12	
	Excellent	0	8	
Operator Satisfaction	Poor	13	0	< 0.001 ^c
	Moderate	14	7	
	Good	3	9	
	Excellent	0	14	

Values are presented as median (percentage 25–75) or number (percentage), VAS — visual analogue pain scale; ^aMann-Whitney U test; ^bIndependent Sample t test; ^cChi-square test

DISCUSSION

The findings from this double-blind, randomized study showed that intravenously-administered lidocaine can be used as an alternative to other procedures in order to reduce pain and increase operator and patient satisfaction during colposcopy-directed biopsies and ECC that are performed in office settings. We believe that the duration of the procedure was short in Group L owing to patient compliance and comfort of the operator.

Most women find colposcopy procedures performed in combination with cervical biopsies and ECC procedures to be uncomfortable and painful. It is thought that the fear of pain is a large obstacle in reaching patients for gynecological procedures. This concern may delay the early diagnosis of patients. For clinicians, it is essential to demonstrate the safety and effectiveness of various pain control methods.

The upper vagina, cervix, and lower uterine segment are innervated by parasympathetic fibers belonging to the S2 and S4, and the cervix together with uterine blood vessels at the 3- and 9-o'clock levels [13]. Because of the visceral innervation of the cervix, it is thought that anesthetics are ineffective in reducing pain during CEB [14]. However, many studies in the literature describing the effectiveness of anesthetics during colposcopic biopsy procedures show contradictory results. Topical anesthetic procedures, nonsteroidal anti-inflammatory drugs, administration of submucosal lidocaine for paracervical block, as well as various nonpharmacological procedures such as the cough trick technique and hypnosis were reported to be effective in many studies [15–17]. The present study examined the administration of intravenous lidocaine, which, to the best of our knowledge, has not been used in short procedures less than 10 minutes such as colposcopy to date, but whose effectiveness has started to be realized in recent years for postoperative analgesia during long term operations [18, 19]. In a recent study similar to our design lidocaine infusion during colonoscopy procedure resulted in a 50% reduction in propofol dose requirements [20]. Different from our study procedure time is approximately thirty minutes for each group.

Lidocaine is an amide group local anesthetic agent that has been defined as having analgesic, anti-hyperallergic, and anti-inflammatory characteristics [12, 21]. Because its half-life is brief (60–120 min), toxicity symptoms are transient at low doses; however, its analgesic effect lasts longer than expected [22, 23]. Intravenously-injected lidocaine has been reported to be effective in pain management at outpatient clinics, including operation theaters [12]. Studies have demonstrated that lidocaine is effective in non-emergency settings when used for perioperative pain and neuropathic pain. Toxicity symptoms of IVL generally occur in a manner that can be predicted from its levels in the blood. In addition, when administered as rapid infusion or push within

a period of few minutes, symptoms can progress rapidly and first lead to cardiovascular toxicity. In a review that included 45 randomized controlled studies and analyzed over 2500 patients, only 17 of the studies reported undesirable side effects, and no serious side effects associated with lidocaine were reported [24]. In a study on the use of IVL during neuropathic pain, patients were administered high doses of IVL, such as 5 mg/kg for 30 min; however, no serious side effects occurred in any of the patients [25, 26]. In the present study, the patients were administered IVL at a dose of 1.5 mg/kg, and it was observed that paresthesia of the tongue occurred in only two patients. No serious side effects were seen in any of the patients.

The literature suggests using doses not higher than 1.5 mg/kg when administering a bolus, and recommends that cardiac and vital findings should be monitored during the procedure [22]. To save time in our study, the patients were administered the analgesic 15 min before colposcopy while the setting of the procedure was being prepared.

IVL can be a suitable alternative for pain management in cases where nonsteroidal anti-inflammatory drugs (NSAIDs) are ineffective or when they are not used due to their side effects and complications. NSAIDs such as ibuprofen are known to reduce pain by inhibiting cyclooxygenase and inhibiting prostaglandins in circulation. These drugs have been effective in certain gynecological procedures, especially in terms of reducing postoperative pain [13]. In a randomized controlled study, Church et al. [27], compared 800 mg ibuprofen and topical benzocaine gel administered 30 min before colposcopy, and found no significant difference between the two groups in terms of cervical biopsy and ECC. The present study showed that NSAID combined with IVL based on multi-model analgesia had superior analgesic effects and resulted in superior patient satisfaction compared to the use of NSAIDs alone.

Because intravenous injection causes discomfort in patients, local anesthetic particularly submucosal administered lidocaine is frequently used in minor gynecological procedures. However, to ensure safety, it is necessary to prevent toxicity to recognize and manage toxicities in a timely manner. The most used local anesthetics in office settings, such as lidocaine or bupivacaine, are associated with fewer allergic reactions. For paracervical block, a dose of 200 mg lidocaine (20 mL of 1% lidocaine) is used, which is below the toxicity threshold [13]. In a study in which paracervical block was performed with an injection of 0.5 mL of 1% lidocaine, Oyama et al. [28] detected a significant decrease in pain scores. In a study by Schmid et al. [15], the cough trick technique, a nonpharmacological method, was compared with injection of 1% lidocaine to the cervix and no statistically significant difference between the two methods was found. However, Naki et al. [16], showed

that the cough trick technique was not effective compared with the control group. However, because injection itself can cause additional pain and hemorrhage, many studies in the literature have discussed topical agents to avoid the disadvantages associated with infiltration anesthesia in colposcopic procedures. In a study that compared the use of local anesthetic agents in the form of sprays with placebos, no significant reduction in pain was identified [8]. However, in another study, the use of lidocaine in the form of a spray was compared with paracervical block during loop electrosurgical excision procedure, and it was reported that LS could be used instead of paracervical block for pain management [29].

The procedures performed in office settings have two objectives: completing the procedure successfully safely and facilitating patient comfort. Additionally, patient comfort influences the clinician's ability to complete the procedure in a safe and effective manner. The safe use of anesthesia in office settings, the varying reactions from the patients to these drugs, and the fast fluctuations in sedation levels require focused planning. Therefore, the use of anesthesia in office settings necessitate space-specific arrangements, advanced life support training for practitioners, availability of cardiac monitoring and resuscitation equipment, and an experienced team.

The limitations of the present study include, first, the short-term administration of intravenous lidocaine and the fact that an adequate plasma level could not be reached. It might have been necessary to measure the plasma level of lidocaine as well. Second, no other sedative and opioid agent except midazolam was used in any of the patients to ensure that all of the patients could assess their VAS scores consciously. A study including opioid and sedative use could have made a more objective evaluation.

Under present conditions, intravenous lidocaine can be accepted as an alternative method for pain management during colposcopy. To ensure its use in office settings, there is a need for higher numbers of prospective randomized studies conducted with more patients that investigate its efficacy and safety. Studies that assess the dose, infusion time, or drug interactions might be helpful to determine safe threshold values.

CONCLUSIONS

In conclusion, for the management of pain that develops during gynecological procedures performed in office settings, IVL can be used to reduce pain and improve patient and operator satisfaction.

Ethics committee approval

Ethics committee approval was received for this study from the ethics committee of Ataturk University.

Financial disclosure

The authors declared that this study received no financial support.

Conflict of interest

No conflict of interest was declared by the authors.

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