Dexketoprofen effectively reduces postoperative pain and meperidine consumption after lumbar discectomy and laminectomy

Lomber Diskektomi ve Laminektomi Operasyonlarında Preoperatif ve Postoperatif verilen Deksketoprofen Trometamolün Postoperatif Analjezi ve Meperidin Tüketimi Üzerine Etkisi

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Abstract: Postopeartive pain is a major contributor to increased morbidity. Analgesia is important in reducing postoperative morbidity and hospital stay. We aimed to determine the efficacy and side effect profile of preemptive and postoperative multimodal use of dexketoprofen added to meperidine patient-controlled analgesia infusion in patients undergoing lumbar discectomy and laminectomy. In this randomised, prospective, single-blind placebo-controlled trial, 60 patients undergoing laminectomy and discectomy were randomly (1:1) divided into two: Group I received placebo whereas Group II received 50 milligrammes dexketoprofen intravenously 30 minutes before surgery and 8 hours after the first dose. VAS scores, overall patient satisfaction, analgesic related side effects (nausea, vomiting, dyspepsia, bleeding, headache, hypotension, bradycardia, respiratory distress, pruritus) at hours 1, 4, 8, 12 and 24 were collected after surgery. Bleeding was recorded as the total value of aspirations during surgery, a number of sponges used during surgery and postoperative bleeding from vacuum drainage tubes. Groups were distributed similarly regarding age, sex, weight, ASA, anaesthesia and surgery time. Intraoperative and postoperative bleeding was similar. First time for PCA analgesic requirement was shorter in Group I. Group II had lower VAS scores on postoperative hours 1, 4, 8, 12 and 24. The total dosage of meperidine was lower in Group II at the 4th, 12th and 24th hours. Group II had lower rates of gastrointestinal side effects and headache related with analgesic use and had higher rates of satisfaction in regards of postoperative analgesia. Current study shows the multimodal use of dexketoprofen is a safe and effective analgesia option in patients undergoing lumbar discectomy and laminectomy. Dexketoprofen is not associated with increased frequency side effects or bleeding.

Key Words: dexketoprofen, postoperative pain, meperidine, laminectomy

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Özet: Postoperatif ağrı morbiditeyi arttıran başlıca etkenlerdendir. Analjezi postopeatif morbiditenin azaltılmasında ve hastanede kalışın kısaltılmasında etkilidir. Lomber diskektomi ve laminektomi uygulanacak hastalarda hasta kontrollü analjezide kullanılan meperedin ile birlikte multimodal analjezi amacıyla preemptif ve postoperatif dönemde uygulanan deksketoprofenin etkinliğini ve yan etki profilini değerlendirmeyi amaçladık. Randomize, prospektif ve tek kör plasebo kontrollü çalışmada lomber laminektomi ve diskektomi uygulanacak hastalar randomize olarak iki gruba ayrıldı. Grup I kontrol-plasebo grubu, Grup II'ye indüksiyondan 30 dakika önce intravenöz 50 miligram deksketoprofen ve ikinci doz ilk dozdan 8 saat sonra 50 mg deksketoprofen verildi. VAS skorları, hasta memnuniyeti, analjezik ilişkili yan etkiler (bulantı, kusma, dispepsi, kanama, baş ağrısı, hipotansiyon, bradikardi, solunum sıkıntısı, kaşıntı) postoperatif dönemde 1,4,8,12 ve 24 saatlarde kaydedildi. Kanama cerrahi sırasında aspiratörde biriken kan, kullanılan spançlar ve postoperatif dönemde vakum drenlerden gelen kan olarak toplanarak kaydedildi. Gruplar arasında yaş,cinsiyet, ağırlık, ASA skorları, anestezi ve cerrahi sürelerinde farklılık bulunmadı. İntaroperatif ve postoperatif kanama miktarları benzerdi. Grup 1' de PCA'dan analjezik kullanımı ihtiyacı daha erken oldu. Grup II'de; postopeartif 1, 4, 8, 12 ve 24. saat VAS değerleri daha düşük bulundu. Grup 2'de kullnaılan meperidin dozları 4,12 ve 24. saatlerde daha düşüktü. Grup 2' de analjezik kullanımına bağlı gastrointestinal yan etkiler ve baş ağrısı oranları düşüktü ve hasta tatmin oranları daha yüksek bulundu. Çalışmamız lomber laminektomi ve diskektomi olgularında multimodal analjezide deksketoprofen kullanımının kanama ve diğer yan etki oranlarında artma olmadan güvenli ve etkili bir seçenek olduğunu göstermiştir.

Anahtar Kelimeler: deksketoprofen, postoperatif ağrı, meperidin, laminektomi

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1. Introduction

Moderate to severe pain experienced after lumbar discectomy and laminectomy is a major contributor to increased morbidity. Effective analgesia is important in reducing postoperative morbidity and hospital stay (1,2). Opioid analgesics are routinely used in patients undergoing lumbar disc surgery postoperatively. Commonly, opioid basal-bolus infusions are used with a patient-controlled analgesia (PCA) device, which increases patient satisfaction, decrease patient anxiety, reduce healthcare costs and further reduce postoperative pain (3). However, opioid use is limited due to side effects such as sedation, respiratory depression, urinary retention, nausea and vomiting (4).

To reduce opioid-related sid e effects and increase analgesia, non-opioids analgesics are increasingly used postoperatively (5,6). Multimodal analgesia usually involves the use of non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs show their effects on both central nervous system and peripheral tissues, and they are better tolerated than opioid analgesics (7,8). NSAID multimodal analgesia may decrease opioid dosage up to 30% (9). However, NSAIDs can have haematological, gastrointestinal and renal side effects; also, bleeding potential due to prostaglandin synthesis inhibition by NSAIDs should be kept in mind during postoperative period (10). Furthermore, pre-operative administration of multimodal analgesia is based on creating an analgesic effect before any painful stimuli and inflammation takes place, therefore reducing postoperative analgesia and opioid dose (11). At the same analgesic doses, preemptive analgesia was shown to be more effective than postoperative analgesia (12). Therefore, preemptive analgesia is another method to reduce postoperative analgesic doses as well.

Dexketoprofen, a nonselective NSAID, is an active S-enantiomer of racemic ketoprofen. Previous studies have shown the effectiveness of intramuscular and intravenous dexketoprofen on moderate to severe acute pain (13). Severe side effects such as myocardial infarction or gastrointestinal bleeding were not reported with dexketoprofen use; dyspepsia was commonly reported in repeating doses (14).

Previous studies in the literature are inconsistent regarding the postoperative opioid sparing effect of dexketoprofen. Furthermore, there are no published studies regarding the effect of dexketoprofen use and quantitative early postoperative amount of bleeding. In this randomised, single-blind placebo-controlled trial, we aimed to determine the efficacy and side effect profile of preemptive and postoperative multimodal use of dexketoprofen added to meperidine PCA infusion in patients undergoing lumbar discectomy and laminectomy.

2. Materials and Methods

Following local ethics committee approval and individual informed consent, sixty American Society of Anesthesiologists (ASA) I-II patients between the ages of 18-60 undergoing elective lumbar laminectomy and discectomy were included in this prospective, single-blind, placebo-controlled study. Patients with known NSAID hypersensitivity reaction, active or possible gastrointestinal bleeding or ulcer, a history inflammatory bowel disease, cardiac/respiratory/hepatic insufficiency, haematological or oncological disease, asthma, coagulopathy, anticoagulant use, a chronic history pain, routine NSAID use and drug or alcohol abuse were excluded from this study.

At the preoperative physical examination, patient vitals and laboratory results were evaluated. Patients were educated regarding the use of visual analogue scale (VAS) and patient controlled analgesia (PCA). VAS scale consisted of an unmarked 10 cm line, which one end represented no pain and the other end represented the worst imaginable pain. VAS has been previously shown to be a safe subjective method to assess postoperative pain and postoperative analgesic requirement (15). Patient-controlled analgesia was shown to be a safe method to assess total postoperative analgesic requirement. Also, PCA has

advantages over intermittent opioid use in regards to better analgesia, shorter hospital stay, fewer side effects, less patient anxiety and more patient satisfaction (3).

Patients who were not able to comply with VAS or PCA due to cultural or educational reasons were further excluded from the study. Patients were randomly (1:1) divided into two groups: Group I (n=30) received placebo 100 ml saline solution 30 minutes before induction and 8 hours after the first dose. Group II (n=30) received 50 mg of dexketoprofen trometamol intravenously in 100 ml saline within 30 minutes 1 hour before anaesthesia induction and 8 hours after the first dose.

Patients did not receive any pain medication one day before surgery. Midazolam (0.5 mg/kg) was used 2 hours before surgery as premedication. Patients uniformly underwent anesthesia induction with thiopental (5-7 mg/kg), fentanyl (1.5 mg/kg) and vecuronium (1 mg/kg). Maintenance of anaesthesia was with sevoflurane (1.5-2.5%) with an equal mixture of oxygen and medical air. Additional doses of remifentanil and vecuronium were used during surgery according to clinical need. Neostigmine (0.04 mg/kg) and atropine (0.5 mg) was used at the end of the surgery to reverse residual neuromuscular blockade. During surgery, vitals were recorded and monitored. Patients were uniformly followed up in the post-surgery care unit for at least one hour.

Patients were connected to PCA and discharged from the post-surgery care unit when Aldrete score was higher than 9. PCA was loaded with 500 mg meperidine in 100 ml saline and set to a demand dose of 10 mg with a lock-out time of 10 minutes and continuous infusion of 10 mg. Maximal dose within 4 hours was set to 100 mg. Time to first bolus consumption and total consumption of meperidine was recorded. Side effects of meperidine such as vomiting and dyspepsia were treated symptomatically with intravenous metoclopramide andintravenous famotidine as needed. No rescue analgesia was used in this study.

VAS scores, patient vitals, postoperative Ramsey Sedation Scores and analgesic related side effects (nausea, vomiting, dyspepsia, bleeding, headache, hypotension, bradycardia, respiratory distress and pruritus) at postoperative 1, 4, 8, 12 and 24th hours were collected . Overall patient satisfaction regarding postoperative analgesia at the 24th hour of surgery was recorded as well (subjectively valued between 1 to 5, one being worst and five best). Postoperative bleeding was recorded as the total value of aspirations during surgery (excluding irrigation solution), a number of sponges used during surgery and postoperative bleeding from mini-vacuum drainage tubes.

SPSS for Windows 17.0 was used for statistical analysis. Kolmogorov-Smirnov test for normality was used. Quantitative data were presented as the mean and standard deviation or median where applicable, qualitative data was presented in frequency and percentages. Independent sample t-test or Mann-Whitney-U tests for significance were used for continuous variables. Wilcoxon signed rank test was used for analysing related samples. Pearson chi-square tests were used in analysing differences between categorical groups. A p value of <0.05 with 95% confidence interval was considered significant.

3. Results

Groups were distributed similarly regarding age, sex, weight and ASA. Patients had similar anaesthesia and surgery time. Intraoperative and postoperative bleeding was similar as well. The first time for PCA analgesic requirement was shorter in Group I (Table 1). Preoperative, intraoperative and postoperative patient vitals (oxygen saturation, systolic and diastolic blood pressure, heart rate and respiratory rate) and postoperative Ramsey Sedation Scores were similar between groups as well (data now were shown).

Table 1.
Patient demographics, surgery and analgesia statistics.

	Group I (n=30)	Group II (n=30)	P
Age (years)	47.8±10.8	49.5±9.7	0.5
Sex (Male/Female)	10/20	10/20	1
Weight (kg)	74.0±12.6	77.6±11.5	0.25
ASA (I/II)	23/7	26/4	0.31
Anesthesia duration (min)	136±50	124±37	0.314
Surgery duration (min)	120±48	106±22	0.19
Bleeding (intraoperative and 24-hour postoperative) (mL)	283±64	260±57	0.148
First time to analgesic (min)	16±5	26±6	0.001

Pain experienced by patients wasdemonstrated by VAS and was graded on a scale of 0 to 10. Group II had lower VAS scores on postoperative hours 1, 4, 8, 12 and 24 (p=0.001, 0.001, 0.001, 0.001 and 0.004, respectively) (Figure 1).

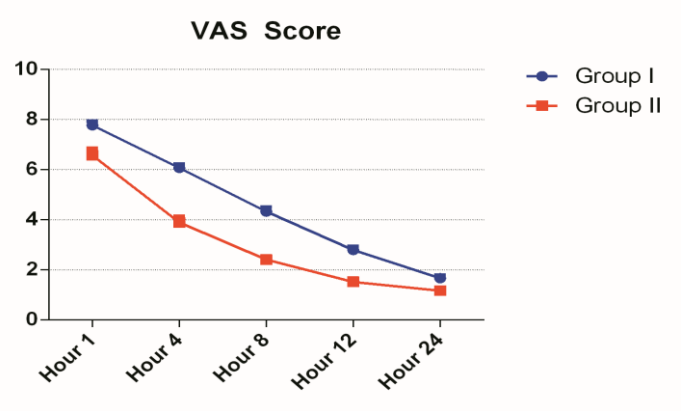

Figure 1. Graphical representation of visual analog scale results of study groups by the hour. (Mean±SEM)

Meperidine consumption was conducted by a PCA device, and total dosage of meperidine (bolus and infusion) was recorded at postoperative hours 1, 4, 8, 12 and 24. While meperidine consumption was lower in Group II at hour 4, 12 and 24; difference failed to reach a significance at hours 1 and 8 (Figure 2).

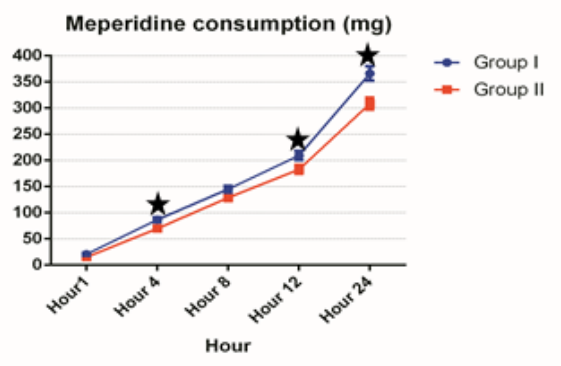

Figure 2. Graphical representation of meperidine consumption of study groups by hour. (Mean±SEM)

Groups had similar rates of hypotension, bradycardia, respiratory distress and pruritus. However, Group II had lower rates of gastrointestinal side effects and headache related to analgesic use. Interestingly, groups had similar bleeding rates (Table 2).

Table 2.
Side effects regarding analgesic use. Group II had lower gastrointestinal side effects and headache.

	Group I (n=30)	Group II (n=30)	P
Nausea/Vomitting	27 (90%)	17 (56.6%)	0.003
Dyspepsia	6 (20%)	1 (3.3%)	0.01
Headache	17 (56.6%)	7 (23.3%)	0.08
Bleeding	1 (3.3%)	1 (3.3%)	1.0

In both groups none of the patients stated "very bad" or "bad" satisfaction, in regards of postoperative analgesia, at 24 hours postoperatively. Group II had higher rates of very good satisfaction in regards of postoperative analgesia.

4. Discussion

In this randomised, single blind placebo controlled trial aiming to determine the efficacy and side effect profile of preemptive and postoperative multimodal use of dexketoprofen added to meperidine PCA infusion in patients undergoing lumbar discectomy and laminectomy, we demonstrated the use of dexketoprofen effectively reduced VAS pain scores and meperidine consumption during the postoperative period. Furthermore, patients had the better overall analgesic satisfaction and fewer side effects related to opioid use. Interestingly, we did not observe an increase of intraoperative and postoperative cumulative quantitative amount of bleeding related to dexketoprofen use.

Several authors studied and compared the multimodal analgesic effect of dexketoprofen in postoperative period as well. Kesimci et al. (1) studied the analgesic and opioid-sparing effects of preemptive oral single doses of 25 milligrammes of dexketoprofen and 500 milligrammes of paracetamol after lumbar disc surgery in 75 patients. They showed that pain scores were similar among groups, but dexketoprofen reduced morphine consumption compared with placebo; side effects were similar between dexketoprofen and paracetamol. Yazar et al. (10) included 60 patients and randomised patients either to recieve two doses of 50 milligrammes of dexketoprofen 30 minutes prior and 12 hours after surgery or placebo. They found dexketoprofen reduced pain intensity and cumulative tramadol consumption, and conversely, nausea and vomiting were lower with dexketoprofen use compared to placebo.

Tunali et al. (16) studied the comparative effect of 1 gr am paracetamol every 6 hours versus 50 milligrammes of dexketoprofen every 8 hours on postoperative pain and morphine consumption in 60 patients undergoing discectomy and/or laminectomy. They demonstrated a decrease in postoperative pain in the dexketoprofen group but not in paracetamol group. However, they failed to demonstrate a change in cumulative morphine consumption. Side effects were similar. Kelsaka et al. (17) studied 50 patients undergoing microdiscectomy, patients were randomised to receive either preemptive 50 milligrammes dexketoprofen or placebo. Dexketoprofen reduced postoperative pain and postoperative tramadol consumption. Side effects were similar between groups.

The current study demonstrated both opioid sparing and analgesic effect of 50 milligrammes of intravenous dexketoprofen. Our results are consistent with the literature regarding increased analgesic effect of multimodal analgesia, however, opioid sparing effect postoperatively is not universally displayed. However, these differences are probably based on dosing and schedule. Interestingly, Yazar et al (10) demonstrated dexketoprofen use reduced nausea and vomiting. We demonstrated a similar effect with dexketoprofen use as well. Furthermore, preemptive use of dexketoprofen is associated with less postoperative pain and morphine consumption when compared with the postoperative use of dexketoprofen, as demonstrated by Gelir et al. on 50 patients undergoing elective abdominal hysterectomy (18). Therefore, preemptive use of multimodal analgesia may be a better option in treating postoperative pain and reducing related complications and increased hospital stay.

Our study has several limitations. In our study, we used a single-blind method; however, similar studies in the literature were double blind. The sample size was small for multiple subgroup analysis. We did not use any biochemical markers to show inflammation associated postoperative pain, such as interleukin-6 levels. Furthermore, we used meperidine infusion rather than morphine or tramadol infusion. However, we included a small number of homogenous patient group undergoing both laminectomy and discectomy; other studies in the literature included either included mixed or laminectomy only/discectomy only patients. We also demonstrated dexketoprofen use did not increase intraoperative and postoperative cumulative quantitive amount of bleeding in these patients.

5. Result

The current study shows the preemptive and multimodal use of dexketoprofen is a safe and effective analgesia option in patients undergoing lumbar discectomy and laminectomy. Dexketoprofen use is not associated with increased frequency side effects or bleeding. Further studies regarding multimodal analgesiadosing and timing before and after surgery are recommended.

❖ *This study was carried out at Osmangazi University Medical Faculty.*

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