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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Comparing efficacy of preemptively used lornoxicam and tramadol for postoperative pain in patients underwent laparoscopic cholecystectomy

Laparoskopik kolesistektomi uygulanan hastalarda, ameliyat öncesi uygulanan lornoksikam ve tramadol'un postoperatif ağrı üzerine olan etkilerinin karşılaştırılması

Pakize Kırdemir[1], Anıl Marşan[2]

ABSTRACT

Objectives: The management of postoperative pain is an important problem in Anesthesiology. This randomized double-blind study compared the analgesic efficacy of preemptively used lornoxicam and tramadol in patients underwent laparoscopic cholecystectomy.

Methods: A total of 76 patients were randomly divided into four groups. All patients received tablets 4 hours before the operation. Preemptively Group PL received 4 mg lornoxicam, Group PT received 50 mg tramadol and Group L and T received placebo. After the operation Group PL received 0.8 mg/h infusion and 1 mg bolus lornoxicam; Group L 1.6 mg loading, 0.8 mg/h infusion and 1 mg bolus lornoxicam; Group PT 5 mg/h infusion and 10 mg bolus tramadol; Group T 20 mg loading, 5 mg/h infusion and 10 mg bolus tramadol for 24 hours. Pain intensity and pain relief at 0, 1st, 2nd,3rd, 6th,10th, 24th hours and overall assessment of pain relief was done at 24th hour.

Results: Demographic features, operation time, heart rate and mean arterial blood pressure values were not different between four groups. Both Group PL and PT had lower pain intensity and higher pain relief values than Group L and T. Group PL and PT had lower total drug consumption and higher pain relief. Overall assessment of pain relief was highest in Group PL. Pain intensity was highest in Group T and lowest in Group PL at all time points.

Conclusion: Onset of analgesia with lornoxicam was faster and greater patient-controlled analgesia (PCA) demand was observed with tramadol. Postoperative pain relief was similar with lornoxicam and tramadol administrated by PCA. This study suggests that preemptive administration of lornoksikam and tramadol may result in more postoperative pain relief. *J Clin Exp Invest 2010; 1(1): 1-6*

Key words: Preemptive analgesia, lornoxicam, tramadol, postoperative, pain relief

ÖZET

Amaç: Postoperatif ağrı, akut ağrının en sık nedenlerinden biridir. Postoperatif ağrı tedavisinin klasik şekli parenteral opioid uygulamasıdır. Bu randomize çift-kör çalışmada preemptif uygulanan lornoksikam ve tramadolün analjeziklerin etkinliklerinin karşılaştırılması amaçlandı.

Hastalar ve Yöntem: Toplam 76 hasta rastgele dört gruba ayrıldı. Tüm hastalar operasyondan 4 saat öncesi tablet aldılar. Grup PL preemptif olarak 4 mg lornoksikam, Grup PT 50mg tramadol alırken, Grup L ve T ise plasebo tablet aldılar. Operasyon sonunda Grup PL'ye 8 mg/saat infüzyon ve 1 mg bolus lornoksikam; Grup L'ye 1.6mg yükleme, 8 mg/saat infüzyon ve 1 mg bolus lornoksikam; Grup PT'ye 5 mg/saat infüzyon ve 10 mg bolus tramadol; Grup T'ye 20 mg yükleme, 5 mg/saat infüzyon ve 10 mg bolus tramadol hasta kontrollü (PCA) ile 24 saat boyunca uygulandı. Ağrı şiddeti 0,1., 2., 3., 6., 10., 24. saatlerde kaydedildi ve 24 saat sonunda genel ağrı iyileşmesi değerlendirildi.

Bulgular: Gruplar arasında demografik bulgular, operasyon süresi, kalp hızı ve ortalama kan basınç değerleri bakımından anlamlı fark gözlenmedi. Grup PL ve PT de Grup L ve T ye göre daha düşük ağrı şiddeti ve daha hızlı ağrı iyileşmesi görüldü. Grup PL ve PT'de daha az total analjezik tüketimi ve daha yüksek ağrı tedavisi memnuniyeti bulundu. Tüm gruplar birbirleriyle karşılaştırıldığında, 24 saatlik ağrı tedavisi en iyi Grup PL'de bulundu. Ağrı şiddeti tüm zamanlarda Grup T'de en yüksek, Grup PL'de ise en düşük bulundu.

Sonuç: Analjezi etkisi lornoksikam grubunda daha önce başlarken, ilaç ihtiyacı tramadol gruplarında daha fazla idi. Cerrahi girişim sonunda PCA kullanımı ile benzer ağrı iyileşmesi görüldü. Bu çalışma postoperatif ağrı tedavisinde analjeziklerin preemptif uygulanmasının daha fazla analjezi sağlayabileceğini düşündürmektedir. *Klin Den Ar Derg 2010; 1(1): 1-6*

Anahtar kelimeler: Preempetif analjezi, lornoksikam, tramadol, postoperatif, ağrı giderilmesi

[1]*Süleyman Demirel University, Department of Anaesthesiology and Reanimation- Algology section- Isparta.*
[2]*SB İstanbul Göztepe Training Hospital, Anesthesiology and Reanimation Clinics- İstanbul, Türkiye*
Yazışma Adresi /Correspondence: *Doç. Dr. Pakize Kırdemir, SDÜ, Anestezi ve Reanimasyon Anabilim Dalı, Algoloji BD-Isparta – Türkiye* **Email:** pkirdemir@gmail.com
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INTRODUCTION

After surgery, severe pain is experienced by 50% -70% of patients postoperatively, while a further 20%-40% of patients experience moderate pain[1].

Postoperative pain not only causes considerable distress to the patient, it also contributes to prolonged recovery time and may adversely affect patient outcome[2]. Despite well known disadvantages including respiratory depression and hypotension, opioid analgesics are the traditional first-line treatment in postoperative pain[3]. Although opioids are effective analgesic drugs with no ceiling in their analgesic effect, their efficacy is often limited by their tolerability profile, therefore inadequate postoperative analgesia has been a problem for several decades[4]. Nonsteroid anti-inflamatuar drugs (NSAID) provide effective analgesia in patients with acute pain after surgery, either as a substitute or as an adjunct to opioid analgesia[4,5]. The major advantage of NSAIDs is relatively well tolerability in selected patients for short-term postoperative analgesia[6].

Tramadol is centrally acting opioid analgesic and provides effective postoperative pain relief especially for abdominal, gynecological and orthopedic procedures[7,8]. On the basis of its potency, tramadol has comparatively few disadvantages associated with other opiates, such as cardiovascular reactions, respiratory depression and physical dependency[9].

Injectable NSAID have recently become recognized as useful agents in the treatment of postoperative pain. Short usage effectiveness provides alternative to morphine[4]. Lornoxicam is a new NSAID belonging to enolic acid chemical class. Its analgesic potency in animal pain models exceeds that of tenoxicam and piroxicam by approximately 12- and 3- fold respectively, and that of indomethacin and diclofenac by 4- and 6-fold, respectively[10]. Effective preemptive treatment of postoperative pain has been one of the main goals of clinicians and researchers. For this reason, we decide to give lornoxicam and tramadol preemptively to see if we could be able to reduce postoperative analgesic need and have good analgesia.

This study aimed to compare efficacy of preemptively used tramadol and lornoxicam for the postoperative pain relief in patients underwent laparoscopic cholecystectomy.

PATIENTS AND METHODS

After the approval of the Ethical Committee and obtaining the written consents, we performed a double-blind randomized study on 76 ASA I-II patients aged between 18 and 65 undergoing laparoscopic cholosystectomy. The patients and the data collectors were blinded to the treatment regimen and had no Access to the anesthesia record. Patients sensitive to NSAID, gastric ulcer complains last 6 months, coagulopaty, abnormal biochemistry results, using drugs interaction with tramadol or NSAID, receiving cytotoxic agents and alcohol or drug addict patients were excluded from the study.

Preemptively, patients were instructed on the use of the 5-point verbal rating scale (5-VRS) for pain severity before the operation. Scoring was determined as, 0= no pain, 1=mild pain, 2= tolerable pain, 3=severe and 4=pain resist. Pain severity recorded postoperative 0, 1st, 2nd, 3rd, 6th, 10th and 24th hours by using 5-VRS. Patients satisfaction were evaluated by the help of linear Pain Relief Scala (pain …-… no pain) as it was easy for the patients to understand and give an answer to the questions: 1= excellent (no pain) 2= very good (mild pain), 3=good (tolerable pain), 4= fair (slight decrease in pain) and 5= bad (pain resist).

Seventysix patients were randomized into four groups. Patients were studied after an eight hours period of fast. No premedication were given. Control haemodynamic parameters of the patients were recorded after their arrival to the operating room. Heart rate (HR) and noninvazive mean arterial pressure (MAP) were recorded every 15 minutes during the operation.

All patients were given tablets 30 minutes before the operation. Group PL received 4 mg lornoxicam, Group PT received 50 mg tramadol and Group L and T received placebo tablets orally. Group Preemptive lornoxicam (PL, n=20) received 4mg lornoxicam, Group Preemptive Tramadol (PT, n=18) received 50 mg tramadol and Group Lornoxicam (L, n=20) and Group Tramadol (T, n=18) received placebo. Anesthesia was induced in all groups with thiopental 4 mg/kg intravenously (IV) and vecuronium 0.1 mg/kg IV. Anesthesia maintenance was achieved with isoflurane 1-1.5%, O_2 / N_2O 50%, and maintenance of muscle relaxation was provided with 0.01 mg/kg vecuronium. After the operation

Group PL received 0.8 mg/h infusion and 1 mg bolus lornoxicam; Group L 1.6 mg loading, 0.8 mg/h infusion and 1 mg bolus lornoxicam; Group PT 5 mg/h infusion and 10 mg bolus tramadol; Group T 20 mg loading, 5 mg/h infusion and 10 mg bolus tramadol IV PCA for 24 hours. At end of the 24th hour patients' satisfaction, total drug demand and side effects were also recorded. All the data were evaluated by using Chi-square and t-tests.

RESULTS

According demographical data, operation period, HR and MAP all groups were similar and there were no significant differences between the groups ($p>0.05$) (Table 1).

Groups preemptively received lornoxicam and tramadol (Group PL and PT) had low pain intensity and high pain relief when compared with other groups and these differences were statistically significant ($p<0.05$) (Table 2).

Table 1. Patients' characteristics (mean±SD)

	Group PL (n=20)	Group L (n=20)	Group PT (n=18)	Group T (n=18)
Gender (M/F)	12/8	16/4	12/6	8/10
Age (year)	38±13.7	36.3±13.1	38.2±14.4	47.3±13.5
Weight (kg)	71.9±8.8	67.1±4.1	69.4±8.9	67.6±9.1
Height (cm)	168.6±10.3	165.8±7.9	166.1±10.6	162.9±6.9
Op. period (min)	71.3±17.5	72.3±30.3	80±18.3	76.4±45

Group PL:preemptive lornoxicam, Group L:lornoxicam, Group PT:preemptive tramadol, Group T:tramadol, M/F: Male/Female, kg:kilogram, cm:centimetre, min.: minute

Table 2. Visual analogue scores (mean±SD)

Postoperative	Group PL	Group L	Group PT	Group T
0	1.13±0.36*	1.6±0.9	1.2±0.4	2.4±0.9
1st hour	0.38±0.7*	0.7±0.6	1	1.9±0.9
2nd hour	0.13±0.36*	0.3±0.5	0.9±0.3	1.4±0.5
3rd hour	0.13±0.36*	0.3±0.5	0.4±0.5	0.7±0.8
6th hour	0	0	0	0.3±0.5
10th hour	0	0	0	0.3±0.5
24th hour	0	0	0	0.3±0.5

Grup PL: preemptive lornoxicam, Grup L: lornoxicam, Grup PT: preemptive tramadol, Grup T: tramadol *p<0.05 between the groups

In Group L postoperative values at 1, 2 and 3rd hours were lower than Group PT but were not statistically significant.

Also in Group PL and Group PT total analgesic demand were low ($p<0.05$) and patients' satisfaction were significantly high ($p<0.05$) (Table 3).

Patients' satisfactions were in Group PL 85 % excellent and very good, in Group PT 78.2%, in Group L 70% and Group T 66.5%. Regarding these results groups receiving preempetively lornoxicam had the highest values of patients'satisfaction and these results were significant comparing with other groups ($p<0.05$) (Table 4).

Pain intensity was highest in Group T and lowest in Group PL in all times.

Table 3. Total analgesic demand (mg)

	Group PL	Group L	Group PT	Group T
Total analgesic demand (mg)	17.1±4	18..9±5.6	229.1±54.7	275.8±64.6

Group PL: preemptive lornoxicam, Group L: lornoxicam, Group PT: preemptive tramadol, Group T: tramadol, mg: miligram

Tablo 4. Patients' satisfaction scores, n (%)

	Grup PL (n=20)	Grup L (n=20)	Grup PT (n=18)	Grup T (n=18)
Excellent	12 (60.0)	8 (40.0)	10 (56.0)	7 (38.8)
Very good	5 (25.0)	6 (30.0)	4 (22.2)	5 (27.7)
Good	2 (10.0)	4 (20.0)	3 (16.6)	3 (16.6)
Fair	1 (5.0)	2 (10.0)	1 (5.5)	3 (16.6)
Bad	-	-	-	-

Group PL: preemptive lornoxicam, Group L: lornoxicam, Group PT: preemptive tramadol, Group T: tramadol

DISCUSSION

Postoperative pain is the most common form of acute pain and affects the majority of patients undergoing surgery. The provision of adequate analgesia is not only important from a humanitarian perspective but also been shown to improve postoperative recovery and outcome. The most commonly used agents for the control of postoperative pain are parenteral opioid analgesics. Although these agents are potent and extremely effective, fears about addiction and respiratory and cardiovascular depression can result in a reluctance to administer sufficient medication and may lead to inadequate management of postoperative pain[11]. This clinical research has demonstrated satisfactory postoperative analgesia and lower analgesic demand when preemptive drugs were administrated. According to these results, we used lornoxicam and tramadol preemptively so as to have good analgesia with lower analgesic demand. Preemptive analgesia prevents secondary hyperalgesia, which supports a role for central sensitization in the generation of postoperative pain[12].

Tramadol; fulfills the requirements of an analgesic for treatment of moderate postoperative pain such as abdominal, gynecological and orthopedic surgery[7]. Houmes et al. designed a study to investigate the efficacy of intravenous tramadol and morphine in 150 patients experiencing moderate or severe pain. The results of that study showed that whereas the analgesic potency of tramadol and morphine were similar, tramadol has markedly less clinically significant respiratory depressive effects than morphine[7]. Perhaps this is because the analgesic effects of tramadol are mediated by non-opioid receptor mechanisms of action. Karslı et al., compared preemptive tramadol 50 mg and meperidine 50 mg IV were found to be effective on postoperative pain and also total analgesic consumption for 24 hours was lower according placebo group[13]. Also another study designed by Yeğin et al. for post-thoracotomy pain relief. They found that intrapleural and intercostal analgesia were more effective than IV preemptive tramadol[14]. In that study, administration of additional local anesthetic via intrapleural catheter resulted in more effective analgesia.

Unlike opioids, NSAIDs do not cause respiratory depression, dependency, sedation, reduced gut motility or significant haemodynamic effects, and this has undoubtedly aided their rise in popularity. Numbers of NSAIDs have been shown to produce analgesia equivalent or superior to that gained with opioids in a variety of postsurgical setting[15]. Lornoxicam is rapidly eliminated and its plasma half-life after the intravenous dose is 3.5 to 4.5 hours; this suggests a suitably acute action for use in postoperative pain control[16]. In the studies done by Norholt, Rosenow and Ilias, lornoxicam has been shown to be as affective as morphine, meperidine and tramadol for the treatment of postoperative pain[15,17,18]. Also Berry, Caruso and Bernstein showed in their studies that lornoxicam has demostrated clinical efficacy in relieving chronic pain associated with osteoartritis, rheumatoid artritis and ankylosing spondylitis[19,20,21].

Staunstrup and et al. compared the analgesic effects of IM lornoxicam and tramadol for arthroscpic surgery and they showed that IM lornoxicam offers

a useful alternative to tramadol for the treatment of moderate to severe postoperative pain[11].

İlias et al. conducted multiple-dose study, 80 patients with pain after gynecologic surgery received IV 4 mg or 8 mg lornoxicam and 50 mg tramadol. They found out that 8 mg lornoxicam was well tolerated and more effective than others[18].

Preemptive analgesia is an, antinociseptive treatment that prevents establishment of altered processing of afferent input which amplifies postoperative pain[22]. It is important to start before incision and cover both the period of surgery and initial postoperative period[23].

Patient control analgesia provides effective pain treatment, adjusts the dose according to personal need and keeps plasma analgesic levels at a constant level[24].

There are several studies preemptively done. In his study Wang had 3 groups receiving PCIA (Patient control intravenous analgesia) Morphine, Tramadol and Tramadol+Lornoxicam respectively. Tramadol+Lornoxicam had the same good analgesia and less immunity depression than other groups[25]. Karaca et al. administered preemptively Tramadol and Lornoxicam via PCA pump for gynecological surgery. Adequate analgesia was achieved in both groups but tramadol has beter analgesia than lornoxicam during the first 12 hours postoperatively[26]. Kemal et al.[27] have given preemptively Tramadol, Tramadol+Metamizol and Tramadol+Lornoxicam and found that tramadol combinations had efficient postoperative analgesia with less side effects. Ölmez et al.[28] have compared efficacy of Tamadol and Lornoxicam during transrectal ultrasound guided biopsy of the prostate. Patients received 100 mg Tramadol and 8 mg Lornoxicam IM 30 minutes prior the procedure. Both had lower VAS scores compared to the control group but pain and discomfort were least in the Tramadol group[28]. In their study Karaman et al. aimed to examine the effect of Lornoxicam before and after skin incision. Preemptively given Lornoxicam improved the quality of analgesia and leaded to reduced consumption of postoperative analgesic[29]. According all these studies we saw that preemptively given analgesics provided good analgesia than postoperative administreted analgesics[25-29]. Combinations had always better results[25,27]. Some of the authors found tramadol more effective than lornoxicam[26,28].

Although preemptively given, lornoxicam and tramadol both improved postoperative analgesia, while lornoxicam group had statiscally significant lower VAS values than the other groups. These results show similarity to the study done by Rosenow et al[30]. But in present study we did not see any side effects. The administration of preemptive lornoxicam improved postoperative analgesia, resulting analgesic consumption with highest patients' satisfaction.

In conclusion, the results of this study suggested that both drugs were effective in the treatment of moderate postoperative pain and well tolerated when administered preemptively.

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