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The preemptive analgesic effect of lornoxicam in patients undergoing major abdominal surgery: A randomised controlled study☆

Yucel Karaman[a,*], *Eyup Kebapcı*[b], *Alp Gurkan*[b,*]

[a]*Tepecik Hospital, Department of Anaesthesiology, Izmir 35120, Turkey*
[b]*Tepecik Hospital, Department of General Surgery, Izmir, Turkey*

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ABSTRACT

Introduction: The aim of this study was to examine the effect of lornoxicam used in preemptive analgesia on the intensity of pain and requirement for analgesics in the perioperative period for major abdominal surgery.

Methods: Sixty patients scheduled for elective major abdominal surgery were randomly assigned to three groups after ethics committee approval. Patients in Group PRE ($n = 20$) received lornoxicam i.v. 8 mg 20 min before incision and saline i.v. after skin closure; patients in Group POST ($n = 20$) received saline i.v. 20 mins before incision and lornoxicam i.v. 8 mg after skin closure; patients in Group C ($n = 20$) received saline i.v. 5 min before incision and after skin closure. A standardized general anesthetic was used. All patients were started on i.v. tramadol patient-controlled analgesia during the postoperative period. Pain intensity was measured using the visual analog scale (VAS), and tramadol consumption. In addition, the incidences of side effects were recorded at the end of the study period.

Results: There were no significant differences among the three groups of the demographic data. Groups PRE and POST demonstrated significantly reduced pain scores compared to Group C at various points in time. Group PRE also demonstrated a weakly significant reduction in analgesic consumption of tramadol postoperatively compared to Groups POST and C.

Conclusion: Lornoxicam administered preemptively appears to improve the quality of postoperative analgesia and leads to reduced consumption of tramadol postoperatively in patients undergoing major abdominal operations.

1. Introduction

The use of a single analgesic to treat moderate to severe postoperative pain has proved inadequate to ensure optimal analgesia. Multimodal analgesia is currently recommended for effective postoperative pain control.[1] Principles of a multimodal strategy include control of postoperative pain of the patient to allow early mobilization, early enteral nutrition, education, and attenuation of the perioperative stress response through the use of a combination of analgesic agents.[1,2]

A multimodal strategy to control postoperative pathophysiology and facilitate rehabilitation results in accelerated recovery and decreased length of hospitalization.[3] Patients undergoing major abdominal procedures and who participate

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* *Corresponding authors*. Fax: +90 (232) 4595901.
E-mail address: alpgurkan@superonline.com (A. Gurkan).

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in a multimodal strategy have a reduction in hormonal and metabolic stress, preservation of total-body protein, shorter times to extubation, lower pain scores, earlier return of bowel function, and earlier fulfillment of intensive care unit discharge criteria.[2] The multimodal approach may even reduce the length of hospitalization for patients undergoing colon resection from a median of 6–10 days to 2 days.[4] This approach may decrease perioperative morbidity, and improve patient satisfaction without compromising safety.

Preemptive analgesia is one of the components for multimodal strategy. The concept of preemptive analgesia consists of an antinociceptive treatment that prevents central neural sensitization that amplifies postoperative pain. This implies that the treatment has been established when the noxious stimulus starts.[2] Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly administered as adjuvants during the preoperative period because of their ability to improve the control of postoperative pain while reducing the need for opioid analgesics.[1] However, the possible preemptive analgesic effect of NSAIDs is currently being debated.

Lornoxicam is a relatively new thienothiazine derivative of the oxicam class of NSAIDs. In animal studies, lornoxicam has demonstrated cylo-oxygenase inhibitory activity approximately 100 times more powerful than that of tenoxicam, along with analgesic activity approximately 10 times greater than that of either tenoxicam or piroxicam.[5] Additionally, and in contrast to other oxicams, lornoxicam has a short plasma half-life of approximately 4–6 h. This may translate into a better tolerability profile for lornoxicam, since NSAIDs with long plasma half-lives have been associated with a higher incidence of adverse effects.[5]

In the present study, we tried to assess the effect of intravenous lornoxicam administered before incision or after incision on tramadol consumption in the postoperative period.

2. Methods

The study protocol was approved by the hospital Ethics Committee, and a written informed consent was obtained from all patients before the study. The study included 60 adult patients undergoing major abdominal surgery (upper or upper and lower medial laparotomy) and treated postoperatively in the surgical intensive care unit. Exclusion criteria were as follows: preoperative use of analgesics, allergy to NSAIDs, history of peptic ulcer disease, coagulopathy, or renal dysfunction. Sixty patients were randomly assigned to three groups.

On arrival at the preanesthetic room, standard monitoring equipment consisting of electrocardiography, noninvasive blood pressure monitoring, and pulse oximetry was installed. Patients in Group PRE ($n = 20$) received lornoxicam (Nycomed GmbH, Austria) i.v. 8 mg 20 min before incision and saline i.v. after skin closure; patients in Group POST ($n = 20$) received saline i.v. 20 min before incision and lornoxicam i.v. 8 mg after skin closure; patients in Group C ($n = 20$) received saline i.v. five minutes before incision and after skin closure. All medicines were prepared by a nurse who had no other involvement in the study. None of the patients and managing anaesthetists was aware of the randomization code. One day before the operation, patients received instructions about the use of a patient-controlled analgesia (PCA) device (APM®, Abbott Laboratories, North Chicago, IL) and the visual analog scale (VAS; 0 = "no pain" and 10 = "worst pain imaginable") for pain.

A standardized general anesthetic was used. Induction was achieved with 10 μg/kg atropine, 1 μg/kg remifentanil, 2 mg/kg propofol. Atracurium (0.5 mg/kg) was given to facilitate orotracheal intubation. Maintenance of anesthesia consisted of desflurane 4–6% (end-tidal) and 60% nitrous oxide in oxygen. Remifentanil infusion was started at an initial rate of 0.5 μg/kg/min. After intubation, remifentanil infusion rate was reduced by 50%. At the completion of skin closure, muscle relaxation was reversed and patients extubated.

After tracheal extubation, patients were transferred to the PACU. Postoperative pain was assessed using a visual analog scale. Postoperative analgesia was provided by i.v. PCA tramadol (Salutas Pharma GmbH, Germany). Patients were connected to the PCA-device on arrival in the PACU. The PCA solution contained tramadol 3 mg/mL. The administration variables were as follows: initial dose, 50 mg; demand dose, 20 mg; lockout interval, 10 min; 4-h limit, 300 mg; and no basal infusion. Pain was assessed using VAS (at rest, on exertion) at 1 h, 2 h, 4 h, 12 h, and 24 h after surgery. Patients were given additional analgesic (lornoxicam 8 mg i.m.) when analgesia was inadequate (VAS > 3). Total and incremental tramadol consumption at these times was also recorded from the PCA-device. Patients were evaluated for the presence of adverse events such as nausea, vomiting, dizziness, drowsiness, sedation, anxiety, dyspepsia, indigestion. Nausea was evaluated using a two point scale; 0 = absent, 1 = positive. Metoclopramide was given in the case of vomiting or after two successive episodes of nausea. The degree of sedation was rated on a four-point scale; 0 = awake, 1 = drowsy, 2 = asleep but rousable, 3 = unrousable. All measurements were recorded by the same anesthesia resident who was blinded to the study drugs administered. At the end of the study, patient satisfaction was questioned (excellent, good, fair, poor).

The postoperative tramadol consumption was used as the main criterion for statistical analysis. We calculated that 15 patients in each group would be necessary for the assessment of a 20% decrease in tramadol consumption for treatment groups with a Type 1 error value of 0.05 and power of the study 80%. Demographic characteristics were analyzed using Student's *t*-test, while the VAS pain scores and PCA tramadol usage were analyzed using Fisher's exact test. The Chi-square test was used to analyse the frequency of nausea, vomiting or pruritus. Statistically testing was performed using SPSS 10.0 program for Windows (SPSS Inc., Chicago, IL), with a P value <0.05 considered statistically significant.

3. Results

The demographic characteristics were similar, and there were no significant differences with respect to duration of surgery (Table 1).The VAS scores were significantly higher in the control group compared with the Group PRE and Group POST at 1 h, 2 h, 4 h, and 12 h after surgery ($P < 0.05$) (Tables 2 and 3). The VAS scores at 1 h, 2 h, 4 h, and 12 h in Group PRE were