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Comparison of Lidocaine Spray in Conjunction with Intrauterine Lidocaine versus Paracervical Block for Pain Relief in Fractional and Curettage: A randomized controlled trial

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ABSTRACT

Objectives: To compare lidocaine spray plus intrauterine lidocaine versus paracervical block alone for pain relief during and at 30 minutes after fractional curettage.

Materials and Methods: One hundred and twelve women with abnormal uterine bleeding at Khon Kaen Hospital from January to April, 2018 were randomly allocated into two groups, receiving lidocaine spray in conjunction with intrauterine lidocaine (n = 56) versus paracervical block (n = 56) before fractional curettage. Pain score during fractional curettage was measured by 100-mm visual analogue scale (VAS). Pain score after procedure and all adverse events were observed and recorded at 30 minutes after procedure by other doctors who did not perform fractional curettage. Moreover, additional analgesia or sedation, and inadequacy of specimen were also recorded.

Results: Baseline characteristics were similar between groups. Median pain score during procedure in lidocaine spray in conjunction with intrauterine lidocaine group was significantly lower than paracervical block group (71.5 (53.5-82.5) vs 50.5 (39-63), 95% Confidence interval12.70-28.25, $p < 0.001$). There were no significant differences in pain score after procedure, adverse events, additional analgesia or sedation and inadequacy of specimen.

Conclusion: Lidocaine spray in conjunction with intrauterine lidocaine had significant difference for pain reduction when compared with paracervical block during fractional curettage without serious adverse events.

Keywords: fractional curettage, lidocaine spray, intrauterine lidocaine, paracervical block, pain score, visual analog scale

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ผลของการพ่นยาชาที่ปากมดลูกร่วมกับการฉีดยาชาเข้าโพรงมดลูกเปรียบเทียบกับการฉีดยาชาข้างปากมดลูกเพื่อลดความปวดในการขูดมดลูกแบบแยกส่วน:การทดลองแบบสุ่ม

ภิญญา เอื้อพงศ์การุณ, ชินวัฒน์ ศรีนิล, มาลีชาติ ศรีพิพัฒนะกุล, ทุมวดี ตั้งศิริวัฒนา

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาการใช้ยาชาชนิดพ่นร่วมกับการฉีดยาชาเข้าโพรงมดลูก เปรียบเทียบกับการฉีดยาชาข้างปากมดลูก ในการลดความปวดระหว่างการขูดมดลูกแบบแยกส่วน และหลังจากขูดมดลูก 30 นาที*

วัสดุและวิธีการศึกษา: *สตรีที่มีภาวะเลือดออกผิดปกติทางช่องคลอดและมีข้อบ่งชี้ในการขูดมดลูกที่เข้ารับการรักษาระหว่างเดือนมกราคมถึงเดือนเมษายน ปี 2561 จำนวน 112 คน ถูกสุ่มแบ่งเป็นสองกลุ่มเพื่อรับการพ่นยาชาที่ปากมดลูกร่วมกับฉีดยาชาเข้าโพรงมดลูก เปรียบเทียบกับการฉีดยาชาข้างปากมดลูก โดยประเมินความเจ็บปวดขณะและหลังขูดมดลูก 30 นาทีโดยแพทย์ที่ไม่ได้ทำการขูดมดลูก รวมทั้งประเมินภาวะแทรกซ้อนจากการใช้ยา ความต้องการยาแก้ปวดชนิดอื่นๆ เพิ่มเติม และความสามารถในการอ่านผลชิ้นเนื้อ ตัววัดที่สำคัญคือคะแนนความเจ็บปวดในขณะและหลังขูดมดลูก 30 นาที*

ผลการวิจัย: *ลักษณะทางประชากรศาสตร์ไม่แตกต่างกันระหว่างกลุ่ม ระดับความปวดในกลุ่มที่ได้รับการพ่นยาชาที่ปากมดลูกร่วมกับฉีดยาชาเข้าโพรงมดลูกน้อยกว่ากลุ่มที่ได้รับการฉีดยาชาข้างปากมดลูกซึ่งแตกต่างกันอย่างมีนัยสำคัญทางสถิติ (ค่ามัธยฐานของกลุ่มทดลอง 71.5 คะแนน (53.5-82.5), กลุ่มควบคุม 50.5 คะแนน (39-63), p < 0.001) และไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของระดับความปวดหลังขูดมดลูก 30 นาที ภาวะแทรกซ้อนรุนแรง ความต้องการยาแก้ปวดชนิดอื่น และชิ้นเนื้อที่ไม่สามารถแปลผลได้ในงานวิจัยนี้*

สรุป: *การพ่นยาชาที่ปากมดลูกร่วมกับฉีดยาชาเข้าโพรงมดลูก สามารถลดความปวดขณะขูดมดลูกได้อย่างมีนัยสำคัญทางสถิติเมื่อเทียบกับการฉีดยาชาข้างปากมดลูก และไม่พบภาวะแทรกซ้อนที่อันตราย*

คำสำคัญ: *การขูดมดลูกแบบแยกส่วน, การฉีดยาชาเข้าโพรงมดลูก, การฉีดยาชาข้างปากมดลูก, การพ่นยาชาที่ปากมดลูก, การให้คะแนนความปวดโดยใช้มาตรวัดด้วยสายตา*

Introduction

Fractional curettage is a common procedure for investigating causes of abnormal uterine bleeding. Patients frequently experience moderate to severe pain during this procedure. Many studies showed pain scores with cervical biopsy and cervical curettage ranging from 4-6 and endometrial biopsy ranging from 5-7 on visual analogue scale (VAS)[1].

General anesthesia is recommended by the Royal Thai College of Obstetricians and Gynecologists (RTCOG) for pain reduction during fractional curettage. It provides amnesia and hypnotic effect and associated with increased mortality and morbidity[2].

Paracervical block is effective for pain reduction by relieving pain in the lower part of uterus and cervix through the uterovaginal plexus and was recommended by RTCOG 2013 in fractional curettage guideline. However, it does not provide completely pain relief and need to use adjunctive medications including intravenous sedative drugs, oral nonsteroidal anti-inflammatory drugs (NSAIDs) or anxiolytic drugs. Moreover, it can be associated with adverse events such as numbness around month, dizziness to convulsion and respiratory arrest[3].

Systematic review[4] showed that there was no evidence that paracervical block reduced pain when compared to alternative regional anesthetic methods or systemic analgesics and sedatives.

Lidocaine spray can be used for pain relief during gynecologic operations. This drug is simple and convenient to use. It acts by reduction of peripheral pain impulses or damaged nociceptors below the application site[5]. Therefore, it can reduce pain during tenaculum placement and during endocervical curettage. However, the adverse effects of lidocaine spray remains unclear.

Intrauterine lidocaine acts by blocking nerve endings in the uterine corpus and fundus. It is logical to add intrauterine lidocaine to lidocaine spray to enhance anesthetic effect.

However, it remains controversial about pain relieving effect in gynecologic procedures and there is still no consensus that which type of analgesia should be used in patients undergoing fractional curettage. Thus, the objective of this study was to compare lidocaine spray in conjunction with intrauterine lidocaine versus paracervical block for pain reduction during fractional curettage.

Materials and Methods

This randomized controlled trial was conducted at Khon Kaen Hospital, Thailand from January to April, 2018. This study was approved by Khon Kaen Hospital Institute Review Board in Human Research. All participants were informed about the study and signed the consent form before enrollment.

We included women with abnormal uterine bleeding age 35 years old or more who were scheduled for fractional curettage. Women with severe genital organ infection, cervical stenosis, history of lidocaine hypersensitivity, impaired liver function, coagulopathy or women who took anticoagulant or antiplatelet drugs, pregnant women and those who were unable to understand how to score VAS were excluded.

Eligible participants were randomized by computer generated with block of four and randomly assigned into two groups; lidocaine spray in conjunction with intrauterine lidocaine and paracervical block. The random numbers were put in the sequentially sealed, opaque envelopes.

The study group received two puffs of lidocaine spray administered on cervical surface and wait for three minutes to allow the anesthetic to take effect, then tenaculum was placed. Afterwards, intrauterine lidocaine was performed by using 5 ml of 2% lidocaine with 1:100,000 epinephrine administered into the uterine cavity through a 2-inch, 16-gauge venous catheter inserted through the cervical canal and was left for 3 minutes to prevent back flow and to allow contact time to take effect. After that, endocervical and endometrial curettage were performed, respectively.

The control group received paracervical block performed by using 23-gauge spinal needle injected at 3 and 9 o'clock of cervicovaginal reflection at depth of 1 cm then push 5 ml of 2% lidocaine with epinephrine 1:100,000 into each side and wait for 5 minutes. Then,

endocervical and endometrial curettage were performed, respectively.

The fractional curettage was performed by using tenaculum grasped the anterior lip of the cervix and endocervical curettage was performed by using a curette number 00, after that we used uterine sound to measure uterine depth and then uterine curettage was performed by curette number 0. Women were observed for two to four hours at gynecology ward by nurses. Vital signs were recorded immediately when lidocaine spray, intrauterine lidocaine, paracervical block, endocervical curettage and endometrial curettage was performed, and also monitored at 30 minutes, 2 and 4 hours after procedure. All adverse events were observed and recorded at 30 minutes after procedure. We made an appointment at 14 days after procedure to inform pathological report.

The primary outcome was pain score during endometrial curettage (15 seconds after inserting curette number 0 and endometrial curettage was performed for the first time) which was first pain perception and other doctors asked patients to mark VAS pain score immediately for reducing recall bias. The secondary outcomes were pain score at 30 minutes after procedure, adverse events, additional analgesia or sedation and inadequacy of specimen.

The sample size was calculated from pilot study. We used formula for test of difference in two independence means with alpha of 0.05, power of 90% and 10% dropouts. The sample size was 56 cases per group.

$$n/\,group = \frac{2(Z_{\alpha/2} + Z_{\beta})^{2}\delta^{2}}{(\mu_1 - \mu_2)^2}$$

Statistical analysis was performed using SPSS 17.0 software. Categorical variables were analyzed by Chi-square test or Fisher's extract test. Continuous variables were analyzed by student t-test and Mann-Whitney U-test depended on data distribution. The primary outcome was presented as median with interquartile range with 95% confidence interval. Other outcomes were presents as percentage and median with interquartile range (IQR). P value less than 0.05 was represented statistical significance.

Results

One hundred and twelve women with abnormal uterine bleeding at Khon Kaen Hospital from January to April, 2018 were randomly allocated into two groups, group 1 received lidocaine spray in conjunction with intrauterine lidocaine (n = 56) and group 2 received paracervical block (n = 56) before performed fractional curettage. There was no dropout in this study. Subjective pain experience was measured by100-mm VAS (Fig. 1).

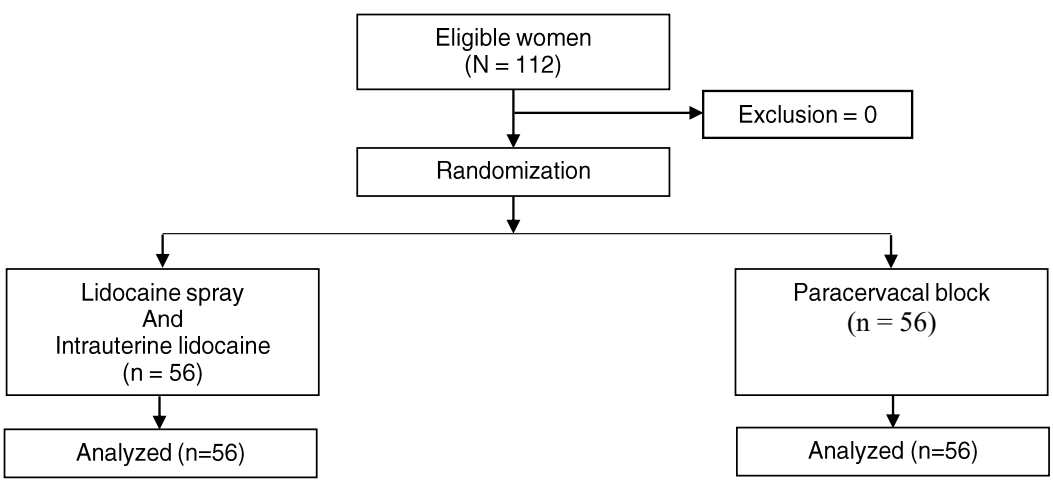

Fig. 1. Study flow diagram.

Baseline characteristics including age, body mass index (BMI), parity, prior curettage, menopausal status and indication for fractional curettage were similar between groups (Table 1). Median pain score (IQR) in lidocaine spray in conjunction with intrauterine lidocaine was significantly lower than paracervical block (71.5 (53.5-82.5) versus 50.5 (39-63), 95% CI 12.70-28.25, p<0.001). Pain score 30 minutes after procedure which was lower in study group but no statistical significance between two groups (Table 2). None of the patients requested termination of fractional curettage or rescue medication. Adverse events found in both groups but without significant difference (lightheadedness, palpitation, numbness of lips, tinnitus and hypotensive event). There was also no difference in inadequacy of specimen (Table 3).

Table 1. Baseline characteristics.

Characteristics	Lidocaine spray and intrauterine lidocaine (n = 56)	Paracervical block (n=56)	p value
Age (years), median (IQR)	46.50 (40 - 50)	46 (43 - 50)	0.606
BMI (kg/m^2), mean (sd)	26.65 (4.81)	25.29 (4.15)	0.178
Multipara, n(%)	44 (78.57)	49 (87.50)	0.157
Prior curettage, n(%)	3 (5.36)	9 (16.07)	0.062
Post menopausal status, n(%)	7 (12.50)	7 (12.50)	1.000
Indication, n(%)			0.733
- Abnormal uterine bleeding	46 (82.14)	46 (82.14)	
- Post menopausal bleeding	8 (14.29)	6 (10.71)	
- Endometrial hyperplasia	1 (1.79)	3 (5.36)	
- Tamoxifen used	0	0	
- Other	1 (1.79)	1 (1.79)	

IQR: interquartile range,
BMI: body mass index,
SD: standard deviation

Table 2. Primary and secondary outcomes.

VAS pain score	Lidocaine spray and intrauterine lidocaine (n=56)	Paracervical block (n=56)	p value	95% CI
During procedure, median (IQR)	50.50 (39 - 63)	71.50 (53.50 - 82.50)	< 0.001	12.70 - 28.25
After procedure, median (IQR)	11.50 (1.50 - 27.50)	20 (0.50 - 37.50)	0.190	-2.14 - 12.78

VAS: visual analogue scale,
CI: confidence interval,
IQR: interquartile range

Table 3. Adverse events, Additional analgesia and inadequacy of specimen.

Characteristics	Lidocaine spray and intrauterine lidocaine (n = 56)	Paracervical block (n=56)	p value
Adverse events, n (%)			
- Lightheadedness	2 (3.57)	3 (5.36)	0.647
- Palpitation	1 (1.79)	1 (1.79)	1.000
- Numbness of lips	0	0	
- Tinnitus	2 (3.57)	0	0.154
- Hypotensive event	4 (7.14)	5 (8.93)	0.121
Additional analgesia, n (%)	0	0	
Inadequacy of specimen, n (%)	8 (14.29)	5 (8.93)	0.783

Discussion

The present study demonstrated that lidocaine spray in conjunction with intrauterine lidocaine had significantly lower pain score than paracervical block during performing endometrial curettage. The combinations of lidocaine spray and intrauterine lidocaine have synergistic effects on both uterus and cervix. Pelvic splanchnics nerves (S2-4) or known as Frankenhauser plexus innervate lower part of uterus and cervix which is blocked by paracervical block. However, uterus also receives nerve supply from sympathetic nerves (T10-L1) or hypogastric nerves which innervate uterine fundus and body blocking by intrauterine lidocaine. Moreover it can reduce other pain perception by blocking nerve plexus on endometrium[11,12], whereas mucosal surface of cervix also receives innervation by ascending and descending roots which is the limitation of paracervical block to block these nerves but intrauterine lidocaine has this action. Therefore, addition of lidocaine spray has effect to damage nociceptors on cervix and endocervix by reducing peripheral pain impulses[5].

From previous studies and systematic review[4] showed that no evidence of paracervical block alone can reduce pain when compared to alternative regional anesthetic methods or systemic analgesics and sedatives. By the way, there was no study comparing lidocaine spray in conjunction with intrauterine lidocaine versus paracervical block as this study.

Aashima et al[7] conducted randomized controlled trial in 84 patients with abnormal uterine bleeding undergoing fractional curettage. All patients received NSAIDs and paracervical block in conjunction with either 5 ml of 2% intrauterine lignocaine or saline. They figured out statistically significant difference in the pain score between two groups (5.36±1.2 versus 6.81±1.4, $p < 0.001$). In addition, a randomized controlled trial study in 230 patients by Leelawattanakul et al[8] found that intrauterine lidocaine and paracervical block statistically reduce pain during fractional curettage when compared with paracervical block alone (45 (3-61) versus 53 (35-82), $p = 0.002$).

Gökhan et al[9] conducted a randomized controlled trial in 144 patients undergoing fractional and curettage. They compared 2 puffs of lidocaine spray, 25 mg of oral dexketoprofen trometamol, 100 mg of subcutaneous pethidine, 1,000 mg of intravenous paracetamol and 75 mg of oral diclofenac versus placebo and found that every interventions reduced pain perception with statistical significance (4 (2-6) versus 5.5 (4-8) versus 5 (4-5.5) versus 6 (5-8) versus 5 (5-7.5) versus 9 (7-10), p value < 0.001), respectively, but without statistical significance between intervention groups. However, there was a limitation about sample

size among intervention groups which was too small.

Another problem of using anesthetic agents is their adverse effects which range from mild toxicity such as numbness of lips, tinnitus and dizziness to severe toxicity such as convulsion and respiratory arrest. Therefore, some studies monitored lidocaine toxicity by evaluating plasma lidocaine level[13]. In our institute, we could not provide plasma lidocaine level, therefore, we observed clinical of lidocaine toxicity such as numbness of lips, lightheadedness, tinnitus, hypotensive event and convulsion. Adverse events from lidocaine that found in this study such as lightheadedness, palpitation, tinnitus and hypotensive event were not statistically different.

In addition, we concerned about adequacy of specimen because of using intrauterine lidocaine which was infiltrated into uterine cavity might have an affect on obtaining endometrium but there was no statistically significant between two groups.

The strengths of this study were no patients who loss to follow-up and the interventions were easy to perform but we cannot blind doctors and nurses who performed procedure which was the weakness of this study.

Conclusion

Lidocaine spray in conjunction with intrauterine lidocaine had better pain relief during fractional curettage than paracervical block without serious adverse events.

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Potential conflicts of interest

The authors declare no conflict of interest.

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