Postoperative analgesic effects of lornoxicam after thyroidectomy: A placebo controlled randomized study

Mustafa Arslan*, Bilge Tuncer*, Avni Babacan*, Ferit Taneri, Yener Karadenizli*, Erhan Onuk**, Bahadır Ege****

ÖZET

Lornoksikamın tiroidektomi operasyonlarında postoperatif analjezik etkinliği: Plasebo kontrollü, randomize çalışma

Bu çalışmanın amacı lornoksikamın postoperatif ağrıda ne derece etkili olduğunu ve tramadol kullanımını ne oranda azalttığını ortaya koymaktır. Çalışmaya elektif tiroidektomi ameliyatı yapılan ASAI-II grubundan, 18-70 yaş arasında, 40 hasta, randomize olarak kabul edildi. GrupL'deki
hastalara operasyon bitiminde i.v. lornoksikam 8 mg uygulandı ve 12 saat arayla 2x8mg olacak şekilde postoperatif ilk 24 saatte verildi. GrupP'deki hastalara i.v. 4cc SF uygulandı ve 12 saat arayla 2x4cc olacak şekilde postoperatif ilk 24 saatte verildi. Ek analjezi (tramadol 100 mg) ihtiyacı olup olmaması 0-6, 6-12, 12-24 saatlik periyotlarda takip edildi. Ağrı skoru VAS ile postoperatif 15. dk, 1, 2, 4, 6, 8, 12, 18 ve 24. saatlerde kaydedildi. İlk analjezik gereksinim zamanı GrupL'de ortalama 101.7 dakika iken GrupP'de 37.9 dakika bulundu, süre anlamlı şekilde artmıştı (p<0.001). VAS GrupL'de 15. dakika, 1, 8, 12 ve 18. saatlerde anlamlı olarak düşük bulundu. Grupların postoperatif 24 saat boyunca tüketilen toplam tramadol miktarı GrupP ile karşılaştırıldığında GrupL'de anlamlı olarak düşük bulundu (p<0.05). GrupL'de tüketilen tramadol miktarı GrupP'ye göre %60 az olarak bulundu (100 mg, 250 mg (ortalama), sırasıyla). GrupP'de hastaların %100'ü ek analjezik kullandı, GrupL' de ise hastaların %60'ı ek
analjezik kullandı (p=0.002). GrupL'de hastaların %95'i, GrupP'de ise %25'i ağrı kontrolü için kullanılan yöntemi mükemmel buldu (p<0.000). GrupP'de olguların onsekizinde, GrupL'de ise dokuzunda bulantı şikayeti oluştu (p=0.002). GrupP'de olguların onbeşinde, GrupL'de ise sekizinde kusma görüldü (p=0.025). Troid ameliyatlarında lornoksikam kullanımı; opioid ihtiyacını ve bulantı kusma oranını azaltmış, ilk analjezik gereksinim zamanını uzatmış ve postoperatif ağrı skorlarında belirgin azalma sağlamıştır.

Anahtar kelimeler: Postoperatif analjezi, tiroidektomi, lornoksikam, tramadol

SUMMARY

The purpose of the present study was to determine the postoperative analgesic effects of lornoxicam and the reduction in tramadol consumption. Fourty patients of ASA class I-II, 18-70 years of age, undergoing thyroidectomy were assigned in a randomized manner into two groups: GroupL received 8 mg of lornoxicam i.v. at the end of the operation followed by 8 mg of lornoxicam b.i.d., i.v. for 24 hours postoperatively. GroupP received 4 ml of saline solution i.v. at the end of the operation and the same amount b.i.d., i.v. for 24 hours postoperatively. The requirements for supplemental analgesics were recorded at 0-6, 6-12 and 12-24 hour intervals. Postoperative pain scores were evaluated at 15th min. and 1, 2, 4, 6, 8, 12, 18 and 24th hours using Visual Analogue Scale (VAS). The time to first analgesic requirement was significantly longer in GroupL compared to GroupP (101.7 vs 37.9 min, p<0.001). Pain scores were significantly lower in GroupL compared to GroupP at 15th min, 1, 8 ,12 and 18th hours. Twenty four hour analgesic consumption was significantly lower in GroupL compared to GroupP (p<0.05). The amount of tramadol consumed in GroupL was 60% lower compared to GroupP (100 mg and 250 mg (mean), respectively). 100% of the patients in GroupL and 60% of the patients in GroupP needed supplemental analgesics. The degree of satisfaction with postoperative pain management was excellent in 95% of patients in GroupL and 25% of patients in GroupP. Eighteen patients in GroupP and 9 patients in GroupL had nausea (p=0.002), and fifteen patients in GroupP and 8 patients in GroupL had vomiting (p=0.025). Lornoxicam decreased the opioid need, the incidence of nausea and vomiting and postoperative pain scores. Moreover, it was observed that the time needed for the first analgesic requirement was prolonged following thyroidectomies.

Key words: Postoperative analgesia, thyroidectomy, lornoxicam, tramadol

(*) Gazi Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı
(**) Gazi Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı

Başvuru adresi:
Dr. Mustafa Arslan, Gazi Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon A.nabilim Dalı, 06500 Ankara
Tel: (0312) 202 50 19 e-posta: mustarslan@gmail.com

(*) Gazi University Faculty of Medicine, Department of Anesthesiology and Reanimation
(**) Gazi University Faculty of Medicine, Department of General Surgery

Correspondence to:
Mustafa Arslan, MD, Gazi University Faculty of Medicine, Department of Anesthesiology and Reanimation, 06500 Ankara TURKEY
Tel.: (+90 312) 202 50 19 e-mail: mustarslan@gmail.com

Introduction

Patients undergoing thyroidectomy have moderate to severe pain in the postoperative period (Dejonckheere and Desjeux 2001). Although opioids are traditionally consumed in managing postoperative pain, their side effects such as respiratory depression, sedation, constipation, urinary retention and itching limit their use (Austrup and Korean 1999). On the other hand, non-steroid anti-inflammatory drugs (NSAIDs) found a widespread use in postoperative pain management. Their peripheric and central analgesic effects, anti-inflammatory properties and relatively more tolerability, with no side effects which are observed in opioids made these drugs of choice in postoperative analgesia (Beilin et al. 2003, Mc Crory et al. 2002).

Lornoksikam (Xefo®), an oxicam group of NSAID, has been recently used in our country. Besides its inhibitory effects on COX-I and COX-II in peripheric receptors, it also increases prostaglandin, endogenous dinorphin and beta-endorphin levels promoting central analgesic and antiinflammatory effects. Lornoxicam has been successfully used in prevention and treatment of postoperative pain (Zhao et al. 2005, Trampitsch et al. 2003, Gong et al. 2001, Ilias and Jansen 1996). Besides postoperative pain management, its analgesic effects in chronic pain states such as osteoarthritis, romatoid arthritis and ankylosing spondylitis has also been demonstrated (Hyllested et al. 2002, McCormack 1999).

The strong analgesic and antiinflammatory effects of this new, short acting NSAID lornoxicam, have been demonstrated in several clinical studies, but there is limited number of studies concerning its opioid sparing effect. Lornoxicam is a potent analgesic with excellent antiinflammatory properties in a range of painful and inflammatory conditions including postoperative pain and rheumatoid arthritis (Radhofer-Welte and Rabasseda 2000, Balfour et al 1996). Studies showed that lornoxicam provides an alternative to morphine and tramadol for the treatment of postoperative pain with fewer adverse events after hysterectomy (Gong et al. 2001, Ilias and Jansen 1996). It was reported that lornoxicam was a useful alternative to tramadol following arthroscopic reconstruction of anterior cruciate ligament (Staunstrup et al 1999). Nikoda et al. reported that lornoxicam allows reduction of promedol dose and the incidense of adverse effects (Nikoda et al. 2001). Also, lornoxicam administered preemptively improved the quality of postoperative analgesia and opioid consumption in patients undergoing gynecological operations (Trampitsch et al. 2003). Application of lornoxicam to patient controlled analgesia in patients undergoing abdominal surgeries was also effective with less adverse reactions compared with fentanyl (Zhao et al. 2005). Following lumbar disk surgery, equivalent pain reief was obtained with lornoxicam and morphine when administered by patient controlled analgesia, but lornoxicam was associated with fewer adverse events (Rosenow et al. 1998).

Studies with parecoxib, diclofenac and ketorolac, showed that opioid consumption and side effects were less postoperatively (Hubbard et al. 2003, Alexander et al 2002). The aim of this randomized, double-blind, placebo controlled study was to investigate the analgesic effects of lornoxicam in postoperative pain and decreasing tramadol (Contramal®) consumption.

Material and Method

Forty patients having American Society of Anesthesiologists (ASA) class I or II physical status, 18-70 years of age, scheduled to undergo thyroidectomy in our hospital were included in this study. After obtaining approval from the local research ethics committee, all patients were informed about the procedure and the anesthetic technique. Then informed written consent was obtained from each patient.

Exclusion criteria were severe systemic disease, allergy to NSAIDs, long term treatment with analgesics, consumption of analgesics within 24 h of surgery, history of gastric or duodenal ulcers and refusal by the patient.

All patients were familiarized with a 10 cm visual analog scale (VAS) preoperatively with 0: no pain and 10: the worse imaginable pain. Preoperative VAS scores were obtained from all patients. Patients were told to indicate the degree of their pain by VAS, when they were asked to evaluate the intensity of their pain.

Premedication was not administered. Patients were assigned in a randomized manner into 2 groups, using a sealed envelope technique. Standard monitoring techniques were used, including heart rate (HR), non-invasive mean arterial pressure (MAP) (Bruker Physiogard SM 786, 1995 France), respiratory rate (RR) and pulse

oximetry (SpO2) (Odam Physiogard SM 786, 1995 France). Normal saline solution or Lactated Ringer's solution (5 ml kg-1 h-1) was infused via an I.V. 22 G catheter. Preoperative heart rate HR, MAP, RR and SpO2 were recorded (baseline value).

All patients received standard general anesthesia which was induced intravenously with thiopental 5mg kg-1, fentanyl 1µg kg-1 and atracurium 0.5 mg kg-1 and maintained with isoflurane (1%) with N2O (66%) in oxygen (33%). Mean arterial pressure, HR and SpO2 were recorded before and after induction, after intubation and every 5 min intervals until the end of the operation. The concentration of volatile anesthetic was decreased to 0.4% during skin suturing. Volatile anesthetic and nitrous oxide were discontinued simultaneously and the lungs were manually ventilated with 100% oxygen with a fresh gas flow of 4 L min-1 until spontaneous ventilation started. Residual neuromuscular blockade was reversed with atropin 0.01 mg kg-1 and neostigmine 0.03 mg kg-1 and patients were extubated. At the end of the procedure anesthesia and surgery times were recorded.

GroupL (lornoxicam) received 8 mg of lornoxicam iv at the end of the operation followed by 8 mg of lornoxicam 2x1 i.v. for 24 hours postoperatively.

GroupP (placebo) received 4 ml of saline solution iv at the end of the operation and the same amount 2x1 i.v. for 24 hours postoperatively.

In case of inadequate analgesia (VAS score greater than 4), patients of both groups received tramadol, i.m. 100 mg of starting dose and the same dose was repeated with a maximum dose of 400 mg daily.

After the operation, patients were transferred to the recovery room where they stayed for 1 hour and were then transferred to their rooms where they were followed up for 24 hours. The time to first analgesic requirement use and 24 hour total analgesic consumption were recorded. Analgesic duration was defined as the time from completion of surgery until the first request for tramadol. The requirements for supplemental analgesics were recorded at 0-6, 6-12 and 12-24 hour intervals. Postoperative pain scores were evaluated at 15 min and 1, 2, 4, 6, 8, 12, 18 and 24 hours using VAS. The presence of side effects such as nausea, vomiting, allergic reactions, urinary retention and hypotension were recorded postoperatively for each patient. Patients in both groups were asked to indicate the degree of overall satisfaction with postoperative pain management on a 4-point satisfaction scale before discharge: 0=unsatisfied/poor, 1=somewhat satisfactory/adequate, 2=satisfactory/adequate, 3=very good, 4=excellent.

Statistical Analysis: Statistical analysis was computer processed. p values < 0.05 were considered significant. The results of the study were expressed as mean, median [± SS, (25-75%) (min-max), n (%)]. Demographic data, duration of anes-

Table I: Demographic properties, and operation and anesthesia duration [Mean ± SD (min-max)]

	Group L (n=20)	Group P (n=20)
Gender (M/F)	5/15	2/18
Age (year)	44.5±8.9 (31-64)	49.5±12.1 (25-70)
Weight (kg)	67.8±10.1 (50-87)	73.1±8.9 (58-90)
Height (cm)	164.0±5.2 (158-175)	163.4±6.8 (155-182)
ASA (I/II)	16/4	15/5
Operation duration (min)	122.6±12.6 (75-175)	129.6±11.6 (85-185)
Anesthesia duration (min)	125.1±12.0 (70-172)	132.3±10.4 (80-190)

Table II: Postoperative VAS values [Median (25-75%) (min-max)].

VAS	15. min	1. h	2. h	4. h	6. h	8. h	12. h	18. h	24. h
GroupL (n=20)	2.5(2-3) (1-8)	4.0(2.5-5.5) (1-8)	3.5(2-5) (1-8)	2.0(2-3) (0-5)	2.0(1-3) (0-8)	1.0(1-2) (0-3)	1.0(0-3) (0-4)	0.5(0-2)† (0-2)	0.0(0-75) † (0-1)
GroupP (n=20)	7.5(4-8)* (3-10)	6.5(4.5-8)* (3-8)	3.0(3-4) † (2-7)	3.0(2-5.5) † (1-8)	2.5(1.5-3) † (1-8)	3.0(2-4)* † (0-7)	4.0(4-6)* † (0-8)	2.0(1-3)* † (0-6)	0.0(0-1) † (0-2)
p	0.000	0.001	0.62	0.22	0.24	0.005	0.000	0.004	0.80

* $p<0.05$: compared to GroupP

† $p<0.05$: compared to 15. min

Table III: First analgesic requirement time and postoperative analgesic requirements [Mean ± SD, (min-max), n].

	GroupL (n=20)	GroupP (n=20)	*p*
First analgesic requirement time (min)	101.7±72.3 (35-280)	37.9±15.1* (15-70)	0.001
Analgesic consumption (mg)	100±45.5 (100-200)	250±104.6* (100-400)	0.000
Number of patients requiring supplemental analjesic in first 6 h (n)	12/20	20/20*	0.002
Number of patients requiring supplemental analjesic in 6-12 h (n)	2/20	10/20*	0.006
Number of patients requiring supplemental analjesic in 12-24 h (n)	0/20	12/20*	0.000
Number of patients requiring supplemental analjesics (n)	12/20	20/20*	0.002

* $p<0.05$: compared to GroupP

thesia and surgery and the first analgesic time between the groups were analyzed using students t test. VAS pain scores were analyzed using ANOVA and Bonferroni adjustment was used for comparing intragroup VAS values. Total analgesic consumption of the groups was compared using Mann-Whitney U-test. Sex, ASA, incidence of side effects, number of patients requiring supplemental analgesics at 0-6, 6-12, 12-24 hour intervals and patient satisfaction between the groups were analyzed with Fisher's test and χ^2 test.

Results

There were no significant differences between the groups with regard to demographic variables (age, gender, weight and height) and ASA physical status or the mean duration of anesthesia and surgery in minutes (Table 1).

The changes in postoperative VAS pain scores are shown in Table 2. VAS pain scores recorded at 15 min, 1, 8, 12 and 18 h after the operation were higher in GroupP, compared to GroupL ($p<0.05$). Pain scores at 18 and 24 h were significantly lower compared to pain scores at 15. min in GroupL ($p=0.003$, $p<0.0001$, respectively), whereas pain scores at all times except 1st hour were significantly lower than pain scores at 15 min in GroupP (Table 2).

There was a significant difference with respect to the first analgesic requirement time between two

Table IV: Patient satisfaction [n (%)].

Patient satisfaction	GroupL (n=20)	GroupP (n=20)	*p*
2: satisfactory/adequate	0 (0)	8 (40)	0.000
3: very good	1 (5)	7 (35)	
4: excellent.	19 (95)	5 (25)*	

c2=20.67, p<0.001

* $p<0.001$: compared to GroupP

Table V: Incidence of side effects (%).

	GroupL (n=20)	GroupP (n=20)	*p*
Nausea	9 (% 45)	18 (90)*	0.002
Vomiting	8 (% 40)	15 (% 75)*	0.025
Allergic reaction	-	1 (% 5)	0.500
Hypotension	-	3 (% 15)	0.231
Urinary retention	-	-	-

* $p<0.05$: compared to GroupP

groups. Time to first analgesic requirement was longer in GroupL (101.7 min) compared to GroupP (37.9 min) ($p<0.05$) (Table 3). The 24 h total tramadol consumption was more in GroupP compared to GroupL ($p<0.05$) (Table 3). The 24 h total tramadol consumption of GroupL was 60 % less compared to GroupP (100 mg and 250 mg respectively) ($p<0.05$) (Table 3). Supplemen-tary analgesics were used in 100% of the patients in GroupP and 60% of the patients in GroupL. The number of patients requiring supplemental analgesics at 0-6, 6-12 and 12-24 h was significantly lower in GroupL compared to GroupP ($p<0.05$) (Table 3).

The degree of satisfaction with postoperative pain management was excellent in 95 % of patients in GroupL and 25 % of patients in GroupP ($p<0.05$) (Table 4).

The side effects are presented in Table 5. The incidence of postoperative nausea and vomiting was significantly higher in GroupP compared to GroupL ($p<0.05$). No significant difference was found between the groups with regard to other side effects. The most frequent side effect in both groups was nausea. 18 patients in GroupP and 9 patients in GroupL complained of nausea and 15 patients in GroupP and 8 patients in GroupL vomitted ($p<0.05$). Three patients in GroupP had hypotension, while all patients in GroupL were normotensive. One patient in GroupP had allergic reaction.

Discussion

This study demonstrates that lornoxicam produces significant opioid sparing effects compared to placebo in postoperative patients following thyroidectomies. It decreased 24 h total opioid consumption and increases the time to first analgesic use, thus its analgesic effect was not enough as a sole agent.

Besides their analgesic effects, anti-inflammatory properties of NSAIDs make them rational analgesics. Therefore, we performed our study with lornoxicam, a NSAID, in patients undergoing thyroidectomy. Lornoxicam has been successfully used in prevention and treatment of postoperative pain (Zhao et al. 2005, Trampitsch et al. 2003,

Gong et al. 2001, Ilias and Jansen 1996). It was reported that i.v. 8 mg of lornoxicam was equianalgesic with 20 mg of morphine (Norholt et al. 1996), 50 mg of pethidine (Dejonckheere and Desjeux 2001) and 50 mg of tramadol (Ilias and Jansen 1996) and 16 mg of lornoxicam had a superior analgesic effect compared to 100 mg of tramadol (Staunstrup et al. 1999).

The most frequent side effects are nausea and vomiting. However, the type of surgery, anesthetics, hypotension and the supplemental agents used should all be considered (Watcha and White 1992). In our placebo controlled study, surgery type and general anesthesia applied was standard and there was no difference between the groups in peroperative hemodynamic values. Visceral and pelvic pains are frequent causes of postoperative nausea and vomiting. Studies reported the improvement of nausea after treatment of pain (Keeny 1994, Adrews 1992, Lerman 1992). Dejonckheere and Desjeux (Dejonckheere and Desjeux 2001) reported an increased incidence of nausea with tramadol compared to propacetamol (injectable prodrug of acetaminophen). In our study, the incidence of nausea was 90 % in GroupP and 45 % in GroupL, and the incidence of vomiting was 75 % and 40 % respectively. Three patients in GroupL had hypotension, whereas none of the patients in GroupL had hypotension. The reason for high incidence of nausea and vomiting in GroupP may be due to higher consumption of opioids in the postoperative period, hypotension and pain.

In a study performed in 38 patients undergoing arthroscopic knee surgery, 16 mg of lornoxicam was applied and 2 patients had gastrointestinal side effects and 2 patients had urinary retention (Hubbard et al. 2003). Norhold et al. reported a dose dependent increase in side effects after im 8 mg and 16 mg of lornoxicam and found that the most frequent side effect was sensitivity at the site of injection (Norhold et al. 1996).

One of the main reasons in avoiding NSAID consumption for postoperative pain is the fear to cause bleeding. NSAIDs are known for their tendency to bleeding, as a result of inhibition of cyclooxygenase and trombocyte aggregation (McCormack 1999, Cooper and Hesch 1996, Nuutinen et al. 1993). In a meta-analysis of 1368 patients undergoing tonsillectomy, Krishna et al. (Krishna et al. 2003) reported that the incidence of postoperative bleeding was not affected by NSAID consumption. This finding was also confirmed by Moiniche et al. (Moiniche et al. 2003). Moiniche et al. (Moiniche et al. 2003) also related postoperative bleeding to ASA group and surgical technique. ASA class I and II had no increase in tendency to bleeding. In our study, none of the patients had postoperative bleeding.

In conclusion, this study demonstrated the early postoperative analgesic effect of 16 mg of lornoxicam in patients undergoing thyroidectomy. Because of providing decreased opioid consumption with lower side effects, lornoxicam can be safely used in postoperative pain management.

References

Alexander R, El-Moalem HE, Gan TJ: Comparison of the morphine-sparing effects of diclofenac sodium and ketorolac tromethamine after major orthopedic surgery. J Clin Anesth 2002; 14: 187-192.

Andrews PLR: Physiology of nausea and vomiting. Br J Anaesth 1992; 69: 10-19.

Austrup ML, Korean G: Analgesic agents for the postoperative period. Opioids. Surg Clin North Am 1999; 79: 253-273.

Balfour JA, Fitton A, Barradell LB: Lornoxicam. A review of its pharmacology and therapeutic potential in the management of painful and inflammatory conditions. Drugs 1996; 51: 639-657.

Beilin B, Besler H, Mayburd E, Smimov G: Effects of preemptive analgesia on pain and cytokine production in the postoperative period. Anesthesiology 2003; 98: 151-155.

Cooper SA, Hesch VE: Lornoxicam: Analgesic efficicacy and safety of a new oxicam derivate. Advances in therapy 1996; 13: 67-77.

Dejonckheere M, Desjeux L: Intravenous tramadol compared to propacetamol for postoperative analgesia following thyroidectomy. Acta Anaesth. Belg 2001; 52: 29-33.

Gong ZY, Ye TH, Qin XT, Yu GX, Guo XY, Luo AL: Patient-controlled analgesia with lornoxicam in patients undergoing gynecological surgery Zhongguo Yi Xue Ke Xue Yuan Xue Bao 2001; 23: 472-475.

Hyllested M, Jones S, Pedersen LJ, Kehlet H: Comparive effect of paracetamol, NSAIDs or their combination in postoperative pain management: qualitative review. Br J Anaesth 2002; 88: 199-214.

Hubbard RC, Naumann TM, Traylor L, Dhadda S: Parecoxib sodium has opioid-sparing effects in patients undergoing total knee arthroplasty under spinal anesthesia. Br J Anaesth 2003; 90: 166-172.

Ilias W, Jansen M: Pain control after hysterectomy: An observer-blind, randomised trial of lornoxicam versus tramadol. BJCP 1996; 50: 197-202.

Keeny GMC: Risk factors for postoperative nausea and vomiting. Anaesthesia 1994; 49: 6-10.

Krishna S, Hughes LF, Lin SY: Postoperative hemorrhage with nonsteroidal anti-inflammatory drug use after tonsillectomy: a meta-analysis. Arch Otolaryngol Head Neck Surg 2003; 129: 1086-1089.

Lerman J: Surgical and patient factors involved in postoperative nausea and vomiting. Br J Anaesth 1992; 69: 24-32.

McCormack K: The evolving NSAİD: Focus on lornoxicam. Pain 1999; 6: 262-278.

Mc Crory CR, Sten G, Lindahl GE: Cyclooxygenase inhibition for postoperative analgesia. Anesth Analg 2002; 95: 169-176.

Moiniche S, Romsing J, Dahl JB: Nonsteroidal antiinflamatory drugs and the risk of operative site bleeding after tonsillectomy: A quantitative systemic review. Anesth. Analg 2003; 96: 68-77.

Nikoda VV, Maiachkin RB, Bondarenko AV, Mikhailov IE, Anosova NP: Use of lornoxicam for analgesia in the early postoperative period. Anesteziol Reanimatol. 2001; 6: 47-50.

Norholt ES., Pedersen S, Larsen U: Pain control after dental surgery: a double blind, randomised trial of lornoxicam versus morphine. Pain 1996 ; 67: 335-343.

Nuutinen LS, Laitinen JO, Salomaki TE: A risk-benefit appraisal of injectable NSAİDs in the management of postoperative pain. Drug Safety 1993; 9: 380-393.

Radhofer-Welte S, Rabasseda X: Lornoxicam, a new potent NSAID with an improved tolerability profile. Drugs Today (Barc). 2000;36: 55-76.

Rosenow ED, Alberchtsen M, Stolke D: A comprasion of patient-controlled analgesia with lornoxicam versus morphine in patients undergoing lumbar disk surgery. Anesth. Analg 1998; 86: 1045-1050.

Skjodt NM., Davies NM: Clinical pharmacokinetics of lornoxicam. Clin Pharmacokinet 1998; 34: 421-428.

Staunstrup H, Ovesen J, Larsen T: Efficacy and tolerability of lornoxicam versus tramadol in postoperative pain. J of Clin Pharmacol 1999; 39: 1-8.

Trampitsch E, Pipam W, Moertl M, Sadjak A, Dorn C, Sittl R, Likar R: Preemptive randomized, double-blind study with lornoxicam in gynecological surgery. Schmerz 2003; 17: 4-10.

Watcha MF, White PF: Postoperative nausea and vomiting: its etiology, treatment and prevention. Anesthesiology 1992; 77: 162-184.

Zhao H, Ye TH, Gong ZY, Xue Y, Xue ZG, Huang WQ: Application of lornoxicam to patient-controlled analgesia in patients undergoing abdominal surgeries. Chin Med Sci J 2005; 20: 59-62.