

THE EFFECTIVITY OF EUTECTIC MIXTURE OF LOCAL ANESTHETICS CREAM AS EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY ADJUVANT ANALGESIA IN SOETOMO GENERAL HOSPITAL

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ABSTRACT

Objective: The Extracorporeal Shockwave Lithotripsy (ESWL) procedure is the first choice for kidney stone therapy with the size ≤ 20 mm. One of the complications of ESWL is the pain. Pain control during ESWL is essential to maintain the focus point of ESWL and give enough time to achieve complete stone fragmentation. Until now there is still no data about the effectiveness of Eutectic Mixture of Local Anesthetics (EMLA) cream as an adjuvant analgesic for ESWL procedure in Soetomo Hospital Surabaya. To compare the onset of pain and ESWL Wong-Baker Pain Scale (WBPS) between the EMLA group and placebo group. **Material & Methods:** The design of this study was a single-blind randomized control trial comparing the onset of pain and Wong Baker pain scale between the patient in EMLA group and placebo one. WBPS is assessed in minute 15, 30, 45, and 60 of ESWL sessions and 60 minutes post ESWL procedure. The results were analyzed with SPSS. Pain onset and differences of WBPS were tested by using independent T-test if the data is normally distributed and using Mann-Whitney test if the data is not normally distributed. **Results:** 10 patients were obtained in each group. The mean onset of pain in the EMLA group was longer than the mean onset of pain in the placebo group but statistically not significant ($p > 0.05$). The WBPS in the EMLA group was significantly lower compared with the placebo group in the 30, 45, and 60 minutes of ESWL ($p < 0.05$). **Conclusion:** EMLA cream application before ESWL was effective and safe as an adjuvant analgesic to reduce pain during ESWL.

Keywords: Eutectic mixture of local anesthetics cream, extracorporeal shockwave lithotripsy, Wong-Baker pain scale.

ABSTRAK

Tujuan: Prosedur ESWL menjadi pilihan utama untuk terapi batu ginjal dengan ukuran ≤ 20 mm. Salah satu komplikasi ESWL adalah nyeri. Pengendalian nyeri selama ESWL sangat penting untuk tetap menjaga fokus ESWL sehingga fragmentasi batu tetap maksimal. Masih belum ada data efektivitas penggunaan krim EMLA sebagai analgesik ESWL di RSUD Dr. Soetomo Surabaya. Membandingkan onset nyeri dan skala nyeri Wong-Baker (WBPS) saat ESWL antara kelompok EMLA dengan kelompok plasebo. **Bahan & Cara:** Penelitian ini merupakan single-blind randomized control trial membandingkan onset nyeri dan WBPS kelompok EMLA dengan kelompok plasebo. Skala nyeri diukur pada menit ke-15, 30, 45, dan 60 menit saat ESWL dan 60 menit setelah tindakan ESWL. Data diolah dengan program SPSS. Onset nyeri dan perbedaan WBPS diuji menggunakan uji independent T-test bila data berdistribusi normal dan menggunakan uji Mann-Whitney jika distribusi data tidak normal. **Hasil:** Didapatkan 10 pasien pada masing-masing kelompok. Rerata onset nyeri pada kelompok EMLA lebih lama dibandingkan pada kelompok placebo tetapi tidak bermakna secara statistik ($p < 0.05$). WBPS pada kelompok EMLA secara signifikan lebih rendah dibandingkan pada kelompok plasebo pada menit ke-30, 45, dan 60 saat ESWL ($p < 0.05$). **Simpulan:** Pemberian krim EMLA sebelum ESWL merupakan analgesik ajuvan yang efektif dan aman untuk menurunkan nyeri pada prosedur ESWL.

Kata Kunci: Krim eutectic mixture of local anesthetics, extracorporeal shockwave lithotripsy, skala nyeri Wong-Baker.

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INTRODUCTION

Urinary tract stones disease causes pain, obstruction, and infection.¹ In Indonesia urinary tract stone disease accounts for the largest number of patients in urology clinics.² Worldwide, appro-

ximately 1-12% of the population suffer from urinary tract stones.^{3,4} Urinary tract stones disease that causes problems should be expelled to prevent more severe complications.⁵ ESWL procedure was the first choice for kidney stone therapy with size ≤ 20 mm with the success rate ranged from 33-91%.⁶

Research conducted by Ridha in 2014 at Soetomo General Hospital Surabaya showed that the success rate of ESWL was 65.5%.⁷

One of the complications of ESWL is pain.⁸ Pain occurs when shock waves delivered from the device reach the superficial structure of the body and stimulate pain receptors in the skin region and or on the deeper structures such as muscle and viscera.⁹ In 2014, Ballesteros reported 2 cases of burns in the skin of the flank area because of ESWL procedure.¹⁰

Pain control during ESWL is essential to minimize patient movement caused by excitatory pain. Cooperative and calm patients are important to keep the ESWL focus point unchanged and stone fragmentation optimal. Convenient ESWL procedure will affect patient compliance if additional sessions are required. Premedication analgesics are administered before ESWL to provide effective pain reduction during ESWL. Analgesics may be intravenous, intramuscular, oral, suppository, or topical.¹¹ Ketoprofen suppository is premedication analgesic used in Soetomo Hospital Surabaya.

Adjuvant analgesics are drugs with a primary indication other than pain that have analgesic properties in some painful conditions. A topical agents addition is one of the alternative of adjuvant analgesic during ESWL. Eutectic Mixture of Local Anesthetics (EMLA) cream contains 2.5% lidocaine eutectic mixture and 2.5% prilocaine. EMLA cream is the option to reduce pain during ESWL. The use of EMLA as a local anesthetic will block the peripheral nerves in the skin and muscle so that the pain impulse is not transmitted to the spinal cord.¹²

OBJECTIVE

There is currently no research that examines the effectiveness of EMLA cream as an adjuvant analgesic for ESWL procedure in Soetomo Hospital Surabaya. This study aimed to compare the effectiveness of EMLA cream with placebo cream in reducing patient's onset of pain and Wong-Baker Pain Scale (WBPS) during ESWL in Soetomo Hospital Surabaya.

MATERIAL & METHODS

This was a single-blind randomized control trial comparing the onset of pain and WBPS between EMLA groups and placebo one.

The sample of this study was patient with

kidney stone who underwent ESWL procedure in Soetomo General Hospital Surabaya that meets the inclusion criteria of kidney stone size >5mm and ≤20mm, radioopaque stone, age more than 18 years to 65 years, routine blood examination, normal hemostasis, and electrolyte serum, and willing to follow and sign the research inform consent. The exclusion criteria were body mass index of less than 18 or more than 30kg/m², renal anatomical abnormality (horseshoe kidney, ureteropelvic junction stenosis, infundibulum stenosis), patients with a history of open ipsilateral flank surgery with ESWL, patients with kidney disease comorbid (Creatinine serum >2g/dl), severe liver disease (SGOT/SGPT >100mg/dl), and unregulated diabetes mellitus (GDA >200mg/dl), patients with coronary artery disease and stroke, pregnant, as well as patient history of drug allergy lidocaine or prilocaine.

HK Classlith V brand is ESWL machine used in Soetomo General Hospital Surabaya. Gradually energy raises per 100x shot, from 5kV to maximum 14kV with the frequency of shock 60-70 waves/min (for 60 minutes). All patients were given ketoprofen 100mg suppository 60 minutes before ESWL procedure. Patients were divided into two groups: EMLA group and placebo one.

In the EMLA group, 5 grams of (Emla®) was applied on flank area skin 60 minutes before ESWL procedure. The cream was applied on the flank area skin of 15x15cm and closed with opsite. In the placebo group, 5 grams of placebo cream (Biocream®) was applied on the flank area skin of 15x15cm and closed with opsite 60 minutes before ESWL procedure. Opsite were removed shortly before ESWL procedure.

WBPS was measured on 15, 30, 45 and 60 minutes during ESWL and then measured again 60 minutes post-ESWL. The onset of pain is the first pain felt (WBPS >2). The onset of pain was noted and compared between two groups. Patients with WBPS >6 were given an intravenous injection of tramadol 100 mg with vital sign monitoring.

The results were analyzed with the 23rd version of SPSS. The onset of pain between groups was tested with independent T-test if the data were normally distributed. If the data was not normally distributed, Mann-Whitney test was used. Similarly, the comparison of WBPS was tested with independent T-test if data normally distributed. If data were not normally distributed, Mann-Whitney test was used. Normality of data was tested with

Shapiro-Wilk. Data were normally distributed if $p < 0.05$ and vice versa. This study was approved by Soetomo General Hospital Ethical Committee.

RESULTS

The total sample of the study were 10 patients for each EMLA and placebo group. The mean age in the EMLA group was 48 ± 15.85 years while in the placebo group was 49.90 ± 15.68 years. The most of patients were male in both EMLA and placebo group. In the EMLA group, most of stone was located in the middle pole while in placebo group most of the stone was located in the lower pole. The body mass index between two groups was comparable. The mean size of the stones in the placebo group was 0.75 (0.6-1.6) cm while the

EMLA group was 0.65 (0.6-1.5) cm.

The pain onset in the EMLA group was longer than the placebo one, respectively 28 ± 16.87 minutes and 18 ± 7.53 minutes. Nevertheless based on independent T-test, there was no significant difference between the EMLA and the placebo group ($p > 0.05$).

Based on the Mann-Whitney test, there was no significant WBPS the 15th minute of ESWL between EMLA group and placebo one, $p > 0.05$. While in the 30th, 45th and 60th minutes of ESWL the WBPS in the EMLA group were lower than the placebo one and statistically significant ($p < 0.05$). However, at 60 minutes post-ESWL there was no significant difference between EMLA group and placebo group ($p > 0.05$).

Table 1. Characteristic of samples.

| Characteristics | EMLA | Placebo | p value |
|------------------------------|------------------|-------------------|---------|
| Age (year) ^a | 48 ± 15.85 | 49.90 ± 15.68 | 0.10 |
| Sex ^b | | | |
| Male | 7 (70 %) | 6 (60%) | 1.00 |
| Female | 3 (30%) | 4 (40%) | |
| Body weight ^a | 55.4 ± 5.19 | 58 ± 3.56 | 0.20 |
| Body height ^a | 162.6 ± 5.81 | 164.5 ± 3.41 | 0.20 |
| Body mass index ^a | 20.92 ± 1.1 | 21.42 ± 0.85 | 0.20 |
| Stone location | | | |
| Pyelum | 1 (10%) | 3 (30%) | |
| Upper pole | 1 (10%) | - | |
| Middle pole | 5 (50%) | 1 (10%) | |
| Lower pole | 3 (30%) | 6 (60%) | |
| Stone size ^c | 0.6 (0.5 – 1.5) | 0.9 (0.6 – 1.8) | 0.13 |

a: Independent T-test (mean \pm SD); b : Chi-Square ; c: Mann-Whitney (Min-Max)

Table 2. Pain onset in EMLA and placebo group.

| Characteristic | EMLA (n = 10) | Placebo (n = 10) | p value |
|----------------|----------------|------------------|---------|
| Pain onset | 28 ± 16.87 | 18 ± 7.53 | 0.10 |

Table 3. Wong Baker pain scale in EMLA and placebo group.

| Time | EMLA | Placebo | p value |
|--------------------------|-----------|-----------|---------|
| 15 th minutes | 1 (0 – 2) | 2 (0 – 2) | 0.37 |
| 30 th minute | 1 (0 – 4) | 2 (0 – 4) | 0.04* |
| 45 th minutes | 2 (0 – 4) | 4 (2 – 4) | 0.00* |
| 60 th minutes | 2 (0 – 4) | 3 (2 – 4) | 0.04* |
| 60 minutes post ESWL | 0 (0 – 2) | 0 (0 – 2) | 0.34 |

DISCUSSION

Urinary tract stones were the largest number of patients in urology clinics. Peak incidence occurs at the 3rd until 5th decade of life. Procedure on kidney stones increased because the availability of noninvasive methods, in which ESWL totally covers 86% of all procedure (ESWL, PNL, and open surgery).¹³

ESWL is the first choice for kidney stones therapy with size less than 20mm. One of the complications of ESWL is the pain. The mechanical factor of shock waves passing through the flank skin and muscle toward the focus point causes stimulation of the nociceptors. Inflammation in the skin, muscle, and visceral tissue caused by ESWL waves will produce arachidonic acid that will be converted to prostaglandins by COX-2. Further, prostaglandin stimulates transduction process in peripheral nerve endings. The impulse of the pain will be transmitted to the dorsal ganglia and then modulated in the thalamus. Finally, pain is perceived in the brain cortex.

Pain control during ESWL includes oral, intravenous, intramuscular, suppository, and topical analgesics. An adequate pain control will increase ESWL stone-free rate by maintaining focus point of ESWL and giving enough time to achieve complete stone fragmentation.¹⁴ A convenient ESWL procedure will improve patient compliance if the additional session is required. Based on EAU guidelines, premedication with NSAID or midazolam will decrease the need for opioid during ESWL procedure.¹⁵ In Soetomo General Hospital, ketoprofen suppository is the analgesic premedication during ESWL procedure.

Intravenous opioid combined with sedation agents can be used in ESWL procedure. Nevertheless, monitoring with ECG, blood pressure, and oxygen saturation must be carefully done because of the side effect of the opioid such as nausea, vomiting, and respiratory depression. The opioid is indicated for severe pain with Wong-Baker pain scale 7-10. In this research, maximal Wong-Baker pain scale was 4, so opioid was not indicated yet.

EMLA cream is an alternative because of its simplicity, less side effect, and noninvasive application. EMLA cream blocks the impulse of the pain that has been formed in nociceptors. The previous study showed different results. A study conducted by Gajral et al., showed that EMLA

reduced pain and decreased the need for opioid until 23%.¹⁶ Monk et al., compared IV Fentanyl with EMLA in ESWL. EMLA provided cutaneous analgesia but no opioid sparing effect.¹⁷ Result from Basar et al., study, EMLA cream was effective as Fentanyl, Diclofenac, and Tramadol with Midazolam for premedication during ESWL.¹⁸

Results from our research showed that mean onset of the pain in EMLA group was longer than placebo one. Nevertheless, this result was not statistically significant. During ESWL procedure, there was no WBPS significant different on 15 minutes. This result may be related to the power of ESWL during that period. But on 30, 45, and 60 minutes during ESWL WBPS in EMLA group was lower with statistically significant than the placebo group. EMLA cream effectiveness was seen with the increasing intensity of pain because of the increase in power ESWL during that period.

In 60 minutes after ESWL procedure, there is no significant WBPS in EMLA group and placebo group. This result was related to the peak onset of action of ketoprofen that was reached in 2.5 hours. Beside of that, during this period the mechanical and inflammation stimulation had been stopped. In this study, we found no flank hematoma complication in all patients after ESWL procedure and irritation because of the EMLA cream application.

The application of EMLA cream may be considered as an adjuvant analgesic on ESWL. The effectiveness of EMLA cream is seen as the intensity of the pain increases. However, further studies with larger numbers of samples are still needed to determine the efficacy of EMLA cream in ESWL procedures. In addition, to obtain an optimal analgesic option, a further study comparing the various analgesics is still required.

CONCLUSION

Application of EMLA cream before ESWL was effective and safe as an adjuvant analgesic to reduce pain during ESWL.

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