Comparison of the Efficacy of Intravenous and Intramuscular Lornoxicam for the Initial Treatment of Acute Renal Colic: A Randomized Clinical Trial

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Purpose: We aimed to find out if there was any difference between intramuscular and intravenous administration of lornoxicam in terms of efficacy and side effects.

Materials and Methods: This study was a single-blind parallel-group randomized clinical trial. A total of 51 patients who were diagnosed with acute renal colic at our clinic were included in the study. Pain severity prior to treatment was rated using the Visual Analogue Scale (VAS). Patients were randomized into 2 groups: Group 1 (n = 27) received intramuscular 8mg lornoxicam and Group 2 (n=24) received intravenous 8mg lornoxicam. Pain severity was reassessed 30 minutes after the treatment. Pre- and post-treatment VAS scores and the mean change in the VAS scores of the 2 groups were statistically compared.

Results: The mean VAS scores decreased significantly from 7.65 to 2.07 in Group 1, from 7.96 to 1.38 in Group 2, and from 7.79 to 1.75 in total ($P < 0.001$). No statistically significant difference was observed between Groups 1 and 2 in terms of VAS score reduction ($P = 0.128$). None of the patients suffered any side effects except for 1 (2%) patient who had dyspepsia.

Conclusion: Parenteral lornoxicam provides significant pain relief in patients with acute renal colic. However, no significant difference was found between intramuscular and intravenous administration in terms of analgesic efficacy.

Keywords: lornoxicam; parenteral treatment; acute renal colic; urolithiasis

INTRODUCTION

Pain is one of the most common presenting complaints in the emergency department (ED).[1] Renal colic is a common cause of pain and patients usually present with severe flank and/or abdominal pain which requires immediate analgesic treatment in the ED.[2] About 85% of renal colic cases are caused by urolithiasis, but renal colic may also arise from different etiologies such as extrinsic ureteral compression, urinary neoplasms, and anatomic anomalies.[3]

The prevalence of renal colic varies between 5-15% throughout the world.[4] Providing pain relief is the most important step of the treatment and various types of medications are used for pain relief in the clinical practice. When selecting first-line analgesic drugs in the ED, the efficacy, safety, and rapid applicability of the drug, and the logistics involved are taken into consideration.[5] Given their prostaglandin synthesis-inhibiting effects and the current evidence on their efficacy, international guidelines recommend the use of non-steroid anti-inflammatory drugs (NSAID) as first-line analgesic treatment.[6,7] However, to date, no gold standard protocol has been established for pain management in patients with renal colic. Lornoxicam is an NSAID which belongs to the oxicam class and has analgesic and antipyretic properties. Like the other members of the oxicam class, lornoxicam acts by inhibiting prostaglandin synthesis. It has a short plasma elimination half-life of 3-4 hours, which makes it eligible for treating acute pain.[8] Previous studies have shown that the analgesic efficacy of NSAIDs is at least as potent as opioids.[9,10] Parenteral lornoxicam can be administered via intramuscular (IM) and intravenous (IV) routes.

We aimed to find out if there was any difference between intramuscular and intravenous administration of lornoxicam in terms of efficacy and side effects.

PATIENTS AND METHODS

Study Population

After local ethics committee approval was obtained, fifty-one patients who presented to the ED of İnönü University Turgut Özal Medical Center between February 1, 2006, and April 30, 2006, with severe flank pain and whose radiological findings were indicative of urolithiasis were included in the study. The study was carried out in compliance with the Helsinki Declaration of 1964 and its later amendments.

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Table 1. Patient characteristics.

	Group 1 (IM)	Group 2 (IV)	*P*-value
Total number, (male-female)	27 (15-12)	24 (12-12)	-
Age (years), mean±SD	38.2 ± 2.7	36.7 ± 2.7	0.799
Stone location (kidney-urether)	5-22	8-16	-
Urea (mg/dL) mean±SD	15.5 ± 5.1	16.2 ± 5	0.807
Creatinine (mg/dL) mean±SD	1 ± 0.2	1 ± 0.3	0.972
Hydronephrosis n(%)	17 (63)	17 (71)	-

Inclusion and exclusion criteria

The exclusion criteria for this randomized controlled study were as follows: history of analgesic use within the last 2 hours prior to presentation, active urinary tract infection and pyuria accompanying renal colic, age < 18 or >65 years, history of gastrointestinal bleeding or ulcer, liver failure, coagulopathies, moderate or severe renal failure, severe heart failure, pregnancy, lactation, hypovolemia and dehydration, known or suspected cerebrovascular bleeding, known allergies to lornoxicam or other NSAIDs.

Procedures and evaluations

Blood and urine samples were obtained from each patient. Complete blood count, blood urea nitrogen, serum creatinine and electrolyte levels, urine dipstick testing, and urine microscopy results were recorded for each patient. All patients underwent plain abdominal radiography and urinary ultrasonography. In patients whose plain abdominal radiography and urinary ultrasonography results were negative, a non-contrast computerized tomography was performed to confirm the stone. The blood pressure, heart rate, respiratory rate and body temperature of all patients were recorded. The severity of pain was evaluated using the Visual Analogue Scale (VAS) score.[11] The VAS is a 100 mm horizontal line, marked from 0 to 10 at 10mm intervals, with 0 representing "no pain" and 10 representing "worst possible pain". Patient randomization and all VAS measurements were performed by the same physician. Informed consent was obtained from each patient prior to treatment. This study was a single-blind parallel-group randomized clinical trial. The parallel design, which is the most popular design in randomized clinical trials, was used. Patients were randomly allocated into 2 groups using a random numbers table.[12-13] Group 1 (n=27) received IM and Group 2 (n=24) received IV 8mg lornoxicam (Nycomed GmbH, Austria) which was diluted in distilled water. The duration of IV of injection was at least 15 seconds and the duration of IM administration was at least 5 seconds. All patients were monitorized before administration and were followed-up for 1 hour to observe any side effects and complications. On the 30th minute, pain was reassessed using the VAS score and vital signs were measured.

Statistical Analysis

All statistical analyses were performed using the SPSS statistical software (SPSS for Windows, version 22.0; SPSS, Inc., Chicago, IL, USA). Pre- and post-treatment VAS scores were compared using the non-parametric Wilcoxon signed ranks test. The age and VAS scores of the two groups were evaluated using the non-parametric Mann Whitney U test. A p-value<0.05 was considered statistically significant.

RESULTS

The mean age was 37.4 ± 1.9 years (range 18-65). The mean age in Groups 1 and 2 were 38.2 ± 2.7 and 36.7 ± 2.7 years, respectively. No statistically significant difference was found between the two groups in terms of age (P = 0.799). The characteristics of patient groups are presented in **Table 1**. All patients had flank and/or abdominal pain, costovertebral angle tenderness, and some patients had abdominal tenderness on the affected side.

On the 30th minute, the mean VAS scores decreased significantly: from 7.79 to 1.75 in the whole study group; from 7.65 to 2.07 in Group 1; and from 7.96 to 1.38 in Group 2 (P < 0.001) (**Table 2**). The decrease in Group 2 was greater than Group 1 but the difference was not statistically significant (P = 0.128). In 5 patients from Group 1 and in 8 patients from Group 2, the VAS score decreased to zero. Four patients from Group 1 whose pain scores did not decrease below 4 were given rescue analgesics. None of the patients from Group 2 required rescue analgesia.

None of the patients developed any allergic reactions or complications. Side effects were observed in only one (2%) 60-year-old female who developed dyspepsia. A single dose of IM or IV lornoxicam was well-tolerated by all patients. None of the patients in the intramuscular or intravenous groups experienced any perioperative coagulopathies due to lornoxicam use.

DISCUSSION

Renal colic is a condition which mostly stems from urinary stone disease and it is the most painful and the most commonly encountered urologic disease in the ED.[14] According to the results of our study, lornoxicam was found to be an effective NSAID in the treatment of renal colic, both through IM and IV routes.

Table 2. The VAS scores of the patients in the study group.

Groups	Pre-treatment VAS Score	Post-treatment VAS Score	*p*-value	Amount of Decrease in Pain (%)
Group 1 (IM, n:27) mean ± SD	7.65 ± 1.32	2.07 ± 1.54	< 0.001	72.9%
Group 2 (IV, n:24) mean ± SD	7.96 ± 1.12	1.38 ± 1.20	< 0.001	82.7%
Total (n:51) mean ± SD	7.79 ± 1.23	1.75 ± 1.42	< 0.001	77.6%

Abbreviations: VAS,Visual Analogue Scale; IM, Intramuscular; IV, Intravenous; SD, Standard Deviation.

In patients with renal colic, pain is generated by the increased urinary tract wall pressure and ureteral smooth muscle spasms caused by the ureteral obstruction. The edema, inflammation, and increased peristalsis and pressure caused by the stone contribute to the pain.[15] In addition, there is an increased sensitivity to pain in these patients.[16] The inflammation and obstruction of the urinary tract induces the local release of prostaglandins, and leads to diuresis and vasodilation and results in an increase in the intrarenal pressure.[17,18]

The prostaglandin synthesis-inhibiting effects of the NSAIDs explain their high efficacy in the analgesia of patients with renal colic.[19] However, given the lack of a gold standard treatment approach, the optimal treatment is still unclear.

In the past, opioid drugs, which act through the central nervous system, were accepted as the first-line treatment for renal colic. However, physicians were often reluctant to administer additional doses to achieve sufficient analgesia, given the risk of adverse events.[20] Extensive use of opioids may lead to various side-effects, such as ventilatory depression, drowsiness, sedation, nausea, vomiting and urinary retention.[21] There are numerous studies stating that parenteral NSAIDs bear the advantage of possessing analgesic properties similar to those of opioid analgesics, without causing the undesirable opioid-related side effects.[9,10,20] However, it should be kept in mind that NSAIDs have their own side effect profile and may cause gastric irritation, gastrointestinal hemorrhage, coagulopathy, and nephrotoxicity.[21] In this context, an NSAID with a low side effect profile, high efficacy and rapid onset of action might well be the optimal analgesic for the initial treatment of acute renal colic.

Lornoxicam has been on the market for over two decades and its benefit/risk profile is considered to be validated.[22] In 2009, its analgesic effects in acute pain were analyzed by a Cochrane systematic review.[23]

An important side effect of NSAIDs is gastrointestinal bleeding. In a placebo-controlled study by Warrington et al which evaluated the gastrointestinal effects of lornoxicam, patients were treated with either lornoxicam 4 mg twice daily or indomethacin 50 mg twice daily for 28 days.[24] No difference was observed between the groups in terms of fecal blood loss, and no lornoxicam-induced ulcers were detected on endoscopic evaluation. Similarly, safety studies on the human gastrointestinal system indicate that single doses of lornoxicam (up to 160 mg) do not cause any serious side effects.[25]

Another side effect of NSAIDs is reduced platelet function. Lornoxicam inhibits platelet aggregation like other non-selective NSAIDs. However, its effects on perioperative bleeding are clinically insignificant.[22] In a prospective randomized study by Isik et al., adult patients undergoing tonsillectomy received either lornoxicam 8 mg IV or 50 mg tramadol IV just before the induction of general anesthesia, and none of the patients experienced significant bleeding with lornoxicam.[24] In another study by Mowafi et al, no significant differences were found between IV 16 mg lornoxicam and normal saline in terms of intraoperative bleeding in patients undergoing tonsillectomy.[26]

Lornoxicam is distinguished from the other members of the oxicam class with its short elimination half-life of 3-5 h.8 Its short elimination half-life makes lornoxicam an effective analgesic for patients with acute pain such as renal colic and also renders the drug more tolerable compared to other NSAIDs. However, there are only a limited number of studies on the use of lornoxicam in patients with renal colic. Bilir et al found that the analgesic effect of a single dose of IV lornoxicam 8 mg is significantly better compared to tenoxicam 20 mg and placebo. In another study, Cevik et al. compared IV lornoxicam, tenoxicam, and dexketoprofen trometamol in patients with renal colic in terms of efficacy and safety.[27] The fastest VAS score reduction was achieved with lornoxicam, which provided pain relief within 30 minutes. In accordance with the literature, both the IV and the IM groups in our study demonstrated VAS score reductions 30 minutes after the administration of lornoxicam. This outcome suggests that intravenous administration is faster in terms of pain reduction, and thus, slightly superior to intramuscular administration. In patients with renal colic, IV route is preferred over oral, rectal or IM administration due to its more rapid effect and ease of titration.[28] In our study, it is worth noting that no difference was found between the IV and IM routes in terms of VAS score reduction. However, all 4 (7.8%) of the patients who required rescue analgesia were in the IM group. In the light of the above data, we speculate that the analgesic effects of IM lornoxicam may start later compared to IV lornoxicam. Thus, when using the IM route, it might be wise to wait longer before administering rescue analgesia. We believe that future studies with larger sample sizes will help enlighten this issue.

Other than its efficacy in renal colic, lornoxicam has also been shown to exhibit potent analgesic effects in patients undergoing various urologic procedures. Mazrais et al. found that lornoxicam is superior to paracetamol in terms of postoperative analgesia in patients undergoing open retropubic prostatectomy.[29] Similarly, Ozkan et al. reported that lornoxicam is superior to paracetamol and tramadol in patients undergoing shock wave lithotripsy.[24]

This study has some limitations. Firstly, VAS scores were not evaluated after the 30th minute. Secondly, the parenteral administrations of lornoxicam were not compared with oral administration. The absence of a placebo control group also constitutes a limitation of this study. However, this study is significant in terms of showing that lornoxicam is a well-tolerated drug which is equally effective via the IM and IV routes in terms of providing analgesia within 30 minutes.

CONCLUSIONS

The parenteral use of lornoxicam, which is an NSAID that belongs to the oxicam class, provides effective pain relief in patients with acute renal colic. However, no significant difference was found between IM and IV administration in terms of analgesic efficacy.

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CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

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