The Analgesic Effect of Cryotherapy on Patients Undergoing Extracorporeal Shock Wave Lithotripsy: A Randomized Controlled Trial

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ABSTRACT

Objective: To compare the degree of pain between cryotherapy and standard preoperative care in the treatment of urolithiasis with extracorporeal shock wave lithotripsy (ESWL).

Materials and Methods: A total of 180 ESWL patients were randomly assigned to experience the standard preoperative method, or additional cryotherapy (ice pack application on the ESWL site) for 10 minutes before ESWL. The primary outcome was the maximum difference of pain intensity score from baseline during ESWL and the secondary outcomes, which were analgesic consumption, pulse rate, adverse events, stone free rate, and complications that were gathered and analyzed.

Results: The maximum change in pain intensity score from baseline during ESWL in the cryotherapy group was significantly lower than in the control group (VAS score 4.0±1.9 vs. 5.2±2.7, p=0.002). The cryotherapy group showed significantly less total fentanyl consumption than the control group (85.3±22.0 mcg vs. 93.6±25.6, p=0.021). We found no significant difference in stone free rate, adverse events or complications in either group.

Conclusion: Preoperative cryotherapy using ice packs for 10 minutes can provide an effective analgesic for ESWL. Adequate pain control with cryotherapy should be an option of pain management during ESWL.

Keywords: Cryotherapy; ESWL; pain; urolithiasis (Siriraj Med J 2022; 74: 85-90)

INTRODUCTION

Extracorporeal shock wave lithotripsy (ESWL) has been a less-invasive option for the treatment of the majority of patients with urolithiasis since 1980.[1] The advancement of the new-generation lithotripter machines has made ESWL more effective with minimal morbidity, making it possible to perform ESWL without the need for general or spinal anesthesia.[2] However, this procedure can be painful because the continuous shock waves act on the cutaneous superficial skin nociceptors and visceral nociceptors, such as the renal capsule, peritoneal, and musculoskeletal pain receptors.[3] Adequate pain control is an important role in achieving successful ESWL treatment. Opioid and sedative drugs are common analgesics for ESWL, but certain amounts of opioids may cause nausea, vomiting, and delayed recovery of patients.[4]

Cryotherapy involves cold applications, which have effects on both the local site around the treatment area and at the level of the spinal cord via neurologic and vascular mechanisms.[5] It is hypothesized that cold applications can control pain by increasing the pain threshold and tolerance by reducing nerve conduction velocity, as described by the gate control theory, whereby pain is transmitted to the dorsal horn of the spinal cord

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via C-fibers and Aß fibers; C-fibers release substance P, which opens the gate and Aß fibers close the gate. Cold applications activate the Aß fibers, thereby stopping the transmission of pain stimuli.[6,7] Many studies have been published in regard to cryotherapy for pain reduction, for example with knee operations, thoracic operations, gynecologic operations, and abdominal operations.[8–11] However, no previous study has reported the analgesic effect of cryotherapy on ESWL.

The aim of this study was to evaluate the effectiveness of cryotherapy regarding pain control during ESWL for urolithiasis treatment.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Buri Ram Provincial Hospital, Buri Ram, Thailand. The protocol of this research was reviewed and approved by the ethical review board of Buri Ram Hospital (BR 0032.102.1/46) and registered in the Thai Clinical Trials Registry (TCTR20201226002). Patients with indication for ESWL treatment were randomly assigned into two groups. Patients in the first group were given ice pack compression at the skin on the ESWL site while patients in the second group were given standard preoperative ESWL. Between October 2020 and March 2021, kidney and ureteric stone patients scheduled for ESWL aged 18 to 80 years with the American Society of Anesthesiologists (ASA) physical status of I, II or III were eligible for the study. This study excluded patients with a history of allergies to the drugs that were used for the ESWL treatment, patients with psychological disorders, neurological disorders, dermatologic disorders (inflammation or eczema within the field of cold therapy), and patients that were unable to comprehend or use the visual analog scale (VAS).

After obtaining the informed written consent, the patients that met the criteria were enrolled and divided into two groups using computer-generated random numbers and opaque sealed envelopes. The patients in group I received cryotherapy; ice pack compression before ESWL. The ice pack was kept at -10°C in a thin cloth bag ready for future use. The ice pack was then placed on the skin at the site of the ESWL for 10 minutes before beginning the procedure. Control group II received standard preoperative care. Both groups received premedication-1000 mg paracetamol and 5 mg diazepam-orally 30 minutes before the ESWL. Initial intravenous fentanyl 1 mcg/kg began five minutes before the beginning of the ESWL for every patient from both groups and a supplementary dose of fentanyl 20 mcg intravenously was given to patients whose pain score was greater than 4 or whose pain tolerance was low. All patients underwent ESWL using a Dornier Delta III Lithotripter machine in a fully integrated operating room, and the procedure was carried out using a similar protocol. An anesthetic nurse, who was not involved in the study, recorded the patients' perioperative anesthetic parameters every five minutes. These parameters included blood pressure, pulse rate, respiratory rate, oxygen saturation, sedative score, pain score, and nausea/vomiting. The pain scores were placed on an 11-point visual analog scale (VAS) and ranged from 0 to 10, with 0 representing no pain and 10 representing the worst pain.

The primary outcome was the maximum of changes in the pain intensity score from baseline during the ESWL, using the VAS score. The secondary outcomes were total fentanyl consumption, pulse rate, perioperative nausea/vomiting, stone free rate at one month after ESWL, and any adverse events or complications.

Statistical analysis

A preliminary study containing 40 patients (20 per group) was conducted. The preliminary study reported the VAS score at 4.9±2.1 in the control group and 3.8±2.1 in the experimental group. The mean scores from the preliminary study were used to calculate an appropriate sample size for the main study. The sample size calculation for the two independent mean tests using a power 90% and a significance level of 0.05 revealed a minimum sample size of 81 participants in each group. We added 10% of the subjects in order to accommodate the projected dropout rate. Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range, IQR) and were analyzed between the two groups by using a t-test or the Mann-Whitney U test. The categorical data were expressed as number and percentage and were compared using a chi-squared test or Fisher's exact probability test. Statistical significance was set at p-value <0.05.

RESULTS

One hundred and eighty-two ESWL cases were enrolled in the study and control groups. Two patients in our study were excluded. Each group was composed of 90 cases (Fig 1). There was no difference in the demographic data for either group, including age, sex, body mass index (BMI), ASA physical status, stone location, time of ESWL, lateralization, or stone size (Table 1). Intra-operative parameters, base line pain score, pulse rate, and initial fentanyl doses were not statistically different between the two groups. The maximum of change in the pain intensity score from baseline during the ESWL in the cryotherapy group was significantly lower than in the

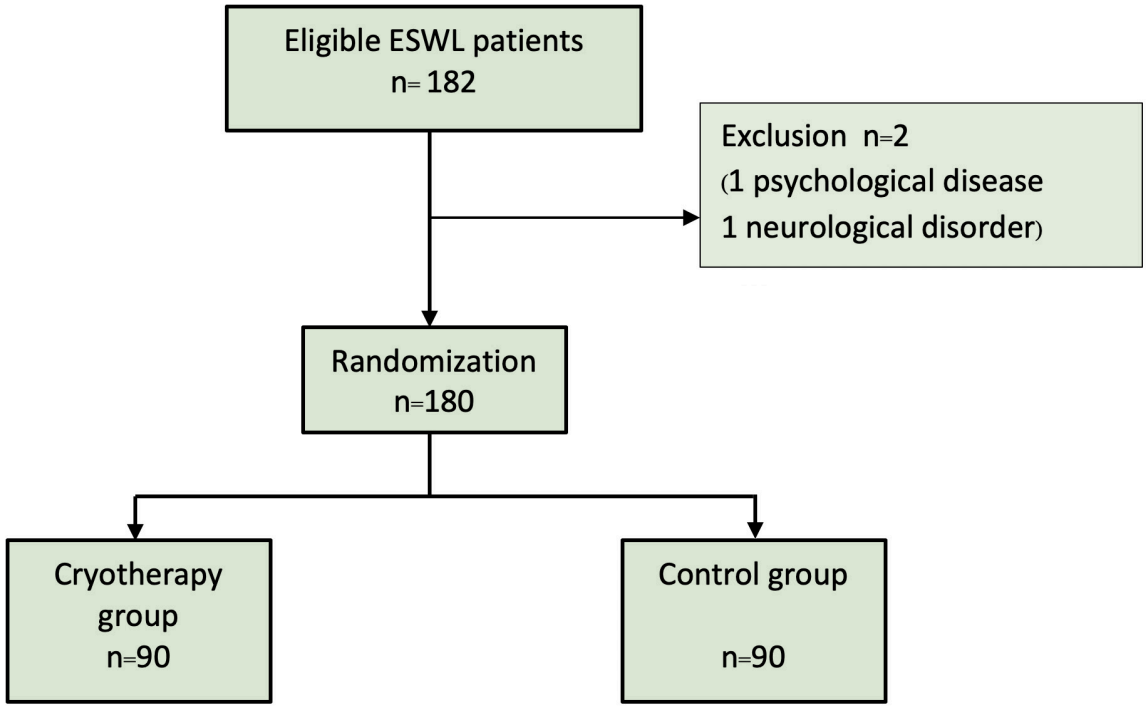

Fig 1. Consort diagram demonstrating the flow of participants through each stage of the randomized trial.

TABLE 1. Knowledge of the warning symptoms of stroke (n=312).

	Cryotherapy group (n=90)	Control group (n=90)	*p*-value
Gender			
Male n (%)	56 (62.2)	56 (62.2)	1.00
Age, year mean±SD	55.5±11.6	55.9±11.0	0.812
BMI, kg/m^2 mean±SD	24.3±3.9	24.4±4.8	0.862
ASA n (%)			0.875
1	29 (32.2)	31 (34.4)	
2	50 (55.6)	50 (55.6)	
3	11 (12.2)	9 (10.0)	
Stone location n (%)			0.414
Renal calculi	61 (67.8)	66 (73.3)	
Ureteric calculi	29 (32.2)	24 (26.7)	
Stone lateralization n (%)			
Right side	49 (54.4)	45 (50.0)	0.551
Time of ESWL n (%)			
First time	32 (35.6)	33 (36.7)	0.877
More than 1 time	58 (64.4)	57 (63.3)	
Stone size, mm median (IQR)	10.0 (10.0,15.0)	10.0 (9.5,15.0)	0.450

control group (VAS score 4.0±1.9 vs. 5.2±2.7, p=0.002). The cryotherapy group showed significantly lower total fentanyl consumption than the control group (85.3±22.0 mcg vs. 93.6±25.6 mcg, p=0.021). The stone free rate at one month after procedure was not difference between both groups (58.8% in the cryotherapy group vs. 62.2% in the control group. We found no significant difference in terms of adverse events regarding nausea/vomiting and bradycardia in either group (Table 2).

DISCUSSION

The introduction of ESWL has been revolutionary for the treatment of urolithiasis since 1980[1], and new-generation lithotripter machines have made ESWL more effective with less morbidity, less pain, shorter recovery time, and shorter hospital stays.[2] Nevertheless, the most common complaint is pain and discomfort during the treatment.[3] The pain experienced during ESWL is due to the continuous shock waves acting on its targets, whether from cutaneous tissue or deeper afferent nerves.[3] An adequate analgesia is mandatory for maintaining patient comfort and improving treatment outcomes[12], but sometimes the patients discharge from the hospital is delayed because of persistent sedation, and nausea and vomiting due to the anesthetic medication administered, so non-pharmacological methods may attract some attention.[13] Cryotherapy for pain relief has been used for many years, based on the gate control theory; cold application can inhibit cutaneous input to the spinal cord and reset the pain threshold in the central nervous system.[6,7,9] By this means, cryotherapy is able to block pain sensation from urinary calculi, whether its origin is from the skin or from the deeper structures. However, the major concern about cryotherapy is the decline in the patient's body core temperature and the local effects on the areas exposed to cryotherapy. The decline in the patient's body temperature has harmful physiological effects, such as Raynaud's phenomenon, while exposure to extreme cold can cause cold urticaria and frostbite of the skin.[14,15] The study by Palmieri et al. showed that

TABLE 2. Outcomes

	Cryotherapy group (n=90)	Control group (n=90)	*p*-value
VAS score			
At baseline median (IQR)	0.0 (0.0,0.0)	0.0 (0.0,0.0)	0.946
Maximum VAS during ESWL mean±SD	4.3±1.7	5.5±2.6	<0.001*
Change of maximum VAS from baseline mean±SD	4.0±1.9	5.2±2.7	0.002*
Pulse rate mean±SD			
At baseline	63.3±9.4	65.7±11.9	0.135
At 15 minutes	63.2±9.4	65.5±11.6	0.144
At 30 minutes	61.2±10.7	63.5±11.4	0.170
Initial fentanyl dose (mcg) mean±SD	69.9±19.4	74.3±20.3	0.140
Total fentanyl consumption (mcg) mean±SD	85.3±22.0	93.6±25.6	0.021*
Nausea and vomiting n (%)	2 (2.2)	2 (2.2)	1.00
Bradycardia n (%)	11 (12.2)	9 (10.0)	0.635
Skin complication (necrosis or frostbite) n (%)	0 (0)	0 (0)	NA**
Stone free rate (%)	58.8	62.2	0.760

* p-value <0.05
** NA = not applicable

a cold application at the skin site for 10-20 minutes did not decline the body core temperature.[16] Thienpont et al. demonstrated that continuous cryotherapy of not more than 20 minutes did not cause frostbite on the skin flap after knee arthroplasty.[15] Further, Natalia et al. demonstrated that a cryotherapy application of not more than 20 minutes was safe and not uncomfortable for any participants.[17] In this study, our protocol applied 10-minute cryotherapy and close monitoring for any adverse event from cryotherapy during the procedure.

Many studies have used cryotherapy to decrease pain in musculoskeletal surgery, gynecologic surgery, cardiothoracic surgery, and abdominal surgery. The overall results revealed beneficial outcomes in terms of pain reduction and pain management.[8–11] The present study is the first to emphasize the effects of cryotherapy or cold application in ESWL treatment. In addition, this study used the change of maximum VAS score from baseline for the primary outcome instead of the patient's stated VAS score after he or she had his/her operation. Traditionally the VAS score is clinically meaningful from the patient's perspective and clinical decisions are made based on such. However, the VAS mean scores cannot capture the complete pain experience because pain is both subjective and multidimensional.[18] Thus this study used the change of maximum VAS score from baseline for the primary outcome, which offers an alternative measurement of the analgesic effect during the actual procedure for the main outcome of our study. We found that the pain intensity score in the cryotherapy group was significantly lower than in the control group (VAS score 4.0±1.9 vs. 5.2±2.7, p=0.002).

Regarding the objective parameter, we used total fentanyl consumption for the secondary outcome. The cryotherapy group showed significantly lower total fentanyl consumption than the control group (85.3±22.0 mcg vs. 93.6±25.6 mcg, p=0.021).

In our study, bradycardia was a common side effect, which may have been caused by both opioid usage and cryotherapy; nevertheless, the pulse rate and bradycardia events did not differ between the two groups (12.2% in the cryotherapy group vs. 10.0% in the control group, p=0.635), as the incidence was likely to be a minor adverse effect of opioids rather than the effect of cryotherapy.[13] The emetic effect of opioids has been documented; in our study, there was no significant difference in nausea or vomiting between both groups (2% in the cryotherapy group vs. 2% in the control group, p=1.000). Local skin complications from cryotherapy were not present in our study. Taking into consideration the significant benefit of pain management from cryotherapy during ESWL, we believe that cryotherapy is a safe, inexpensive, practical, and effective adjuvant pain relief method.

There were some limitations in this study. First, we could not blind the cold application between the cryotherapy group and the control group. Secondly, the VAS score for pain was subjective and multidimensional. Even though this study used the change of maximum VAS score from baseline as an alternative measurement, this measurement is prone to variation regarding the patient's pain tolerance level. In our study the stone free rate was not significant difference between both groups. Thus, future studies should consider using a more objective measurement regarding outcome evaluation such as the success rate of the stone treatment.[3,12,19,20]

CONCLUSIONS

In this study we demonstrated that preoperative cryotherapy using an ice pack for 10 minutes can provide an effective analgesic for ESWL treatment. Adequate pain control with cryotherapy should be an option of pain management during ESWL.

REFERENCES

1. Chaussy C, Brendel W, Schmiedt E. Extracorporeally induced destruction of kidney stones by shock waves. Lancet. 1980 Dec 13;2(8207):1265–8.
2. Gupta NP, Kumar A. Analgesia for pain control during extracorporeal shock wave lithotripsy: Current status. Indian J Urol. 2008 Apr;24(2):155–8.
3. Huang Y, Chai S, Wang D, Li W, Zhang X. Efficacy of Eutectic Mixture of Local Anesthetics on Pain Control During Extracorporeal Shock Wave Lithotripsy: A Systematic Review and Meta-Analysis. Med Sci Monit. 2020 May 13;26:e921063-1-e921063-9.
4. Berwin JT, El-Husseiny T, Papatsoris AG, Hajdinjak T, Masood J, Buchholz N. Pain in extracorporeal shock wave lithotripsy. Urol Res. 2009 Apr;37(2):51–3.
5. Nadler SF, Weingand K, Kruse RJ. The physiologic basis and clinical applications of cryotherapy and thermotherapy for the pain practitioner. Pain Physician. 2004 Jul;7(3):395–9.
6. Mendell LM. Constructing and deconstructing the gate theory of pain. Pain. 2014 Feb;155(2):210–6.
7. Ropero Peláez FJ, Taniguchi S. The Gate Theory of Pain Revisited: Modeling Different Pain Conditions with a Parsimonious Neurocomputational Model. Neural Plast. 2016;2016:4131395.
8. Tedesco D, Gori D, Desai KR, Asch S, Carroll IR, Curtin C, et al. Drug-Free Interventions to Reduce Pain or Opioid Consumption After Total Knee Arthroplasty: A Systematic Review and Meta-analysis. JAMA Surg. 2017 Oct 18;152(10):e172872.
9. Gorji HM, Nesami BM, Ayyasi M, Ghafari R, Yazdani J. Comparison of Ice Packs Application and Relaxation Therapy in Pain Reduction during Chest Tube Removal Following Cardiac Surgery. N Am J Med Sci. 2014 Jan;6(1):19–24.
10. Chumkam A, Pongrojpaw D, Chanthasenanont A, Pattaraarchachai J, Bhamarapravatana K, Suwannarurk K. Cryotherapy Reduced Postoperative Pain in Gynecologic Surgery: A Randomized Controlled Trial. Pain Res Treat. 2019;2019:2405159.

11. Ravindhran B, Rajan S, Balachandran G, Mohan LN. Do Ice Packs Reduce Postoperative Midline Incision Pain, NSAID or Narcotic Use? World J Surg. 2019 Nov;43(11):2651–7.
12. Bovelander E, Weltings S, Rad M, van Kampen P, Pelger RCM, Roshani H. The Influence of Pain on the Outcome of Extracorporeal Shockwave Lithotripsy. Curr Urol. 2019 Mar 8;12(2):81–7.
13. Cannata F, Spinoglio A, Di Marco P, Luzi M, Canneti A, Ricciuti G, et al. Total intravenous anesthesia using remifentanil in extracorporeal shock wave lithotripsy (ESWL). Comparison of two dosages: a randomized clinical trial. Minerva Anestesiol. 2014 Jan;80(1):58–65.
14. Stocks JM, Taylor NAS, Tipton MJ, Greenleaf JE. Human physiological responses to cold exposure. Aviat Space Environ Med. 2004 May;75(5):444–57.
15. Thienpont E. Does advanced cryotherapy reduce pain and narcotic consumption after knee arthroplasty? Clin Orthop Relat Res. 2014 Nov;472(11):3417–23.
16. Palmieri RM, Garrison JC, Leonard JL, Edwards JE, Weltman A, Ingersoll CD. Peripheral ankle cooling and core body temperature. J Athl Train. 2006 Jun;41(2):185–8.
17. Vargas E Silva NCO, Rubio AL, Alfieri FM. Pain Tolerance: The Influence of Cold or Heat Therapy. J Chiropr Med. 2019 Dec;18(4):261–9.
18. Myles PS, Myles DB, Galagher W, Boyd D, Chew C, MacDonald N, et al. Measuring acute postoperative pain using the visual analog scale: the minimal clinically important difference and patient acceptable symptom state. Br J Anaesth. 2017 Mar 1;118(3):424–9.
19. Yayik AM, Ahiskalioglu A, Alici HA, Celik EC, Cesur S, Ahiskalioglu EO, et al. Less painful ESWL with ultrasound-guided quadratus lumborum block: a prospective randomized controlled study. Scand J Urol. 2019 Dec;53(6):411–6.
20. Çift A, Benlioglu C. Effect of Different Musical Types on Patient's Relaxation, Anxiety and Pain Perception during Shock Wave Lithotripsy: A Randomized Controlled Study. Urol J. 2020 Jan 26;17(1):19–23.