EMLA Cream and Intraperitoneal Lidocaine Decrease Intraoperative Pain During Postpartum Tubal Sterilization

SHUSEE VISALYAPUTRA, M.D.*,
PREMRUDEE ARIYANON, M.D.**,
LUDDA PERMPOLPRASERT, B.Sc.*,
UMAPORN LATTHIKAVIBOON, B.Ed.**,
TAWEESAK SANTIVARANGKANA, M.D.*,
NUCHSAROCH PETHPAISIT, M.D.*,
SUDTA PARAKKAMODOM, B.N.*,
PARICHAD APIDECHAKUL, B.Sc.*,
ATICHA LIMSAKUL, M.D.*,
PREYAPA SIRILERTMAKASAKUL, B.N.**

Abstract

We conducted a randomized, double blinded, placebo controlled trial to evaluate the effectiveness of EMLA cream together with intraperitoneal lidocaine for pain relief in postpartum tubal ligation. In a factorial designed study, 90 postpartum patients were randomly assigned to have 5 g of EMLA or placebo cream applied to the skin in 2 groups of 45 patients and to have intraperitoneal instillation of 20 ml of either 1 per cent, 2 per cent lidocaine or normal saline in 3 groups of 30 patients. A numerical rating pain score (0-10) was used during skin check, skin infiltration and uterine tube manipulation. The pain scores were significantly lower in the EMLA group as compared with the placebo group during the skin forceps check ($p<0.001$) and during local skin infiltration ($p<0.05$). The pain scores were also significantly lower during intraabdominal manipulation in the group using either 1 per cent or 2 per cent intraperitoneal lidocaine as compared with the group using normal saline ($p<0.001$), but no difference was found between the groups using 1 per cent and 2 per cent lidocaine.

Implications : Five g of EMLA cream applied to the skin together with 20 ml of 1 per cent lidocaine instilled into the abdominal cavity effectively decrease intraoperative pain in patients undergoing postpartum tubal sterilization under local anesthesia.

Key word : EMLA Crem, Intraperitoneal Lidocaine, Tubal Sterilization, Local Anesthesia

VISALYAPUTRA S, PETHPAISIT N, ARIYANON P, et al
J Med Assoc Thai 2002; 85 (Suppl 3): S942-S947

* Department of Anesthesiology,
** Department of Obstetric and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Evidence indicates that low resource settings have maintained an excellent safety record for tubal sterilization performed under local anesthesia (1). How ever, local anesthesia, with a lower risk of complications, lower cost and a shorter recovery time as compared with major regional or general anesthesia, provides inadequate pain relief. Although instilling 80 ml of 0.5 per cent lidocaine in to the abdominal cavity effectively decreases intra-operative pain during postpartum tubal ligation(2,3), patients still have pain during local skin infiltration. And sometimes, this large volume of 80 ml may interfere with locating the uterine tubes.

EMLA cream, a eutectic mixture of lidocaine and prilocaine cream, (Astra Zeneca, Bangkok, Thailand) is widely use to alleviate skin pain in both adults(4-8) and children(9,10). Its use in postpartum tubal ligation has not been reported. The objective of this study was to evaluate whether EMLA cream applied to the skin together with intraperitoneal instillation of 20 ml of either 1 per cent lidocaine or 2 per cent lidocaine can effectively decrease pain in postpartum tubal sterilization performed under local anesthesia.

METHODS

We performed a randomized, double-blinded, placebo controlled, factorial designed study to answer two research questions with a small but adequate sample size. Patients were ASA physical status I or II who agreed to undergo postpartum tubal sterilization within 48 h of delivery under local anesthesia. Patients with a history of pelvic inflammatory disease, liver disease, allergy to local anesthetics, or a body mass index >32 kg/m^2 were excluded from the study. After approval of the hospital ethics committee, 90 patients gave their written informed consent and were randomly divided into 6 groups of 15 patients to have either EMLA (E) or placebo (P) cream applied to the skin in each 3 of 6 groups (total 45 patients received EMLA, 45 patients received placebo). 2 out of 6 groups received a 20 ml intraperitoneal instillation of either normal saline (NS) or 1 per cent lidocaine (L1) or 2 per cent lidocaine (L2), (gr. ENS, EL1, EL2, PNS, PL1 and PL2).

During the preoperative visit, the patients were asked to practice scoring their pain verbally using the numerical rating score (NRS). Pain was rated on a scale of 0-10 (0 = no pain at all, 10 = the most severe pain). About 2 h before the operation, either 5 g of EMLA or placebo cream were applied to the skin area just below the umbilicus over an area measuring 3 x 1.5 inch to cover the incision line which had been previously marked by the obstetrician who was our coinvestigator and was the only one who performed the operations. The cream was then sealed with a plastic covering (Tegaderm, 3M Health Care, Bangkok, Thailand) and was wiped off two hours later. Patients were then brought into the operating room where an IV infusion of Ringer's Lactate solution was started and noninvasive monitoring (electrocardiogram, automated blood pressure and pulse oximetry) was begun. The evaluator was allowed to enter the operating room only after the skin had been scrubbed and covered so that she remained "blind" to whether EMLA or placebo had been used because of the change in color of the skin that can be seen when using EMLA. Skin numbness was checked by pinprick, followed by a forceps pinching. Patients were asked to rate the NRS during the skin check. If the NRS score ≥3, 10 ml of 1 per cent lidocaine was infiltrated into the skin and subcutaneous tissue. Since we did not expect an analgesic effect of EMLA to the sheath and peritoneum, another 5 ml of 1 per cent lidocaine was injected beneath the sheath in every patient. After the abdominal cavity was opened, either 20 ml of NS or 1 per cent lidocaine or 2 per cent lidocaine was instilled into the abdominal cavity. The abdominal opening was lifted to allow 10 ml of the solution to be instilled to each side of the adnexa with a 20-ml syringe without a needle. After waiting 1 minute, the surgeon started searching for the uterine tubes, and the patient was asked to rate the pain using the verbal NRS. If the pain score was <3, no rescue drugs were given. If it was ≥3, initially IV fentanyl 1 μg/kg was given up to 2 μg/kg. Patients who had pain scores of 3-5 received only fentanyl. If pain score ≥6, initially iv ketamine 0.5 mg/kg was given, up to 2 mg/kg if needed. If the surgery could not be performed after the administration of ketamine, general anesthesia with endotracheal intubation would be given.

In the recovery room, vital signs were observed for 2 h after surgery. On the postpartum ward, paracetamol (two 500-mg tablets) was administered every 4 h if the patient required pain relief. Side effects such as nausea, vomiting, fever, or urinary retention were observed and recorded until the patient was discharged, which was usually within 48 hours.

The results of the pilot study were used to estimate the sample size for the current study (n = 90) based on a power of 0.8 and a type I error probability of 0.05. Differences among continuous outcome variables were tested by using a student *t*-test for the comparison of 2 groups and one- way analysis of variance for the comparison of 3 groups. Post hoc pairwise comparisons were conducted using the Bonferroni correction to adjust for multiple comparisons. The χ^2 test was used to test association of categorical variables and the Kruskal-Wallis test was used for ranked variables and when variables had nonparametric distributions.

RESULTS

There were no significant differences in demographic characteristics between the two groups. The duration of applying EMLA cream and the duration of surgery were similar (Table 1). The mean NRS during the needle and forceps check was significantly lower (p<0.001) in the group using EMLA cream (0.9 and 1.46) compared to the placebo group (1.7 and 4.6 respectively). About 65 per cent of the patients in the EMLA group did not require local skin infiltration as compared with 0 per cent of the patients in placebo group (p<0.001). The mean NRS during local infiltration was significantly lower (p< 0.05) in the 16 patients in the the EMLA group who needed local infiltration (4.6) as compared with 45 patients in the placebo group (6.2) and only 17.8 per cent of the patients in the EMLA group had NRS ≥5 during local infiltration, as compared with 80 per cent in the placebo group (p<0.001), (Table 2). There were no significant differences in demographic characteristics among the three groups of 30 patients (Table 3). The intraabdominal NRS pain score means the highest intraperitoneal NRS rated at searching, picking up and occlusion of both uterine tubes if ketamine was not given, or it was the highest NRS rated before ketamine was given. The mean intraabdominal NRS was significantly lower (p<0.001) in both groups using lidocaine (2.5 and 2.1 in group 1 per cent and group 2 per cent, respectively) than in the group using NS (5.2), but there were no signi-

Table 1. Demographic characteristics, duration of application of EMLA and duration of surgery.

	Placebo cream (45)	EMLA cream (45)
Age (yr)	29.4 ± 4.8	29.7 ± 4.7
Weight (kg)	63.5	62.5
Height (cm)	155.6 ± 4.7	156.9 ± 5.7
BMI (kg/m2)	26.5 ± 3.7	25.5 ± 3.9
EMLA time (min)	143.4 ± 31.5	137.2 ± 33.1
Duration of Surgery (min)	19.6 ± 6.3	18.9 ± 6.5

Values are mean ± SD

Table 2. Numerical rating score (NRS), patients requiring rescue drugs, and patients with a NRS ≥5.

	Placebo Cream(45)	EMLA Cream(45)	P
NRS during needle check	1.75 ± 1.8	0.91 ± 0.1	<0.001
NRS during forceps check	4.64 ± 2.5	1.46 ± 1.9	<0.001
Patients with NRS <3	0 (0)	29 (64.5)	<0.001
Patients with NRS ≥5	36 (80)	8 (17.8)	<0.001
NRS during local infiltration (no = 45 : 16)	6.2 ± 2.1	4.6 ± 1.9	<0.05
NRS during skin incision	1.0 ± 1.4	1.3 ± 1.4	0.32
NRS during sheath incision	1.9 ± 1.7	2.8 ± 2.7	0.21
Postoperative paracetamol use (tablets)	5.6 ± 2.9	5.1 ± 2.7	0.41

Value are mean ± SD or n (%)
(If NRS <3 = not required local infiltration, NRS ≥5 = in moderate to severe pain)

Table 3. Demographic characteristics and duration of surgery.

	Group NS (30)	Group 1% Lidocaine (30)	Group2%Lidocaine (30)
Age (yr)	30.3 ± 5.0	28.6 ± 4.6	29.8 ± 4.5
Weight (kg)	65.1 ± 10.1	61.4 ± 8.0	62.3 ± 9.7
Height (cm)	157.1 ± 5.1	155.4 ± 4.9	156.4 ± 4.8
BMI (kg/m^2)	26.6 ± 4.1	25.4 ± 3.3	25.8 ± 4.0
Duration of surgery (min)	22.2 ± 8.8	17.7 ± 4.5	17.9 ± 3.7

Values are mean ± SD

Table 4. Numerical rating score (NRS), patients requiring rescue drugs, and postoperative paracetamol use.

	Group NS (30)	Group 1% Lidocaine (30)	Group 2% Lidocaine (30)	P
Intraabdominal NRS pain scores(0-10)	5.2 ± 3.0	2.5 ± 2.3	2.1 ± 2.0	<0.001
Patients requiring fentanyl	9 (30)	6 (20)	5 (16.6)	0.434
Patients requiring ketamine	20 (66.7)	2 (6.7)	0 (0)	<0.001
Postop. Paracetamol use (tablets)	5.6 ± 2.6	4.8 ± 3.2	5.4 ± 2.8	0.48

Values are mean ± SD or n (%)

ficant differences in mean intraabdominal NRS between the 1 per cent group and the 2 per cent group. The percentages of patients who required ketamine were significantly lower ($p<0.001$) in both groups using lidocaine (6% and 0%) than the group using NS (66%). There were no differences in the proportions of patients who required fentanyl and no patients needed general anesthesia with intubation (Table 4).

The hemodynamic changes, indicated by systolic, diastolic blood pressure and heart rate measuring during the operation, showed no differences among the three groups. There were no clinical differences in observed side effects. Vomiting occurred in 5, 3 and 6 patients in the NS group, the 1 per cent group and the 2 per cent group respectively. During the postoperative period, the paracetamol tablet requirement was not significantly different between the 3 groups.

DISCUSSION

The results in Table 2 demonstrate that EMLA cream is an effective analgesic for local skin infiltration. Our study agrees with other studies, which used EMLA cream for skin anesthesia[4-10]. Browne J, et al.[4] reported that EMLA significantly reduced pain associated with digital ring block for ingrowing toenail correction. In our study, 64.5 per cent of the patients needed no local infiltration. Gupta and Sibbald[8] demonstrated that EMLA cream provided effective anesthesia for excisional biopsy of cutaneous lesions in 87 per cent of the patients. Other than the differences in surgical procedure, their study was done in both male and female up to 90 years old, who usually have higher pain threshold compared with the female patients in our study. Lander, et al. [11] demonstrated that factors which predicted success or failure of EMLA included the type of procedure, the duration of application and anxiety. We applied EMLA cream for 2 h because it has been demonstrated that adequate cutaneous analgesia at a depth of 1-2, 2-3 or 6 mm can be made by applying EMLA cream for 60, 120 or 3-4 h respectively[12]. The maximal depth of analgesia (approx 5 mm) was also observed for a 30 and a 60 min period after a 90 and 120 min application of EMLA cream respectively[13].

The results in Table 4 demonstrate that 20 ml of intraperitoneal lidocaine either 1 per cent or 2 per cent is effective for intraabdominal pain relief. The effectiveness of pain relief in this study confirms the results of previous studies[5,6] that used 80 ml of a 0.5 per cent. solution. As compared with 80 ml of the solution, 20 ml would obscure less of the operative field. The maximal dosage of lidocaine used in this study was 550 mg, which is similar to the 550 mg used in our previous study and 500 mg used by Deep and Viechnicki[14]. The highest mean plasma lidocaine concentration in our previous study,

2.7 μg/ml[2] was similar to the level of 2.2 μg/ml reported by Deep and Viechnicki. Ryan, et al.[15] reported that the level of lidocaine that caused a convulsion in a child during cardiac catheterization was 8.7 μg/ml, although non-life threatening signs of toxicity, such as light headness, tinnitus or circumoral numbness were seen at 4 μg/ml, and muscle twitching at 8 μg/ml[16]. Since the plasma lidocaine concentration in previous studies[2,14] using the same dosage of lidocaine as this study was far below that considered to be toxic, although the different volumes used might produce a different rate of absorption, plasma lidocaine levels in this study should still be within a safe range.

The few side effects observed in our patients included a few cases of nausea-vomiting, which was most likely due to fentanyl usage. One case of ileus occurred in each group of patients which is unlikely to have been caused by lidocaine. Although Cruikshank, et al[3] observed 2 cases of urinary retention, it was not found in our study.

Ketamine was used in 2 cases of the group using 1 per cent lidocaine, this was probably due to the low pain threshold of the individual patient or the unexpected difficulty in finding the uterine tube. Although ketamine expected side-effects[17], it should be explained to the patient that intraperitoneal lidocaine may not be effective and that fentanyl or ketamine may be needed in addition.

After the intraperitoneal lidocaine instillation, we waited for 1 minute before starting to search for the uterine tubes, instead of the 3 minutes in our previous study[2]. However, to know the exact onset and duration of the intraperitoneal lidocaine anesthesia, further study is needed. Since there was no significant differences in the NRS pain scores or the requirement for rescue drugs between the groups using 1 per cent or 2 per cent lidocaine, 1 per cent lidocaine should be selected for intraperitoneal pain relief.

In conclusion, EMLA cream applied to the skin together with 20 ml of 1 per cent lidocaine instilled into the abdominal cavity is a safe, effective and easy technique that should be used to decrease suffering in patients who undergo postpartum tubul sterilization under local anesthesia.

(Received for publication on 6 May 2002)

REFERENCES

1. Pati S, Cullins V. Female sterilization. Evidence. Obstet Gynecol Clin North Am 2000; 27: 859-99.
2. Visalyaputra S, Lertakkyamanee J, Pethpaisit N, et al. Intraperitoneal lidocaine decreases intraoperative pain during postpartum tubal ligation. Anesth Analg 1999; 88: 1077-80.
3. Cruikshank DP, Laube DW, De Backer LJ. Intraperitoneal lidocaine anesthesia for postpartum tubal ligation. Obstet Gynaecol 1973; 42: 127-30.
4. Browne J, Fung M, Donnelly M, Cooney C. The use of EMLA reduces the pain associated with digital ring block for ingrowing toenail correction. Eur J Anaesthesiol 2000; 17: 182-4.
5. Koscielniak NZ, Hesselbjerg L, Brushoj JJ, Pederson HS. EMLA patch for spinal puncture. A comparison of EMLA patch with lignocaine infiltration and placebo patch. Anaesthesia 1998; 53: 1218-22.
6. Joly LM, Spaulding C, Monchi M, et al. Topical lidocaine - prilocaine cream (EMLA) *versus* local infiltration anesthesia for radial artery canulation. Anesth Analg 1998; 87: 403-6.
7. Tschaikowsky K, Hemmerling T. Comparison of the effect of EMLA and semicircular subcutaneous anaesthesia in the prevention of tourniquet pain during plexus block anaesthesia of the arm. Anaesthesia 1998; 53: 390-3.
8. Gupta AK, Sibbald RG. Eutectic lidocaine/prilocaine 5 per cent cream and patch may provide satisfactory analgesia for excisional biopsy or curettage with electrosurgery of cutaneous lesions. A randomized, controlled, parallel group study. J Am Acad Dermatol 1996; 35: 419-23.
9. Gall O, Annequin D, Ravault N, Murat I. Relative effectiveness of lignocaine/prilocaine emulsion and nitrous oxide inhalation for routine pre-operative laboratory testing. Paediatr Anaesth 1999; 9: 305-10.
10. Taddio A, Ohlsson A, Einarson TR, et al. A systemic review of lidocaine/prilocaine (EMLA) in acute pain in neonates. Pediatrics 1998; 101: E1.
11. Lander J, Hodgins M, Nazarali S, et al. Determinants of success and failure of EMLA. Pain 1996; 64: 89-97.
12. Wahlgren CF, Quiding H. Depth of cutaneous analgesia after application of a eutectic mixture

of the local anesthetics lidocaine and prilocaine (EMLA cream). J Am Acad Dematol 2000; 42: 584-8.
13. Bjerring P, Arendt-Nielsen L. Depth and duration of skin analgesia to needle insertion after application of EMLA cream. Br J Anaesth 1990; 64: 173-7.
14. Deep JR, Viechnicki MB. Laparoscopic tubal ligation under peritoneal lavage anesthesia. Reg Anesth 1985; 10: 24-7.
15. Ryan CA, Robertson M, Coe JY. Seizures due to lidocaine toxicity in a child during cardiac catheterization. Pediatr Cardiol 1993; 14: 116-8.
16. Cass N, Cass L. Pharmacology for anaesthetists. Edinburgh: Churchill Livingstone, 1994: 116.
17. Weerasekera DS, Gunawardene KK. Ketamine as an anesthetic agent for tubal sterilization. Ceylon Med J 1996; 41: 102-3.

ประสิทธิผลของเอมลาครีมและการใส่ลิโดเคนเข้าช่องท้องในการระงับปวดขณะผ่าตัดทำหมันหลังคลอด

ชูศรี พิศลยบุตร, พ.บ., นุชสโรช เพ็ชรไพศิษฏ์, พ.บ.*, เปรมฤดี อริยานนท์, พ.บ.**, สุตตา ปรักกโมดม, พย.บ.*, ลัดดา เพิ่มผลประเสริฐ, วท.บ.*, ปาริชาติ อภิเดชากุล, วท.บ.*, อุมาพร ลัฐิกาวิบูลย์, ค.บ.**, อาทิชา ลิ่มสกุล, พ.บ.*, ทวีศักดิ์ ศานติวรางคณา, พ.บ.*, ปรียาภา สิริเลิศเมฆาสกุล, พย.บ.***

เพื่อศึกษาประสิทธิผลของการใช้ EMLA cream ร่วมกับการใส่ยาชา lidocaine เข้าช่องท้องเพื่อระงับปวดจากการผ่าตัดทำหมันหลังคลอดโดยวิธีสุ่ม ปกปิดสองทาง และควบคุมโดยยาหลอก ผู้ป่วยหลังคลอดจำนวน 90 คนถูกแบ่งโดยวิธี factorial ออกเป็น 2 กลุ่ม ๆ ละ 45 คน เพื่อรับ EMLA cream หรือ placebo cream ขณะเดียวกันถูกแบ่งออกเป็น 3 กลุ่ม ๆ ละ 30 คนเพื่อรับ 1% lidocaine, 2% lidocaine หรือน้ำเกลือนอร์มัล จำนวน 20 มล. ใส่ลงในช่องท้องก่อนการหยิบจับตัดท่อรังไข่ การวัดคะแนนความเจ็บปวดใช้ numerical rating score (0–10) ทำในขณะตรวจเช็คความรู้สึกที่ผิวหนัง ขณะฉีดยาชาที่ผิวหนังและขณะทำผ่าตัดบริเวณท่อรังไข่ ผลพบว่าคะแนนความเจ็บปวดขณะตรวจเช็คความรู้สึกที่ผิวหนังด้วย forceps ในกลุ่มที่ใช้ EMLA cream ต่ำกว่ากลุ่มที่ใช้ placebo cream อย่างมีนัยสำคัญทางสถิติ ($p<0.001$) และขณะฉีดยาชาที่ผิวหนัง ($p<0.05$) นอกจากนี้คะแนนความเจ็บปวดขณะตัดท่อรังไข่ในกลุ่มที่ใส่ยาชา lidocaine เข้าช่องท้องก็ต่ำกว่ากลุ่มที่ใช้น้ำเกลือนอร์มัล ($p<0.001$) อย่างไรก็ตามไม่มีความแตกต่างระหว่างกลุ่มที่ใช้ยาชา 1% หรือ 2% lidocaine ใส่เข้าช่องท้อง

สรุปได้ว่า การใช้ EMLA cream 5 กรัมทาบริเวณผิวหนังที่จะผ่าตัดร่วมกับการใช้ 1% lidocaine 20 มล. ใส่ลงในช่องท้องมีประสิทธิผลดีในการลดความเจ็บปวดขณะทำผ่าตัดในผู้ป่วยที่มาทำหมันหลังคลอด

คำสำคัญ : เอมลาครีม, การผ่าตัดทำหมันหลังคลอด, การใส่ลิโดเคนเข้าช่องท้อง

ชูศรี พิศลยบุตร, นุชสโรช เพ็ชรไพศิษฏ์, เปรมฤดี อริยานนท์, และคณะ
จดหมายเหตุทางแพทย์ ฯ 2545; 85 (ฉบับพิเศษ 3): S942–S947

* ภาควิชาวิสัญญีวิทยา,
** ภาควิชาสูติศาสตร์–นรีเวชวิทยา, คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10700