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ORIGINAL ARTICLE

Postoperative analgesic efficacy of preemptive and postoperative lornoxicam in femoropopliteal bypass surgery

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SUMMARY

Objectives: In this study, we analyzed the effect of the application time of intravenous (IV) lornoxicam in preventing postoperative pain.

Methods: This placebo-controlled study was conducted on 72 patients undergoing elective femoropopliteal bypass surgery. The patients were randomly divided into three groups. Group I (n=25) was administered IV 8 mg lornoxicam 20 minutes before incision and IV 2 mL saline at the end of the surgery; Group II (n=24) was administered IV 2 mL saline 20 minutes before incision and IV 8 mg lornoxicam at the end of the surgery; Group III (n=23) was administered IV 2 mL saline 20 minutes before incision and IV 2 mL saline at the end of the surgery. All patients used IV morphine via a patient-controlled analgesia device. Postoperative pain was measured using the visual analog scale (VAS), and patients with a VAS score >3 were administered intramuscular 75 mg naproxen sodium.

Results: The VAS scores were significantly higher in Group III compared with Group I at the 0th, 1st, 2nd, and 3rd hours and with Group II at the 1st, 2nd, and 3rd hours ($p<0.05$). As far as 24-hour morphine and naproxen sodium consumption were concerned, there was a significant statistical difference between the three groups ($p<0.05$); comparing Group I and II, there was no difference ($p>0.05$).

Conclusion: Regardless of the time it is applied, lornoxicam reduces postoperative pain and consumption of opioids within the initial 3 hours.

Keywords: Non-steroidal anti-inflammatory agents; pain management; postoperative pain; vascular surgical procedures.

Introduction

Postoperative pain is an acute pain that occurs with surgical trauma. It disappears as the tissue heals.[1] The perioperative period can be divided into three phases: preoperative pain, intraoperative pain due to tissue dissection, and postoperative inflammation. Each of these phases contributes to both peripheral and central sensitization, exacerbating the pain response. Apart from these three factors, surgical procedures, tissue characteristics, duration of surgery, pharmacological interventions, and the presence or absence of intraoperative and postoperative analgesia may also lead to acute pain. To mitigate the adverse effects of these factors, interventions are needed in all three phases to prevent sensitization from occurring and continuing.[1,2]

Preemptive analgesia is described as a treatment initiated before surgery to prevent the onset of central sensitization due to surgical or inflammatory injury. Because of its protective effect on the nociceptive system, it may be more efficient than similar postoperative analgesic treatments. This proactive strategy not only reduces postoperative pain but also reduces nociceptor sensitivity to prevent chronic pain development.[1,2] Opioid analgesics have traditionally been the primary treatment for postoperative pain management. However, their utility is limited by adverse effects such as sedation, respiratory depression, constipation, and urinary retention.[3]

Non-steroidal anti-inflammatory drugs (NSAIDs) have been a good option in postoperative pain treatment. In the short term, their efficacy and toler-

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ability make them a favorable alternative to opioid analgesics.[4,5] Lornoxicam is an NSAID from the oxicam group, and its strong analgesic and anti-inflammatory effects have been shown in clinical trials.[6]

In this study, we investigated the effects of intravenous (IV) lornoxicam in the application period in patients undergoing femoropopliteal bypass surgery.

Material and Methods

Ethical approval for this study was obtained from the Research Ethics Committee of the Medical Faculty, Ege University. The study was conducted according to the ethical standards of the institutional research committee and the 1964 Helsinki Declaration and its later amendments.

This single-center, prospective, randomized-controlled study included 72 patients with an ASA I-II, who were scheduled for elective femoropopliteal bypass surgery. The exclusion criteria were a history of peptic ulcer disease, allergy to NSAIDs, and impaired renal and coagulation function. At the preoperative anesthesia evaluation, the patients were informed about the use of patient-controlled analgesia (PCA) and the visual analog scale (VAS; 0 "no pain" and 10 "worst pain imaginable").

The patients were randomly assigned to three groups using the sealed envelope method. If a patient agreed to participate in the study, an envelope was opened, and the anesthesiologist administered the patient's assigned treatment regimen. Group I (preemptive group, n=25) received IV 8 mg lornoxicam 20 minutes before incision and IV 2 mL saline after skin closure; Group II (postoperative group, n=24) received IV 2 mL saline before incision and IV 8 mg lornoxicam after skin closure; and Group III (control group, n=23) received IV 2 mL saline both 20 minutes before incision and after skin closure.

Patients were taken to the operating room, and standard monitoring was performed, consisting of electrocardiography, non-invasive blood pressure, pulse oximetry, and temperature. Anesthesia induction was achieved with 2% lidocaine (1 mg/kg), fentanyl (2 µg/kg), propofol (2 mg/kg), and rocuronium (0.6 mg/kg). Anesthesia was maintained through desflurane (1–1.5 MAC) and 50% air in oxygen. After skin closure, muscle relaxation was reversed with neostigmine. The patients were extubated in the operating room and transferred to the intensive care unit.

The VAS scores were recorded at 0 minutes (baseline), 1, 2, 3, 4, 8, 12, and 24 hours after surgery. For postoperative analgesia, all patients received IV morphine PCA with a loading dose of 1 mg, a basal infusion of 0.3 mg/h, a bolus dose of 1 mg, and a locked time of 15 minutes, with a 4-hour limit of 10 mg. Additional analgesia (naproxen sodium 75 mg intramuscular) was administered when VAS scores were greater than 3. Over 24 hours, patients' morphine and naproxen sodium consumptions were recorded, along with any side effects such as sedation, respiratory depression, ileus, dizziness, drowsiness, anxiety, dyspepsia, indigestion, and nausea and vomiting (PONV). Patients with PONV were treated with 10 mg metoclopramide as an antiemetic. At the end of the study, patient satisfaction was queried (1=bad, 2=poor, 3=fair, 4=good, 5=excellent). All measurements were recorded by the same consultant anesthesiologist blinded to study groups.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics v21 (SPSS, Inc, Chicago, IL, USA) for Windows. Data were presented as mean±standard deviation, median (minimum–maximum) for continuous variables, and number (n) and percentage (%) for categorical variables.

The distribution of data was checked using the Kolmogorov-Smirnov test. To determine the significance of factors like age, body mass index, morphine consumption, duration of anesthesia, and duration of surgery, ANOVA with Bonferroni Test was used. For categorical variables including gender, ASA status, presence of complications, NSAIDs consumption, and patient satisfaction, the chi-squared test was applied. The relationship between groups and the VAS scores was assessed using the Kruskal-Wallis test. Statistically significant was defined if the p value was ≤0.05.

A sample size was calculated to ensure adequate statistical power, aiming for an effective size of 0.449 with 90% power at a significance level of 0.05. Assuming a difference of more than 30% in VAS scores (2.1±2.1 points) between the placebo and lornoxi-

Table 1. Demographic characteristics and operation duration of the treatment groups

	Group I (n=25)	Group II (n=24)	Group III (n=23)
Age (year)	59.1±9.4	63.3±7.4	63.7±8.5
Gender (male), n (%)	20 (80)	21 (87.5)	23 (100)
BMI (Kg m^{-2})	26.3±4.9	25.8±3.1	25.3±4.5
ASA I/II/III	0718/7	1/15/8	0/21/2
Duration of anesthesia (min)	204.4±70.5	202±57.7	169.1±55.6
Duration of surgery (min)	169.4±69.4	166.4±52.5	134.3±53.8

Data are presented as mean±standard deviation, number (n) and percentage (%). F: Female; M: Male; BMI; Body Mass Index; ASA; American Society of Anesthesiologists; Min: minute; n: Number of patients.

Table 2. Postoperative Visual Analog Scale scores after surgery

Time (hour)	Group I (n=25)	Group II (n=24)	Group III (n=23)
0^{th}	5 (0–10)	6 (2–10)	7 (4–10)*
1^{st}	4 (0–8)	4 (1–8)	6 (3–8) *+
2^{nd}	3 (0–8)	3 (1–10)	5 (2–7)*+
3^{rd}	3 (0–8)	3 (1–8)	5 (2–6)*+
4^{th}	3 (0–8)	2.5 (1–8)	4 (2–6)
8^{th}	2 (0–5)	2 (1–5)	3 (1–5)
12^{th}	2 (0–4)	2 (1–5)	2 (1–4)
24^{th}	1 (0–2)	1 (1–4)	1 (0–3)

Data are presented as median (minimum–maximum). *: P<0.05: Comparison of group III vs group I ; +: P<0.05: Comparison of group III vs group II

Table 3. Postoperative total morphine and naproxen sodium consumption

	Group I (n=25)	Group II (n=24)	Group III (n=23)
Total morphine/ 24 hour (mg)	21.1±4.7	21.5±4.9	24.9±3.6 *+
Additional analgesic (Naproxen sodium), n (%)	4 (16)	6 (25)	13 (56.5) *+

Data are presented as mean±standard deviation, number (n) and percentage (%). *: P<0.05: Comparison of group III vs group I; +: P<0.05: Comparison of group III vs group II.

cam groups and incorporating a 10% margin of error, this study required a total of 72 patients (G*Power software, ANOVA, One-way analysis).

Results

The mean age of all patients was 62.01±8.68 years, and only 11% were women. Except for gender, there were no differences in patient demographics, duration of anesthesia, and surgery (Table 1).

When comparing the VAS scores between the three groups, it was demonstrated that Group III had higher scores than Group I at four postoperative time points (0, 1, 2, and 3 hours) and higher scores than Group II at three postoperative time points (1, 2, and 3 hours) (p<0.05) (Table 2).

Morphine and naproxen sodium consumptions at 24 hours postoperative were found to have a significant difference between the three groups (p<0.05). However, when groups I and II were compared, there was no difference (p>0.05) (Table 3).

In all three groups, only PONV were observed as side effects. There was no difference in the incidence of nausea (p=0.065) and vomiting (p=0.388) between the groups. No patient experienced severe sedation, anxiety, dyspepsia, ileus, or respiratory depression (Table 4).

Table 4. Adverse events

	Group I (n=25)	Group II (n=24)	Group III (n=23)
Nause (yes), n (%)	4 (16)	2 (8.3)	8 (34.8)
Vomiting (yes), n (%)	2 (8)	1 (4.2)	0 (0)

Data are presented as number (n) and percentage (%).

Table 5. The patient satisfaction

	Group I (n=25)	Group II (n=24)	Group III (n=23)
Excellent, n (%)	12 (48)	10 (41.7)	2 (8.7)
Good, n (%)	7 (28)	9 (37.5)	11 (47.8)
Fair, n (%)	5 (20)	5 (20.8)	10 (43.5)
Poor, n (%)	0 (0)	0 (0)	0 (0)
Bad, n (%)	1 (4)	0 (0)	0 (0)

Data are presented as number (n) and percentage (%). Group III vs I: p=0.016; Group III vs II: p=0.014; Group II vs I: p=0.880.

When patients' satisfaction was compared, both Group I and Group II expressed higher satisfaction than Group III (p=0.020) (Table 5).

Discussion

Despite advancements in medications, techniques, and research, managing acute pain remains challenging. Nearly three-quarters of surgical patients experience acute pain, with 80% reporting moderate to severe pain.[7]

Møiniche et al.[8] emphasized that the duration and efficacy of analgesic treatment are more critical than the timing of administration. Their analysis of randomized controlled studies spanning from 1983 to 2000 found no significant impact of timing on postoperative pain management. They concluded that preemptive analgesia, while not superior in alleviating postoperative pain, remains a valuable strategy. Murphy et al.[9] found no difference in the use of indomethacin for preemptive versus postoperative patients undergoing thoracotomy. A meta-analysis including 36 studies compared the efficacy of preemptive versus postoperative NSAIDs. The analysis showed that preemptive analgesics slightly reduced pain levels within the first six hours after surgery. Importantly, no serious side effects associated with NSAIDs developed, such as bleeding, myocardial infarction, or renal failure. In addition, pain scores within the first 24 to 48 hours after surgery and PONV were found to be similar between the two groups.[5]

Similarly, our study observed that IV lornoxicam effectively reduced postoperative pain scores compared to placebo, regardless of the timing of administration. Furthermore, the use of NSAIDs during intraoperative or postoperative periods correlated with reduced need for additional analgesics and increased patient satisfaction.

Trampitsch et al.[10] administered 24 mg lornoxicam divided equally into three doses for 24 hours to 66 patients in preemptive, postoperative, and placebo groups. Consistent with our results, significantly lower pain scores were observed in the preemptive and postoperative groups. However, morphine consumption was lower only in the preemptive group. Other studies have also demonstrated the preemptive efficacy of NSAIDs in various surgical procedures.[11–13] Kaila et al.[11] found that the use of preemptive lornoxicam resulted in a pain-free period of 7 hours after the surgical extraction of the third molar. No adverse events were reported, and patients tolerated it well. Inanoglu et al.[12] demonstrated that the administration of lornoxicam 30 minutes before surgery resulted in better postoperative analgesia than when administered after surgery. In addition, Mowafi et al.[13] reported that the administration of 16 mg lornoxicam before tonsillectomy provided more effective analgesia than a placebo.

Lornoxicam improves the quality of postoperative analgesia and reduces opioid consumption follow-

ing different surgical procedures.[10,14] After IV administration, the peak analgesic effect of lornoxicam occurs within 20 to 30 minutes, with an elimination half-life of 3 to 5 hours.[15] Due to the rapid onset of lornoxicam action, there may be no differences between Group I and Group II in the VAS scores, morphine consumption, use of additional analgesics, and patient satisfaction. In our study, lornoxicam reduced the consumption of analgesic medications in Group I and II. After the 4th hour, the VAS scores were similar in all groups because of its short effect.

The most serious side effects associated with NSAIDs include gastrointestinal bleeding and perforation, with PONV reported in previous studies with lornoxicam.[16] Liao et al.[17] compared the analgesic efficacy of lornoxicam and tramadol. They found that tramadol gave rise to a higher incidence of PONV than saline, with no difference between tramadol and lornoxicam. One of the main reasons for avoiding NSAIDs for postoperative pain management is the risk of bleeding due to their inhibitory effects on cyclooxygenase and platelet aggregation.[18] A meta-analysis of a large number of studies found that NSAIDs have a very low potential for side effects.[19] In our study, we did not observe any side effects except for PONV, which were observed in the group that did not receive lornoxicam. Therefore, we attributed these side effects to high pain scores and morphine consumption.

This study has several limitations. First, the VAS scores, analgesic consumption, and complications were recorded for only 24 hours. Second, naproxen sodium consumption could not be standardized, and thus the VAS scores may have been influenced.

Conclusion

In conclusion, IV lornoxicam effectively reduces postoperative pain and opioid consumption, regardless of administration timing, particularly within the first three hours. However, preemptive administration did not prove superior to postoperative administration.

Ethics Committee Approval: The Ege University Research Ethics Committee granted approval for this study (date: 18.06.2009, number: 09-2/3).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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