Original Article

Topical Lidocaine-Prilocaine Cream Versus Lidocaine 1% Subcutaneous Infiltration During Nexplanon Insertion: A Randomized Controlled Study

Ahmed Nasr[1], Mohamed Khalaf[1], Eman El-said[2], Ahmed M. Abbas[1] and Mohamed M. Abdallah[1]

Department of Obstetrics and Gynecology, [1]Assiut University, Assiut, [2]Luxor General Hospital, Luxor, Egypt

ABSTRACT

Background: Subcutaneous injection of lidocaine 1% is a widely used anesthetic method in implant insertion. However, lidocaine injection may be painful due to the penetration of the skin by the needle. This may also cause bleeding or edema which may mislead the intact subdermal insertion of the implant .Lidocaine-prilocaine (LP) cream is an oil/water emulsion in which the oil phase is a eutectic mixture of two anesthetics: lidocaine 2.5% and prilocaine 2.5% in a ratio of 1:1 by weight.

Objectives: Our objective is to compare the anesthetic effect of LP cream versus lidocaine subcutaneous infiltration during insertion of Nexplanon.

Methods: The study was conducted on department of obstetrics and gynecology faculty of medicine Assiut and Luxor University. Eligible women requesting Nexplanon insertion for contraception were randomized to LP cream (n=130) vs. lidocaine 1% subcutaneous infiltration (n=130)

Results: Statistical analysis of current results showed that visual analog scale (VAS) at nexplanon insertion was significantly higher however overall pain was significantly lower in cases "lidocaine- prilocaine cream" compared to control "lidocaine subcutaneous injection" group. Duration of application was significantly higher in cases compared to control group due to the time needed for the effect of used cream. Complications during insertion were significantly lower in cases compared to control group. Patient's satisfaction was insignificantly different between both groups.

Conclusion: Topical application of lidocaine-prilocaine cream before Nexplanon insertion significantly reduces the induced pain with subsequent easier insertions and less rate of procedure-related complications.

Key Words: Lidocaine, nexplanon, subdermal implants.

Received: 16 November 2023, **Accepted:** 02 January 2024

Corresponding Author: Mohamed M. Abdallah, Department of Obstetrics and Gynecology, Assiut University, Assiut, Egypt, **Tel.:** +20 10 6105 6747, **E-mail:** dr_mabdallah1988@yahoo.com

ISSN: 2090-7265, 2025, Vol.15

INTRODUCTION

Long-acting reversible contraception, which include intrauterine devices (IUDs) and subdermal hormonal implants, are gaining popularity due to high efficiency rates in preventing unintended pregnancy. Use of subdermal implant since 2002, for adolescents and adults ages 15 to 44 years, has increased (0.3% to 0.8%)[1].

Nexplanon is a contraceptive implant pre-loaded in a disposable applicator. The implant contains 68 mg of etonogestrel. Etonogestrel is synthetic female hormone resembling progesterone. A small amount of the hormone is continuously released into the blood stream for three years. The rod itself is made of ethylene vinylacetate copolymer, a plastic that will not dissolve in the body. It also contains small amount of barium sulfate (which renders it visible under x- ray) and magnesium stearate[2].

Adequate anesthesia is an important procedural step when inserting contraceptive implants. Subcutaneous injection of lidocaine 1% is widely used anesthetic method in implant insertion. It produces anesthesia by inhibiting excitation of nerve endings or by blocking voltage-dependant sodium channels[3]. However, lidocaine injection may be painful due to penetration of the skin by the needle and there is a theoretical risk of needle stick injury. This may also cause bleeding or edema which may mislead the intact sub dermal insertion of implant. It also requires certain time to be anaesthized.

Therefore, the use of anesthetic cream such as lidocaine –prilocaine cream may decrease the side effects of injection. Lidocaine- prilocaine topical cream is used on the skin or in the genital area to cause numbness or loss of feeling before certain medical procedures to decrease pain scores associated with insertion[4].

Lidocaine-prilocaine cream is an oil/water emulsion in which the oil phase is a eutectic mixture of two anesthetics: lidocaine 2.5% and prilocaine2.5% in a ratio of 1:1 by

DOI:10.21608/EBWHJ.2024.249234.1277

weight[5]. This eutectic mixture has a melting point below room temperature and therefore both local anesthetics exist as liquid oil rather than as crystals. The current study aims to compare the analgesic effect of lidocaine-prilocaine cream versus lidocaine subcutaneous injection during insertion of nexplanon.

SUBJECTS AND METHODS

Patients' Data

This study is a randomized open-labelled controlled study conducted at Gynecology & Obstetrics Department, Assiut woman's Health Hospital, Egypt and Gynecology & Obstetrics Department, Luxor general hospital, Egypt. An informed consent was obtained from each patient and all the study procedures were approved by the Medical Ethics Committee (Institutional Review Board), Faculty of Medicine, Assiut University (Approval number: 200406). The first group (cases) included 130 women, aged 20-45 years attended the family planning clinic for nexplanon insertion and had no contraindication for subdermal implants insertion and no contraindication to or history of allergic reaction to lidocaine- prilocaine. They used lidocaine- prilocaine anesthetic cream placed on their skin prior to insertion of nexplanon. The second group (control) included 130 women age-matched, had lidocaine subcutaneous injection instead. We excluded women with Lidocaine- prilocaine allergy or with any contraindication to subdermal implants insertion.

Method of application

We randomly assigned women who had chosen nexplanon as their contraceptive into two groups. randomized into 2 equal groups; group 1 (cases): had lidocaine- prilocaine anesthetic cream placed on their skin prior to insertion of nexplanon and group 2 (control): had lidocaine subcutaneous injection instead. The level of pain at three different time points on a 10-point visual analogue scale (VAS) and the patients' satisfaction with the procedure was compared between the two groups. Randomization was conducted using a computer-generated table of random numbers with allocation concealment. Allocation concealment was done by using serially numbered closed opaque envelope. Counselling for participation was done before recruitment. Once allocation has been done, it could not be changed.

Participants, after informed consent, were randomized in a 1:1 ratio to both groups. The demographic data (age, body mass index, history of vaginal delivery, cesarean section and abortion) was collected. After randomization, Povidone iodine solution was used to sterilize the skin. In group 1, it was applied on the insertion site. Nexplanon rod was inserted after 5 minutes of cream application. In group 2, 2 ml of 1% lidocaine was slowly injected through a 24 G needle at the nexplanon insertion site of skin with the depth of 2-3 mm, until at least 5mm of wheel was observed.

The needle was further advanced under the skin in the direction of nexplanon insertion and the remaining lidocaine was injected subcutaneously. Nexplanon rod was inserted within 3 minutes afterwards. The client pain at analgesic application, nexplanon insertion, 15 minutes after insertion and overall pain was assessed using 100 mm visual analogue scale (VAS) with 'no pain' written at the left end of the scale (0mm) and 'worst pain imaginable' was written at the right end (100mm) as recommended by Bouhassira *et al*[6]. The client will be instructed to rate their pain by making a mark on a 100 mm visual analogue scale by themselves.

Client and doctor satisfaction will be measured using a five-point Likert scale (very unsatisfied, unsatisfied, neutral, satisfied, and very satisfied). Duration of the procedure, time from the beginning of analgesic administration to the end of implant insertion will be also collected[6].

Statistical analysis

The collected data was be coded; tabulated and analyzed by using the statistical package for social science programs (SPSS) Chicago, IL, USA, version 21. Quantitative data was expressed as mean and standard deviation and was analysed by using Student's t test. Qualitative data was expressed as frequency and percentages and was analyzed by Chi-square test. Pearson's correlation analysis was performed to analyze the patient's risk factors and its relation to pain scores. Level of significance "*P*" value was evaluated, where *P value* <0.05 was considered statistically significant.

Sample size was calculated using the Open Epi software program, version 2.3.1. Previous study reported that the mean pain score using VAS with lidocaine infiltration was 2.75[7]. Using two-sided chi-square (χ^2) test with α error of 0.05, a minimum sample size of 260 women (130 in each group) is needed, using 80% power to detect 50% decrease in the VAS pain score with the use of Lidocaine-prilocaine cream [Odds Ratio=0.41].

RESULTS

Clinical characteristics of PE patients

The present study included 260 women. The mean age of patients 30 years (range, 26-36 years). The demographic data of PE patients are summarized in (Table 1).

Table 1: Demographic data of the studied groups

	Cases (n=130)		Control (n=130)		*P. value*
	Mean ± SD		Mean ± SD		
Age	30.95±5.64		30.17±5.84		0.272
	No.	%	No.	%	
Residency					
Rural	102	78.5	96	73.8	0.383
Urban	28	21.5	34	26.2	
Education					
Illiterate	12	9.2	14	10.8	0.695
Primary school	36	27.7	43	33.1	
High school	65	50.0	56	43.1	
College	17	13.1	17	13.1	

Evaluation of visual analog scale(VAS) distribution and duration of application in both groups

The results showed VAS at analgesic application, and overall pain were significantly lower in cases group compared to control group. VAS at nexplanon insertion was significantly higher in cases group compared to control group. VAS 15 min after insertion was insignificantly different between both groups and the duration of application was significantly higher in cases group compared to control group (*P value* <0.001). (Table 2).

Table 2: VAS distribution and duration of application between the two groups

VAS	Cases (n=130)	Control (n=130)	*P. value*
	Mean ± SD	Mean ± SD	
Analgesic application	1.01±0.09	5.57±1.64	<0.001*
Nexplanon insertion	3.46±1.38	2.55±0.99	<0.001*
15 min after insertion	2.22±0.9	2.03±0.71	0.068
Overall pain	2.98±1.25	4.32±1.28	<0.001*
Duration of application (min)	8.23±0.89	7.49±0.66	<0.001*

Complications and side effects during insertion

We also found that complications were significantly lower in cases group compared to control group (*P* <0.001) (Figure 1). We reported that the occurrence of side effects was significantly lower in case group than control group (Table 3).

Table 3: Side effects in both groups

	Cases (n=130)		Control (n=130)		*P. value*
	No.	%	No.	%	
Side effects					
Yes	26	20	56	43.1	
No	104	80.0	74	56.9	
Bruising	0	0.0	20	15.4	
Bruising 3 days	0	0.0	2	1.5	
Bruising and itching	0	0.0	6	4.6	
Bruising and pain	0	0.0	1	0.8	
Bruising and pain for 10 days	0	0.0	1	0.8	
Bruising for 10 days	0	0.0	1	0.8	
Bruising for days	7	5.4	0	0.0	
Bruising for days and edema	0	0.0	1	0.8	
Bruising for few days	0	0.0	1	0.8	
Bruising for one week	0	0.0	1	0.8	
Bruising and edema	0	0.0	6	4.6	<0.001*
Edema	0	0.0	8	6.2	
Edema and itching	0	0.0	1	0.8	
Itching	0	0.0	3	2.3	
Itching and pain	0	0.0	2	1.5	
Minimal bruising	2	1.5	0	0.0	
Pain	0	0.0	1	0.8	
Severe bruises	0	0.0	1	0.8	
Slight bruising	9	6.9	0	0.0	
Slight itching	1	0.8	0	0.0	
Slight pain in next day	6	4.6	0	0.0	
Slight bruising and itching	1	0.8	0	0.0	

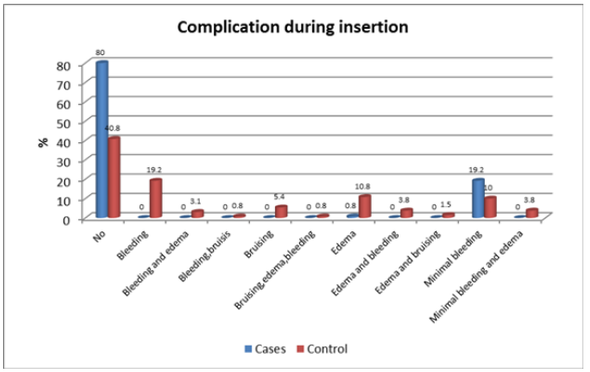

Fig. 1: Clustered cylindrical chart showing percentage of complication during insertion distribution between two groups

Time of insertion, arm used, day of the menstrual cycle and patient satisfaction between both groups

Our study reported that were no significant differences between both groups as regarding time of insertion, arm used and day of the menstrual cycle (Table 4).

Table 4: Time of insertion, arm used , day of the menstrual cycle and patients satisfaction between both groups

	Cases (n=130)		Control (n=130)		*P. value*
	No.	%	No.	%	
Time of insertion					
Menstrual	55	42.3	54	41.5	0.130
Post abortion	2	1.5	8	6.2	
Post-partum	47	36.2	51	39.2	
Post contraceptive	26	20.0	17	13.1	
Arm					
Rt	3	2.3	8	6.2	0.123
Lt	127	97.7	122	93.8	
	Mean ± SD		Mean ± SD		
Day of menstrual cycle	5.19±1.57		5.07±1.33		0.670

As regard patient satisfaction, the results showed no statistically significant differences between both groups (Figure 2)

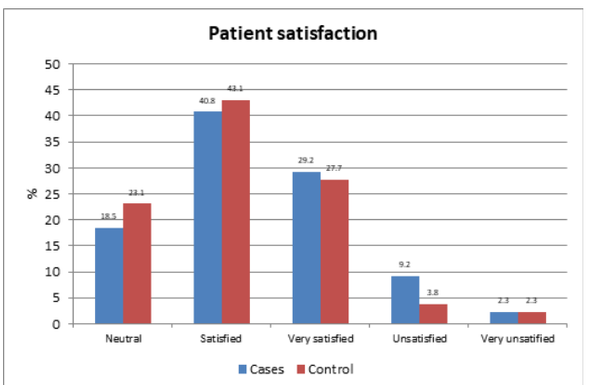

Fig. 2: Clustered cylindrical chart showing percentage of patient satisfaction distribution between two groups

DISCUSSION

When it comes to implanting contraceptive devices, having adequate anaesthetic is crucial. Lidocaine 1% subcutaneous injection is a common form of implant insertion anaesthetic[8]. However, because the needle penetrates the skin, lidocaine injections can be uncomfortable, and there is a potential danger of needle stick injuries[9].

As a result, the usage of anesthetic creams such as lidocaine–prilocaine cream may help to reduce the injection's negative effects[10].

According to our knowledge there were only three previous studies compared between the analgesic effect of lidocaine-prilocaine cream/spray versus lidocaine subcutaneous injection during insertion of nexplanon

Regarding basal demographic and clinical data; statistical analysis of current results showed that there were no significant difference between study groups regarding age, residency, education, parity, obstetric history "vaginal delivery, abortion and cesarean section", time of insertion, used arm and day of the menstrual cycle.

Regarding VAS distribution; statistical analysis of current results showed that VAS at nexplanon insertion was significantly higher however overall pain was significantly lower in cases "lidocaine- prilocaine cream" compared to control "lidocaine subcutaneous injection" group. Techasomboon *et al* (2017)[6] agreed with current study and stated that clients in lidocaine injection group reported more pain during anesthetic administration and also overall pain than in ethyl chloride spray group ($p < 0.01$). Mapaisankit *et al* (2021)[11] agreed with current study and stated that median VAS during anesthetic administration and overall pain reported by patients in the ethyl chloride spray group was significantly lower than the lidocaine group (0 vs 3 cm; $p < 0.001$ and 1 vs 2.9 cm; $p < 0.001$, respectively). However, the median VAS during the procedure in the ethyl chloride spray group was found to be significantly higher than the lidocaine group (1 and 0 cm; $p = 0.001$).

Regarding duration of application; it was significantly higher in cases compared to control group (*P value* <0.001) due to the time needed for the effect of used cream. Techasomboon *et al* (2017)[6] disagreed with current study and stated that 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, $p < 0.01$) that might be due to spray had easier application compared with cream of our study. Mapaisankit *et al* (2021)[11] disagreed with current study and stated that significantly shorter duration was found in the contraceptive implant removal in the ethyl chloride spray group, compared to lidocaine group.

The duration difference is approximately 13.5 seconds (median 31 vs 44.5 seconds; $p = 0.007$) that might be due to spray had easier application compared with cream of our study.

Regarding complications during insertion in both groups "bleeding, edema, bruises and itching"; statistical analysis of current results showed that they were significantly lower in cases compared to control group ($P < 0.001$). Techasomboon *et al* (2017)[6] disagreed with current study and stated that none of the participants experienced adverse effect with both anesthetic agents that might be due to different techniques of application of study medications and criteria of study population.

Regarding patient's satisfaction; statistical analysis of current results showed that it was insignificantly different between both groups. Techasomboon *et al* (2017)[6] disagreed with current study and stated that both clients and doctor's satisfaction in ethyl chloride spray group were better than that in lidocaine injection group ($p < 0.05$) that might be due different population size and more potent effect of ethyl chloride spray compared with cream of our study. Mapaisankit *et al* (2021)[11] agreed with current study and stated that participant and procedure assistant satisfaction in the ethyl chloride spray group was significantly higher than in the lidocaine group.

CONCLUSION

In conclusion, During insertion of nexplanon implant, lidocaine- prilocaine cream had higher overall analgesic effect and lower side effect compared with lidocaine subcutaneous injection but with longer duration of application, higher pain scores with implant insertion and no difference in patient's satisfaction.

RECOMMENDATION

We recommend further research to determine the efficacy of using lidocaine- prilocaine cream during insertion of nexplanon subdermal implants

CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCES

1. Mestad R, Secura G, Allsworth JE, Madden T, Zhao Q and Peipert JF. Acceptance of long-acting reversible contraceptive methods by adolescent participants in the Contraceptive CHOICE Project. Contraception. 2011;84(5):493-8.

2. Mansour D. Nexplanon®: what Implanon® did next. BMJ Sexual & Reproductive Health. 2010;36(4):187-9.

3. Golzari SE, Soleimanpour H, Mahmoodpoor A, Safari S and Ala A. Lidocaine and pain management in the emergency department: a review article. Anesth Pain Med. 2014;4(1):e15444.

4. 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(5):1335-9.

5. Friedman PM, Mafong EA, Friedman ES and Geronemus RG. Topical anesthetics update: EMLA and beyond. Dermatol Surg. 2001;27(12):1019-26.

6. Techasomboon M, Wattanayingcharoenchai R, Bartlett JM and Aimjirakul K. Efficacy of Topical Ethyl Chloride Spray versus Subcutaneous 1% Lidocaine Injection in Reducing Pain from One Rod System Implant Insertion. Thai Journal of Obstetrics and Gynaecology. 2017:266-74.

7. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, *et al*. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain. 2005;114(1-2):29-36.

8. Romero J, Bello J, Díaz JC, Grushko M, Velasco A, Zhang X, *et al*. Tumescent local anesthesia versus general anesthesia for subcutaneous implantable cardioverter-defibrillator implantation. Heart Rhythm. 2021;18(8):1326-35.

9. Schlich M, Primavera R, Lai F, Sinico C and Decuzzi P. Needle-Free Jet Injectors for Dermal and Transdermal Delivery of Actives. Imaging Technologies and Transdermal Delivery in Skin Disorders. 2019:201-22.

10. Razavi BM and Fazly Bazzaz BS. A review and new insights to antimicrobial action of local anesthetics. Eur J Clin Microbiol Infect Dis. 2019;38(6):991-1002.

11. Mapaisankit N, Chandeying P and Tangthasana S. Efficacy of Ethyl Chloride Spray versus Subcutaneous 1% Lidocaine Injection for Relieving the Pain of One-rod Contraceptive Implant Removal: A single-blinded randomized controlled trial. Thai Journal of Obstetrics and Gynaecology. 2021:82-91.