Medicinska istaživanja 2024; 57(2):33-40 | DOI 10.5937/medi57-48031

OPEN ACCESS

Medical Research | Published by Faculty of Medicine University of Belgrade

ORIGINAL ARTICLE

Preemptive administration of oral, fast-acting tapentadol compared to tramadol/ketoprofen i.m. to reduce acute pain during and after ESWL procedure in renal stone disease

Vuksanović Aleksandar[1,2], Lađević Nikola[1], Jovičić Jelena[2,3], Petrović Nataša[2,3], Jovanović Vesna[2,3], Likić Lađević Ivana[2,4], Lađević Nebojša[2,3], ✉Miloš Lazić[3]

[1]Clinic for Urology, University Clinical Centre of Serbia, Belgrade, Serbia
[2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia
[3]Center for Anesthesiology and Reanimatology, University Clinical Centre of Serbia, Belgrade, Serbia
[4]Clinic for Gynecology and Obstetrics, University Clinical Centre of Serbia, Belgrade, Serbia

Recived: 05 December 2023
Revised: 31 January 2024
Accepted: 29 February 2024

Check for updates

Funding information:
The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Competing interests:
The authors have declared that no competing interests exist

✉ **Correspondence to:**
Miloš Lazić
51, Resavska Street, 11000 Belgrade, Serbia
Email: m.lazic1003@gmail.com

Summary

Introduction: Extracorporeal shock wave lithotripsy (ESWL) used to be performed under general anesthesia. Today, although it is a painful procedure, it is performed under analgosedation. The aim of the study was to determine the severity of acute pain associated with ESWL using two comparative protocols for preemptive analgesics: tramadol vs. ketoprofen plus tapentadol.

Methods: A clinical prospective randomized cohort study included 200 patients of both sexes aged 18-80 years who were divided into two groups: group 1 received a combination of ketoprofen 100 mg/ tramadol 50 mg i.m. 30 minutes before surgery; group 2 received tapentadol IR 50 mg orally, 1 hour before surgery. Pain intensity (NRS) and complications were recorded before, during and at the end of the procedure, respectively.

Results: No difference was found in the preoperative characteristics of patient population, size and localization of the stone. Dimensions of kidney-localized stones were significantly higher in group 2 compared to group 1 (T test .000). There was a statistically significant increase in pain intensity before and during the procedure as well as pain intensity decrease during and after the procedure in each group (T test .000). In group 2, 10% of patients experienced severe pain during the procedure, compared to 3%of patients in group 1 (Mann-Witney 0.005). In the severe pain subgroups of each patient group, drowsiness occurred in 5% of patients in group 2, which was significantly more than the 1% in group 1 (overall incidence in both groups was 25%).

Conclusion: Although both protocols offered average moderate pain intensity during the procedure, severe pain and nausea were observed more frequently in the tapentadol group, which was related to stone size and JJ stent insertion.

Keywords: preemptive analgesia, tapentadol, ESWL procedure

Cite this article as: Aleksandar V, Lađević N, Jovičić J, Petrović N, Jovanović V, Likić Lađević I, Lađević N, Lazić M. Preemptive administration of oral, fast-ascting tapentadol compared to tramadol/ketoprofen i.m. to reduce acute pain during and after eswl procedure in renal stone disease; Medicinska istaživanja 2024; 57(2):33-40 DOI: 10.5937/medi57-48031

INTRODUCTION

After the introduction of extracorporeal shock wave lithotripsy (ESWL), the procedure was performed under general anesthesia. Technical improvement of the ESWL device made it possible to perform the treatment without general anesthesia, although less energy is used to break up the stone. Nevertheless, ESWL is still generally considered a painful procedure. This may be because shock waves reach superficial (skin and muscles) and deeper structures (ribs, nerves and kidney capsule) (1,2).

Pain is generally believed to affect the outcome of ESWL, as involuntary pain is caused by movements and excessive breathing excursions during the procedure, which interferes with the surgeon's efforts to focus on the stone. A high pain sensation may also limit the ability to apply the appropriate dose of energy (3,4). In addition, pain that limits the patient's cooperation may limit the energy and number of shock waves and lead to more complications, such as a higher rate of renal hematoma due to increased blood pressure (5).

To date, there are no guidelines for pain management during ESWL treatment, and different treatment protocols and different medications are used. Traditionally, non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac, ketorolac and piroxicam are used, but sometimes opioids such as morphine, pethidine and fentanyl are also used (6,7).

Pain caused by shock waves is usually described as burning and stabbing (8,9).

Non-steroidal anti-inflammatory drugs (NSAIDs) are the most widely used analgesics in the world, mainly because of their analgesic and anti-inflammatory properties (10,11). In 1991, molecular biologists discovered that there are two different gene codes for cyclooxygenases - COX1 and COX2 (12). Both enzymes are distributed differently in the organism and are regulated differently. COX 1 is a constitutively present enzyme in most tissues of the body. They most likely influence the production of a constant amount of eicosanoids (prostaglandins and similar substances) to maintain physiological homeostasis in many organs such as the kidneys, lungs, stomach, etc. COX2 is found in macrophages and other cells of inflamed tissue (13). The expression of this enzyme is suppressed by glucocorticoids (14, 15). Opioids are substances with morphine-like effects, including both agonists and antagonists as well as natural and synthetic opioid peptides.

Opioids exert their pharmacological effects by binding to the opioid receptors MOP(μ), KOP(κ), DOP(δ), NOP - nociceptive orphanin FQ receptors, also known as ORL (opioid receptor-like). The receptors achieve their efficacy by binding to the inhibitory G protein. When using opioids, precautions are necessary in cases of liver and kidney disease, emphysema, asthma, pneumonia, head injuries, allergic reactions, interactions with antihistamines, sedatives, antiemetics and MAO inhibitors (16,17).

The group of weak opioid drugs is named this way because they have an upper limit of effectiveness, meaning there is a maximum effective daily dose that can be used in the treatment of moderate pain intensity score. Weak opioids are most commonly combined with non-opioids, such as: acetylsalicylic acid, acetaminophen and other NSAIDs. Weak opioids include: tramadol, tapentadol, codeine, dihydrocodeine, dextropropoxyphene (18).

THE AIM

The aim of the study was to evaluate the severity of acute pain related to ESWL procedure of kidney stones under preemptive analgesia with tramadol/ketoprofen combination intramuscular and tapentadol tablets orally as well as to compare analgesic effects of these two protocols in acute pain control for ESWL procedure.

METHODOLOGY

The research was conducted at the University Clinical Center of Serbia in accordance with the Helsinki Declaration and approved by the Ethics Committee (decision number 57/13).The clinical prospective cohort study included 200 consecutive patients of both genders, aged 18-80 years, ASA I-III status, who underwent an elective ESWL (extracorporeal shock wave lithotripsy) procedure for the treatment of kidney stones. The study lasted for 6 months.

Preoperative demographic data, gender, age, body mass index (BMI), place of residence (urban/rural), education, occupation, smoking habit, comorbidities, previous surgeries were collected from all patients. Regarding the procedure, the characteristics of the kidney stone (size, localization) and the presence of a JJ urethral stent were recorded.

The following patients were excluded from the study: those with advanced chronic renal insufficiency, chronic hepatic insufficiency, psychiatric comorbidity, dizzy spells, ASA status IV group, asthma, active peptic ulcer, and previous allergies to administered drugs.

The subjects were divided into two study groups according to the received pain therapy protocols both used as the standard procedure in everyday practice. Group 1 received the combination of ketoprofen 100mg plus tramadol 50mg intramuscularly, 30 minutes before the start of the ESWL procedure. Group 2 received tapentadol IR 50mg orally, 1 hour before the start of the ESWL procedure. Stone-related pain intensity score was recorded before the administration of the medication, during the ESWL procedure and at the end of the ESWL procedure using the NRS scale (numerical rating scale).

Parametric and non-parametric tests were used in the statistical analysis of the data, and the statistical differ-

Table 1. Distribution of preoperative patient characteristics in both study groups

Patient characteristics	Group 1 (n=100) n (%)	Group 2 (n=100) n (%)	Test value/ p(probability)
Gender (male/female)	42 / 58	39 / 61	0.666**/p ≥0.05
Age (years)	51.98±13.18	51.70±13.72	0.884*/ p≥ 0.05
BMI (kg/m2)	24.66±2.85	24.34±3.16	0.453*/ p ≥0.05
Smoking habit (Y/N)	48 / 52	59 / 41	0.120**/ p ≥0.05
Occupation (Y/N)	66 / 34	72 / 28	0.360**/ p ≥0.05
Place of residence (urban/rural)	73 / 27	66 / 34	0.284**/ p ≥0.05
Education (basic/ middle/ faculty)	30 / 40 / 30	33 / 48 / 19	0.199**/ p ≥0.05
Comorbidities (Y/N)	51 / 49	57 / 43	0.396**/ p ≥0.05
Previous surgeries (Y/N)	53 / 47	51 / 49	0.778**/ p ≥0.05

*Student T- test, ** Mann-Witney test; Y- yes, N-no

ence was expressed by two levels of significance (p≥0.05, p<0.05) using SPSS 21 statistic software. The variables were categorized according to the median value.

RESULTS

Two hundred patients were included in the study and classified into two groups according to the study protocol. There was no statistically significant difference between groups in preoperative patient characteristics and stone characteristics (stone size and localization).

In both groups of patients, the majority of respondents were from urban areas (66% vs. 73%), with secondary school degree (48% vs. 40%). In both groups the majority of patients had jobs (72% vs. 66%) but there was no statistically significant difference between the groups related to occupational status. Also, there were no statistically significant differences between groups in the prevalence of tobacco smoking (59% vs. 48%). Patient characteristics in two groups are shown in **Table 1**.

Stone localization was divided into five groups (left kidney, right kidney, left UP segment, right UP segment, ureter) with no statistically significant difference among the groups (X^2 0.856, p≥0.05). The most frequent localization in both study groups was the kidney **(Chart 1)**. The average stone size was 13.24±2.803 mm in group 1 and 13.14±2.370 mm in group 2, also with no statistically significant difference (T test 0.786, p≥0.05). No correlation was found between stone size and localization in group 1 (Pearson X^2 0.150, p≥0.05). A significant correlation was found in group 2 patients between stone size and stone localization (Pearson X^2 .000, p≥ 0.01) related to greater dimensions of kidney-localized stones.

Overall, 33% of patients in group 1 and 25% of patients in group 2 had a protectively placed JJ stent after the procedure. The presence of a JJ stent did not influence pain intensity after the procedure in patients from group 1 (Pearson X^2 0.486, p≥0.05). JJ stent insertion had influence on pain intensity after the procedure in group 2 (tapentadol group) with 21% of patients suffering from mild pain and 4% of patients suffering from moderate pain intensity related to JJ stent insertion (Pearson X^2 0.015, p<0.05).

Pain intensity was measured before, during and immediately after ESWL procedure, and the distribution of mean pain scores is shown in Chart 2.

Chart 1. The distribution of stone position by group (UP segment- ureteropelvic segment)

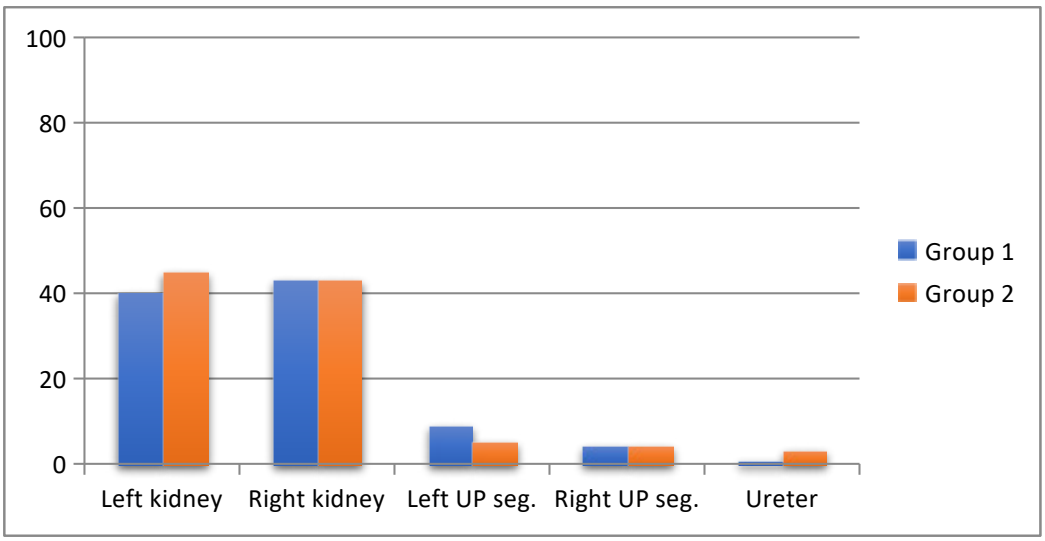
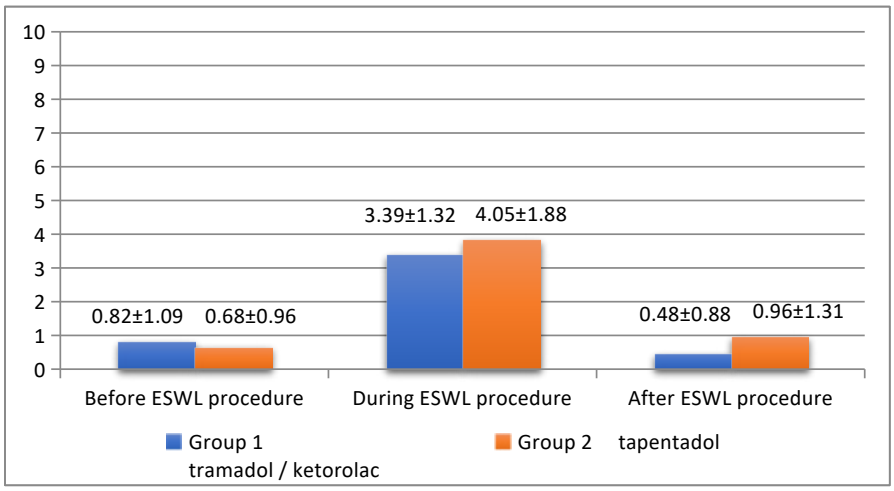


Chart 2. Average pain values measured by the NRS scale before, during and after the ESWL procedure



During the procedure, pain intensity was statistically significantly higher in both groups of patients (T test .000, CI 0.95, p<0.05) compared to pain before and after the procedure. No statistically significant difference was found in pain intensity before –after measurements in group 1 and group 2 patients respectively (T test 0.737 and T test 0.320 CI 0.95, p≥0.05). Before ESWL procedure no statistically significant difference was found in NRS between the groups (T test 0.338 CI 0.95, p≥0.05). Statistical difference was found in NRS during the procedure (T test 0.039 CI 0.95, p≥0.05) and after the procedure close to the level of significance (T test 0.055 CI 0.95, p≥0.05)

Chart 3. Distribution of patients related to pain intensity score during the ESWL procedure (Group 1)

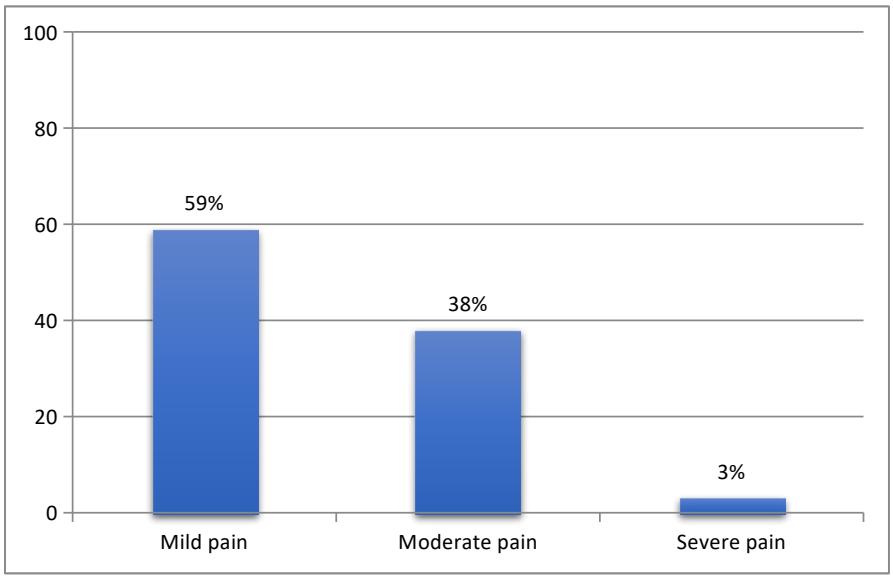


Chart 4. Distribution of patients related to pain intensity score during the ESWL procedure (Group 2)

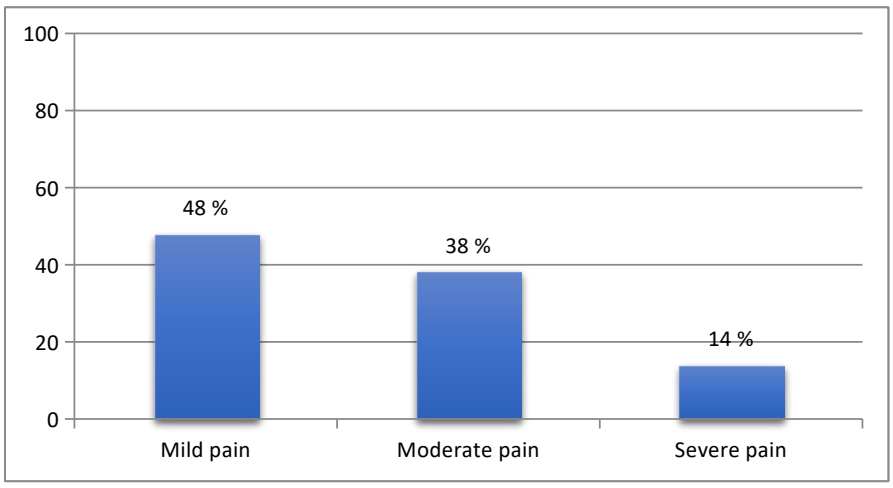
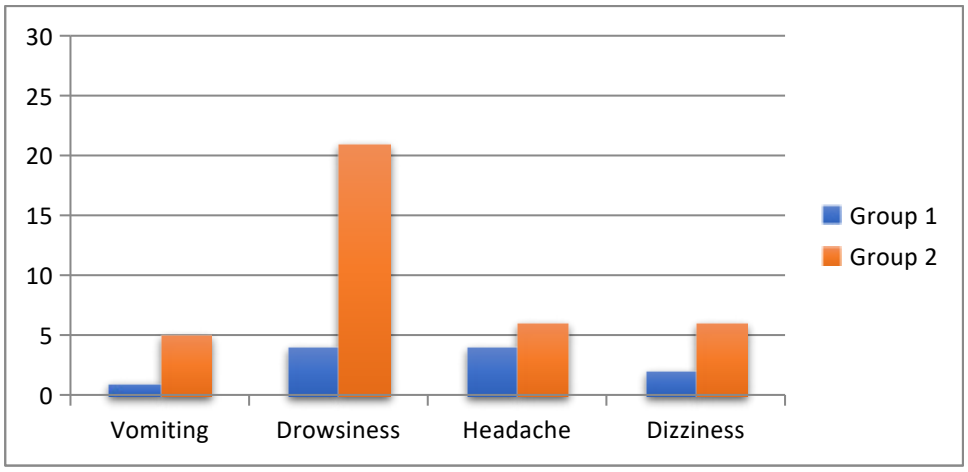


Chart 5. Frequency distribution of vomiting, drowsiness, headache and dizziness (both groups)



between the study groups. In group 1 patients, statistically significant difference was found between NRSs before - during procedure and NRSs during-after procedure (T test .000 CI 0.95, p<0.05). In group 2, a statistically significant difference was found between all three follow-up periods respectively (T test .000 and T test .000 and T test 0.058 CI 0.95, p<0.05). Compared to group1 patients, in group 2 patients average mild pain score recorded before the procedure remained mild pain score after the procedure although statistically significant.

The distribution of pain score within the individual groups is shown in **Chart 3** and **Chart 4**.

Drowsiness was present in 25% of patient population: 21% of patients in group 2 and 4% of patients in group 1 with a statistically significant difference between the groups (X^2 .000, p<0.05). Compared to drowsiness, there was no statistically significant difference among groups in occurrence of vomiting, headache, dizziness respectively (X^2 0.212 and X^2 0.748 and X^2 0.279, p≥0.05), **Chart 5**. In the entire patient population, 12,5% of patients with kidney-localized stones felt drowsiness without statistical difference between groups (X^2 0.229,p ≥0.05). Drowsiness was not reported by the patients with UP segment or ureter stone localizations.

Only during the procedure, severe pain intensity score was recorded in both study groups. Severe pain during the procedure was reported by 10% of patients from tapentadol group and by 3% of patients from tramadol/ketoprofen group. Severe pain was reported with statistical difference in distribution between the groups (X^2 0.005, p<0.05), but it was reported only by 7,6% of those with kidney-localized stones. In tapentadol group (group 2) 5% of patients reported severe pain with drowsiness compared to 1% of patients in tramadol/ketoprofen group (X^2 0.021, p<0.05). Moderate pain intensity after the procedure was reported by 6% of patients in group 2 and 1% of patients in Group1 (X^2 0.059, p ≥0.05). We found weak statistical correlation between drowsiness (with kidney stone localization) and NRS during the procedure (in group 1 Spearman $^{0.020}$, p<0.05 and in group 2 Spearman 0. 028, p<0.05). No correlation was found swithin study groups between drowsiness and NRS after the procedure in both groups of patients (group 1 Spearman $^{0.113}$, p≥0.05 and group 2 Spearman 0.113, p≥0.05). Multivariate regression analysis did not find any correlation between NRS after the procedure and the examined variables except for drowsiness with the statistical level close to significant (Sig. 0.072, CI 0.95, t -1.772).

DISCUSSION

The introduction of ESWL was revolutionary for the treatment of urolithiasis. However, ESWL causes shock wave pain during the treatment. The right dose of analgesics is mandatory to maintain the patient's comfort and can improve the result of the treatment (19). The pathogenesis of pain related to ESWL procedure has not been fully understood yet, but cavitations seem to play a key role rather than direct mechanical effects on the nociceptive nerve endings. The formation, movement and implosion of the resulting shock wave, microbubbles in body fluids or tissues lead to the stimulation of superficial nociceptors in the skin as well as deeper visceral nociceptors in the renal capsule, periosteum, pleura, peritoneum and muscles. Another component of pain associated with shock waves is the movement of the stone caused by the impact of the shock waves (6).

It has been found that several physical variables influence the treatment of pain: the type of shock wave source, the size and location of the stone load (e.g., an upper pole stone near the ribs), the peak pressure of shock waves, the diameter of the focal zone, and the size of the shock wave source orifice, which reflects an important role of the surface area of the shock wave entering the skin. In addition, patient-related factors such as age, gender and habitus are responsible for the sensation of pain during ESWL (7,8).

In our study, the mean pain score during the procedure ranged from NRS 3.39± 1.32 to NRS 4.05± 1.88 (moderate pain) depending on the subject group. Even though statistical significance in pain intensity was recorded between follow-up periods in tapentadol group, a

clinical significance was not found (average pain intensity scores < 1/10 NRS). Also, in tramadol/ketoprofen group there was no clinical and statistical significance in perioperative pain scores (before and after the procedure). Only 6,5% of the patient population reported severe pain during procedure (NRS 7/10) with statistical significance between the groups. After completing the procedure, average mild pain intensity was reported in both groups of patients. Both results indicate good pain control after the procedure related both applied analgesic regimens. Bovelander E. et al. reported the mean pain score described as "5", which is a relatively high pain score, considering that analgesics are administered (20). In addition, one third of the patients had severe pain (pain score 7–10). These data show that high pain scores are associated with lower intensity during ESWL. This suggests that pain avoidance protocol is not sufficient and should be revised. Additional analgesics (and a combination of paracetamol, NSAIDs and opioids) reduced the mean pain score and improved the patients' well-being. Also, they reported no significant difference in pain scores between the patients who received additional opioids (n = 46) and those who did not. This is likely due to the small group of patients who received opioids. The study by Tokgoz et al. which analyzed pain perception during ESWL supports these findings by describing the mean pain score for the first ESWL session as 4.67 on the NRS scale (1).

Even with the latest generation of lithotripters, ESWL is still a potentially painful procedure and adequate analgesia is essential for good treatment outcomes. General anesthesia should be reserved for selected cases and the treatment of children; the same applies to spinal anesthesia. Both guarantee optimal pain control but have high personnel, resource and management requirements leading to a longer recovery time, making them less suitable for ESWL as an outpatient procedure.

In this context, inhalation anesthesia with nitrous oxide is another very interesting option as it provides good analgesia, is easy to use and does not lead to a prolonged recovery period. Subcutaneous infiltration with local anesthetics has also proven to be effective in terms of pain control and safety, as it avoids the side effects of opioids. The concept of dermal anesthesia is not new, but remains an interesting option due to the ease of application and convenience for the patient, but it has not shown the best results.

Opioids, sometimes in combination with sedatives or NSAIDs, are classic pain control agents for ESWL. They have a very good analgesic effect, but sometimes unpleasant side effects as well, they require monitoring the patient and lead to a delayed discharge of the patient. Analgosedation and patient-controlled analgesia lead to good pain relief and patient satisfaction, but are expensive and also limited in the outpatient setting.

NSAIDs are very convenient for both surgeons and patients. They are easy to use, do not require patient monitoring and patients can be discharged immediately after surgery. NSAIDs mainly act in the area of pain transmission and modulation. Peripheral prostaglandins influence the development of hyperalgesia, and for many years it was thought that inhibition at the site of inflammation was the main mechanism of action of NSAIDs. Prostaglandins stimulate a certain number of primary afferent nerve fibers, the so-called "silent" nociceptors, and thus cause primary hyperalgesia via tetrodoxin-resistant Na+ channels. Prostaglandins act on nociceptors in the periphery, also produced in the dorsal horns of the spinal cord in response to peripheral inflammation (16,17).

Substances such as paracetamol and tamsulosin are often used for other indications and have recently come into focus, but do not have a significant place in ESWL analgesia. Their very favorable side effect profile makes them very interesting, although the analgesic component, especially of tamsulosin, is not convincing (21).

A study by Hashem A et al. compared safety and efficacy of xylocaine gel and ketorolac as opioid-sparing analgesics versus pethidine for shock wave lithotripsy (ESWL) pain (22). A single-blind, randomized, controlled trial (RCT) was conducted in 132 patients with renal and upper ureteral stones which were eligible for treatment with the ESWL procedure.

The first group of patients received intravenous pethidine and placebo gel; the second group received IV ketorolac plus placebo gel; the third group received topical lidocaine gel plus IV normal saline. Dissolution of the stone was classified as none (no change from baseline by kidney, ureter, X-ray, or ultrasound), partial (fragmented and residual fragments > 4 mm), and complete (≤4 mm residual fragments).

The disintegration of the stone was assessed by X-ray of the bladder and ultrasound. Pain was assessed using the Numerical Pain Rating Scale (NRS). NRS scores were highest in the xylocaine group at 10, 20 and 30 minutes (p=0.0001), with no significant difference between the ketorolac and pethidine groups except at 10 minutes (p=0.03) and almost significant difference at 30 minutes (p=0.054) in favor of ketorolac. The results for stone dissolution (no, partial or complete dissolution) were as follows: 25 (50.0%), 23 (46.0%), and 2 (4.0%) for pethidine; 19 (35.8%), 23 (43.4%), and 11 (20.8%) for ketorolac; and 26 (89.7%), 3 (10.3%), and 0 (0.0%) for lidocaine (p=0.008). The authors concluded that the use of ketorolac was a safer and more effective alternative to morphine derivatives for ESWL analgesia. Lidocaine gel should not be used as monoanalgesia for ESWL (23).

Bovelander E. and colleagues showed in their study that there was a correlation between the severity of pain and the success of the ESWL procedure (24,25). Non-steroidal anti-inflammatory drugs such as diclofenac or ketoprofen and opioids such as tramadol are most commonly used to prevent and treat pain during and immediately after the ESWL procedure (26). Tramadol is a synthetic analgesic. It acts via NOP, KOP and DOP receptors and

then unfolds its effect as an opioid analgesic, i.e. it inhibits its nociception. Another mode of action of tramadol is to block the uptake of serotonin and noradrenaline and then act as a non-opioid analgesic. The properties of tramadol are reflected in the rapid absorption, the effect after 30 minutes, the manifestation of the maximum effect after 1-2 hours and the application intervals of 5-6 hours (27).

Today, oral pain therapy is increasingly used for acute pain. Tapentadol is a new central analgesic with a dual mechanism of action in a single molecule: μ-opioid receptor agonist and noradrenaline reuptake inhibitor (MOR-NRI) (19,20). Moderate affinity for the μ-opioid receptor and the opioid-sparing effect of noradrenaline reuptake inhibition allow for the occurrence of fewer side effects. Effects are compared to other μ-agonists (28,29). The most recent recommendations of the European Association of Palliative Care (from 2012) did not include this new drug as it was not available until after they were produced (30).

Viscisi ER et al. showed good analgesic properties of tapentadol and its excellent tolerability in the treatment of acute postoperative pain (31).

All these studies have shown so far that there is no universal combination of drugs that prevents the occurrence of pain 100% and that this depends on a number of factors. However, it is also clear that our respondent groups were satisfied with the therapy used and that analgesics should be used,even per os in the form of the opioid tapentadol if administered at the right time.

CONCLUSION

Severe pain was reported only during the ESWL procedure in both study groups with no statistical difference between the groups. In tapentadol group of patients, statistically significant difference was also found in pain intensity scores before and after the procedure compared to tramadol/ketoprofen group. Severe pain intensity score during the procedure was reported only by the patients with kidney stone localization. The size of the stone had no effect on the intensity of pain during ESWL but it influenced drowsiness whose occurrence was related to stone localization. Although statistical difference was noted, the clinical significance in terms of pain intensity scores before and after the procedure was not found. Both protocols ensured safety and low pain intensity scores after the procedure.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

All authors contributed to the study conception and design. Material preparation and data collection were performed by Aleksandar Vuksanović and Nikola Lađević. The first draft of the manuscript was written by Aleksandar Vuksanović, Nikola Lađević, Jelena Jovičić, Vesna Jovanović, Nataša Petrović and Miloš Lazić. Nebojša Lađević and Ivana Likić Lađević edited the manuscript. All authors read and approved the final manuscript.

Consent to participate

Written informed consent was obtained from the patient.

Consent to publish

The authors affirm that the patient provided informed consent for publication.

REFERENCES

1. Tokgoz H, Hanci V, Turksoy O, Erol B, Ak¬duman B, Mungan NA: Pain perception during shock wave lithotripsy: does it correlate with patient and stone characteristics? J Chin Med Assoc 2010; 73:477–482.
2. Ucer O, Ceylan Y, Ekren F, Ozan E, Mu¬ezzinoglu T: Effect of anxiety and pain on success of shockwave lithotripsy (SWL) for treatment of proximal ureteral and renal pel¬vic stones. Urolithiasis 2016; 44:559–564.
3. Vergnolles M, Wallerand H, Gadrat F, Mau¬rice-Tison S, Deti E, Ballanger P, Ferriere JM, Robert G: Predictive risk factors for pain during extracorporeal shockwave lithotripsy. J Endourol 2009; 23:2021–2027.
4. Berwin JT, El-Husseiny T, Papatsoris AG, Hajdinjak T, Masood J, Buchholz N: Pain in extracorporeal shock wave lithotripsy. Urol Res 2009; 37:51–53.
5. Tauzin-Fin P et al. Effect of balanced analgesia with buprenorphine on pain response and general anaesthesia requirement during lithotripsy procedures. European Journal of Anaesthesiology 1998;15(2):147–152.
6. Mezentsev VA. Meta-analysis of the efficacy of non-steroidal anti-inflammatory drugs vs. opioids for SWL using modern electromagnetic lithotripters. International Brazilian Journal Urology 2009;35)3): 293–298.
7. Allman DB, Richlin DM, Ruttenberg M, Sotolongo JRJ. Analgesia in anesthesia-free extracorporeal shock wave lithotripsy: a standardized protocol. Journal of Urology 1991;146(3):718–720.
8. Basar H, Yilmaz E, Ozcan S et al. Four analgesic techniques for shockwave lithotripsy: eutectic mixture local anesthetic isa good alternative. Journal of Endourology 2003;17(1):3–6
9. Lussier D, Beauliey P. Rational Taxonomy of Analgesics Drugs. In: Beauliey P, Lussier D, Porreca F, Dickenson A (eds). Pharmacology of Pain. IASP Press, Seatle, 2010: 27-40.
10. Laine L. Aproachesto non-steroidal anti-inflamatory drug use in the high risk patient. Gastroenterology 2001; 120:594-606.
11. Bacchi S, Palumbo P, Sponta A, Coppolino MF. Clinical pharmacology of non-steroidal anti-inflamatory drugs: a review. Anti-inflamatory&Anti-alergy Agents in Medicinal Chemistry 2012; 11:52-64.

12. Kujubu DA et al. TIS 10, a phorbol ester tumor promoter-inducible mRNA from Swiss 3T3 cells, encodes a novel prostaglandin synthase/cyclooxygenase homologue. Journal of Biological Chemistry 1991; 266:12866-1872.
13. Beiche F et al. Upregulation of cyclooxygenase- mRNA in the rat spinal cord following peripheral inflammation. FEBS letters 1996; 390:165-169.
14. Masferrer JL, Seibert K, Zweifel BS, Needleman P. Endogenous glucocorticoids regulate an inducible cyclooxygenase enzyme. Proceedings of the National Academy of Science, USA 1992;89:3917–21.
15. Maihöfner C, Schlötzer-Schrehardt U, Gühring H, Zeilhofer HU, Naumann GOH, Pahl A, Mardin C, Tamm ER, Brune K. Expression of cyclooxygenase-1 and -2 in normal and glaucomatous human eyes. Investigative Ophthalmology & Visual Science 2001:42:2616–24.
16. Baba H, Kohno T, Moore KA, Woolf CJ. Direct activation of rat spinal dorsal horn neurons by prostaglandin E2. Journal of Neuroscience 2001; 21:1750–1756.
17. Ahmadi S, Lippross S, Neuhuber WL, Zeilhofer HU. PGE2 selectively blocks inhibitory glycinergic neurotransmission onto rat superficial dorsal horn neurons. Nature Neuroscience 2002; 5:34–40.
18. Holdcroft A, Power I. Recent developments: Management of pain. British Medical Journal 2003; 326:635-639.
19. Türk C, Knoll T, Petrik A, Sarica K, Skolarikos A, Straub M, Seitz C: Guidelines on urolithiasis. European Association of Urology, 2015.
20. Tzschentke TM, De Vry J, Terlinden R, et al. Tapentadolhydrochloride.Analgesic, mu-opioid receptor agonist,noradrenalin reuptake inhibitor.Drugs Future 2006;31:1053-61.
21. Bach C et al. Drugs for PainManagement in ShockWave Lithotripsy. Pain Research and Treatment 2011: doi:10.1155/2011/259426
22. Hashem A et al. Efficacy of pethidine, ketorolac, and lidocaine gel as analgesics for pain control in shockwave lithotripsy: A single-blinded randomized controlled trial. Investig Clin Urol2019; 60:251-257
23. Daly KM et al. Evaluation of protocols on the use of analgesics for pain management in patients with extracorporeal shock wave lithotripsy (ESWL). Pan Afr Med J 2019; 32:109.
24. Kiaei MM et al. Enteral diclofenac controls pain and reduces intravenous injection during extracorporeal shock wave lithotripsy. Eur J TranslMyol 2018;28(2):7353.
25. Bovelander E et al. The Influence of Pain on the Outcome of Extracorporeal Shockwave Lithotripsy. CurrUrol 2019;12(2):81-87.
26. Türk C, Knoll T, Petrik A, Sarica K, Sko¬larikos A, Straub M, Seitz C: Guidelines on urolithiasis. European Association of Urol¬ogy, 2015.
27. Tzschentke TM, Christoph T, Ko¨ gel B, et al. (-)-(1R,2R)-3-(3-Dimethylamino- 1-ethyl-2-methyl-propyl)-phenol hydrochloride (tapentadol HCl): a novel m-opioid receptor agonist/norepinephrine reuptake inhibitor with broad-spectrum analgesic properties. J Pharmacol Exp Ther2007; 323:265-76.
28. Shafer M. Novel concepts for analgesia in severe pain: current strategies and future innovations. Eur J Pain 2009; (Suppl 3):6-10
29. Caraceni A, Hanks G, Kaasa S, et al. Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. Lancet Oncol 2012;13:e58-68.
30. Riemsma R, Forbes C, Harker J, et al. Systematic review of Tapentadol in chronic severe pain. Curr Med Res Opin2011; 27:1907-30.
31. Viscusi ER et al. Tapentadol immediate release for moderate to severe acute post-surgery pain. J Opioid Manag 2019;15(1):51-67.

PREVENTIVNA PRIMENA ORALNOG TAPENTADOLA SA BRZIM DEJSTVOM NASPRAM PRIMENE INTRAMUSKULARNOG TRAMADOLA/KETOPROFENA SA CILJEM SMANJENJA BOLA TOKOM I NAKON EKSTRAKORPORALNE LITOTRIPSIJE UDARNIM TALASIMA KOD BUBREŽNOG KAMENA

Vuksanović Aleksandar[1,2], Lađević Nikola[1], Jovičić Jelena[2,3], Petrović Nataša[2,3], Jovanović Vesna[2,3], Likić Lađević Ivana[2,4], Lađević Nebojša[2,3], Miloš Lazić[3]

Sažetak

Uvod: Ekstrakorporalna litotripsija udarnim talasom (ESWL) ranije je rađena u opštoj anesteziji, ali se danas, iako bolna procedura, radi u analgosedaciji. Cilj studije je da se utvrdi jačina akutnog bola povezanog sa ESWL-om korišćenjem dva uporedna protokola preeemptivnih analgetika: tramadol plus ketoprofen nasuprot tapentadolu.

Metode: Klinička, prospektivna, randomizovana kohortna studija obuhvatila je 200 pacijenata oba pola starosti od 18-80 godina koji su podeljeni u dve grupe: grupa 1 – primila kombinaciju ketoprofena 100 mg/tramadola 50 mg i.m. 30 minuta pre procedure; grupa 2 – primala tapentadol IR 50 mg oralno 1 sat pre procedure. Intenzitet bola (NRS) i komplikacije su evidentirani pre, tokom i na kraju zahvata.

Rezultati: Nije nađena razlika u preoperativnim karakteristikama populacije pacijenata i veličini i lokalizaciji kamena. Veličina kamena lociranog u bubregu u grupi 2 je bila statistički značajno veća (T- test .000). U svakoj grupi došlo je do statistički značajnog povećanja intenziteta bola pre i tokom operacije (T-test .000) kao i do smanjenja intenziteta bola tokom i nakon procedure bez razlike među grupama. U grupi 2, 10% pacijenata je imalo jake bolove tokom postupka u poređenju sa 3% u grupi 1 (Mann-Whitney 0.005). U podgrupama sa jakim bolom svake grupe pacijenata, mučnina se javila kod 5% pacijenata u grupi 2, što je značajno više od 1% u grupi 1(ukupna incidenca u obe grupe je 25%). **Zaključak:** Iako oba protokola obezbeđuju prosečno umeren intenzitet bola tokom procedure, jak bol i mučnina su češće primećeni u grupi koja je primala tapentadol, što je povezano sa renalnom veličinom kamena i plasiranjem JJ stenta.

Ključne reči: preemptivna analgezija, tapentadol, ESWL procedura

Primljen: 05.12.2023. I **Revizija:** 31.01.2024. I **Prihvaćen:** 29.02.2024.

Medicinska istaživanja 2024; 57(2):33-40