

Comparison of the efficacy of intrauterine lidocaine, paracervical block and oral etodolac for decreasing pain in endometrial biopsy

İntrauterin lidokain, paraservikal blok ve oral etodolak uygulamalarının endometrial biopside ağrıyı azaltmadaki etkinliklerinin karşılaştırılması

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Abstract

Objective: To compare the effectiveness of paracervical block, intrauterine lidocaine and oral etodolac in decreasing the pain caused by pipelle endometrial sampling. A secondary goal of this study was to determine the adverse effects and compare possible effects of these methods on pulse and blood pressure.

Material and Methods: The study was performed between April 2006 and October 2006 in the Obstetrics and Gynecology Department of Van Yüzüncü Yil University Research Hospital. One-hundred twenty patients were randomized into four groups: 1. Group: Paracervical block was performed with 3 ml 2% prilocaine solution. 2. Group: Five ml of 2% lidocaine solution was instilled through the endocervix into the uterine cavity. 3. Group: Subjects received 400 mg oral etodolac tablet 1-1.5 hour before the procedure. 4. Group: No method of anesthesia was used in the control group. Endometrial sampling was performed with pipelle. Severity of pain during the procedure was scored by the subjects according to the "6-point Verbal Rating Scale (VRS)". Blood pressure and pulse rate were measured before, during and 30 minutes after the procedure.

Results: Pain scores in intrauterine lidocaine group (2nd group) were found statistically significantly lower than the other three groups ($p < 0.05$).

Conclusion: Intrauterine lidocaine anesthesia technique decreases pain in endometrial sampling with pipelle more efficiently than paracervical block or oral etodolac. While indication of menorrhagia and endometrial thickness more than 5 mm increased pain scores, intrauterine lidocaine application or paracervical block decreased the scores significantly ($p < 0.05$).

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Endometrial sampling is a diagnostic tool that is frequently applied in outpatient clinics for many disorders, including abnormal uterine bleeding, abnormal cytology, postmenopausal bleeding, hormone therapy monitoring and infertility. Today, although sonographic evaluation of the endometrium is the first step, pathological examination is still "the gold standard" in the diagnostic pathway. Traditionally, the standard method of assessing the endometrium has been dilatation of the cervix and curettage (D&C) of the uterine cavity. Recently,

Özet

Amaç: Endometrial biopsi alınmasında Pipelle kullanımının neden olduğu ağrıyı azaltmada paraservikal blok, intrauterin lidokain ve oral etodolacın etkinliklerinin karşılaştırılması. Bu çalışmada ikincil olarak bu yöntemlerin yan etkileri ile nabız ve kan basıncı üzerindeki olası etkilerinin belirlenmesi ve karşılaştırılması amaçlanmıştır.

Gereç ve Yöntemler: Çalışma Nisan 2006 ve Ekim 2006 tarihleri arasında Yüzüncü Yil Üniversitesi Araştırma Hastanesi Kadın Hastalıkları ve Doğum kliniğinde gerçekleştirildi. Yüz yirmi hasta 4 gruba randomize edildi. Birinci gruba; 3 ml %2'lik prilokain ile paraservikal blok yapıldı. İkinci gruba; intrauterin olarak 5 ml %2'lik lidokain uygulandı. Üçüncü grubtaki olgulara işlemden 1-1.5 saat önce oral olarak 400 mg etodolak verildi. Dördüncü gruba ise herhangi bir yöntem uygulanmadı. Endometrial örnekleme pipelle endometrial örnekleme aleti ile yapıldı. İşlem esnasında duyulan ağrının şiddeti olgular tarafından "6-Nokta VRS (Verbal Rating Scale)" ye göre derecelendirildi. Kan basıncı ve nabız işlemden önce, işlem esnasında ve işlemden 30 dk sonra ölçüldü.

Bulgular: İntrauterin lidokain grubunun (2. grup) ağrı skorları diğer 3 grubun ağrı skorlarından istatistiksel olarak anlamlı şekilde daha düşük bulundu ($p > 0.05$).

Sonuç: Pipelle ile endometrial biopsi alınmasında intrauterin lidokain anestezisi, ağrıyı paraservikal blok veya oral etodolaktan daha etkin biçimde azaltmaktadır. Biopsi endikasyonunun menoraji olması ve endometriyum kalınlığının 5 mm'den fazla olması ağrı skorlarını yükseltirken, intrauterin lidokain veya paraservikal blok uygulamaları skorları belirgin şekilde azaltmaktadır ($p < 0.05$).

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simple, quick, safe and inexpensive methods such as Pipelle, Vabra and Z-sampler have superceded this technique. Pipelle is the most popular of these sampling devices (1, 2). Although pipelle is known to be painless or to cause less pain than conventional methods of endometrial sampling, nearly half of the patients experience moderate-to-severe pain during the procedure (3). Nevertheless, there are only a few studies that have evaluated possible methods of pain-relief during endometrial biopsy using a pipelle (4).

Paracervical block is the most common anesthetic technique which has been used for minor gynecological procedures since 1925. It has been suggested that paracervical block may reduce pain, but the evidence is not strong. The risk of anesthetic intravasation is its main disadvantage (5).

Nonsteroidal antiinflammatory drugs block prostaglandin synthesis and have been shown to be effective in the relief of mild-to-moderate pain related to various obstetrical and gynecological syndromes and procedures, such as dysmenorrhea, intrauterine device insertion, suction curettage, postpartum pain, gynecologic surgery and menorrhagia (6, 7).

Recent studies have investigated the use of local anesthetics (i.e., lidocaine, mepivacaine) to lessen the pain experienced during minor gynecological procedures such as endometrial biopsy and office hysteroscopy. Most, but not all, of these studies reported reduced pain during the procedure (8-10).

The main objective of the present study was to compare the effectiveness of paracervical block, intrauterine lidocaine and oral etodolac in decreasing pain caused by endometrial sampling. A secondary goal of this study was to determine the adverse effects and compare possible effects of these methods on pulse and blood pressure.

Material and Methods

The study was performed between April and October 2006 in the Obstetrics and Gynecology department of Yuzuncu Yil University Research Hospital. One-hundred twenty patients who fulfilled the inclusion criteria and required endometrial biopsy to be taken for various indications were enrolled in the study. Subjects were randomized for paracervical block (1st group), intrauterine lidocaine (2nd group), etodolac (3rd group) and control (4th group) groups. In the 1st group, paracervical block was performed with 3 ml 2% prilocaine (Citanest flacon; AstraZeneca, İstanbul, Türkiye) solution. In the 2nd group, a blue colored feeding catheter (2.70 mm in diameter) was shortened with a sterile scalpel to about 20 cm in length and its tip was inserted into the endometrial cavity up to 2-3 cm distal to the endocervix. Five ml of 2% lidocaine solution were instilled slowly through the catheter into the uterine cavity and the catheter was withdrawn after 3 minutes. In the 3rd group, subjects received 400 mg oral etodolac tablet 1-1.5 hour before

the procedure. In the 4th group no methods of anesthesia was used. Endometrial sampling of all subjects was performed by the same person using the pipelle endometrial sampling device. After completion of the procedure, but before the speculum was taken out, all patients were asked to score the severity of pain they had felt during the procedure according to the "6-point Verbal Rating Scale (VRS)". Blood pressures and pulse rates of all subjects were measured before, during and 30 minutes after the procedure. All subjects were observed in the clinic during the first hour after the procedure and were asked at the end of this time if they needed additional analgesia. Endometrial tissue samples were examined in the pathology laboratory of Yuzuncu Yil University Research Hospital.

Statistical analysis of data was performed using SPSS 13.0 for Windows package programme with Student's-*t* test, Post-hoc LSD test, Chi-square test, One-way ANOVA and Spearman correlation analysis tests.

Results

In Table 1, demographic characteristics of the subjects are demonstrated. Ages of 120 subjects included in the study were between 20-67 years and mean age was 46.1±9.3 years. Of the 120 subjects, 92 (77%) were premenopausal and 28 (13%) were postmenopausal. There were no statistically significant differences in age, gravidity, parity, number of living children or menopausal status of the groups ($p>0.05$). Mean systolic blood pressure of the subjects measured before, during and 30 minutes after the procedure were 125.3±11.7 mmHg, 123.9±11.6 mmHg and 123.2±9.9 mmHg, respectively. Mean diastolic blood pressures were 79.9±7.4 mmHg, 80.6±7.6 mmHg, 78.7±9.3 mmHg, and mean pulse rates were 83.9±7.1 beat/minute, 82.8±5.2 beat/minute and 83.8±4.2 beat/minute, respectively. No statistically significant differences among groups were found in terms of blood pressures and pulse rates ($p>0.05$). For blood pressures and pulse rates, there were also no clinically significant differences between measurements before and during or after the procedure ($p>0.05$).

In Table 2, dispersion of the pain scores of four groups are showed. When pain scores of groups were compared (Table 3), scores in the intrauterine lidocaine group (2nd group) were found statistically significantly lower than in the other three

Table 1. Demographic characteristics of the groups

	1. Group (n=30)	2. Group (n=30)	3. Group (n=30)	4. Group (n=30)	p
Age (year)*	43.3±10.4	44.8±8.8	48.5±8.3	47.8±9.2	p=0.099
Gravidity*	8.7±4.1	7.4±3.6	8.7±3.5	7.6±4.4	p=0.364
Parity*	7.0±3.3	6.2±3.4	7.7±3.3	6.6±3.5	p=0.362
Abortion*	0.6±1.0	0.9±1.6	0.5±0.6	0.7±1.3	p=0.552
Live child*	5.9±3.1	5.1± 2.6	6.6±2.3	6±2.9	p=0.163
Menopausal status					
Pre-menopausal (%)	23 (76.7)	23 (76.7)	23 (76.7)	23 (76.7)	p=1.000
Postmenopausal (%)	7 (23.3)	7 (23.3)	7 (23.3)	7 (23.3)	p=1.000
*Mean±SD					

Table 2. Distribution of patients in groups according to the pain scores

Groups	PAIN SCORE						Total
	0	1	2	3	4	5	
Paracervical block	8	15	0	5	1	1	30
Intrauterine lidocaine	13	8	8	0	0	1	30
Oral Etodolac	3	12	7	4	3	1	30
Control	2	9	11	4	3	1	30
Total	26	44	26	13	7	4	120

0: No pain, 1: Mild pain, 2: Moderately severe pain, 3: Severe pain, 4: Very severe pain, 5: Unbearable pain

Table 3. Comparison of groups for pain scores

GROUPS COMPARED	P VALUES
Group 1-Group 2	p=0.004
Group 1-Group 4	p=0.004
Group 1-Group 3	p=0.057
Group 2-Group 3	p=0.015
Group 2-Group 4	p=0.008
Group 3-Group 4	p=0.911

groups ($p < 0.05$). While the difference between pain scores of paracervical block (1st group) and etodolac (3rd group) groups, and between pain scores of etodolac and control (4th group) groups were not statistically significant ($p > 0.05$), the difference between the scores of paracervical block (1st group) and control (4th group) groups was statistically significant ($p = 0.004$). In ordinal regression analysis, predictors which probably affect pain scores (menopausal status, parity, endometrial thickness, indication for biopsy and type of anesthesia applied) were examined. Of these predictors, indication for endometrial biopsy, thickness of endometrium being less or more than 5 mm and the method of anesthesia/analgesia were all the factors which affected the pain scores. While the indication of menorrhagia ($p = 0.02$) and endometrial thickness more than 5 mm ($p = 0.03$) increased pain scores, intrauterine lidocaine application and paracervical block decreased the scores significantly ($p < 0.05$).

There was no statistically significant difference among groups in terms of additional analgesia requirement ($p > 0.05$). No complications occurred in any of the subjects either during or one hour after the procedure.

Discussion

In many gynecologic examinations, assessment of the endometrium is required. Traditionally, this used to be achieved by dilatation and curettage (D&C) (1, 2). D&C, which had gained wide acceptance by the end of the 1950's, has begun to be questioned after awareness of evidence-based medicine. As

a result, many investigators were forced to find alternative methods.

Since this relatively expensive method, D&C, is not excellent in diagnosis and treatment and also has some complications and problems in its acceptability by patients, many investigators tended to search for alternative methods (11-15). Pipelle is a relatively painless method that does not require dilatation and has low morbidity and 97.5% sensitivity for cancer (16). Many recent studies revealed that pipelle was preferred because of its low cost, easy transport, suitability for peripheral usage and causing less pain. We also preferred pipelle for taking endometrial biopsy in our study.

At the end of the study, a statistically significant difference was determined among groups in terms of pain scores. Although pipelle has been defined as a painless method, in a study by Trolice et al, a moderate degree of pain was reported to be felt by the patients when anesthesia was not applied during pipelle endometrial biopsy (4). Intrauterine anesthesia is a method that have been tried in different gynecologic procedures by some investigators and various data on its effectiveness have been reported. In the study by Guney et al. published in 2006, it was reported that intrauterine lidocaine could be an effective anesthetic method for removing lost IUD's (17). In their 40-patient-study, Edelman et al. reported that 5 ml of 4% lidocaine injected into the endometrial cavity after giving a standard paracervical block decreased the pain significantly more than a placebo in dilatation and curettage of first trimester elective abortions (18). Although these studies are different from ours in terms of material and method, they are significant as they showed that intrauterine anesthesia decreased pain in many gynecologic procedures. A limited number of studies on intrauterine topical anesthesia is available in literature and in most of these studies, the effectiveness of intrauterine anesthesia was investigated either in hysteroscopy or in hysteroscopy combined with endometrial biopsy (5, 8-10, 17). Endometrial biopsy taken during hysteroscopy is more invasive and potentially more disturbing than only endometrial biopsy. Pain and disturbance caused by uterine distension during hysteroscopy are less responsive to the topical anesthesia (10). Considering that endometrial biopsy alone is simpler and less painful than hysteroscopy, intrauterine lidocaine is expected to prevent pain in endometrial biopsy according to these studies. In our study also, this anesthetic method was found effective.

In two different studies by Cicinelli et al., the effectiveness of intrauterine anesthesia in postmenopausal patients was investigated during diagnostic hysteroscopy and endometrial biopsy. In the first (19) of those studies, no statistically significant difference was found between intrauterine anesthesia and placebo. However in the second, which was performed with a larger number of subjects, more effective anesthesia was achieved with application of intrauterine anesthesia and this was statistically significant (10). Although both pre- and post-menopausal patients were included in our study, the second study by Cicinelli et al. supports our results.

In the study by Zupi et al., it was reported that 5 ml 2% mepivacaine applied into the uterus, as in our study, effectively decreased pain in an endometrial biopsy taken during hysteroscopy (9). Chanrachakul et al. also reported that intrauterine lidocaine decreased pain in fractionated curettage without causing any complications (20).

Lau et al. reported in two separate studies that neither paracervical block nor intrauterine anesthesia was effective in decreasing pain in hysteroscopy and endometrial biopsy compared to a placebo (5, 8).

Anesthetic methods were not combined in our study and the nonsteroidal antiinflammatory tablet did not provide sufficient analgesia by itself. Pain scores were similar in the etodolac tablet group and the control group where no form of anesthesia was applied.

In the study by Dogan et al., the pain decreasing effects of intrauterine lidocaine and oral naproxen sodium in endometrial biopsy with pipelle were compared with each other and with their combined usage. Pain caused by pipelle biopsy was evaluated with the 10 cm visual analog scale. They found that intrauterine lidocaine application combined with naproxen sodium given 1 hour before the procedure statistically significantly decreased pain. When applied separately, naproxen sodium and intrauterine lidocaine each decreased pain equally compared to the placebo, but this decrease was not significant statistically. However, when applied together, intrauterine lidocaine and naproxen sodium statistically significantly decreased pain more compared to placebo and to each of them separately (3).

Instead of naproxen, which has been tried before, we aimed to investigate the effectiveness of etodolac, also a nonsteroidal antiinflammatory drug that has not been previously tried for use in endometrial biopsy with pipelle, and had a pain decreasing effect comparable to naproxen. In our study, we did not find a significant difference between the group given nonsteroidal antiinflammatory drug 1 hour before the procedure and the control group to whom no anesthetic or analgesic methods was applied. In Dogan et al.'s study also, no significant differences were determined between the naproxen and placebo groups. Also in that study, in contrast to our findings, intrauterine lidocaine application itself was not found more effective than placebo or naproxen sodium application. However, in our study, intrauterine lidocaine in the same doses were determined to provide significant pain decrease compared to paracervical block and etodolac.

In conclusion; intrauterine lidocaine anesthesia is the anesthesia of choice for pipelle endometrial biopsy, being easily applied without pain and can provide sufficient anesthesia without causing serious complications. Intrauterine lidocaine anesthesia may be an effective method that is safely used mainly for endometrial sampling and also for various other gynecological and obstetrical procedures. It is clear that further clinical studies with larger numbers of patients are required in order to obtain more scientific data on this issue.

Conflict of interest

No conflict of interest is declared by authors.

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