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The contribution of preemptive lornoxicam on postoperative analgesia in spinal surgery

Abstract

Purpose: The purpose of this study is to evaluate the contribution, efficacy and safety of preemptive intravenous lornoxicam 8 mg on postoperative analgesia in patients who shall undergo spinal surgery and instrumentation.

Materials and Methods: 50 adult (18-65) patients from ASA I-II risk group, scheduled for elective spinal surgery were included in clinical prospective, randomized, double blind, placebo controlled study. Lornoxicam 8 mg (in 100 ml physiological serum iv) was administered to the first group (Group L; n=25) and 100 ml physiological serum iv was administered by perfusor to the second group (Group P; n=25) 30 minutes before surgical incision. General anesthesia was applied after standard monitorization. Postoperative analgesia was performed with tramadol (iv) in 2 mg/ml concentration via patient controlled analgesia (PCA); bolus: 20 mg, lock time: 60 minutes and application time: 24 hours. Numerical Rating Scale (NRS) (0-10 points), tramadol used by PCA, frequency of drug request, additional analgesic amount consumed and effective analgesia times were recorded at the end of operation, 2nd, 4th, 6th, 12th and 24th hours.

Results: Total PCA tramadol consumption during 24 hours period and frequency of PCA drug request at the end of operation, 2nd and 12th hours was significantly lower than the values for placebo ($p<0.05$). Total additional analgesic consumption was significantly lower when compared with placebo during the follow up period of 24 hours ($p<0,05$). Effective analgesia time was long in Group L ($p<0,05$).

Conclusion: It was shown that administration of preemptive intravenous lornoxicam 8 mg for pain treatment in patients subjected to spinal surgery, decreased tramadol amount and additional analgesic amount consumed, enhanced quality of analgesia and elongated effective analgesia time.

Keywords: preemptive analgesia, lornoxicam, spinal surgery

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Introduction

In the studies performed it is shown that upon effective performance of pain control after surgery, postoperative recovery is accelerated, duration of stay is decreased, treatment cost, mortality and morbidity is decreased.[1] Although opioids are frequently used for this purpose, side effects like respiratory depression, sedation, constipation, nausea and vomiting limit the usage of them.[2] On the other hand, central and peripheral analgesic action as well as anti-inflammatory features of nonsteroid anti-inflammatory drug (NSAID) are found. NSAIDs are considered as preferred choice in postoperative analgesia because side effects seen in opioids are not detected and they are tolerated relatively better than opioids.[3]

Lornoxicam is an oxicam group NSAID with central analgesic and anti-inflammatory features. The efficacy in postoperative pain and acute pains where inflammation is in forefront, is proven.[4] Preemptive analgesia method, one of the methods used to relieve post-operative pain may be defined as decrease or prevention of post-operative pain by application of analgesic drug or techniques before painful stimulus. For this purpose opioids, NSAIDs and local anesthetics (LA) are used in preemptive analgesia.[5] In spinal surgical interventions and instrumentation applications, moderate postoperative pain is observed. In these cases, nowadays preemptive analgesia applications and PCA applications are frequently preferred to provide effective pain treatment.[6] In our study we planned to investigate the contribution, efficacy and safety of preemptive lornoxicam in patients subjected to spinal surgery.

Material and methods

50 patients between 18-65 ages from ASA I-II risk group, scheduled for elective spinal surgery were included in the study after Faculty Ethics Committee Approval and consent of subjects were obtained. The patients were separated into two groups with lot drawing method; Group P: Placebo (n=25) and Group L: Lornoxicam (n=25). Evaluation of preoperative anesthesia and training for PCA device was performed in the conditions of polyclinics and service. Patients with development of intraoperative complication, hypersensitivity to the drugs to be used, gastric ulcer, bleeding and clotting disorder, liver or renal failure, alcohol or drug addiction were excluded from the study. Patients were premedicated with midazolam 2-3 mg before operation. The patients taken to operation room were monitored as standard with electrocardiography (ECG), pulse oximeter and noninvasive artery pressure (Drager Cicero, PM 8014, Lubek, Germany). 100 ml of isotonic saline and 8 mg of lornoxicam (iv) in saline with the same volume was administered via perfusor before surgical incision respectively to placebo group (Group P) and lornoxicam group (Group L). Standard balanced anesthesia was applied to all patients. Induction was performed with 5-7 mg/kg of thiopental sodium, 1 mg/kg of fentanyl and 0,1 mg/kg of vecuronium. Maintenance of anesthesia was continued with of 1 MAC (minimum alveoler concentration) desflurane and a mixture of 50/50% N^2O/O^2. When operation was completed general anesthesia was terminated, neuromuscular blocking agent was reversed and extubated in patients whose spontaneous respiration was restored and patients were taken

to recovery room. All the patients were monitored in the recovery room. PCA application (2 mg/ml concentration tramadol iv, bolus 20 mg, lock time is 60 minutes and application time is 24 hours) started for postoperative analgesia. Post-operative pain levels were evaluated with NRS between 0-10 (0=n pain, 10= worst possible pain). Metamizol 1000 mg im was used as additional analgesic in patients with NRS ≥ 3. The patients with Modified Aldrete Score ≥ 9 were sent to service. NRS, blood pressure (systolic and diastolic), heart rate (HR), peripheral oxygen saturation, respiratory rate was recorded at the postoperative 2nd, 4th, 6th, 12th and 24th hours by the same employee who was uninformed about working drug. Besides, frequency of drug requests, total tramadol amount (mg) and additional analgesic requirement from PCA device were separately assessed and recorded. The time for requirement of additional analgesic was recorded for PCA applied patients. Side effects like nausea, vomiting, hypotension, hypertension, arythmia, gastrointestinal system irritation (GIS) (stomach ache, heartburn), bleeding disorder, urinary incontinence, distension, respiratory depression were recorded for 24 hours the drug was administered. Coagulation parameters platelet count, prothrombin time (PT), partial thromboplastin time (PTT), INR (International Normalization Ratio) measurements were performed.

Statistical analysis

The statistical analyses of data were performed with SPSS (version 10,0) for Windows. Conformance of data obtained by measurement to normal disturbance was evaluated with KolmogorovSmirnov test. During comparison of measured values for both groups, Student's t test was used for normally distributed values and Mann-Whitney U test was used for non-normally distributed values. Chi square test was used for the comparison of qualitative values. For comparison of intra-group repetitive measurements Variance analysis (and Paired T test post hoc) was used for normally distributed values and Friedman test (and Wilcoxon test post hoc) was used for non-normally distributed values. Data obtained from measurements were presented as arithmetic mean, standard deviation and data obtained through counting (%). Significance level was accepted as $p<0.05$. Significance level in multi comparisons (post hoc) was accepted as "$p<0.05$/number of comparisons".

Results

Statistically significant difference was not detected with regards to demographic values and operation durations of cases included in the study (Table 1). Groups were similar with regards to hemodynamic data (Table 2).

Table 1 Demographic values of patients, ASA risk groups and operation durations (Mean±SS)

	Group L(n=25)	Group P(n=25)	p
Age (year)	47.16 ± 8.45	46.80 ± 7.38	0.873
Weight (kg)	70.86 ± 7.65	71.12 ± 8.22	0.782
Gender (F/M)	15-Oct	15-Oct	1
Operation duration (minutes)	108.40 ± 28.49	104.20 ± 24.48	0.579
ASA I	16 (64%)	18 (72%)	0.762
ASA II	9 (36%)	7 (28%)	

NRS value was lower in lornoxicam group when compared with placebo group in all follow-up periods, but it was not statistically significant ($p>0.05$) (Table 3). Frequency of drug demand of the patients from iv-PCA in postoperative period in group L was found significantly lower when compared with placebo group at the end of operation, at the 2nd and 12th hour ($p<0.05$) (Table 4). 24 hours of total tramadol consumptions of patients with iv-PCA was found significantly lower in Group L than placebo group ($p<0.05$). When compared with placebo group a lower additional analgesic demand was observed in lornoxicam group in all of the follow-up periods. This difference was significant at the end of the operation and at the 2nd hour ($p<0.05$). Also, effective analgesia duration was 316.2±50.07 min. in lornoxicam group and 53.6±57.94 in placebo group and this was statistically significant ($p=0.011$) (Table 5).

Table 2 Hemodynamic data of patients (Mean±SS)

Follow-up periods	Group P(n=25)	Group L(n=25)	p
SBP End of Op	121.20±17.33	125.96±17.34	0.337
2th hour	117.20±14.58	122.80±13.39	0.164
4th hour	112.80±14.29	116.00±16.07	0.461
6th hour	111.60±12.47	116.80±16.00	0.206
12th hour	110.80±11.15	112.00±12.24	0.719
24th hour	112.00±14.72	117.60±16.40	0.138
DBP End of Op	76.40±12.20	81.40±12.81	0.164
2th hour	78.40±10.67	80.80±11.15	0.186
4th hour	74.40±10.83	77.00±11.90	0.423
6th hour	71.60±9.43	75.20±10.50	0.789
12th hour	69.20±7.59	74.00±9.12	0.08
24th hour	69.60±8.88	74.00±11.54	0.138
HR End of Op	81.16±9.68	81.40±11.61	0.937
2th hour	78.32±6.12	78.80±8.00	0.813
4th hour	78.16±5.85	75.68±6.21	0.153
6th hour	77.68±4.38	76.08±5.70	0.272
12thc hour	76.56±5.43	74.80±5.26	0.25
24th hour	78.72±4.82	75.12±7.07	0.065

($p<0.05$ significance limit).

Table 3 Periodic NRS change (Mean±SS)

Follow-up periods	Group P(n=25)	Group L(n=25)	p
End of Operation	3.12±2.02	2.32±2.03	0.131
2th hour	3.04±1.69	2.44±1.80	0.134
4th hour	2.04±1.56	1.56±1.19	0.271
6th hour	1.80±1.65	1.12±1.05	0.09
12th hour	1.00±0.70	1.08±1.28	0.787
24th hour	0.96±1.06	0.68±1.14	0.121

($p<0.05$ significance level).

Table 4 Frequency of drug demand of the patients (Mean±SS)

Follow-up periods	Group P(n=25)	Group L(n=25)	p
End of Op.	0.60±0.50	0.28±0.45	0.024*
2th hour	2.76±2.96	2.04±4.04	0.039*
4th hour	3.20±4.29	1.56±1.82	0.149
6th hour	2.92±2.56	1.76±2.33	0.101
12th hour	5.04±5.63	1.96±1.90	0.013*
24th hour	6.08±6.51	3.24±3.35	0.059

($p<0.05$ significance limit)

Laboratory values (coagulation parameters) of groups were similar in pre and postoperative periods ($p>0.05$). When side effects in postoperative 24 hours (Table 6) were compared, more nausea and vomiting were observed in Group L than Group P. But it was not statistically significant ($p>0.05$). Besides, hypotension was observed

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in one patient in lornoxicam group (4%) and urinary retention was observed in the placebo group in one patient (4%) (Table 6).

Table 5 Total drug consumptions and effective analgesia durations of the groups (Mean±SS)

	Group P(n=25)	Group L(n=25)	p
Total PCA Tramadol consumption (mg)	197.60±102.35	113.60±72.27	0.002*
Total Additional Analgesic Consumption (mg)	1600±1190.23	680±1107.55	0.001*
Effective Analgesia Duration (min)	53.6±57.94	316.2±50.07	0.011*

(p<0.05 significance limit).

Table 6 Number of patients with side effects and percentage incidences

Side effects	Group P(n=25)	Group L(n=25)	p
Nausea (%)	6 (24%)	4 (16%)	0.48
Vomiting (%)	3 (12%)	2 (8%)	0.63
GIS irritation (%)	0	0	
Hypotension (%)	0	1 (4%)	

Discussion

We observed that administration of preemptive lornoxicam (8 mg iv) to adult patients subjected to spinal surgery, decreased analgesic consumption in post-operative 24 hours and increased effective analgesia duration (efficient analgesia duration) and had a positive effect on additional analgesic consumption. Administration time of the analgesic drug that will be used to provide an efficient analgesia during postoperative period is important.[7] Central neural sensitization composed of intraoperative and postoperative noxious stimuli arising from muscle, bone, nerve incisions and wound retraction can be avoided in the intraoperative period with preemptive analgesia. NSAIs used for this purpose indirectly prevent central sensitization by inhibiting prostaglandin synthesis.[8] There is preemptive administration of different NSAIDs in different surgical procedures. Akın et al. showed that the administration of piroxicam (20 mg im) in preemptive and postoperative periods in total hip prosthesis surgery, decreased additional analgesic drug consumption significantly in the preemptive group.[9] Reuben et al. researched preemptive analgesic efficiency of 50 mg Rofecoxibin in arthroscopic knee surgery and showed that it increased post-operative analgesia duration and decreased pain score and opioid use in 24 hours period in preoperative group.[10] Trampitsch et al. found that pre and postoperative administration of lornoxicam 8 mg in patients scheduled for gynecological surgery, increased postoperative analgesia quality and decreased opioid consumption in postoperative 24 hours period.[11] We observed that preemptive administration of lornoxicam 8 mg increased effective analgesia duration and decreased PCA tramadol consumption and the need for additional analgesia in patients who had spinal surgery.

In order for opioids to provide effective analgesia in spinal surgeries with accompanying instrumentation applications, high doses of opioids are needed. Alternative analgesia methods were needed due to possible side effects that could develop related to high doses. Nikoda V et al. showed that lornoxicam administration (24 mg/day), with analgesic and anti-inflammatory characteristics in early postoperative period, decreased opioid demand in 35% of patients and steroid use by 25-50%.[12] In our study we found that preemptive lornoxicam 8 mg administration decreased postoperative analgesic consumption by 43%. Pain scores and PCA application used in evaluating postoperative pain severity are recommended as an objective method. Thompson et al.[13] administered preemptive meloxicam (15mg) - a NSAID – by rectal route to patients who had abdominal hysterectomy and evaluated postoperative pain scores with VAS (0-100mm) and despite significant decrease in VAS values they did not determine any decrease in iv morphine consumption with PCA method and concluded that VAS values and morphine consumption were not correlated.[13] On the other hand, although Ong et al.[14] determined that preemptive administration of NSAI drugs decreased total analgesic consumption and increased effective analgesia duration in a meta-analysis that consisted of 3261 patients where they evaluated the efficacy of preemptive analgesia practice in post-operative acute pain treatment, they demonstrated that there was not any statistically significant difference in VAS values in postoperative period.[15] While we similarly did not detect any significant difference between groups with regards to NRS values, a pain measurement score with PCA method, in patients who were administered iv tramadol observed a significant decrease in PCA drug demand frequency and postoperative analgesic drug consumption. As the other studies, we too consider that there may not be a significant correlation between pain scores and other analgesia success parameters always.

One of the criteria used for the evaluation of postoperative analgesia is "effective analgesic duration". The effect of preemptive NSAID administration to effective analgesic duration has been researched in mild to medium grade surgeries. O'hanlon et al. detected that effective analgesic duration following administration of tenoxicam (20mg iv) 30 minutes before operation to patients subjected to breast biopsy was 87.5 ± 32.5 minutes.[15] Kılıçoğlu et al.[16] determined that effective analgesic duration was 78 ± 62.66 with preemptive administration of lornoxicam 8mg in patients subjected to open cholecystectomy.[17] Salah et al. found that the effective analgesia duration was 684 ± 328 following administration of lornoxicam (16 mg iv) 30 minutes before tonsillectomy operation.[17] In our study effective analgesic duration was 312.2±50.07 minutes in 8 mg lornoxicam administered group. We considered that this was correlated with half-life of the drug.

One of the primary complications expected in the treatment with NSAI drugs is inhibition of aggregation of thrombocyte with increase in bleeding tendency.[18] In the literature it is reported that doses of lornoxicam used in the study, do not increase risk of bleeding and it can be administered safely due to short effect duration.[19,20] By means of intraoperative and postoperative monitoring for follow-up of bleeding a significant increase was not observed in the amount of surgical bleeding. There are some limitations of this study. First, we enrolled relatively a small sample size, so we could not perform any power analysis in this study. Second, we administered the same dose of lornoxicam (8mg of lornoxicam in100ml of isotonic saline) to the patients. We could not calculate a dose of the drug per body weight. We agree with the need of further studies related to the bigger study groups and a different dosage of lornoxicam. However, we can suggest the readers in their clinical applications to control of the postoperative pain may begin with 8mg of lornoxicam in the preoperative period. In conclusion we consider that preoperative lornoxicam (8mg iv) in the treatment of postoperative pain in spinal surgery increases the quality of analgesia in postoperative 24 hours and it is a reliable postoperative pain treatment method.

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None.

Conflicts of interest

The authors declare there is no conflict of interests.

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