

## Both EMLA and Placebo Cream Reduced Pain during Extracorporeal Piezoelectric Shock Wave Lithotripsy with the Piezolith 2300

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**Background:** The objectives were to determine whether a eutectic mixture of local anesthetic (EMLA) or placebo cream reduces pain during extracorporeal piezoelectric shock wave lithotripsy (EPSWL), and to determine which of the components of the application (*i.e.*, the occlusive dressing, the cream, or the local anesthetic) contributes to analgesia.

**Methods:** A randomized, double blind, crossover study (part 1) was performed in 12 patients who were scheduled for EPSWL procedures on an ambulatory basis who received the first treatment without any intervention and who had verbal pain scores of 70 or more (on a 0-to-100 scale). For the next two treatments at 2-week intervals, patients were randomly assigned to receive either 10 g EMLA or 10 g placebo cream and then crossed over to receive the other. The cream and occlusive dressing were left in place and immersed in water throughout the procedure. Verbal numeric pain score was assessed at 5 min after receiving the maximal tolerable intensity of shock wave and at the end of the procedure. The study continued (part 2) in 202 ambulatory patients; 125 men and 77 women, American Society of Anesthesiologists physical status I and II, subjected to EPSWL were randomly allocated into five groups who received (1) nothing on the skin (control), (2) plastic occlusive dressing, (3) placebo cream and plastic occlusive dressing, (4) EMLA cream and plastic occlusive dressing, (5) EMLA cream and plastic occlusive dressing for 60 min to achieve cutaneous anesthesia, which was

removed before EPSWL. Pain score was evaluated 10 min into the procedure and at the end of the procedure.

**Result:** Both parts of the study showed that patients who received either EMLA or placebo cream with dressing throughout the procedure experienced less pain and tolerated higher energy levels compared with the control. Patients who received only pre-EPSWL cutaneous anesthesia of EMLA and who received only the occlusive dressing did not have a reduction in pain score.

**Conclusions:** EMLA and placebo creams under occlusive dressing reduced pain during EPSWL. The presence of the cream itself as a coupling medium contributed to analgesia. This may be a useful, simple, safe, and economical adjuvant technique to reduce pain during immersion EPSWL. (Key words: Ambulatory; anesthesia; renal stone; topical; treatment.)

TREATMENT with the third-generation piezoelectric lithotripter has been described as painless.<sup>1-5</sup> However, 28% of patients experienced severe pain when undergoing the treatment without anesthesia.<sup>6</sup> A eutectic mixture of local anesthetic (EMLA) cream (2.5% lidocaine, 2.5% prilocaine) provides sufficient topical anesthesia to perform superficial skin surgery, split-thickness skin grafting, and even circumcision.<sup>7-9</sup> The objectives of the study were to determine whether EMLA cream under a plastic occlusive dressing reduces pain during extracorporeal piezoelectric shock wave lithotripsy (EPSWL), and, if so, which component (cutaneous anesthesia, the cream, or the occlusive dressing) contributes to analgesia.

## Materials and Methods

### Part 1

This randomized, double blind, crossover design was approved by the institutional review board of Siriraj Hospital, Mahidol University. After obtaining informed consent, 12 patients (American Society of Anesthesiologists physical status I-II) with large renal stones scheduled for multiple EPSWL procedures performed on an ambulatory basis (anticipated at least three treatments)

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using a Wolf Piezolith 2300 Shock Wave Lithotripter (Richard Wolf GmbH, Hamburg, Germany) were evaluated. These patients received the first treatment without any intervention and reported pain scores of 70 or more (on a 0-to-100 scale). Only patients whom urologists evaluated by renal stone size, location, and the response to the first treatment, who would need at least two more treatments were approached and recruited after the first treatment. For the next two treatments, they were randomly allocated to receive either EMLA or placebo cream of identical physical characteristics (consistency, color, and smell) and then crossed over to receive either placebo or EMLA cream 2 weeks apart. Both creams were kept in identical tubes with code numbers. Doctors, nurses, and patients were blind to the content of the tubes. The codes were broken at the end of the study for statistical analysis.

Ten grams EMLA or placebo cream from identical 10-g tubes was applied on the skin of the flank at the area of entry of the shock wave marked by the urologist. The cream was spread 2 or 3 mm thick and covered an area of approximately  $5 \times 7$  cm. An occlusive plastic sheet (Steri Drape; 3M, St Paul, MN) was applied over the area. Meticulous attention was given to avoid air bubbles trapped under the occlusive dressing. The cream was applied for at least 60 min before starting the treatment to allow the local anesthetics to penetrate the skin and produce cutaneous anesthesia. The applied cream with the occlusive plastic dressing was immersed in the water and was left in place throughout the procedure and removed after the completion of the treatment.

There are four levels of EPSWL intensity used with the Piezolith 2300. The shock wave energy at the acoustic focus of intensity 1 is 31 Mpa (310 bar), intensity 2 is 40 megapascals (Mpa; 400 bar), intensity 3 is 62 Mpa (620 bar) and intensity 4 is 102 Mpa (1020 bar).<sup>3</sup> The frequency of the shock wave is 1.5–1.7 shock/s. The lithotripsy treatment started with intensity 1 and increased to intensities 2 and 3 within 5 min, then increased to intensity 4 and, if pain was tolerable, continued until the completion of 4,000 shocks. If pain was intolerable, the shock wave intensity after receiving the maximal intensity 4 for 5 min was decreased to intensity 3, and if it still was intolerable, 50  $\mu$ g intravenous fentanyl was administered. Numeric verbal pain scale of 0–100 (no pain = 0, the most severe pain = 100) was used to evaluate pain when patients received 5 min of shock wave intensity 3 and 5 min of intensity 4 and at the end of the treatment. Pain score was evaluated by an assistant who was blind to the content of the cream.

### Part 2

The study was a randomized controlled trial and was approved by the institutional review board of Siriraj Hospital, Mahidol University. Two hundred two adult patients who were American Society of Anesthesiologists physical status I–II and scheduled for EPSWL using the Piezolith 2300 lithotripter on an ambulatory basis (regardless of the number of treatments) participated in the study. After obtaining informed consent, they were randomized into one of five groups. Group A (control) received no intervention (nothing to the skin). Group B received a plastic occlusive dressing (Tegaderm; 3M) applied to the skin at the shock wave entry site and immersed in water. Group C received 10 g placebo cream, and groups D and E received 10 g EMLA cream covered by a plastic occlusive dressing for at least 60 min before the start of EPSWL. The dressing in group E was removed just before EPSWL. The plastic occlusive dressings in groups B, C, and D remained in place and immersed in water during EPSWL treatment and were removed after the completion of the procedure.

No premedication was administered to any patient in either part of the study. EPSWL was performed in the same manner as in part 1. Pain was evaluated at 10 min (after 5 min of maximum shock wave intensity) and at the end of the procedure using a verbal numeric score, as in part 1.

The sizes of renal stone on the plain radiograph of the abdomen were measured in square millimeters by a clear plastic sheet of  $1 \times 1$  mm grid before EPSWL and 2 weeks after. The difference in sizes before and after treatment was used to compare the effectiveness of EPSWL in reducing stone size among different groups. After EPSWL, the number of days of frank hematuria; the presence or absence of chill, nausea, or vomiting; and the presence and severity of post-treatment abdominal colic, deep pain on the flank, and cutaneous tenderness were recorded.

### Statistical Analysis

The standard deviation of pain scores from part 1 of the study was used to plan the sample size of part 2. Because pain scores in the EMLA and placebo groups were significantly lower than in the control group, the calculated sample size was very small. Because part 1 was performed in patients who had previous pain scores of 70 or more, the sample size of each group in patients in part 2 were increased to 40 to compensate for patients who had all ranges of pain.

A paired *t* test was used to compare pain scores in part

# EMLA AND PLACEBO CREAMS REDUCED PAIN IN EPSWL

**Table 1. Pain Scores at 5 min after EPSWL at Intensity 3, 4, and at the End of EPSWL in the Control, EMLA, and Placebo Groups, and Number of Patients Who Tolerated Maximum-Intensity Shock Wave until Completion of the Treatment (Part 1)**

	Control (n = 12)	EMLA (n = 12)	Placebo (n = 12)
Pain score			
Intensity 3	62 ± 10	25 ± 7**	44 ± 11*
Intensity 4	83 ± 6	46 ± 21*	54 ± 19*
At end of the procedure	82 ± 5	43 ± 24**	46 ± 23**
Number tolerated maximum intensity	6	12	12

Data are mean ± SD.

\*  $P < 0.01$ .

\*\*  $P < 0.001$  compared with control.

EMLA = eutectic mixture of local anesthetics; EPSWL = extracorporeal piezoelectric shock wave lithotripsy.

1. In part 2, after testing of homogeneity of variances using the Levene statistics and Komologov-Smirnov goodness-of-fit test for normal distribution, continuous variables (*i.e.*, age, weight, and pain scores) were compared using analysis of variance. If there were statistically significant differences among groups, then the Dunnett *t* test (one-sided) was used to compare pain scores by treating group A as a control and to compare all other groups (B, C, D, and E) against it. The chi-square test was used for comparing discrete variables and the Kruskal-Wallis test was used for comparing rank data. A *P* value less than 0.05 was considered to be statistically significant.

## Results

### Part 1

Eight men and four women, aged 23–67 yr (mean, 41 ± 13 years) participated in the study. The size of renal

stones measured on the plain abdominal film ranged from 1 × 2 to 1.5 × 4 cm. All patients completed the three treatments and received 4,000 shocks/treatment. The duration of each treatment was 35–45 min (mean, 41 ± 3 min). Pain scores in the EMLA and placebo groups were significantly lower than the control scores, as shown in table 1. All patients in the EMLA and placebo groups, but only 6 of 12 in the control group, tolerated the maximum intensity shock wave. Two patients (control group) required supplemental analgesia (fentanyl).

### Part 2

In this study, 125 men and 77 women participated. There were no differences among groups regarding demographic data, stone sizes, and procedure duration, as presented in table 2. Pain scores are shown in table 3. Pain scores in groups C and D were significantly lower than in group A after 10 min of the treatment, but, at the end of the procedure, only group C had lower pain scores than the control group A. Application of EMLA or placebo resulted in fewer patients having severe pain. Seventy patients (34.6%) requested and received reduced-intensity shock waves. Seven patients among these could not even tolerate shock wave intensity 3, and the intensity had to be reduced to intensity 2 until completion of EPSWL. Of these seven patients, four were from group A, two from group E, and one from group B. None were in groups C or D. None of the patients in any group received intravenous rescue analgesic. The incidence of inability to tolerate maximum shock wave intensity during the procedure did not differ between groups.

There were no differences among the five groups regarding the size of renal stone measured on the plain films before and after the treatment and the difference between them (table 2).

There was no difference in the side effects and oral

**Table 2. Demographic Data, Duration of EPSWL, Size and Differences between Renal Stone before and after EPSWL (Part 2)**

	Group A (n = 41)	Group B (n = 42)	Group C (n = 41)	Group D (n = 39)	Group E (n = 39)
No. of men (%)	24 (59)	24 (57)	27 (66)	26 (67)	24 (62)
Age (yr)	41 ± 9	39 ± 11	41 ± 10	38 ± 12	38 ± 11
Weight (kg)	60 ± 10	61 ± 10	62 ± 10	59 ± 9	60 ± 10
Duration (min)	36 ± 5	36 ± 5	37 ± 5	37 ± 5	38 ± 7
Renal stone before (mm <sup>2</sup> )	30 ± 19	42 ± 24	29 ± 17	32 ± 23	32 ± 22
Renal stone after (mm <sup>2</sup> )	17 ± 15	27 ± 24	15 ± 12	18 ± 13	12 ± 10
Size reduction of stone (mm <sup>2</sup> )	13 ± 10	15 ± 10	14 ± 11	14 ± 9	20 ± 16

Data are mean ± SD.

EPSWL = extracorporeal piezoelectric shock wave lithotripsy.

responsible for analgesia. Unfortunately, absence of a no-treatment control group made it impossible to determine whether the observed reduction in pain scores at follow-up EPSWL was related to the creams or was simply because a second subsequent EPSWL is intrinsically less painful. A previous study showed that pain scores in the second treatment did not differ from pain scores in the first treatment.<sup>6</sup> We continued the study to determine which component of the application (*i.e.*, the occlusive dressing, the placebo cream, the EMLA cream, or the topical cutaneous anesthesia) contributes to analgesia.

The result of part 2 confirmed that patients who received either the placebo cream (group C) or the EMLA cream (group D) with occlusive dressing immersed in water during EPSWL had lower pain scores than the control patients who received nothing on the skin (group A). The nondifference in pain scores between group A (control) and groups B (plastic occlusive dressing alone) and E (cutaneous anesthesia) suggested that the plastic occlusive dressing and the topical cutaneous anesthesia effect of EMLA cream *per se* did not provide analgesia for this procedure. The presence of the carrier cream as the only common factor in group C and group D and its absence in group B and group E suggests that the carrier cream is the component responsible for analgesia.

The principle of acoustic shock wave physics provides a likely explanation of the mechanism of this analgesia. During ESWL and EPSWL, shock waves travel from the source through water, skin, soft tissue, renal parenchyma, and then the renal stone at the acoustic focus. As the wave continues through the media, it follows acoustic principles.<sup>18,19</sup> As the wave passes from one medium to another with different acoustic conductance, there is reflection, absorption, and transmission of shock wave energy at the interface between the media. Acoustic impedance is a characteristic of a medium and is equal to the product of density and sound velocity. The larger the difference of the acoustic impedance between the two adjacent media, the greater the reflection and absorption of energy at the interface. At the water-skin interface, reflection and absorption of the shock wave causes skin trauma, contusion, and superficial pain of the skin. When EMLA cream or placebo cream was applied under an occlusive dressing and was left in place and immersed in water, the cream became a coupling medium. The acoustic impedance of the cream is nearer to that of skin than that of water to skin. At the cream-skin interface, there is less reflection and absorption of shock wave

energy than at the water-skin interface and, hence, less pain, less skin trauma, and more energy transmission through skin to soft tissue and kidney and renal stones.

There are several limitations in the application of the result of the study to clinical use. The study was performed in patients treated with the third-generation Piezolith 2300, which causes less pain and does not necessitate general or regional anesthesia. It may not be readily applicable to patients treated with the first- or the second-generation lithotriptors (*e.g.*, the Dornier lithotripter [Marietta, GA], which causes severe pain and necessitates either general or regional anesthesia).<sup>18</sup> For the third-generation lithotripter, patients with a low pain threshold and who experienced severe pain during previous treatment may benefit from the application of cream and occlusive dressing and may have a greater reduction in pain scores than a patient who experienced only mild to moderate pain.

Side effects of lithotripsy did not receive attention from surgeons or the anesthesiologist. This is similar to postoperative pain a few decades ago. Even the third-generation lithotripter causes a high incidence of hematuria, abdominal colic, deep flank pain, skin tenderness, shivering, nausea, and vomiting. More attention and further study is necessary to alleviate the suffering of patients.

In conclusion, this study showed that the EMLA and placebo creams under an occlusive dressing reduce pain during EPSWL. The local cutaneous anesthetic effect of EMLA cream is less important than the effect of the cream itself, which may function as a coupling medium, thereby reducing pain. Although the difference in pain scores was marginal, this could increase dramatically in a select group of patients who had high pain scores, and further study is now planned. The use of a coupling medium is a useful adjuvant during an immersion lithotripsy procedure. It may provide a simple, safe, economical technique to reduce pain in select patients during EPSWL and ESWL without causing side effects.

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## References

1. Spirnak JP, Bodner D, Udayashankar S, Resnick M: Extracorporeal shock wave lithotripsy in traumatic quadriplegic patients: Can it be safely performed without anesthesia? *J Urol* 1988; 139:18-9

2. Knudsen F, Jorgensen S, Bonde J, Andersen JT, Mogensen P: Anesthesia and complication of extracorporeal shock wave lithotripsy of urinary calculi. *J Urol* 1992; 148:1030-3
3. Marberger M, Turk C, Steinkogler I: Painless piezoelectric extracorporeal lithotripsy. *J Urol* 1988; 139:695-9
4. Marberger M, Turk C, Steinkogler I: Piezoelectric extracorporeal shock wave lithotripsy in children. *J Urol* 1989; 142:349-52
5. Vallancien G, Aviles J, Munoz R, Veillon B, Charton M, Brisset JM: Piezoelectric extracorporeal lithotripsy by ultrashort wave with EDAP LT 01 device. *J Urol* 1988; 139:689-94
6. Tritrakarn T, Lertakyananee J, Tuntiwong A, Raksamani A, Jitrapapai S: Evaluation of pain during extracorporeal piezoelectric lithotripsy with Piezolith 2300. *Thai J Anesthesiol* 1992; 18:15-8
7. Ehrenstrom Reiz GM, Rhiz SLA: EMLA a eutectic mixture of local anaesthetic for topical anaesthesia. *Acta Anaesth Scand* 1982; 26:596-8
8. Juhlin L, Evers H, Broberg A: A lidocaine prilocaine cream for superficial skin surgery and painful lesions. *Acta Dermatovenereol Stockholm* 1980; 60:544-6
9. Tritrakarn T, Raksamani A, Thaosuwan A, Khaowichit S, Thaipratharn A: EMLA cream produce adequate anesthesia to perform circumcision in children. *Reg Anesth* 1992; 17(suppl 3):51
10. Ganapathy S, Razoi H, Moote C, Parkin J, Yee I, Gverzdys S, Dain S, Denstedt J: Eutectic mixture of local anaesthetics is not effective for extracorporeal shock wave lithotripsy. *Can J Anaesth* 1996; 43:1030-4
11. Monk TG, Ding Y, White PF, Albala DM, Clayman RV: Effect of topical eutectic mixture of local anesthetic on pain response and analgesic requirement during lithotripsy procedure. *Anesth Analg* 1994; 79:506-11
12. Bromage PR: Effect of topical eutectic mixture of local anesthetics on pain response and analgesic requirement during extracorporeal shock wave lithotripsy. *Anesth Analg* 1995; 80:1059
13. McDonal PF, Berry AM: Topical anaesthesia for extracorporeal shock wave lithotripsy. *Br J Anaesth* 1992; 69:399-400
14. Lichtenberg MH, Miskowiak J, Mogensen P, Andersen JT: Local anesthesia for extracorporeal shock wave lithotripsy: A study comparing eutectic mixture of local anesthetic cream and lidocaine infiltration. *J Urol* 1992; 147:96-7
15. Bierkens AF, Maes RM, Hendrikx AJM, Erdos AF, Vries JDM, Debruyne FMJ: The use of local anesthesia in second generation extracorporeal shock wave lithotripsy: Eutectic mixture of local anesthetics. *J Urol* 1991; 146:287-9
16. Barcena M, Rodriguez J, Gude F, Vidal MI, Fernandez S: EMLA cream for renal extracorporeal shock wave lithotripsy in ambulatory patients. *Eur J Anaesthesiol* 1996; 13:373-6
17. Tiselius HG: Cutaneous anesthesia with lidocaine prilocaine cream: A useful adjunct during shock wave lithotripsy with analgesic sedation. *J Urol* 1993; 149:8-11
18. Eisenberger F, Miller K, Rasseiler J: Extracorporeal shock wave lithotripsy (ESWL), Stone Therapy in Urology. New York, Thieme Medical Publisher, 1991, pp 29-82
19. Hunter PT: The physics and geometry pertinent to ESWL, Principle of Extracorporeal Shock Wave Lithotripsy. Edited by Ricehlle RA. New York, Churchill Livingstone, 1987, pp 13-27