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Efficacy of Topical Ethyl Chloride Spray versus Subcutaneous 1% Lidocaine Injection in Reducing Pain from One Rod System Implant Insertion

Monthinee Techasomboon, M.D.*,
Rujira Wattanayingcharoenchai, M.D.*,
Jittima Manonai Bartlett, M.D.*,
Komkrit Aimjirakul, M.D.*.

** Department of Obstetrics and Gynaecology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand*

ABSTRACT

Objectives: To compare the efficacy of topical ethyl chloride spray and subcutaneous 1% lidocaine injection in reducing pain from one rod system implant insertion.

Materials and Methods: Eighty-four women undergoing one rod implant insertion during February 2014 to December 2015 were enrolled and randomly allocated to ethyl chloride spray and 1% lidocaine injection groups. After skin was sterilized, the assigned anesthetic method was administered before insertion of one rod implant according to the standard pro-cedure. Pain during anesthetic administration, implant insertion, 20 min after insertion, and overall pain were evaluated, using a 100-mm visual analogue scale (VAS). Patient and doctor satisfaction were measured using a five-point Likert scale.

Results: All basis clinical characteristics between two groups did not differ. There was no significant difference in VAS during and 20 min after implant insertion between 2 anesthetic groups ($p > 0.05$). Median VAS during anesthetic administration and overall pain in ethyl chloride spray group (1.50 and 1.60) were significant lower than lidocaine injection group (3.75 and 2.75) ($p < 0.01$). Patient and doctor satisfaction scores were significant higher in ethyl chloride spray group ($p < 0.05$).

Conclusion: Ethyl chloride spray can be used as anesthetic option for one rod system implant insertion. It provides comparable analgesic effect to lidocaine injection but with less pain from anesthetic administration.

Keywords: ethyl chloride spray, lidocaine, one rod system implant

Correspondence to: *Monthinee Techasomboon, M.D., Department of Obstetrics and Gynaecology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand, E-mail: monthineetecha @gmail.com*

การศึกษาเปรียบเทียบประสิทธิภาพของยาชาชนิดพ่นเอทธิลคลอไรด์และยาชาชนิดฉีดลิโดเคน 1% ในการระงับความปวดที่เกิดจากกระบวนการฝังยาคุมกำเนิดชนิดหนึ่งหลอด

มณฑินี เตชะสมบูรณ์, รุจิรา วัฒนายิ่งเจริญชัย, จิตติมา มโนนัย บาร์ทเล็ทท์, คมกฤช เอี่ยมจิรกุล

บทคัดย่อ

วัตถุประสงค์: *เพื่อเปรียบเทียบประสิทธิภาพระหว่างยาชาชนิดพ่นเอทธิลคลอไรด์ และยาชาชนิดฉีด 1% ลิโดเคนใต้ผิวหนังในการลดความปวดที่เกิดจากกระบวนการฝังยาคุมกำเนิดชนิดหนึ่งหลอด*

วัสดุและวิธีการ: *สตรีที่รับการบริการยาฝังคุมกำเนิดชนิดหนึ่งหลอดจำนวน 84 ราย ระหว่างเดือนกุมภาพันธ์ 2557 ถึงเดือนธันวาคม 2558 ถูกสุ่มแยกเป็นกลุ่มที่ได้รับยาชาชนิดพ่นเอทธิลคลอไรด์ และกลุ่มได้รับยาชา 1% ลิโดเคนฉีดใต้ผิวหนัง โดยหลังจากทำความสะอาดผิวหนังบริเวณที่จะฝังยาคุมกำเนิดด้วยยาฆ่าเชื้อ ทุกรายจะได้รับการระงับความปวดด้วยวิธีที่สุ่มไว้แล้ว ก่อนทำการฝังยาคุมชนิดหนึ่งหลอดตามวิธีมาตรฐาน ประเมินระดับความปวดขณะให้การระงับความปวด, ขณะฝังยาคุม, หลังจากฝังยาคุม 20 นาทีและความปวดโดยรวม โดยใช้ visual analogue scale (VAS) และวัดระดับความพึงพอใจของผู้ให้และผู้รับบริการโดยใช้มาตรวัดของลิเคิร์ท 5 ระดับ*

ผลการทดลอง: *ลักษณะพื้นฐานทางคลินิกของผู้ป่วยทั้งสองกลุ่มไม่มีความแตกต่างกัน ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของความปวดประเมินโดย VAS ขณะฝังยาคุมและหลังจากฝังยาคุม 20 นาที ในการระงับความปวดทั้ง 2 วิธี ($p > 0.05$) ค่ามัธยฐานความปวดประเมินโดย VAS ขณะให้การระงับความปวดและความปวดโดยรวมในกลุ่มยาชาชนิดพ่นเอทธิลคลอไรด์ (1.50 และ 1.60) ต่ำกว่ากลุ่มฉีดยาชา 1% ลิโดเคนใต้ผิวหนัง (3.75 และ 2.75) อย่างมีนัยสำคัญ ($p < 0.01$) คะแนนความพึงพอใจของผู้ป่วยและแพทย์ในกลุ่มยาชาชนิดพ่นสูงกว่าอย่างมีนัยสำคัญ ($p < 0.05$)*

สรุป: *ยาชาชนิดพ่นเอทธิลคลอไรด์สามารถใช้เป็นทางเลือกหนึ่ง ในการลดความปวดจากการฝังยาคุมกำเนิดชนิดหนึ่งหลอดได้ โดยสามารถลดความปวดที่เกิดขณะฝังยาคุมได้ไม่แตกต่างจากยาชาลิโดเคนชนิดฉีด แต่มีความปวดขณะให้การระงับปวดต่ำกว่า*

คำสำคัญ: *เอธิลคลอไรด์ สเปร์ย, ลิโดเคน, ยาฝังคุมกำเนิดชนิดหนึ่งหลอด*

Introduction

Contraceptive implant is the one of the most effective long acting reversible contraception comparing with other reversible contraceptive methods. It was first introduced in Finland since 1983, as a 6-rod system containing levonorgestrel (Norplant®)[1-3]. Problem related to insertion and removal of Norplant leads to the development of newer implant. In 1998, a one rod system subdermal implant contained 68 mg etonogestrel (Implanon®) was introduced into the market. It has led to easier insertion and removal[1-3].

In 2011, one rod subdermal etonogestrel implant with new device for easier inser-tion, Implanon-NXT® or Nexplanon® was developed. A pre-loaded applicator was designed to facilitate insertion of the implant subdermally in a one-handed action. Moreover, barium sulphate was added to the implant core allowing x-ray detection in non-palpated implant[4, 5].

Although single rod etonogestrel implant has been introduced in Thailand since 2000, its utilization rate is still low. From the reproductive health survey of Ministry of Public Health, Thailand in 2014, contraceptive prevalence of implant is only 0.22% of all methods used in reproductive age women[6]. Factors that may affect the implant utilization include lack of provider's knowledge and skill, fear of side effects, problem of confidentiality due to the potential visibility of the implant, and high contraceptive cost. Fear of pain with implant insertion is also an important factor for impediment to implant use[7].

Subcutaneous injection of 1% lidocaine is a widely used anesthetic method in implant insertion. It produces anesthesia by inhibiting excitation of nerve endings or by blocking voltage-dependent sodium channels[8]. However, lidocaine injection itself may be painful due to penetration of the skin by the needle and there is the theoretical risk of needle stick injury. It also requires certain time to be anaesthetized.

Ethyl chloride spray is another method that provides local anesthesia. Rapid evaporation of the volatile liquid spray from the skin surface causes a decrease in temperature from 33°C to below 10°C after a 10-second application. This cooling effect results in temporary interruption of pain sensation, possibly through desensitization of pain receptors or activation of ion channels involved in pain transmission which finally produces immediate skin anesthesia[9-11]. Regarding the skin sterility, although ethyl chloride topical anesthetic spray is not labeled as sterile, its application do not alter the sterility of the injection sites [12].

Due to the rapid onset ethyl chloride spray, it has been used in minor procedures with short operative time including intravenous cannulation and incision and drainage. Comparing to lidocaine injection, ethyl chloride may help reducing pain at anesthetic administration and risk of needle stick injury. The efficacy of ethyl chloride spray in decreasing cannulation pain has been less clear cut. Several previous studies demonstrated its efficacy[13-18] but some studies did not[19, 20]. At present, there are no published study that assessed pain from implant insertion nor evaluated efficacy of different anesthetic methods in reducing pain from implant insertion. The objectives of this study were to compare the efficacy of topical ethyl chloride spray and subcutaneous 1% lidocaine injection in reducing pain from one rod system implant insertion and compare client and doctor satisfaction between these two anesthetic methods.

Materials and Methods

This was a randomized controlled trial study, conducted in women attending the family planning clinic, Department of Obstetrics and Gynaecology, Ramathibodi Hospital, Bang-kok, Thailand, during February 2014 to December 2015. This study was approved by the Ethics Committee on human rights related to research involving human subjects, based on Declaration of Helsinki, Faculty of Medicine, Ramathibodi Hospital, Mahidol University and registered with the Thai Clinical Trials Registry (TCTR20150925002).

The inclusion criteria were Thai literate women who prefer to use one rod system contraceptive implant, no contraindication for one rod system implant. The exclusion criteria included known allergic to either analgesic methods, known underlying dermatologic

condition that relate to cold temperature, removal and reinsertion of subdermal implant at the same time, received pain killer within 4 hours prior to the procedure. All eligible participants received a verbal and written explanation about the research study and signed written informed consent.

On enrollment, all participants were randomly allocated to one of two anesthetic groups; 1% lidocaine injection and topical ethyl chloride spray, using computer-generated numbers. The randomized treatment assignments were sealed in opaque envelopes and opened individually for each participant who agreed to be in the study. Before the procedure, the participants were informed about the study drugs, the implant insertion procedure and how to use the visual analogue scale (VAS) for pain assessment. The demographic data (age, body mass index (BMI), history of vaginal delivery, cesarean section and abortion) and level of provider were collected.

After randomization to either 1% lidocaine injection or topical ethyl chloride spray, every client underwent the same skin preparation technique. Povidone iodine solution was used to sterilize skin. In Ethyl chloride spray group, implant insertion site was sprayed con-stantly for 5 seconds from about a 15 cm distance as shown in Fig. 1a[12, 18]. One rod sys-tem implant was inserted within 10 seconds of spray administration. In 1% lidocaine injec-tion group, 2 ml of 1% lidocaine without adrenaline was slowly injected through a 24 G needle at the implant insertion site of skin with the depth of 2-3 mm, until at least 5 mm of wheal was observed. The needle was further advanced under the skin in the direction of implant insertion and the remaining lidocaine was injected subcutaneously as shown in Fig. 1b. One rod system implant was inserted 60 seconds afterward[18].

Fig. 1. a) Ethyl chloride spray application b) Lidocaine injection.

The client's pain at analgesic application, implant insertion, 20 minutes after implant insertion and overall pain were assessed using 100 mm visual analogue scale (VAS) with 'no pain' written at the left end of the scale (0 mm) and 'worst pain imaginable' written at the right end (100 mm) as recommended by Ho et al[21]. The clients were instructed to rate their pain by making a mark on a 100 mm visual analogue scale by themselves. Client and doctor satisfaction were measured using a five-point Likert scale (very unsatisfied, unsatisfied, neutral, satisfied, very satisfied). Duration of the procedure, time from the beginning of analgesic administration to the end of implant insertion, was also collected. The consort flow diagram is shown in Fig. 2.

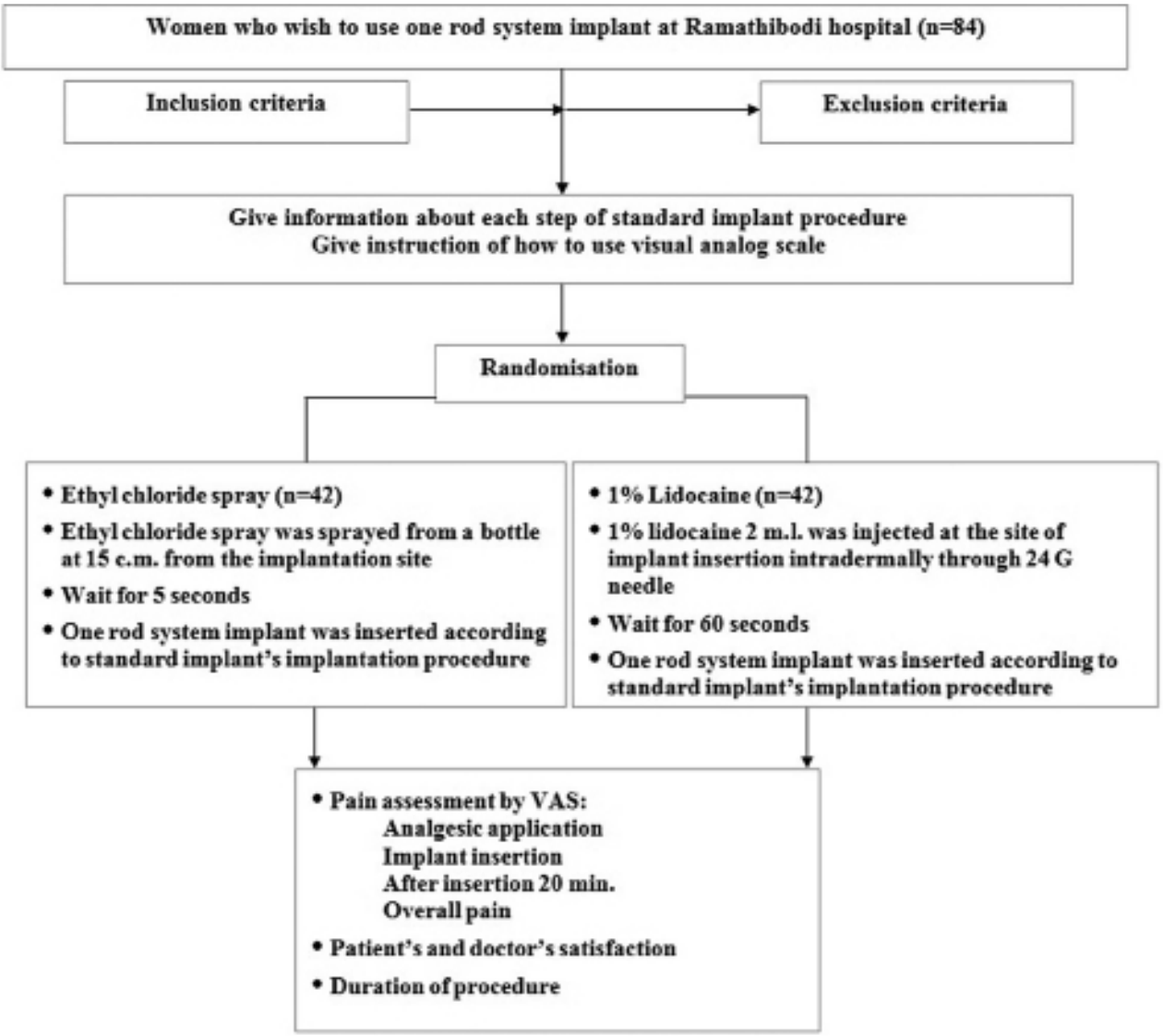

Fig. 2. Consort diagram flow chart.

Sample size calculation

The sample size was calculated from the formula for comparing mean where Zβ was set as 1.96 with a type I error of 5%, Zβ was set as 1.28 with a power of 90%. From the pilot study included 20 subjects; 10 in each anesthetic group, mean VAS score of overall pain from implant insertion in subcutaneous lidocaine injection group was 4.17 (SD 2.05) and in ethyl chloride spray group was 2.7 (SD 2.01). The calculated number was then added with 5% of the calculated number of subjects who might be excluded due to data loss. Therefore, 42 subjects were needed to be enrolled in each group.

Statistical analysis

Statistical analyses were performed using PASW (Predictive Analytics Software) Statistics 18.0.0. Continuous data were reported as the mean and standard deviation. Categorical data were shown as the number and percentage. The continuous data (age, BMI, VAS) were tested for normal distribution using Kolmogorov-Smirnov test.

The statistical analysis was carried out using independent student's t test for parametric continuous data, Mann-Whitney U test for non-parametric and ordinal data, and Pearson Chi-square test for categorical data. All reported probability values are two-tailed; $p < 0.05$ was considered to be statistically significant.

Results

Eighty-four of women, 42 in ethyl chloride spray group and 42 in lidocaine injection group were recruited in the analysis. The demographic characteristics of subjects are presented in Table 1. There were no statistical difference in age, BMI, previous delivery modes and level of provider.

VAS pain scoring at analgesic application, implant insertion, 20 minutes after implant insertion and overall pain of both anesthetic groups are shown in Table 2. There was no statistically significant difference in VAS pain score during implant insertion and 20 minutes after implant insertion between 2 anesthetic groups ($p > 0.05$). However, clients in lidocaine injection group reported more pain during anesthetic administration and also overall pain than in ethyl chloride spray group ($p < 0.01$).

Regarding the satisfaction with the procedure, both clients and doctor's satisfaction in ethyl chloride spray group were better than that in lidocaine injection group ($p < 0.05$) (Table 3). Moreover, duration of the procedure using ethyl chloride spray as anesthetic agent was obviously shorter than that using lidocaine injection (12.04 ± 0.63 sec vs 144.26 ± 57.15 sec, respectively, $p < 0.01$). None of the participants experienced adverse effect with both anesthetic agents.

Table 1. Demographic Characteristics.

Demographic data	Ethyl chloride spray (n=42)	Lidocaine injection (n=42)	p value
Age (year), mean ± SD	23.17±6.44	23.79±7.70	0.69[a]
BMI (kg/m^2), mean ± SD	23.53±4.28	22.96±4.03	0.53[a]
Parity, median (range)	1 (1-3)	1 (0-3)	< 0.05[b]
Previous vaginal delivery, n (%)	29 (69.0)	22 (52.4)	0.09[c]
Previous cesarean section, n (%)	12 (28.6)	14 (33.3)	0.81[c]
Previous abortion, n (%)	26 (61.9)	34 (81.0)	0.09[c]
Level of provider, n (%)			0.41[c]
- Resident 1	32 (76.2)	36 (85.7)	
- Resident 2 and 3	10 (23.8)	6 (14.3)	

[a] Independent Student T test, [b] Mann-Whitney U test, [c] Chi square test

Table 2. VAS Pain Scoring.

VAS Pain score median (IQR)	Ethyl chloride spray (n=42)	Lidocaine injection (n=42)	p value
Analgesic administration	1.50 (1.20, 2.05)	3.75 (2.45, 5.10)	< 0.01[a]
Implant insertion	0.65 (0.30, 1.40)	0.90 (0.10, 2.00)	0.87[a]
20 minutes after implant insertion	0.25 (0.10, 0.93)	0.00 (0.00, 1.18)	0.11[a]
Overall pain	1.60 (1.30, 2.20)	2.75 (1.50, 4.38)	< 0.01[a]

[a] Mann-Whiney U test

Table 3. Client and Doctor Satisfaction.

Satisfaction median (range)	Ethyl chloride spray (n=42)	Lidocaine injection (n=42)	p value
Client	5 (3-5)	4 (2-5)	0.04[a]
Doctor	5 (4-5)	5 (3-5)	0.03[a]

[a] Mann-Whitney U test

Discussion

Local lidocaine injection is widely used as anesthetic of choice for many minor operative procedures. Its efficacy in decreasing pain was proved in previous studies. But the method itself causes painful administration[15, 17, 18, 22, 23]. It also requires certain period of time to achieve anesthesia which results in incomplete anesthesia especially in emergent procedures. Ethyl chloride spray has long been used in the relief of acute and chronic painful conditions. Due to its rapid onset and short duration of action, it is also used in minor procedures with short operative time.

A one rod subdermal etonogestrel implant with new pre-loaded applicator, Implanon-NXT® was developed for easier and safer insertion. The average time for insertion is less than one minute. Therefore, ethyl chloride spray may be useful in avoidance of analgesic administered pain from lidocaine injection.

In this study, the results showed a significant higher analgesic administered pain in lidocaine injection group than in ethyl chloride spray group. This was similar to the study of Page[17]. But Armstrong's study found no significant difference in anesthetic administered pain between lidocaine injection and ethyl chloride[18]. This might be due to the different in administration technique. This study injected 2 ml of lidocaine via a 24 G needle, whereas Armstrong's study injected only 0.2 ml of lidocaine via a 25 G needle. The less amount of drug and a small-caliber needle may produce less pain.

The efficacy of ethyl chloride in decreasing pain form intravenous cannulation had been reported with inconsistent results. In this study, VAS pain score at time of subdermal implant insertion in ethyl chloride and lidocaine injection group was not differ significantly. From the literature review, there was no previous published study comparing the anesthetic efficacy of these two analgesic methods in implant insertion. Prior study compared the anesthetic effect of ethyl chloride spray and lidocaine injection in prevention of pain from intravenous cannulation[17, 18]. Those studies reported significant lower VAS pain score in lidocaine injection group. This might be due to the different in the procedure. Insertion of the newer one rod system implant in this study required very short duration of procedure (12.04 ± 0.63 sec). In intravenous cannulation procedure, it might be difficult and time consuming in some cases. Ethyl chloride has shorter analgesic duration of action, compared to lidocaine injection. It might become less effective in pain reduction in the procedure with possible longer duration.

Regarding satisfaction of the procedure, client's satisfaction was significantly higher in ethyl chloride spray group. This was supported by lower overall VAS and anesthetic ad-ministered pain in ethyl chloride spray group. Doctor's satisfaction was also significantly higher in ethyl chloride spray group. This might be explained by shorter duration of the pro-cedure, less exposure to needle that leads to decrease risk of needle stick injury.

The findings of this study indicated the advantage of ethyl chloride spray over subcutaneous lidocaine injection; less administered pain, easy administration technique, less equipment use, shorter application time, but with similar efficacy in decreasing implant insertion pain. This can be applied for use as analgesic option for one rod system implant insertion in certain circumstances such as seropositive patients, service in ambulatory setting.

The limitation of this study was inability to blind to both investigators and partici-pants due to the obvious different intervention. It might have the potential assessment bias. However, all participants were received similar information about two anesthetic agents us-ing in the study, the step of implant insertion procedure, and how to use the VAS for pain assessment which might help reduction in this bias.

The strength of this study was a randomized controlled trial, using computer-generated numbers to allocate the participants. Randomized assignment numbers were kept in sealed opaque envelopes contains and opened individually for each participant who agreed to be in the study. It is the first RCT comparing between 2 analgesic methods in implant insertion. Providers who performed the procedure had been standardized with the same one rod system implant insertion technique and the same instruction for application each analgesic methods. Moreover, pain at different steps of the procedure was assessed. Client and provider satisfaction which might reflect their acceptability were also collected.

Conclusion

Ethyl chloride spray provides similar efficacy in decreasing implant insertion pain with lidocaine injection. It has significantly less anesthetic administered pain. It requires less exposure to needles and shorter administration time. Ethyl chloride spray can be used as standard anesthesia for one rod system implant insertion.

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Potential conflicts of interest

The authors declare no conflict of interest.

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