



Postoperative Analgesic Efficacy of Preemptive and Postoperative Lornoxicam or Tramadol in Lumbar Disc Surgery

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Abstract

Objective: To compare preemptive and postoperative analgesic efficacy of tramadol and lornoxicam administered before anaesthesia induction in lumbar discectomy.

Methods: This randomised, double-blind trial was conducted on 60 ASA I and II patients undergoing lumbar discectomy. Group L (n=30) received 3×8 mg day⁻¹ lornoxicam, and Group T (n=30) received 3×1.5 mg kg⁻¹ day⁻¹ tramadol. A verbal rating scale (VRS), the duration of effective analgesia, the number of additional analgesics used, adverse effects and patient satisfaction were evaluated at the postoperative 30th minute and 1st, 2nd, 4th, 6th, 8th, 12th and 24th hours.

Results: There were no significant differences between Groups L and T regarding demographic and clinical characteristics, the number of additional analgesics and the duration of effective analgesia, adverse effects and patient satisfaction. VRS scores of the patients in Group T were significantly higher than those in Group L at the postoperative 30th minute (p=0.050) and the 1st hour (p=0.005).

Conclusion: Lornoxicam, which was used for preemptive and postoperative analgesia in lumbar disc surgery, had provided adequate and effective analgesia such as tramadol. Moreover, preemptive analgesia was quite effective in prevention and treatment of postoperative pain.

Keywords: Analgesia, lornoxicam, lumbar disc surgery, tramadol

Introduction

Postoperative pain is a type of acute pain that starts with surgical trauma, decreases gradually, and ends up with tissue healing. Goals of treatment of postoperative pain are to remove or minimise pain; to facilitate recovery; to prevent complications such as neuroendocrine system, respiratory system, cardiovascular system and gastrointestinal system dysfunction caused by increased stress response and hypermetabolism due to pain and to provide cost-effective treatment. The pathophysiology of pain focuses on the theorem that central neural hyperexcitability, which causes postoperative pain, can be reduced or prevented. Preemptive analgesia is the treatment for prevention of the development of central hypersensitivity, which plays a role in postoperative pain. Central sensitisation can be inhibited by preemptive analgesia and thus memory of pain that occurred in the central nervous system can be regressed. Therefore, this method can not only reduce the intensity and duration of postoperative pain but also delay its onset. A good preemptive analgesia accelerates recovery from surgery and reduces the incidence of morbidity and mortality (1-3).

Opioid analgesics have been the first-line therapy in the treatment of postoperative pain for years. However, side effects such as respiratory depression, sedation, constipation and urine retention limit opioid use. Non-steroid an-

ti-inflammatory drugs (NSAIDs) provide efficient analgesia in acute pain following minor and major surgical procedures, and they substitute for opioid analgesics or are used additionally. The major advantage of NSAIDs is its better tolerability than that of opioid analgesics for short-term postoperative analgesia in selected patients. NSAIDs prevent prostaglandin-mediated sensitisation, which occurs due to mechanical and chemical irritants, by inhibiting cyclooxygenase (4).

Lornoxicam is an oxicam-derived NSAID available in parenteral and oral forms. Animal studies have demonstrated that lornoxicam has 100-fold higher cyclooxygenase-inhibiting effect than tenoxicam and 10-fold higher analgesic potency than tenoxicam and proxicam (5, 6) and provides analgesia equivalent to morphine and pethidine (7, 8). Unlike the other oxicam-derived drugs, lornoxicam has a short plasma half-life (4–6 hours) and fewer side effects (5, 6).

Tramadol is a synthetic opioid derivative with central activity and is a double-action drug with both opioid and non-opioid mechanisms of action. In addition to its weak μ -opioid receptor agonist activity, tramadol inhibits presynaptic reuptake of noradrenaline and serotonin and stimulates the secretion of serotonin (9). It provides equivalent analgesia to morphine in the treatment of moderate–severe postoperative pain. Side effects of tramadol are similar to those seen with opioid use; however, it causes respiratory depression less frequently than morphine (10). The aim of the present study was to compare postoperative analgesic efficacy of lornoxicam and tramadol, which were administered preemptively and postoperatively, in lumbar disc surgery.

Methods

The present single-centre, prospective, randomised, double-blind study was conducted on the American Society of Anaesthesiologists I–II patients between 18 and 60 years of age, who had undergone elective single-level (L1–S1) lumbar discectomy in the Neurosurgery Clinic of Haydarpaşa Numune Training and Research Hospital between May 2007 and April 2008. Patients with cardiovascular, cerebrovascular, pulmonary, hepatic, renal and allergic disorders; those who had a history of chronic pain, epilepsy and peptic ulcer; those who were pregnant or breastfeeding; those who were suffering with alcohol or drug addiction; those who were using monoamine oxidase inhibitors, tricyclic antidepressants or sympathomimetic drugs and those who had coagulation disorders were not included in the study. The patients in whom duration of surgery lasted longer than 2 hours and 30 minutes; those who developed complications, such as severe bradycardia, nausea–vomiting, hypotension or apnoea; those and who had to receive any analgesic other than those in the study protocol were excluded. The present study was

approved by the Local Ethics Committee of Haydarpaşa Numune Training and Research Hospital at February 2007 (Ref. No. 07–20). Patients were informed about the procedure, and their written informed consent was obtained.

Before the surgical procedure, physical examination of the patients was performed, and their vital signs and routine laboratory analyses were evaluated. Premedication with 0.5 mg im atropine and 10 mg im diazepam was performed in all patients 30 minutes before the operation. In the operating room, for all patients, an intravenous (iv) line was opened, and 0.9% NaCl infusion was initiated. Before the induction of anaesthesia, patients were randomised into two equal groups (Group L and Group T) using the sealed envelope method. In Group L, patients were administered 8 mg lornoxicam as a slow-bolus iv first dose at the beginning of induction of anaesthesia and then the other two doses of lornoxicam were applied as 8 mg as a slow-bolus iv at 8 hours intervals during the postoperative period, corresponding to a total dose of 24 mg day⁻¹ (3×8 mg). In Group T, patients were administered 1.5 mg kg⁻¹ tramadol as an iv infusion for 10 minutes first at the beginning of induction of anaesthesia and then at two 8-hour intervals, which corresponded to a total dose of 4.5 mg kg⁻¹ day⁻¹ (3×1.5 mg kg⁻¹ day⁻¹). In both groups, 2 mcg kg⁻¹ fentanyl, 5–7 mg kg⁻¹ thiopental sodium and 0.1 mg kg⁻¹ vecuronium bromide were administered. Maintenance of anaesthesia was performed by 1%–2% isoflurane in 50% O₂+50% N₂O.

During the perioperative period, standard monitoring, including the measurements of electrocardiography, non-invasive systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure, peripheral oxygen saturation (SPO₂), capnography and end-tidal isoflurane concentration using infrared anaesthetic gas monitor, was used. Fluid and blood replacement was performed when necessary. An additional fentanyl dose was not given during the perioperative period.

At the end of the operation, 10 mg metoclopramide was administered to each patient through the iv route during subcutaneous closure. Decurarization was provided through 0.01 mg kg⁻¹ atropine and 0.03 mg kg⁻¹ neostigmine. Drug administration times, duration of anaesthesia and duration of the operation were recorded. Extubation time was considered to be the postoperative time (0 min).

Considering that complete recovery from anaesthesia was provided and the patients were completely conscious, SAP, DAP, heart rate and SPO₂ were recorded at the postoperative 30th minute and at the 1st, 2nd, 4th, 6th, 8th, 12th and 24th hours. Verbal rating scale (VRS) scores were evaluated as 0: no pain, 1: mild pain, 2: moderate pain, 3: severe pain and 4: unbearable pain. Ramsay sedation scale (RSS) scores were evaluated

as 1: restless and agitated; 2: tranquil, cooperative and oriented; 3: responsive to commands only, if the patients were awake and as 4: brisk response to light glabellar tap or loud auditory stimulus; 5: sluggish response to light glabellar tap or loud auditory stimulus and 6: no response to light glabellar tap or loud auditory stimulus, if the patients were asleep. Side effects were evaluated as nausea, vomiting, dizziness, pruritus, dyspepsia, hypotension, bradycardia, convulsion, skin rash and urine retention. Patient satisfaction was evaluated at the postoperative 24th hour as 1: poor, 2: fairly well, 3: good, 4: very good and 5: excellent. Neither the patient nor the physician who performed the evaluations was informed about the analgesic used.

In the postoperative period, 1 g metamizole was administered as a slow-bolus iv for alternative purposes and another derivate as an additional analgesic for the patients with VRS score ≥ 2 . Duration of effective analgesia (time to the first additional analgesic) and the number of additional analgesics were recorded. For the patients with nausea and vomiting, 10 mg metoclopramide was intravenously administered.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences version 15.0 (SPSS Inc.; Chicago, IL, USA). Descriptive statistics were expressed as mean, standard deviation and frequency. For intergroup comparisons, Student’s t-test was used for normally distributed variables (age, height, body weight, duration of effective analgesia, SAP, DAP, HR and SPO₂), and Mann–Whitney U test was used for non-normally distributed variables (VRS, RSS and patient satisfaction). Qualitative data were compared using the Chi-square test (gender, number of additional analgesics, nausea, vomiting and dizziness) and Fisher’s Exact Chi-square test (pruritus and dyspepsia). Data were evaluated within 95% confidence interval and at a significance level of $p < 0.05$.

Table 1. Demographic and clinical characteristics of the patients

Characteristics	Group L	Group T	p
Age, years	42.1±4.4	44.2±9.1	0.331
Gender			
Female	13 (43.3)	19 (63.3)	0.121
Male	17 (56.7)	11 (36.7)	
Body weight, kg	75.3±11.7	72.8±12.8	0.426
Height, m	1.7±0.1	1.7±0.1	0.946
Duration of anaesthesia, minute	161.2±28.4	151.6±23.8	0.161
Duration of surgery, minute	120.7±25.7	118.4±22.5	0.718

Data are presented as mean±standard deviation or n (%), where appropriate.

Results

In the present study, 60 patients with the mean age of 41.68±9.59 years (range: 23–58 years), of whom 32 (53.3%) were female and 28 (46.7%) were male, were included. Patients were randomly divided into two groups as Group L (n=30) and Group T (n=30). There were no significant differences between the study groups in terms of age, body weight, height, gender, mean duration of anaesthesia and mean duration of surgery (Table 1).

There were no significant differences between the study groups in terms of postoperative SAP and DAP, heart rate, SPO₂ and RSS scores. Requirement for additional analgesic use was determined in 10 (33.3%) patients in Group L and in 14 (46.7%) patients in Group T. There were no significant differences between the study groups in terms of the number of additional analgesics and the duration of effective analgesia (Table 2). However, time to the first requirement for additional analgesics was longer in Group L than in Group T.

At the postoperative 30th minute, VRS scores of the patients in Group T were significantly higher than those in Group L ($p=0.050$). Moreover, at the postoperative 1st hour, VRS scores of the patients in Group T were also significantly higher than those in Group L ($p=0.005$). However, there were no significant differences between the study groups in terms of the postoperative 2nd, 4th, 6th, 8th, 12th and 24th hour VRS scores (Figure 1).

There were no significant differences between the groups in terms of the rates of postoperative nausea, vomiting, dizziness, pruritus and dyspepsia. The ratio of nausea/vomiting was 11/8 in Group T, whereas it was 9/4 in Group L. During the postoperative period, hypotension, bleeding, bradycardia, convulsion, skin rash, hiccup and/or urine retention were not observed in any of the patients in both study groups (Table 3).

Table 2. Number of requirements for additional analgesics and duration of effective analgesia (time to the first additional analgesic use) in the study groups

	Group L n=30	Group T n=30	p
Number of requirements for additional analgesics, n (%)			
Once	7 (23.3)	10 (33.3)	0.759
Twice	2 (6.7)	3 (10.0)	
Three times	1 (3.3)	1 (3.3)	
Duration of effective analgesia (time to the first additional analgesic) min, mean±SD	229.0±29.4	214.6±19.7	0.289

SD: standard deviation.

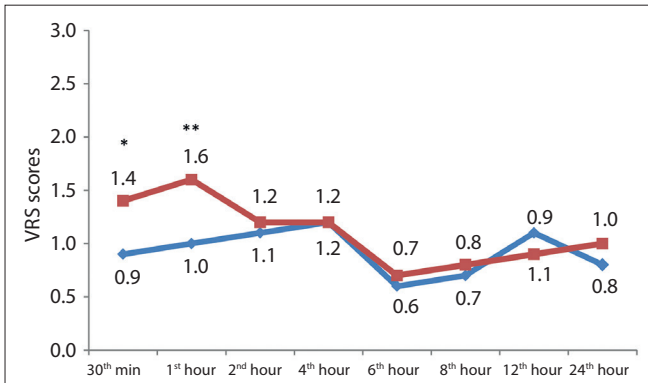


Figure 1. Comparison of verbal rating scale scores of the study groups. The blue line represents Group L, and the red line represents Group T. * p<0.05 and ** p<0.01

There was no significant difference between the study groups in terms of the level of patient satisfaction (p=0.812). In Groups L and T, 90% and 93.3% of the patients, respectively, rated the treatment as “good–very good–excellent”. Three patients in Group L (10%) and two patients in Group T (6.6%) rated the treatment as “poor–fairly well”; however, none of the patients discontinued the treatment.

Discussion

Today, the suggestion that control of postoperative pain from the preoperative period is a critical factor in the prevention of stress response has made the concept “preemptive analgesia” a topical issue (11).

Opioids and NSAIDs are among the medications used for both preemptive and postoperative analgesia (1–3). The site and type of the operation and duration of nociceptive stimulation are important factors in preemptive procedures (11, 12).

Many studies have been conducted to evaluate preemptive efficacy of either lornoxicam or tramadol. In the placebo-controlled study by Olmez et al. (13), a preemptive procedure was performed in cases with transrectal prostate biopsy. The researchers determined that although an adequate analgesia was obtained by 8 mg Lornoxicam and that 100 mg tramadol provided more efficient analgesia. Nevertheless, Isik et al. (14) determined a lower postoperative pain using the preemptive method in a group that received 8 mg lornoxicam than in a group that received 50 mg tramadol. In another study, Güler et al. (15) found that analgesia was inadequate in a group received 8 mg lornoxicam prior to abdominal hysterectomy but that durations of effective analgesia and analgesic efficacy in the first 6 hours were similar to those in groups where 16 mg lornoxicam and 100 mg tramadol were used. In the present study, we compared 8 mg lornoxicam with a higher dose of

Table 3. Distribution of side effects among the study groups

	Group L n (%)	Group T n (%)	p
Nausea	9 (30.0)	11 (36.7)	0.584
Vomiting	4 (13.3)	8 (26.7)	0.197
Dizziness	3 (10.0)	5 (16.7)	0.706
Pruritus	0 (0)	1 (3.3)	1.000
Dyspepsia	2 (6.7)	0 (0)	0.492

tramadol (1.5 mg kg⁻¹) as compared with the those reported in the above-mentioned studies and observed that lornoxicam provided as adequate and effective analgesia as that provided by tramadol.

Yücel et al. (16) found similar analgesic efficacy for 8 mg lornoxicam and 1 mg kg⁻¹ tramadol but durations of effective analgesia were longer with 8 mg lornoxicam than with 1 mg kg⁻¹ tramadol; these doses were postoperatively used in thyroidectomy procedures. Kirdemir et al. (17) compared 4 mg lornoxicam, which was used prior to laparoscopic cholecystectomy, with 50 mg tramadol and also compared the two with two different control groups. They reported that the most efficient analgesia and lowest analgesic consumption were observed in the preemptive lornoxicam group and that the highest pain complaint and analgesic consumption were observed in the postoperative iv tramadol control group.

Trampitsch et al. (18) administered 8 mg lornoxicam either preoperatively or before skin closure in gynaecology patients and demonstrated that the quality of postoperative analgesia was better and opioid consumption was lower in the preoperative lornoxicam group than in the control group. Mowafi et al. (19) explained that 16 mg lornoxicam administered prior to the tonsillectomy procedure provided more effective analgesia than a placebo. In the present study, which comprised no control group, we observed that 8 mg lornoxicam also provided adequate analgesia.

Thienthong et al. (20) administered 16 mg lornoxicam or placebo during an incision closure phase in lumbar disc surgery and monitored the pain through VRS for 2 hours. They reported that 16 mg lornoxicam provided inadequate analgesia similar to that provided by the placebo and that there was no significant difference in terms of duration of effective analgesia between the groups. In the present study, besides tramadol, adequate analgesia obtained by the use of 8 mg lornoxicam was attributed to the preoperative administration of both drugs. In addition, with the assumption of memory of pain being regressed by the preemptive analgesia, we recommended at least 24-hour monitoring to obtain more reliable outcomes.

Wordliczek et al. (21) administered 100 mg tramadol in hemicolectomy patients during induction or the peritoneum closure phase or postoperative period and found that tramadol use was higher in the postoperative group despite similar analgesic efficacy in each group. Karaman et al. (22) compared patients to whom 8 mg lornoxicam was administered prior to the laparoscopic cholecystectomy with the patients who received 1 g paracetamol and with the control group. They reported that lornoxicam and paracetamol had similar analgesic efficacy but the use of analgesics was higher in the lornoxicam group, and the shortest duration of effective analgesia and higher analgesic use were observed in the control group. Kilickaya et al. (23) reported that 8 mg lornoxicam, 75 mg diclofenac sodium or 50 mg dexketoprofen administered prior to the major abdominal surgery provided more effective analgesia compared with the saline group and that the lowest tramadol use was observed in the diclofenac sodium group. Akcali et al. (24) administered 1 g paracetamol, 8 mg lornoxicam or 1 mg kg⁻¹ tramadol prior to extracorporeal shockwave lithotripsy and found that the three drugs caused similar and adequate quality of postoperative analgesia.

Vickers et al. (25) found that the analgesic efficacies of 100 mg tramadol and 5 mg morphine after abdominal surgery were similar. Rosenow et al. (8) expressed that lornoxicam had similar analgesic efficacy to that of opioids and that duration of effective analgesia was 100 min for 8 mg lornoxicam and 75 min for 50 mg pethidine, both administered after laminectomy. In the present study, the duration of effective analgesia was found to be longer for 8 mg lornoxicam (229.0±29.4 min) than that in the above-mentioned study. In addition, lack of additional analgesia use in 66.7% of the patients in Group L was attributed to the preemptive administration.

Ilias et al. (26) reported that 8 mg lornoxicam after hysterectomy provided equivalent analgesia to 50 mg tramadol but better analgesic efficacy and tolerability compared with 4 mg lornoxicam and placebo. In the present study, we observed that 8 mg lornoxicam provided equivalent analgesia to the higher dose of tramadol (1.5 mg kg⁻¹).

Staunstrup et al. (27) reported that a single dose of 16 mg lornoxicam administered after arthroscopic reconstruction of the anterior cruciate ligament provided better analgesia compared with 3×100 mg tramadol. They also reported that the duration of effective analgesia was 5–9 hours for lornoxicam and 4–7 hours for tramadol and that the requirement for additional analgesia was 58% for the lornoxicam group and 77% for the tramadol group. In the present study comparing 8 mg lornoxicam with 1.5 mg kg⁻¹ tramadol, the rate of requirement of additional analgesia was 33.3% in the lornoxicam group and 46.7% in the tramadol group. Shorter duration of effective analgesia in the present study was attributed

to the low dose of lornoxicam, to the first dose of lornoxicam up to 8 mg being given in the preoperative period, and to the different operation type.

Kaygusuz et al. (28) found that 8 mg lornoxicam and 100 mg tramadol administered prior to percutaneous nephrolithotomy provided a higher quality of analgesia and tolerability than the placebo, but Lornoxicam had a shorter duration of effective analgesia compared with tramadol despite similar analgesic use in both drug groups. Kara et al. (29) administered 8 mg lornoxicam through iv, im and oral routes before surgery and found a similar duration of effective analgesia and analgesic efficacy in all patients. In the present study, we preferred a slow-bolus iv administration considering that it was more practical and made no change in the efficacy of treatment. The results of the studies performed with different routes of administration for the same drug were similar to that of the present study (16, 17, 29).

In the postoperative period, nausea and vomiting are the second leading complaints after pain. Nausea and vomiting are the known effects of opioids; however, these side effects are less frequently encountered with NSAIDs. Moreover, the residual effect of anaesthesia and surgical procedures are among the major causes of nausea and vomiting that occurred in the early postoperative period. Kilickaya et al. (23) determined that lornoxicam, diclofenac or dexketoprofen used prior to major abdominal surgery caused nausea and vomiting less commonly as compared with the placebo. Ilias et al. (26) also reported that nausea and vomiting were less frequent in the patients receiving lornoxicam after hysterectomy as compared with those receiving the placebo and tramadol. Staunstrup et al. (27) found lower incidence of nausea and vomiting with lornoxicam than that with tramadol, both administered after arthroscopic reconstruction of anterior cruciate ligament. In the present study, the rates of nausea and vomiting were low and similar in each study group.

Nonsteroidal anti-inflammatory drugs may cause bleeding. Lornoxicam is likely to minimise the side effects as it has a short half-life and allows returning to physiological prostaglandin levels. Aabakken et al. (30) reported lower gastric and duodenal mucosal damage with lornoxicam compared with naproxen in voluntary subjects. In the present study, we determined no sign of bleeding in none of the patients both in the preoperative and postoperative periods.

The right subject who would decide whether analgesic therapy is adequate is the patient him/herself. In the study by Ilias et al. (26), the number of patients who discontinued the study because of “unresponsiveness to the treatment” after hysterectomy was larger in the tramadol and placebo groups as compared with those in the lornoxicam group. In the present

study, three patients in Group L and two patients in Group T rated the treatment as “poor–fairly well”; however, none of the patients discontinued the treatment. Rosenow et al. (8) determined the patient satisfaction to be higher in the patients who received 8 mg lornoxicam and 50 mg pethidine as than I the patients who received 4 mg lornoxicam and the placebo after laminectomy. Staunstrup et al. (27) reported the patient satisfaction as 82% for lornoxicam and 49% for tramadol. In the present study, the patient satisfaction was 90% for lornoxicam and 93.3% for tramadol. These higher rates of patient satisfaction were attributed to the preemptive administration of the drugs.

Kaygusuz et al. (28) conducted a preemptive study and reported the patient satisfaction to be “very good–excellent” both in the lornoxicam and tramadol groups, but “poor–fairly well” in the placebo group. Kirdemir et al. (17) compared lornoxicam and tramadol administered prior to laparoscopic cholecystectomy with two different control groups and found the patient satisfaction in the groups as follows: preemptive lornoxicam+postoperative iv patient-controlled analgesia (PCA) (Lornoxicam)>preemptive tramadol+postoperative iv PCA (Tramadol)>preemptive saline+postoperative PCA (Lornoxicam)>preemptive saline+postoperative PCA (Tramadol).

One of the limitations of our study was only including patients who were ASA I and II and who underwent lumbar disc surgeries, which did not exceed 2 hours and 30 minutes. Another limitation may be the relatively subjective data that possibly occurred both for patients and physicians since pain is an abstract and subjective concept and there are no absolute measurement methods for pain in all studies on pain.

Conclusion

Preemptive and postoperative administration of either lornoxicam (8 mg) or tramadol (1.5 mg kg⁻¹) in the patients undergoing lumbar disc surgery provided adequate and effective analgesia in the treatment of postoperative pain. Moreover, we concluded that preemptive administration was efficient in the prevention and treatment of postoperative pain.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Haydarpaşa Numune Training and Research Hospital (February 2007, Ref. No: 07-20).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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E.D.; Data Collection and/or Processing – E.C.; Analysis and/or Interpretation – E.C., E.D., G.T., A.Ö.; Literature Search – E.C.; Writing Manuscript – E.C., G.T., E.D., A.Ö.; Critical Review – E.C., G.T., E.D., A.Ö.; Other – E.C., E.D., G.T., A.Ö.

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