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Lidocaine Prilocaine Cream in Conjunction with Paracervical Block versus Placebo with Paracervical Block for Pain Relief during Fractional Curettage

Bordin Duangrudeesawat, M.D.*
Sukanya Srinil, M.D.*

** Department of Obstetrics and Gynecology, Khon Kaen Hospital, Khon Kaen, Thailand*

ABSTRACT

Objectives: To study the efficacy of lidocaine prilocaine cream apply at cervix in conjunction with paracervical block versus placebo with paracervical block for pain reduction during fractional curettage.

Materials and Methods: One hundred and six women who underwent fractional curettage at Khon Kaen Hospital were enrolled in a randomized, double-blinded, placebo-controlled trial. The participants were randomly allocated into two groups, received lidocaine prilocaine cream plus paracervical block applied onto cervix (n = 53) versus placebo cream plus paracervical block (n = 53) before performing fractional curettage. Pain score was measured at tenaculum placement, during procedure, immediately after and 30 minutes after the procedure, using a 10 centimeters visual analog scale (VAS). The adverse events and additional analgesia were also recorded.

Results: Baseline characteristics were similar between groups. Mean pain score during fractional curettage in lidocaine prilocaine cream plus paracervical block was significantly lower than placebo cream plus paracervical block (2.80 ± 0.29, 95% confidence interval (CI) 2.21-3.38 vs. 5.34 ± 0.39, 95%CI 4.55-6.13, $p < 0.001$). Adverse events such as lightheadedness, palpitation and tinnitus were found without statistically significant difference between groups. None of the participants requested an additional analgesia.

Conclusion: Lidocaine prilocaine cream in conjunction with paracervical block had better pain relief during fractional curettage than in control group without serious adverse events.

Keywords: fractional curettage, lidocaine prilocaine cream, paracervical block, visual analog scale.

Correspondence to: *Bordin Duangrudeesawat, M.D., Department of Obstetrics and Gynecology, Khon Kaen Hospital, Khon Kaen, Thailand. Email: bordin.dear@gmail.com*

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การศึกษาประสิทธิภาพของการทาครีมยาชาที่ปากมดลูกร่วมกับการฉีดยาชาข้างปากมดลูก เปรียบเทียบกับการทาครีมยาหลอกร่วมกับการฉีดยาชาข้างปากมดลูกในการลดความเจ็บปวดระหว่างการทำหัตถการขูดมดลูกแบบแยกส่วน

บดินทร์ ดวงฤดีสวัสดิ์, สุกัญญา ศรีนิล

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพของการทาครีมยาชาที่ปากมดลูกร่วมกับการฉีดยาชาข้างปากมดลูก เปรียบเทียบกับการทาครีมยาหลอกที่ปากมดลูกร่วมกับการฉีดยาชาข้างปากมดลูกในการลดความเจ็บปวดระหว่างการขูดมดลูกแบบแยกส่วน*

วัสดุและวิธีการ: *สตรีที่มีข้อบ่งชี้ในการทำหัตถการขูดมดลูกแบบแยกส่วนที่เข้ารับการรักษาในโรงพยาบาลขอนแก่น จำนวน 106 คน ถูกสุ่มแบ่งเป็นสองกลุ่ม คือกลุ่มที่ได้รับการทาครีมยาชาที่ปากมดลูกร่วมกับการฉีดยาชาข้างปากมดลูก และกลุ่มที่ได้รับการทาครีมยาหลอกที่ปากมดลูกร่วมกับการฉีดยาชาข้างปากมดลูกก่อนทำหัตถการขูดมดลูกแบบแยกส่วน สตรีทั้งสองกลุ่มได้รับการประเมินความเจ็บปวดโดยใช้มาตรวัดความเจ็บปวดด้วยสายตาจำนวน 4 ครั้ง คือ ขณะใช้อุปกรณ์ยึดจับปากมดลูก ระหว่างทำหัตถการขูดมดลูกแบบแยกส่วน หลังทำหัตถการขูดมดลูกแบบแยกส่วนเสร็จทันที และหลังทำหัตถการขูดมดลูกแบบแยกส่วนเสร็จนาน 30 นาที รวมถึงมีการประเมินภาวะแทรกซ้อนจากการใช้ยาและความต้องการยาแก้ปวดชนิดอื่นเพิ่มเติม*

ผลการศึกษา: *ข้อมูลลักษณะพื้นฐานทางประชากรศาสตร์ของทั้งสองกลุ่มไม่แตกต่างกัน คะแนนความเจ็บปวดระหว่างการทำหัตถการขูดมดลูกแบบแยกส่วนในกลุ่มที่ทาครีมยาชาที่ปากมดลูกร่วมกับการฉีดยาชาข้างปากมดลูก (กลุ่มทดลอง) น้อยกว่ากลุ่มที่ทาครีมยาหลอกที่ปากมดลูกร่วมกับการฉีดยาชาข้างปากมดลูก (กลุ่มควบคุม) อย่างมีนัยสำคัญทางสถิติ (ค่าเฉลี่ยคะแนนความเจ็บปวด ± ส่วนเบี่ยงเบนมาตรฐานของกลุ่มทดลอง และกลุ่มควบคุมมีค่า 2.80 ± 0.29, 5.34 ± 0.39 ตามลำดับ, $p < 0.001$) ภาวะแทรกซ้อนที่พบในทั้งสองกลุ่ม คือ วิงเวียนศีรษะ ใจสั่น และหูอื้อ ซึ่งพบว่าไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ และเป็นภาวะแทรกซ้อนที่ไม่รุนแรง รวมถึงไม่มีการใช้ยาแก้ปวดชนิดอื่นเพิ่มเติมในทั้งสองกลุ่ม*

สรุป: *การทาครีมยาชาที่ปากมดลูกร่วมกับการฉีดยาชาข้างปากมดลูก สามารถลดความเจ็บปวดระหว่างทำหัตถการขูดมดลูกแบบแยกส่วนได้อย่างมีนัยสำคัญทางสถิติ และไม่พบภาวะแทรกซ้อนที่รุนแรงจากการใช้ยา*

คำสำคัญ: *การขูดมดลูกแบบแยกส่วน, ครีมยาชา, การฉีดยาชาข้างปากมดลูก, การให้คะแนนความเจ็บปวดโดยใช้มาตรวัดความเจ็บปวดด้วยสายตา*

Introduction

Fractional curettage is a common procedure for evaluating the causes of abnormal uterine bleeding[1]. In patients that have clinicals or risk factors that mimic endometrial cancer, fractional curettage is needed to investigate before treatment. In patients undergoing this operation in an outpatient setting, the requirement of an analgesic is inevitable. The various procedures during fractional curettage such as placement of the tenaculum for traction of the uterine cervix as well as the curettage itself can cause pain sensation. The analgesic efficacy of various pain-relief procedures has been tested for women undergoing fractional curettage. Although use of general anesthesia provides complete analgesia, it carries higher mortality and morbidity risk than properly administered local anesthetics[2].

The sensory innervation of the female pelvic organs derives from the superior hypogastric plexus or presacral nerve, pelvic nerves and ovarian plexus. Afferent fibers from the upper vagina, uterus, proximal segment of the fallopian tubes, bladder, urethra and rectum pass through the paracervical region and into the uterosacral folds and meet in the hypogastric plexus and pelvic nerves[3]. Paracervical block anesthetizes the second to fourth sacral nerve roots that innervate the cervix and the lower part of the uterine body[4]. The paracervical block is one of the most common procedures used for relief pain in patients undergoing fractional curettage[1], but the pain intensity under paracervical block is still moderate pain[5].

Five percent EMLA® cream is composed of two local anesthetics-lidocaine 25 mg/g and prilocaine 25 mg/g. When 5% EMLA® cream is applied to a mucous membrane, absorption is rapid, so occlusive dressings are not necessary. Ten minutes application time trended to produce the longest duration of analgesia of about 45 min[6,7]. One study reported the application of lidocaine prilocaine cream on the uterine cervix before hysterosalpingogram (HSG) relieved pain during the procedure. Cervical instrumentation was, moreover, the most painful step during the procedure and the use of lidocaine prilocaine cream decreased the pain during this step[8]. It has also been used locally on the uterine cervix before laser ablation and hysteroscopy and was found to reduce the patient's pain[9,10].

The objective of the current study was to evaluate the efficacy of lidocaine prilocaine cream versus placebo in conjunction with paracervical block for pain reduction during fractional curettage.

Materials and Methods

This study was a randomized, double-blinded, placebo-controlled trial. The study was reviewed and approved by Khon Kaen Hospital Institute Review Board for Human Research. All participants were informed about the study and signed informed consent before enrollment.

Between January 2020 and July 2020, we recruited 106 women with abnormal uterine bleeding indicated for fractional curettage at Khon Kaen Hospital. We excluded women with coagulopathy, currently using anticoagulant or antiplatelet drugs, having active liver or kidney disease, having lidocaine hypersensitivity, or being pregnant.

The participants were randomized to two groups using a computer-generated block of four: the study group – lidocaine prilocaine cream in conjunction with paracervical block, and the control group - placebo given in conjunction with paracervical block. The randomization list was kept in a sealed opaque envelope. The fractional curettage was performed by trained physicians not involved in the study. The physicians and assistant nurses were masked to the group assignments.

At first, the participants were in the lithotomy position. After twice rinsing the vagina and cervix with betadine, a paracervical block injection was done with a 23-gauge spinal needle at 3 and 9 o'clock of the cervicovaginal reflection at an estimated depth of 1 cm. Twenty milliliters of 1% lidocaine (without adrenaline) was given to each participant (10 ml at each site).

The study group and control group received 5 g of 5% lidocaine prilocaine cream and placebo, respectively. Due to the awareness of lidocaine toxicity, the maximum dose should not exceed 7 mg/kg. All participants in the study group were given a total 325

mg of lidocaine, which did not reach the toxic level. The 5% lidocaine prilocaine cream or placebo was applied to the cervix and external os using a cotton swab. After waiting 10 minutes, the fractional curettage was performed.

The fractional curettage was performed step-by-step, using a tenaculum grasped at 2 and 10 o'clock at anterior lip of the cervix. A curette number 00 was used for endocervical curettage. A uterine sound was inserted into uterine cavity to measure the uterine depth before performing endometrium curettage using a curette number 0.

The pain score was recorded using a 10-cm visual analog scale (VAS). Zero represented no pain and 10 represented the worst pain. The participants were asked by the assistant nurse to make a mark on the line that corresponded to their level of perceived pain intensity. Each participant was asked to evaluate pain assessment 4 times; at tenaculum placement, during endometrial curettage 15 s after beginning the procedure, immediately after the procedure, and 30 min after the procedure. All participants could ask for additional analgesia if/when needed.

Vital signs and adverse events i.e., lightheadedness, palpitation, numbness of lips, and tinnitus were recorded by a nurse until 2 h after the procedure. Additional analgesia was also recorded. The participants were appointed at three weeks later to inform about pathological report.

The primary outcome was the pain score during fractional curettage. The secondary outcomes were the pain score at the tenaculum placement immediate after and 30 min after the procedure, adverse effects, and the need for any additional analgesia. Baseline characteristics were recorded including age, body mass index (BMI), parity, prior curettage, post-menopausal status and indication for fractional curettage.

The sample size was calculated based on data from the pilot study with 80% power at the 5% level of significance with up to 10% dropout. The appropriate sample size was thus 106 participants (53 in each group). Data were analyzed using STATA version 13. Continuous variables were analyzed using the student t-test presented as means ± standard deviation (SD). Categorical variables were assessed using the chi-square or Fisher's exact test presented as percentages. A p value < 0.05 was considered statistically significant.

Results

During the study, there were 106 women who were indicated for fractional curettage at Khon Kaen Hospital. All of the participants were recruited into the study and randomly allocated into two groups the study group (lidocaine prilocaine cream in conjunction with paracervical block) (n = 53), and the control group (a placebo given in conjunction with paracervical block) (n = 53). There were no dropouts during the study, so the data from 106 women were analyzed (Fig. 1).

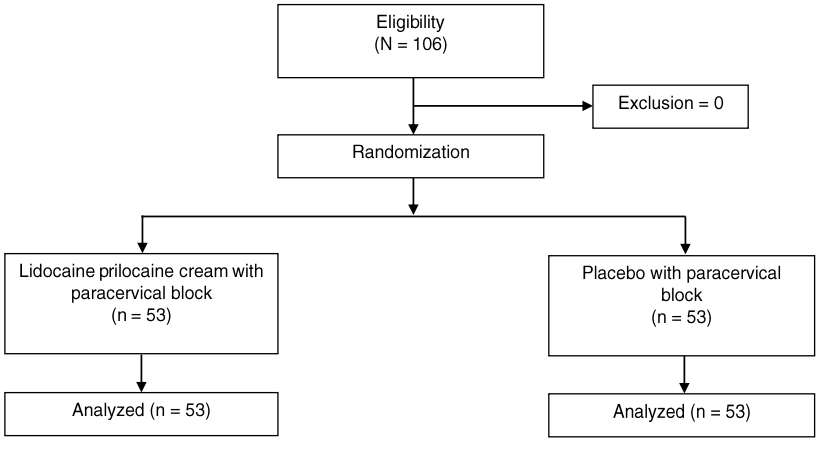

Fig. 1. Study flow diagram.

Both groups had similar baseline characteristics including age, BMI, parity, history of prior curettage, post-menopausal status, and indication for fractional curettage (Table 1).

The primary and secondary outcomes are presented in Table 2. The respective mean pain score was lower in the study vs. the placebo group during fractional curettage (2.80 ± 0.29, 95% confidence interval (CI) 2.21 - 3.38 vs. 5.34 ± 0.39, 95%CI 4.55 - 6.13, p < 0.001); at tenaculum placement (1.45 ± 0.26, 95%CI 0.93 - 1.97 vs. 2.35 ± 0.34, 95%CI 1.66 - 3.04, p = 0.04); and, immediately after treatment (2.91 ± 0.34, 95%CI 2.22 - 3.60 vs. 4.21 ± 0.38, 95%CI 3.44 to 4.98, p = 0.01). The pain score at 30 min was not significantly different between the groups (1.25 ± 0.18, 95%CI 0.89 - 1.60 vs. 1.66 ± 0.29, 95%CI 1.09 - 2.23, p = 0.22).

Table 1. Demographics and characteristics of the cases.

	Lidocaine prilocaine cream with paracervical block (n = 53)	Placebo with paracervical block (n = 53)	p value
Age (years), mean ± SD	49.70 ± 10.58	47.51 ± 8.89	0.25[c]
BMI (kg/m^2), mean ± SD	26.73 ± 4.77	25.12 ± 4.31	0.07[c]
Parity, n (%)			0.18[a]
Nullipara	3 (5.7)	7 (13.2)	
Multipara	50 (94.3)	46 (86.8)	
Prior curettage, n (%)	15 (28.3)	14 (26.4)	0.83[a]
Post-menopausal status, n (%)	17 (32.1)	10 (18.9)	0.12[a]
Indication, n (%)			0.26[b]
Abnormal uterine bleeding	36 (67.9)	39 (73.6)	
Postmenopausal bleeding	14 (26.4)	10 (18.9)	
Endometrial hyperplasia	3 (5.7)	4 (7.5)	
Other	0 (0.0)	0 (0.0)	

[a] chi-square test, [b] Fisher's exact test, [c] student t-test. SD: standard deviation, BMI: body mass index

Table 2. Primary and secondary outcomes.

VAS	Lidocaine prilocaine cream with paracervical block (n = 53)	Placebo with paracervical block (n = 53)	Mean different	95%CI	p value
At tenaculum placement					
mean ± SD	1.45 ± 0.26	2.35 ± 0.34	- 0.90	- 1.75 to - 0.05	0.04[c]
(95%CI)	(0.93 to 1.97)	(1.66 to 3.04)			
During fractional curettage					
mean ± SD	2.80 ± 0.29	5.34 ± 0.39	- 2.55	- 3.52 to - 1.57	< 0.001[c]
(95%CI)	(2.21 to 3.38)	(4.55 to 6.13)			
Immediate after procedure					
mean ± SD	2.91 ± 0.34	4.21 ± 0.38	- 1.30	- 2.31 to - 0.28	0.01[c]
(95%CI)	(2.22 to 3.60)	(3.44 to 4.98)			
Thirty minutes after procedure					
mean ± SD	1.25 ± 0.18	1.66 ± 0.29	- 0.41	- 1.08 to 0.25	0.22[c]
(95%CI)	(0.89 to 1.60)	(1.09 to 2.23)			

[c] student t-test, Significant p < 0.05. VAS: Visual analog scale, CI: confidence interval, SD: standard deviation

Adverse events such as lightheadedness, palpitation, and tinnitus were found in both groups (no significant difference), and none of the participants requested medical treatment or additional analgesia (Table 3).

The pathological report revealed benign endometrial tissue 88.68% (n = 94), endometrial hyperplasia with/without atypia 4.72% (n = 5), malignancy 3.77% (n = 4) and no endometrial tissue obtained 2.83% (n = 3)

Table 3. Adverse events and additional analgesia.

	Lidocaine prilocaine cream with paracervical block (n = 53)	Placebo with paracervical block (n = 53)	p value
Adverse events, n (%)			0.72
Lightheadedness	9 (17.0)	14 (26.4)	0.24[a]
Palpitation	5 (9.4)	5 (9.4)	1.00[a]
Numbness of lips	0 (0.0)	2 (3.8)	0.50[b]
Tinnitus	7 (13.2)	9 (17.0)	0.59[a]
Hypotensive event	0 (0.0)	0 (0.0)	NA
Additional analgesic, n (%)	0 (0.0)	0 (0.0)	NA

[a] chi-square test, [b] Fisher's exact test.

Discussion

Use of lidocaine prilocaine cream in conjunction with paracervical block resulted in a significantly lower pain score than placebo used in conjunction with paracervical block. On the basis that the lower part of uterine body and cervix is innervated by Frankenhauser's plexus (sacral plexus 2 - 4). Paracervical block should thus block not only uterine pain but also cervical pain. Notwithstanding, Thongrong et al[5], demonstrated that although paracervical block alone reduced pain during endometrial curettage, moderate pain persisted. The present study showed that the combination of lidocaine prilocaine cream in conjunction with paracervical block had a synergistic effect for pain reduction during fractional curettage, because lidocaine prilocaine cream anesthetizes the cervix which is innervated by Frankenhauser's plexus which uses the same pathway as the uterine body. The use of lidocaine prilocaine cream in conjunction with paracervical block could help patients to be more comfortable than using paracervical block alone.

Although there has been no study about the efficacy of lidocaine prilocaine cream for the pain reduction during fractional curettage, previous studies on cervical and uterine interventions provide relevant comparisons. Liberty et al[8], reported that the effect of applying lidocaine prilocaine cream on the uterine cervix for pain relief after performing HSG on 84 women who underwent HSG as part of an infertility evaluation. The study found that cervical instrumentation in the lidocaine prilocaine-treated patients was associated with significantly less pain than the placebo (3.3 ± 2.9 vs. 4.9 ± 2.7, p = 0.02).

Tavakolian et al[11], reported on the effect of lidocaine prilocaine cream on the uterine cervix to determine intrauterine device (IUD) insertion pain among 92 women who underwent IUD insertion. The study demonstrated that lidocaine prilocaine cream significantly reduced pain during the use of a tenaculum compared with a placebo (1.52 ± 1.85 vs. 4.30 ± 2.40, p < 0.001). In addition, the mean pain score during insertion of a hysterometer in the lidocaine prilocaine cream group was associated with significantly less pain than the placebo group (3.11 ± 2.53 vs. 5.20 ± 2.31, p < 0.001). The results of two previous studies agreed with our study and indicated that lidocaine prilocaine cream in conjunction with paracervical block significantly reduced the pain score over against placebo in conjunction

with paracervical block.

Besides the primary outcome, we found that the pain score at tenaculum placement and immediately after fractional curettage was significantly lower in the study group (lidocaine prilocaine cream in conjunction with paracervical block) over against the control group (placebo given in conjunction with paracervical block). Lidocaine prilocaine cream produced the longest duration of analgesia (about 45 min) and reduced pain scores (i.e., 30 min after fractional curettage). The pain score 30 min after the procedure was not significantly between groups as mild intensity pain persisted in both groups.

None of the participants requested any additional analgesia. There was no significant difference in adverse events (whether lightheadedness, palpitation, numbness of lips, or tinnitus) between the two groups. These adverse events were mild and resolved within a few minutes without medical treatment. Zilbert[12] reviewed the effect of using lidocaine prilocaine cream for pain relief during minor gynecological procedures and found that it was well-tolerated and adverse reactions were generally mild, local, and transient.

Although the standard procedure for diagnosis of women with abnormal uterine bleeding is endometrial sampling, fractional curettage remains an alternative. Fractional curettage can be obtained from the endocervix and/or the entire of endometrial tissue useful for both diagnosis and therapy, particularly in cases of active uterine bleeding. Fractional curettage under paracervical block can be performed in a minor operative setting without hospital admission. Based on the literature review, fractional curettage causes moderate pain, so our findings have practical implications for reducing pain during such procedures.

The strengths of this study were that it was (a) a randomized, double-blinded, placebo-controlled trial, (b) no patients dropped out, and (c) all participants did their own pain assessment. The limitation was the lack of patients, who are having the difficulty of fractional curettage such as cervical stenosis. Therefore, the study of lidocaine prilocaine cream in conjunction with paracervical block for pain relief in this group of patients may be needed.

Conclusion

Compared with placebo, lidocaine prilocaine cream in conjunction with paracervical block significantly reduced pain during fractional curettage.

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Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Api O, Ergen B, Api M, Ugurel V, Emeksiz MB, Unal O. Comparison of oral nonsteroidal analgesic and intrauterine local anesthetic for pain relief in uterine fractional curettage: a randomized, double-blind, placebo-controlled trial. Am J Obstet Gynecol 2010;203:28.e1-7.
2. Arora A, Shukla A, Saha SC. Effectiveness of intrauterine lignocaine in addition to paracervical block for pain relief during dilatation and curettage, and fractional curettage. J Obstet Gynaecol India 2016;66:174-9.
3. Arnau B, Jovell E, Redón S, Canals M, Mir V, Jiménez E. Lidocaine-prilocaine (EMLA®) cream as analgesia in hysteroscopy practice: a prospective, randomized, non-blinded, controlled study. Acta Obstet Gynecol Scand 2013;92:978-81.
4. Tangsiriwatthana T, Sangkomkamhang US, Lumbiganon P, Laopaiboon M. Paracervical local anaesthesia for cervical dilatation and uterine intervention. Cochrane Database Syst Rev 2013:9:CD005056.
5. Thongrong P, Jarruwale P, Panichkul P. Effectiveness of paracervical block versus intravenous morphine during uterine curettage: a randomized controlled trial. J Med Assoc Thai 2011;94:403-7.
6. Ljunghall K, Lillieborg S. Local anaesthesia with a lidocaine/prilocaine cream (EMLA) for cautery of condylomata acuminata on the vulval mucosa. The effect of timing of application of the cream. Acta Derm Venereol 1989;69:362-5.
7. Van der Burght M, Schønemann N, Laursen J, Arendt-Nielsen L, Bjerring P. Duration of analgesia following application of eutectic mixture of local anaesthetics (EMLA) on genital mucosa. Acta Derm Venereol

1993;73:456.
8. Liberty G, Gal M, Halevy-Shalem T, Michaelson-Cohen R, Galoyan N, Hyman J, et al. Lidocaine–Prilocaine (EMLA) cream as analgesia for hysterosalpingography: a prospective, randomized, controlled, double blinded study. Hum Reprod 2007;22:1335-9.
9. Zilbert A. Topical anesthesia for minor gynecological procedures: a review. Obstet Gynecol Surv 2002;57: 171-8.
10. Zullo F, Pellicano M, Stigliano C, Di CC, Fabrizio A, Nappi C. Topical anesthesia for office hysteroscopy. A prospective, randomized study comparing two modalities. J Reprod Med 1999;44:865-9.
11. Tavakolian S, Doulabi MA, Baghban AA, Mortazavi A, Ghorbani M. Lidocaine-prilocaine cream as analgesia for IUD insertion: a prospective, randomized, controlled, triple blinded study. Glob J Health Sci 2015;7:399.
12. Zilbert A. Topical anesthesia for minor gynecological procedures: a review. Obstet Gynecol Surv 2002;57: 171-8.