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Efficacy of Moderate Sedation for Pain Control in Patients Undergoing Extracorporeal Shock Wave Lithotripsy: a Randomized Clinical Trial

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Abstract

Introduction: Extracorporeal shock wave lithotripsy (ESWL) is a painful procedure. Effective analgesia is mandatory to achieve patient comfort and in cooperating according to the treatment plan. The objective of the study is to evaluate pain relief from moderate to severe (pain score, PS ≥4) to mild pain (PS 0-3) with parenteral propofol-fentanyl (moderate sedation) and preemptive etoricoxib combined with acetaminophen (conventional treatment) during ESWL.

Methods: Seventy patients scheduled for ESWL were randomized by a computer program and sealed envelope. Thirty-five samples were assigned to propofol-fentanyl (PF) as the experimental group, and thirty-five samples were assigned to etoricoxib-acetaminophen (EA) as the control group. The primary outcome was to evaluate the efficacy of moderate sedation for pain control. Pain was assessed using an 11-point numeric rating scale (NRS) and ≤3 was considered adequate analgesia. Secondary outcomes included complications, recovery time, health care and patient satisfaction using the Modified Aldrete score, Modified Post-anesthesia Discharge Scoring System (PADSS) and visual analog scale (VAS) for satisfaction

Results: Sixty-eight patients completed the present study, with no differences in demographics data or baseline vital signs. Group PF reported less PS than group EA (P<0.001). After ranging the severity of pain, moderate to severe pain was 2 (5.9%) and 29 (85.3%), respectively (P<0.001). All patients underwent a planned ESWL without major complications. Most patients achieved a Modified Aldrete score ≥9 within 5 min of the end of ESWL. Although the recovery time of group PF was slower than group EA, it was not clinically significant. The median time for patients to achieve PADSS ≥10 was 10 and 0 min, and the median time for patients to feel full recovery was 40 and 5 min, respectively (P<0.001). Furthermore, group PF had better overall satisfaction than group EA.

Conclusion: A combination of propofol and fentanyl for moderate sedation can provide effective anesthesia during ESWL. Furthermore, it facilitates ESWL to be established plan, safely and increases overall satisfaction.

Keywords: analgesia, extracorporeal shock wave lithotripsy, fentanyl, moderate sedation, propofol

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Introduction

Renal calculi (RC) are common urinary tract problems worldwide and a major health burden. The overall prevalence of RC in the United States increased from 3.2% in 1980 to 10.1% in 2016.[1] In Europe, the prevalence of RC ranges from 0.1 to 14.8, and similar trends are also observed.[2] For Thailand, the highest reported prevalence rate among adults was in the North East (16.9%).[3] The incidence rate in Thai population is higher than 85 per 100,000. Of these cases, more than 40% are from the North East region, or approximately 117 cases per 100,000 population.[2] Stones lodged in the urinary tract often cause severe pain (renal colic), urinary tract infection and renal failure from urinary tract obstruction. In addition to affecting health and quality of life, the chance of recurrence is as high as 26-50% within 5 years.[4] The high recurrence rates lead to higher costs of medical treatment, hospitalization, healthcare expenses, social costs, and indirect costs from time lost from work.[5]

Extracorporeal shock wave lithotripsy (ESWL) is a non-invasive procedure and is considered the treatment of choice for small (less than 1.5-2 cm) RC or ureteric calculi (UC). Shockwave-related pain is one of the most significant side effects of ESWL, which can be caused by many factors. Firstly, external pain is caused by the direct impact of the shock waves on the cutaneous pain receptors. Bruising of the skin may even appear in the area treated with ESWL. Secondly, visceral pain is caused by the distension of the renal capsule around the impact area and a sustained increase in intrapelvic pressure. Finally, the mobility of the stone fragments and the impact of the shock waves on the 12th rib also appear to contribute to pain.[6] Pain during ESWL may lead to disruptive movement and also cause an increased respiratory rate, both resulting in decreased hit rate and reduced stone fragmentation. Additionally, pain may lead to hypertension and a higher rate of renal hematomas. Patients being relaxed and cooperative during procedure is key to maintaining stone targeting for optimal fragmentation.[7] Therefore, proper pain management with minimal adverse effects is essential.

From the retrospective data of Surin Hospital, an average of 3,162 RC and UC patients were diagnosed and approximately 302 patients (9.5%) were treated with ESWL per year. All patients underwent minimal sedation. ESWL was successful at 98.5%, most patients tolerated the experience but were uncomfortable. A 3.8% of patients had severe pain. Therefore, urologists were unable to use shock wave energy properly. It may be assumed that pain directly affects the treatment plan, patient cooperation and patient satisfaction. Based on a pilot study, 15 ESWL patients received enteral etoricoxib and paracetamol; moderate to severe pain (PS ≥4) was observed in 93% of patients (mean PS=4.53). The authors aimed to use moderate sedation to reduce the pain score during ESWL compared with the conventional pain control.

Methods

After obtaining Surin Hospital Human Research Ethics Committee approval (no.31/2565) and registered at the Thai Clinical Trial Registry,

this study was conducted and took place in a tertiary care hospital in Thailand. Patients over 18 years old who scheduled for ESWL were enrolled in this prospective, randomized clinical trial, cooperated and were able to evaluate their pain scores. Patients allergic or contraindicated to the use of drugs (acetaminophen, etoricoxib, fentanyl, midazolam, and propofol), have renal impairment (eGFR less than 30), a history of drug abuse or chronic use of opioids or have previously participated in this study or refused to participate were excluded from the study. The remaining patients were randomly assigned by a computer program and sealed envelopes at the time consent into two groups. Group PF (moderate sedation; n=35) received propofol and fentanyl and group EA (minimal sedation; n=35) received etoricoxib and acetaminophen.

Statistical analysis

Based on a pilot study of 15 subjects who received minimal sedation, the moderate to severe pain was reported by 93.0%. The authors aimed to use moderate sedation to reduce the pain score from moderate to severe pain (PS ≥4) to mild pain (PS ≤3). The clinical significance was 40.0% lower than the control group (56.0%).

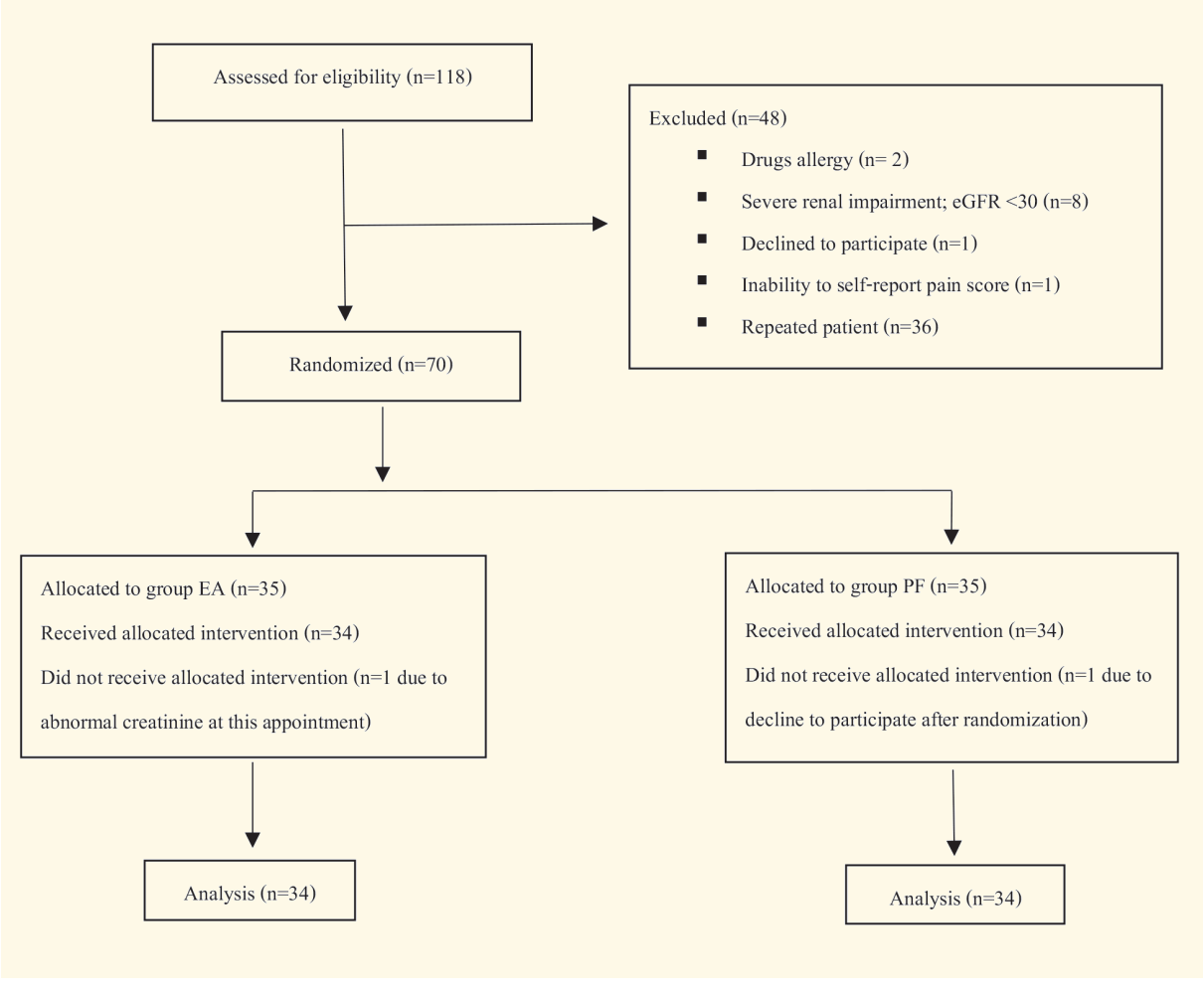


Figure 1 Consort diagram

The sample size was calculated using the nQuery advisor program for two-sided test of equal proportions (odds ratio=1) (equal n's). With a significance level of 0.05, a two-sided test with power set at 90%, a sample size of 28 samples was required per group and reserved for a 20% drop out, so there must be 35 samples per group. Data analyses were performed with PASW Statistics, version 18.0 (SPSS Inc., Chicago, IL, USA), and a *P*-value of less than 0.05 was considered significant. Descriptive statistics were used to summarize demographic characteristics such as age, gender, ASA classification, and underlying diseases. Quantitative data were presented as mean±standard deviation, or median (percentile 25, percentile 75), and qualitative data were presented as frequency (percent).

Results

Between August 15, 2022 and December 31, 2022, 118 patients enrolled in the present study. Of these, 48 patients were excluded due to drugs allergy (n=2), severe renal impairment (n=8), declined to participate (n=1), inability to self-report NRS (n=1), or previously participated this study (n=36). This left 70 patients to be randomized. After randomization, one patient had abnormal creatinine after this appointment and one patient refused to participate. Those mentioned above were excluded from the analysis. (Figure 1) Most of them were male and had RC. The mean age was 56.5±13.5 years. Common comorbidities include hypertension, chronic kidney disease, diabetes mellitus, obesity, hyperlipidemia, gout, and benign prostatic hypertrophy. Intergroup comparisons of the 68 patients analyzed are summarized in Table 1. There were no significant differences in demographic data.

All patients underwent ESWL according to the protocol. The median total dose of fentanyl was 60 (50, 75) mcg in group PF and 20 (20, 40) mcg in group EA. The median total propofol dose in group PF was 100 (80, 130) mg. Two patients in group PF were able to terminate ESWL at 4000 shots due to a completely broken stone. Reporting pain scores showed that the median PS in group PF was 2 (0, 2), while group EA was 4 (4, 5). Therefore, moderate to severe pain was reported by 2 patients in group PF and 29 patients in group EA ($P<0.001$). Although the median time for Modified Aldrete score ≥9 in group PF was not different from that in group EA, the time for PADSS ≥10 and the median time to full recovery in group PF was significantly longer than in group EA. (Table 2)

Intraoperative complications include disruptive movement, hypotension (BP < 90/60 mmHg) and hypertension (BP ≥ 160/100 mmHg) were reported with no differences between the two groups. Additionally, postoperative complications including nausea, vomiting, and pain at the procedure site were also not significantly different. (Table 3) Median satisfaction of urologists, anesthesiologists and patients in group PF was significantly higher than in group EA. While the satisfaction of nurse care after sedation was not different among the two groups. In addition, surgeon, anesthesiologist, post-anesthesia nurse and patient satisfaction were demonstrated in Table 4.

Table 1 Baseline characteristics

	Group EA (n=34)	Group PF (n=34)	*P*-value
Age (yr), mean±SD	55.9±13.0	57.1±13.5	0.730
Gender, n (%)			1.000
Male	21 (61.8)	21 (61.8)	
Female	13 (38.2)	13 (38.2)	
Site, n (%)			>0.999
Renal calculi	28 (82.4)	27 (79.4)	
Ureteric calculi	6 (17.6)	7 (20.6)	
Side, n (%)			1.000
Right	18 (52.9)	18 (52.9)	
Left	16 (47.1)	16 (47.1)	
Visit, n (%)			0.790
1st	21 (61.8)	23 (67.6)	
2nd	10 (29.4)	8 (23.5)	
3rd	3 (8.8)	2 (5.9)	
4th	0	1 (2.9)	
Comorbidity, n (%)			
Hypertension	20 (58.8)	13 (38.2)	0.140
Chronic kidney disease	6 (17.6)	9 (26.5)	0.560
Diabetes mellitus	3 (8.8)	5 (14.7)	0.710
Others	13 (38.2)	13 (38.2)	1.000
Creatinine, median (P25, P75)	0.9 (0.8, 1.2)	0.9 (0.8, 1.1)	0.920
eGFR, median (P25, P75)	70.6 (54.1, 85.9)	74.7 (58.8, 92.7)	0.720
ASA physical status, n (%)			0.900
I	6 (17.6)	5 (14.7)	
II	14 (41.2)	13 (38.2)	
III	14 (41.2)	16 (47.1)	
Body weight (kg), median (P25, P75)	62.0 (54.0, 71.5)	60.0 (53.3, 71.0)	0.770
Body mass index, median (P25, P75)	23.3 (21.1, 27.0)	23.5 (20.8, 27.7)	0.930
Baseline vital signs			
Systolic blood pressure, mean±SD	137.1±18.8	139.7±12.4	0.500
Diastolic blood pressure, mean±SD	80.7±10.9	85.1±11.3	0.110
Heart rate, median (P25, P75)	72.0 (64.0, 94.0)	77.5 (70.0, 82.0)	0.660
Oxygen saturation, mean±SD	97.6±1.3	97.5±1.3	0.930

eGFR=estimated glomerular filtration rate, ASA=American Society of Anesthesiologists

Table 2 Sedation outcomes

	Group EA (n=34)	Group PF (n=34)	*P*-value
Total fentanyl dose (mcg), median	20 (20, 40)	60 (50, 75)	<0.001*
Total propofol dose (mg), median	-	100 (80, 130)	
Success rate of ESWL, n (%)	34 (100.0)	34 (100.0)	1.000
Average intraoperative NRS, median	4 (4, 5)	2 (0, 2)	<0.001*
Moderate to severe pain, n (%)	29 (85.3)	2 (5.9)	<0.001*
Time to Modified Aldrete score ≥ 9 (min), median	0 (0, 5)	5 (0, 5)	0.059
Time to Modified PADSS ≥ 10 (min), median	0 (0, 5)	10 (5, 35)	<0.001*
Full recovery time (min), median	5.0 (0, 26.3)	40.0 (20.0, 101.3)	<0.001*

ESWL=extracorporeal shock wave lithotripsy, NRS=numeric rating scale, PADSS=post-anesthesia discharge scoring system, **P*-value <0.05

Table 3 Complications

	Group EA (n=34)	Group PF (n=34)	*P*-value
Intraoperative complications, n (%)			
Movement	2 (5.9)	2 (5.9)	1.000
Hypotension	1 (2.9)	1 (2.9)	1.000
Hypertension	5 (14.7)	1 (2.9)	0.200
Postoperative complications, n (%)			
Nausea	1 (2.9)	1 (2.9)	1.000
Vomiting	0	1 (2.9)	>0.999
Pain around procedural site	0	1 (2.9)	>0.999

Table 4 Satisfaction

VAS satisfaction	Group EA (n=34)	Group PF (n=34)	*P*-value
Surgeon, median (P25, P75)	98 (95, 98)	98 (98, 98)	0.042*
Anesthesiologist, median (P25, P75)	90 (90, 95)	95 (95, 95)	<0.001*
Post-anesthesia nurse, median (P25, P75)	100 (90, 100)	100 (90, 100)	0.720
Patient, median (P25, P75)	80 (80, 90)	99.5 (90, 100)	<0.001*

VAS=visual analog scale; 100 horizontal lines for satisfaction reports (0=no satisfaction and 100=highest satisfaction), **P*-value <0.05

Discussion

Appropriate pain control for ESWL should provide adequate anesthesia, sufficient sedation, rapid recovery and be easy to use with minimal side effects. At present, there are no standard guidelines for the treatment of pain during ESWL procedures and a variety of treatment protocols and medications are used. General anesthesia and regional anesthesia provide an excellent pain control, but take time to recover. Patients often have to be admitted. Therefore, it should be considered on a case-by-case basis. The current trend in ESWL pain control is the use of sedatives, because patients can recover quickly without hospitalization to reduce medical expenses.[7-9] The depth of sedation also varies according to many factors including the expertise of medical personnel.[10,11]

The main determinant of pain depends on the level of energy and frequency applied during ESWL. After the procedure, there is usually mild pain, so the most commonly used sedatives are short-acting opioids that have no active metabolites such as remifentanil and fentanyl, as shown in several previous studies.[12-16] However, remifentanil is not available in Thailand, so this present study used fentanyl. A previous study confirmed that a combination of fentanyl and propofol was a viable alternative technique for the outpatient immersion lithotripsy.[17] The dose of etoricoxib used in our study was 90 mg. It was smaller than the previous study.[19] Moreover, a selective COX-2 inhibitor (parecoxib) was not as effective as fentanyl in alleviating pain during ESWL and a low-dose opioid should be added for breakthrough pain.[20] Acetaminophen 1 g intravenously could be used safely and effectively for pain control during ESWL.[21] However, there is no IV acetaminophen available at Surin Hospital. Therefore, the control group in this study used an oral etoricoxib combined with acetaminophen and a small dose of fentanyl for breakthrough pain.

The total dose of fentanyl in group PF was significantly greater than that of EA due to different levels of sedation. According to the present study, a combination use of propofol and fentanyl was able to control pain for this procedure, and the complications were lower than in the previous studies.[17,18] The authors postulate that analgesic requirements during the procedure have significantly decreased due to a newer version of lithotripters being less painful than their prototypes. As well, a better understanding of the pathophysiology of ESWL-induced pain allows new investigators to optimize medication and the depth of sedation. While a combination use of oral etoricoxib and acetaminophen, despite administering minimal sedation, the median PS was lower and was similar to the study of Pimratana and colleagues due to the use of multimodal analgesia.[22]

By the severity of pain, the moderate sedation was significantly effective in reducing moderate-to-severe to mild pain. In addition, it also greatly increased satisfaction for urologists, anesthesiologists, and patients. The authors hypothesized the effect of an appropriate sedation level. As a result, the patients are calm and cooperative, the operator can use the energy and frequency according to the treatment plan. While successful in ESWL, complications during and after sedation, recovery period, and nurse satisfaction were not different. Most

patients achieved a Modified Aldrete score ≥9 within 5 min of the end of ESWL was not different. Although the median time to modified PADSS ≥10 and time to full recovery were slower in group PF than in group EA, the discharge time was not affected and also faster than the previous studies.[23] The main reason for delayed discharge was due to the urologist wanting to check the complications after ESWL (observation approximately 4 hours). Consequently, anesthesia-related complications in the present study were not statistically different between the two groups. Limitations of the present study were noted. First, the administration in each group could not be blinded. Second, because of the small number of patients in the present study, there was no serious problem or complication. Serious complications might potentially be observed if more participants were recruited, or the study was extended. Further prospective trials would be warranted with more patients and updated work plans regularly.

Conclusion

Moderate sedation (propofol-fentanyl) can provide an effective anesthesia for pain control during ESWL. Furthermore, it facilitates ESWL procedures to be established plan, safely and increases overall satisfaction.

What is already known on this topic?

Moderate sedation, although better pain control than minimal sedation, may affect the respiratory system such as causing respiratory obstruction, slow respiratory rate or apnea, and aspiration. In addition, there may be cardiovascular complications such as hypotension, and slower heart rate. Therefore, to ensure safety, anesthetic personnels or clinicians need to be trained in the use of sedation and provide knowledge and ability to monitor and resolve complications that may occur in a timely manner are required.

What this study adds?

Before initiating moderate sedation, an appropriate support system should be established by providing a plan for the anesthetic personnel or other competent personnel to care for the patient. As well as regularly updating, the work should constantly plan to achieve safety goals and continually improve performance.

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Conflicts of interest

The authors declare no conflicts of interest.

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