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# Comparison of the Effects of Epidural Levobupivacaine with Tramadol or Morphine Addition on Postoperative Analgesia following Major Abdominal Surgery

Zeynep Türkoğlu[1], Feride Karacaer[2], Ebru Biricik[2], Murat Ilgınel[2], Hakkı Ünlügenç[2]

[1]Erdemli Public Hospital, Mersin, Turkey

[2]Department of Anaesthesiology and Reanimation, Çukurova University School of Medicine, Adana, Turkey

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## Abstract

**Objective:** The study was designed to compare the postoperative analgesic efficacy of epidural tramadol or epidural morphine as adjuvant to levobupivacaine in major abdominal surgery.

**Methods:** Patients in ASA I-II group aged between 18 and 65 years were included in study. Epidural catheter was introduced. Patients were randomised into three groups to receive levobupivacaine (Group L), levobupivacaine+morphine (Group LM) and levobupivacaine+tramadol (Group LT). General anaesthesia was administered to all patients. The solution intended for Group L contained 25 mg 0.5% levobupivacaine+15 mL saline, that for Group LM contained 25 mg 0.5% levobupivacaine+14.5 mL salin+100 µg morphine and that for Group LT contained 25 mg 0.5% levobupivacaine+13 mL salin+100 mg tramadol, which was administered via epidural catheter as loading dose 30 min before the end of the operation. Patient-controlled analgesia device was connected to the epidural catheter to provide postoperative analgesia. Bolus dose was adjusted to 12 mg levobupivacaine in Group L, 12 mg levobupivacaine +1.2 mg morphine in Group LM and 12 mg levobupivacaine+12 mg tramadol in Group LT. Lock-out period was adjusted to 15 min in three groups. Quality of analgesia was evaluated using Visual Analogue Scale; administered and demand doses of levobupivacaine, morphine and tramadol were compared at 30 min, 1, 2, 6, 12 and 24 h postoperatively.

**Results:** Visual Analogue Scale scores were significantly higher in Group L than Groups LM and LT. Nausea and vomiting observed in Group L were lesser than those in Groups LM and LT.

**Conclusion:** Continuous epidural analgesia using levobupivacaine combined with morphine or tramadol is an effective method for managing postoperative analgesia in major abdominal surgery.

**Keywords:** Analgesia, epidural patient-controlled, levobupivacaine, morphine, postoperative pain, tramadol

## Introduction

The ineffective treatment of pain during the postoperative period increases the cardiovascular workload by activating the neuroendocrine and sympathetic nervous system, delaying mobilization, and causing thromboembolic events to develop, which results in the development of atelectasis due to deep breathing and coughing and eventually leads to increased postoperative morbidity and mortality (1, 2).



Corresponding Author: Feride Karacaer E-mail: feridekaracaer@gmail.com



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Although various analgesic methods have been recommended in patients undergoing major abdominal surgery, the epidural analgesia method is accepted as the gold standard for treatment of postoperative pain and is safely performed. However, as important as the method of analgesia is, the agent and dosage also have important roles in the success of postoperative pain treatment.

Local anaesthetics are often used while inducing epidural analgesia. In recent years, levobupivacaine, a bupivacaine S (-) isomer that has a similar onset and duration of action as bupivacaine but with less toxic effects on the cardiovascular and central nervous system, is widely used (3).

Even in isolated clinical doses, the local anaesthetics used for epidural analgesia in regional applications cause significant changes in haemodynamics (4, 5). In order to reduce these side effects of local anaesthetics and to increase analgesic efficacy, adjuvants are frequently added to the treatment. The most commonly used adjuvants are opioids. Although opioids such as fentanyl, sufentanil, and morphine are frequently used with local anaesthetics (6, 7), there are not many studies in which tramadol is used in combination with epidural local anesthetics.

In our study, we aimed to compare the efficacy of epidural levobupivacaine using a patient-controlled analgesia (PCA) device. We also assessed local anaesthetic consumption, patient comfort, haemodynamics, and side effects of levobupivacaine+morphine and levobupivacaine+tramadol combinations in the treatment of postoperative pain in patients undergoing major abdominal surgery.

## Methods

With approval of the Medical Faculty of the University of Cukurova (22.03.2012; 5/10), our prospective, randomized, controlled, and double-blind study included 60 ASA I-II adult patients aged 18-65 years, who were to undergo major abdominal surgery. Patients with systemic or local infection, bleeding diathesis, anticoagulant therapy, central nervous system diseases, local anaesthetic sensitivity, vertebral column deformity, or severe lung, liver, and kidney failure were excluded from the study. In the preoperative period, the subjects were explained the visual analog scale (VAS) which was used to evaluate the epidural patient-controlled analgesia and postoperative pain. For patients who were taken to the operating room without premedication before epidural catheterization, a 20 Gauge cannula was opened and the infusion was started with 0.9% NaCl at a rate of 10 mL $min^{-1}$. Electrocardiography (ECG, Drager Fabius GS ECG monitor), noninvasive blood pressure (Drager Fabius GS Blood Pressure Module) measurement, and measurement of peripheral arterial oxygen saturation ($SpO_2$) (Nellcor Oximax N600x) were used for routine monitoring.

Epidural catheterization for postoperative pain management was performed in all patients before surgery in the sitting position and at L3–4 or L4–5 intervertebral space. Demographic data (age, height, weight, and body mass index (BMI)) were questioned and recorded in all cases.

General anaesthesia was induced with thiopental 5 mg $kg^{-1}$ (0.5 g Pentalyn vial Ibrahim Etem Ulagay, Turkey) and 0.1 mg $kg^{-1}$ vecuronium intravenously (Norcuron vial, MSD, USA) and patients were intubated. In the maintenance of anaesthesia, sevoflurane (Sevorane, Abbvie, USA) and a 50% O2+50% NO2 combination were used. No additional analgesia was given to any patient in the intraoperative period. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), and heart rate (HR) were recorded at baseline and intraoperatively at 5, 15, 30, 45 and 60 minutes.

The 60 adult participants were assigned to 3 groups according to the computerized randomization block table. Accordingly, 30 minutes before the end of the operation the loading dose of the epidural catheter was as follows;

Group L (n=20): 25 mg 0.5% (5 mL) levobupivacaine (chirocain 0.5% Astra Zeneca PLC, UK)+15 mL saline (Total volume=20 mL);

Group LM (n=20): 25 mg of 0.5% (5 mL) levobupivacaine 100 micrograms 14.5 mL saline+morphine (Morphine HCl bulb, Galen Pharmaceuticals, Turkey) (0.5 mL) (total volume=20 mL);

Group LT (n=20): 25 mg of 0.5% (5 mL) levobupivacaine 13 mL saline+tramadol (Tramadol bulb, Abdi Ibrahim, Turkey) 100 mg (2 mL) (total volume=20 mL) was performed.

The drug combination was prepared by an anaesthetist who was blinded to the patient group assignment. The investigators who applied epidural catheterization and collected intraoperative and postoperative data were also not informed of the patient group and the combination of drugs applied.

At the end of the operation, anaesthetic gases were cut in all 3 groups and patients were ventilated with 100% oxygen. Intravenous prostigmine (0.05 mg $kg^{-1}$) and atropine (0.015 mg $kg^{-1}$) were administered to reverse the muscle relaxant effect.

Tracheal extubation was performed when $SpO_2$ was ≥90%, while breathing room air.

Following extubation, the patients were taken to the recovery room and observed for 1 hour. The epidural catheter of the patients was connected to a PCA pump (CADD-Legacy PCA Pump, Smiths Medical, USA) according to their groups. In group L, 100 mg of levobupivacaine was placed into 100 mL of saline (SF), the division dose was adjusted to 10 mL (Levobupivacaine 8.3 mg), and lock time was 15 minutes. The patients in the group LM were given 100 mg of levobupivacaine and 10 mg of morphine in 100 mL of saline, the bolus dose was adjusted to 10 mL (Levobupivacaine 8.3 mg+morphine 0.83 mg), and lock time was 15 minutes. The patients in Group LT were given 100 mg of levobupivacaine and 100 mg of tramadol in 100 mL of saline, the bolus dose was adjusted to 10 mL (Levobupivacaine 8.2 mg+tramadol 8.2 mg), and lock time was 15 minutes.

In the postoperative recovery room, the VAS values recorded in the 1st hour follow-up period and the number of doses given by the PCA device were recorded at 30 minutes and 60 minutes postoperatively. In addition, SBP, DBP, HR, and $SpO_2$ values were followed and recorded in the same process. Hypotension was defined as a fall of the initial value of SBP for more than 20% and bradycardia was defined as a HR <50 beats $min^{-1}$. In case of hypotension, it was planned that the crystalloid infusion would be increased and patients would be treated with iv 5-10 mg ephedrine in cases where no response could be obtained and with iv 0.5 mg atropine in case of bradycardia.

At the end of the 1-hour follow-up, patients who had motor block 0, VAS ≤4 and vital signs stable (normotensive, normocardic, room air Sp02 ≥95%) were sent to service. In patients who did not meet these conditions, the follow-up was continued in the follow-up room and only PCA was used in the treatment of pain in patients with VAS> 4. These patients were sent when VAS was ≤4.

In the evaluation of postoperative analgesia; VAS values of patients, demand counts, doses of levobupivacaine, morphine, and tramadol given as bolus from epidural PCA, and haemodynamic variables (SBP, DBP, HR, and SpO2) and their side effects were evaluated at the 30th hour and 1st hour after the end of the operation and at the following 2nd, 6th, 12th, and 24th hours at follow-up. At the end of the 24th hour, all patients were questioned in terms of patient comfort and their satisfaction levels were recorded. According to this scale; excellent = no pain, no patient discomfort (VAS=0) (4 points); good=very mild pain or discomfort, no additional analgesia required (VAS=1-2) (3 points); moderate=mild analgesia required (VAS=3-4) (2 Points); bad=moderate to severe pain or discomfort requiring general anaesthesia (VAS> 5) (1 point).

The aim of our study was to investigate the effects of morphine or tramadol added to levobupivacaine in postoperative epidural PCA. Our secondary objectives are assessing the efficacy of analgesia, patient satisfaction, haemodynamics, and side effects in patients.

**Statistical analysis**

A pilot study showed that postoperative 24 hour levobupicaine dose was 120±20 mg. The sample size was calculated as 16 patients for each groups for a 20% decrease in levobucaine dose with 5% error and 90% power.

For statistical analysis, it was first checked whether repetitive data showed normal distribution. Normally distributed data were shown as mean±SD and others as median (min-max). Demographic data were analyzed by ANOVA test. One-way analysis of variance was performed in the analysis of haemodynamic data. Post-Hoc Analysis Tukey Test was used for the detection of differences within the groups and the Greenhouse-Geisser test was applied for Repetitive Measurement Analysis. PCA demand and given doses were analyzed by the Kruskal–Wallis test. Mann–Whitney-U test was used to test the differences within each group. Complications were analyzed by chi-square test. $p<0.05$ was considered statistically significant. Statistical analysis was performed using SPSS package program.

## Results

All subjects enroled to our study completed the study and the study was terminated when the intended number of subjects was reached. There was no difference between the demographic variables related to age, height, weight, BMI, and duration of surgery (Table 1).

In the intraoperative period, it was found that HRs decreased statistically ($p=0.0001$); however, this change in time was not significant compared to the groups ($p=0.192$). Decrease in mean SBP and DBP measurements from baseline to 60 minutes were found statistically significant ($p=0.017$, $p=0.017$), however, this change in time was not significant among the groups ($p=0.115$, $p=0.116$).

It was found that VAS values decreased statistically significantly over time in the postoperative 30th minute and in the 1st, 2nd, 6th, 12th, and 24th hours ($p=0.0001$); this change in

**Table 1. Demographic distribution of data by groups**

| | Group L | Group LM | Group LT | p |
|---|---|---|---|---|
| Age (years) | 42.5±12.8 | 44.6±8.4 | 42.4±11.0 | 0.778 |
| Surgical time (min) | 80.7±33.2 | 86.7±31.3 | 83.2±45.3 | 0.877 |
| Length (cm) | 162.7±3.0 | 161.6±6.2 | 161.6±5.9 | 0.096 |
| Weight (kg) | 84.6±19.3 | 73.3±7.2 | 73.9±9.4 | 0.059 |
| BMI | 31.94±7.2 | 28.1±3.3 | 25.1±3.1 | 0.001 |

p: One-way analysis of variance, $p_{1-2}$, $p_{1-3}$, $p_{2-3}$: Post-Hoc Analysis Turkey Test

**Table 2. VAS values according to groups in the postoperative period**

| Group | | 30th minute | 1st hour | 2nd hour | 6th hour | 12th hour | 24th hour | p* |
|---|---|---|---|---|---|---|---|---|
| L | Med (Min-Max) | 4 (0-6) | 4 (0-6) | 4 (0-6) | 4 (0-7) | 4 (0-5) | 4 (2-5) | 0.0001 |
| LM | Med (Min-Max) | 5 (2-6) | 4 (2-6) | 4 (2-6) | 4 (1-4) | 2 (1-4) | 2 (1-4) | |
| LT | Med (Min-Max) | 4 (1-6) | 4 (1-5) | 3 (2-6) | 3 (2-5) | 3 (1-5) | 2 (1-4) | |
| | p | 0.182 | 0.226 | 0.207 | 0.459 | 0.024 | 0,002 | |
| | $P_{1-2}$ | - | - | - | - | 0.008 | 0.0001 | |
| | $P_{1-3}$ | - | - | - | - | 0.231 | 0.028 | |
| | $P_{2,3}$ | - | - | - | - | 0.157 | 0.547 | |

p: Kruskal–Wallis Test, $p_{1-2}$, $p_{1-3}$, $p_{2-3}$: Post-Hoc Analysis Mann–Whitney U Test, p*: Repeated Measurement Analysis, Greenhouse-Geisser test

**Table 3. Distribution of the demand in the postoperative follow-up period according to the groups**

| Demanded Dose Time Group No | | 30th minute | 1st hour | 2nd hour | 6th hour | 12th hour | 24th hour | p* |
|---|---|---|---|---|---|---|---|---|
| L | N | 20 | 20 | 20 | 20 | 20 | 20 | 0.0001 |
| | Med (Min-Max) | 2 (1-4) | 3 (1-5) | 5 (4-10) | 9 (5-16) | 11 (6-17) | 12 (8-20) | |
| LM | N | 20 | 20 | 20 | 20 | 20 | 20 | |
| | Med (Min-Max) | 1 (1-3) | 3 (3-11) | 4 (1-11) | 6 (1-13) | 8 (1-13) | 10 (1-14) | |
| LT | N | 20 | 20 | 20 | 20 | 20 | 20 | |
| | Med (Min-Max) | 1 (1-3) | 2 (2-5) | 3 (2-6) | 5 (2-7) | 7 (4-9) | 8 (6-10) | |
| Total | N | 60 | 60 | 60 | 60 | 60 | 60 | 0.0001 |
| | Med (Min-Max) | 2 (1-4) | 3 (1-11) | 4 (3-11) | 6 (1-16) | 8 (1-17) | 10 (1-20) | |
| | p | 0.080 | 0.289 | 0.0001 | 0.0001 | 0.0001 | 0.0001 | |
| | $p_{1-2}$ | - | - | 0.114 | 0.038 | 0.007 | 0.009 | |
| | $p_{1-3}$ | - | - | 0.0001 | 0.0001 | 0.0001 | 0.0001 | |
| | $p_{2-3}$ | - | - | 0.043 | 0.038 | 0.020 | 0.043 | |

p:Kruskal–Wallis Test, $p_{1-2}$, $p_{1-3}$, $p_{2-3}$: Post-Hoc Analysis Mann–Whitney U Test, p*: Repeated Measurement Analysis, Greenhouse-Geisser test

time is also significant compared to the groups (p=0.0001). VAS values at 12 hours postoperatively were higher in Group L compared to Group LM (p=0.008). VAS scores at 24 hours postoperatively were higher in Group L compared to Group LM and Group LT (p=0.001, p=0.028) (Table 2).

The demand for levobupivacaine was found to be higher in group L than group LT and group LM in all study periods, starting from the 2nd and 6th hour, respectively (p=0.0001). In group LM, it was determined that levobupivacaine demand was higher than group LT in all study periods starting from the 2nd hour (p=0.0001) (Table 3).

The increase in total levobupivacaine doses consumed at the 30th, 1st, 2nd, 6th, 12th, and 24th hours postoperatively was statistically significant (p=0.0001) and this change in time was also significant compared between groups (p=0.0001) (Table

**Table 4. Distribution of total levobupivacaine consumption according to time groups in postoperative follow-up**

| Group | | 30th minute | 1st hour | 2nd hour | 6th hour | 12th hour | 24th hour | p* |
|---|---|---|---|---|---|---|---|---|
| L | Med (Min-Max) | 29 (9-39) | 29 (9-49) | 29 (9-49) | 94 (39-158) | 108 (59-168) | 118 (79-198) | 0.0001 |
| LM | Med (Min-Max) | 19 (9-29) | 29 (9-49) | 49 (19-79) | 59 (29-108) | 84 (39-128) | 108 (49-128) | |
| LT | Med (Min-Max) | 19 (9-29) | 19 (19-29) | 29 (19-39) | 49 (19-59) | 69 (39-79) | 84 (59-108) | |
| | p | 0.032 | 0.046 | 0.0001 | 0.0001 | 0.0001 | 0.0001 | |
| | $p_{1-2}$ | 0.221 | 0.256 | 0.057 | 0.021 | 0.006 | 0.007 | |
| | $p_{1-3}$ | 0.012 | 0.043 | 0.0001 | 0.0001 | 0.0001 | 0.0001 | |
| | $p_{2-3}$ | 0.239 | 0.143 | 0.030 | 0.012 | 0.008 | 0.041 | |

p: Kruskal–Wallis Test; $p_{1-2}$, $p_{1-3}$, $p_{2-3}$: Post-Hoc Analysis Mann–Whitney U Test; p*: Repeated Measurement Analysis, Greenhouse-Geisser test

**Table 5. Distribution of total morphine and tramadol doses over time in postoperative follow-up (median)**

| | 30th minute | 1st hour | 2nd hour | 6th hour | 12th hour | 24th hour |
|---|---|---|---|---|---|---|
| Group LM morphine (Mg) | 2.4 | 3.6 | 4.8 | 6 | 10.8 | 13.2 |
| Grup LT tramadol (Mg) | 24 | 24 | 36 | 60 | 84 | 108 |

**Table 6. Patient comfort distribution in patients according to groups**

| Group | | 24th hour | p* |
|---|---|---|---|
| L | Ave±SD | 2.5±0.8 | 0.003 |
| | Med (Min-Max) | 2.0 (2-4) | |
| LM | Med (Min-Max) | 3.2±0.6 | |
| | | 3.0 (2-4) | |
| LT | Med (Min-Max) | 3.0±0,6 | |
| | | 3.0 (2-4) | |

p: One-way analysis of variance
$p_{1-2}$, $p_{1-3}$, $p_{2-3}$: Post-Hoc Analysis Tukey Test

3). Levobupivacaine consumption was found to be higher in group L compared to group LT in the 30th minute and higher than group LM in the 6th hour in all study periods. In group LM group, levobupivacaine consumption was found to be higher than group LT in all study periods starting from the 2nd hour (p=0.0001) (Table 4).

During the follow-up period, total morphine and tramadol doses consumed at the 30th minute and the 1st, 2nd, 6th, 12th, and 24th hours were statistically significant (p=0.0001), (Table 5).

Patient comfort scores measured at the end of 24 hours were statistically lower in Group L compared to Group LM and Group LT (p=0.003) but there was no statistically significant difference between Group LM and Group LT (Table 6).

In the postoperative period, nausea was observed in 2 patients and both nausea and vomiting were observed in 1 patient in Group L. Nausea was observed in 4 patients and both nausea and vomiting were observed in 1 patient in Group LT. Nausea was observed in 5 patients and both nausea and vomiting were observed in 3 patients in Group LM. In addition, in group LM, 2 patients had tremors at 30 minutes postoperatively that recovered spontaneously. When the incidence of side effects was evaluated, the least incidence of complications was observed in Group L according to Group LM and Group LT.

## Discussion

In our study, levobupivacaine consumption in patients undergoing major abdominal surgery for postoperative analgesia was significantly higher in group L treated with levobupivacaine+saline as compared to Group LM or Group LT, who were supplemented with morphine or tramadol ($p<0.05$).

In the control group (Group L), the side effects were significantly lower but patient satisfaction was the least when compared to groups using morphine (Group LM) or tramadol (Group LT).

In recent years, regional anaesthesia methods have become preferable with the improvements in postoperative pain management. In particular, epidural anaesthesia can provide effective intraoperative analgesia depending on the type of surgery and also provides effective and reliable analgesia for the treatment of pain in the postoperative period. Epidural analgesia technique for postoperative analgesia has been suggested as one of the first choice methods in patients undergoing major abdominal surgery (8). Therefore, in our study, patients who were to undergo major abdominal surgery were preferred.

Today, the most commonly used local anaesthetic for regional anaesthesia and analgesia is bupivacaine. However, levobupivacaine, which is the S (-) isomer of bupivacaine, has been

introduced to clinical use due to bupivacaine has long duration effect, potential of intense motor block action and cardiotoxicity (9-11). The potential for cardiotoxicity and motor block formation is less when compared to bupivacaine, and it has been reported that the duration of sensory block duration is longer in non-statistically significant rates in patients undergoing major nerve block with levobupivacaine as compared to bupivacaine (9, 12). In double-blind clinical studies, the anaesthetic and analgesic effects of levobupivacaine were found to be similar to the same dose of bupivacaine. In addition, a longer sensory block duration and a shorter motor block have been reported by the administration of levobupivacaine epidurally (13).

In regional anaesthesia and analgesia, there are not many studies on the combined use of local anaesthetics with tramadol. Fan et al. (14) aimed to compare the efficacy of fentanyl (3 μg $mL^{-1}$)+epidural ropivacaine at a concentration of 0.125% for a caesarian section to epidural ropivacaine+tramadol (5 mg $mL^{-1}$). In their study, tramadol added to epidural ropivacaine was found to be as safe and effective as fentanyl. In similar studies, it has been reported that the use of tramadol epidurally is safe and effective (15, 16). In addition, the local anesthetic efficacy of tramadol has already been shown (17, 18). The low VAS levels and the increase in the quality of analgesia obtained in our study can be attributed to the additive interaction of levobupivacaine and tramadol.

The aim of postoperative pain management is to support the respiratory and gastrointestinal system functions, allow early mobilization, and to control pain in patients undergoing surgery. In this sense, the prevention or reduction of the stress response to surgical trauma in the postoperative period accelerates the healing and decreases the morbidity and mortality. In our study, an effort was made to decrease the incidence of motor block usually observed with high-dose local anaesthetics by increasing the quality of postoperative analgesia. Morphine or tramadol added to epidural levobupivacaine increased VAS and patient comfort scores without generating a motor block and each patient determined the need for analgesia according to their own pain levels. The drugs or combinations were thus used to provide information about the pain and comfort levels in patients. In our study, VAS scores evaluated at 24 hours postoperatively were significantly higher in Group L than Group LM and Group LT. These data were parallel with patient comfort scores and caused significant reductions in the need for local anaesthetics. This difference was thought to be caused by morphine and tramadol added to levobupivacaine. Similar to our findings, low doses of opioids added to epidural local anaesthetics have been shown to increase analgesic quality by reducing the incidence of motor block (19).

The addition of morphine or tramadol to epidural levobupivacaine also reduced the dose of levobupivacaine consumed. In our study, the requested and given dose rates were statistically significant between the three groups at 2nd, 6th, 12th, and 24th hours (p=0.0001). Group L was shown to demand significantly more local anaesthetic doses as compared to Group LM and Group LT, likewise, Group LM demanded significantly more local anaesthetic doses when compared to Group LT. Levobupivacaine, which is used epidurally at concentrations of 0.125% and above, has been reported to cause a significant amount of motor block while providing adequate analgesia (20). In our study, levobupivacaine was used at a concentration of 0.0625% and no motor block was observed in any of the cases.

Crews et al. (8) compared thoracic epidural 0.25% levobupivacaine administration with 0.25% levobupivacaine+0.005% morphine and only epidural 0.005% morphine groups for pain control after major abdominal surgery. In their study, VAS values measured in the epidural levobupivacaine+morphine group at the 4th and 8th hours were reported to be significantly lower than the other two groups and they found that the duration of analgesia (4.3 hours with levobupivacaine alone, 16 hours with levobupivacaine-morphine), as well as the demand for additional analgesia in the epidural levobupivacaine+morphine group, was longest. In our study, lower VAS values at 12th and 24th hours were obtained in Group LM and Group LT where adjuvants were added to epidural levobupivacaine. Better patient comfort scores and less analgesic requirement were in accordance with the data of Crews et al. (8).

Selecting the most appropriate concentration of local anaesthetics is one of the most important factors for the establishment of the balance between pain control and side effects (21). While Milanesi et al. (22) did not observe any haemodynamic changes in 115 patients who had thoracic, abdominal, and urological surgeries and took levobupivacaine for postoperative analgesia, the infusion of epidural ropivacaine was stopped after the development of hypotension in patients. In our study, levobupivacaine was used at a concentration of 0.0625% and no hypotension has been reported at this concentration in the literature (22). With the agents used in the PCA method, no clinically significant changes were detected in haemodynamic data (systolic blood pressure, diastolic blood pressure and heart rate) and none of the patients needed ephedrine.

In the literature, nausea and vomiting are the most common complications after epidural opioid administration (23). The use of opioids combined with local anaesthetics as compared to epidural opioid use reduces the incidence of side effects by reducing gastrointestinal paralysis, nausea and vomiting in

the postoperative period, visceral reflex activity, and systemic opioid use (24). In contrast, in Group L, which was not an opioid group, we found less nausea and vomiting rates than LM and LT. In our study, higher nausea and vomiting rates of opioid group LM and LT were thought to occur due to the emetic potential of morphine and tramadol.

## Conclusion

Epidural levobupivacaine, levobupivacaine+morphine, or levobupivacaine+tramadol administered by PCA device for postoperative analgesia in patients undergoing major abdominal surgery under general anaesthesia provided effective and adequate analgesia. Levobupivacaine consumption was significantly higher in Group L with levobupivacaine alone, but local anaesthetic consumption was the least in the group with tramadol supplementation. We believe that this difference is not clinically important. Postoperative pain scores were significantly lower in Group LM and Group LT groups, to whom morphine or tramadol were supplied as compared to Group L, and patient comfort scores were significantly higher.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Cukurova University School of Medicine (22.03.2012; 5/10).

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

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