KLİNİK ÇALIŞMA / CLINICAL RESEARCH

TORAKS CERRAHİSİ İÇİN UYGULANAN EPİDURAL LOKAL ANESTEZİKLERİN KARŞILAŞTIRILMASI: BUPİVAKAİN İLE LEVOBUPİVAKAİN

A COMPARISON OF EPIDURAL LOCAL ANESTHETICS ADMINISTERED FOR THORACIC SURGERY: BUPIVACAINE VERSUS LEVOBUPIVACAINE

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SUMMARY

Aim*: We aimed to compare the analgesic efficacy, hemodynamia, and side effects of epidural bupivacaine and levobupivacaine given preoperative, intraoperative, and postoperative periods of thoracic surgery.*

Materials and methods: *Thirty adult patients undergoing elective thoracotomy were divided into two groups receiving thoracal epidural bupivacaine or levobupivacaine. Group I received bupivacaine, whereas Group II received levobupivacaine boluses both 15 min before surgical incision and during the closure of thorax. Continuous epidural infusion of fentanyl combined with either bupivacaine or levobupivacaine was given in intensive care unit. In addition, all patients received iv morphine bolus with patient controlled analgesia device. If shoulder pain persisted, diclofenac sodium was administered. Hemodynamic data, pain scores, and side effects were recorded from preoperative period to 24th hr of epidural infusion.*

Results*: The difference in mean arterial pressures, heart rates, pain scores, and morphine consumptions were not significant between the groups ($p > 0.05$). Decrease in visual analog scale was statistically significant compared to the basal values within the groups during the postoperative period ($p < 0.05$). There were no serious side effects.*

Conclusion: *Bupivacaine and levobupivacaine were found to be comparable in the analgesia, hemodynamia, and side effects for thoracic surgery. In combination with thoracic epidural fentanyl, a continuous infusion of levobupivacaine may be considered as a good alternative to bupivacaine.*

KEY WORDS: *Bupivacaine, levobupivacaine, thoracal epidural analgesia*

ÖZET

Amaç: *Göğüs cerrahisinin pre, intra ve postoperatif dönemlerinde uygulanan epidural bupivakain ve levobupivakainin analjezik, hemodinamik ve yan etkilerinin karşılaştırılmasıdır.*

Gereç ve yöntem: *Elektif torakotomi uygulanan 30 erişkin hasta torakal epidural bupivakain veya levobupivakain alan iki gruba ayrıldı. Hem cerrahi insizyondan 15 dk önce, hem de toraks kapatılırken Grup I'e bupivakain, Grup II'ye levobupivakain bolusları verildi. Fentanil ile bupivakain ya da levobupivakain kombine edilerek yoğun bakım ünitesinde sürekli epidural infüzyonla verildi. Ayrıca bütün hastalara hasta kontrollü analjezi cihazıyla iv morfin bolusu verildi. Dirençli omuz ağrısı olduğunda diklofenak sodyum uygulandı. Hemodinamik veriler, ağrı skorları ve yan etkiler preoperatif dönemden epidural infüzyonun 24. saatine kadar kaydedildi.*

Bulgular: *Ortalama arter basıncı, kalp atım hızı, ağrı skorları ve morfin tüketiminde gruplar arasındaki farklılık anlamlı değildi ($p > 0.05$). Her iki grup içinde postoperatif dönemde bazal değerlere göre vizüel analog skaladaki azalma istatistiksel olarak anlamlı bulundu ($p < 0.05$). Ciddi bir yan etki ile karşılaşılmadı.*

Sonuç: *Bupivakain ve levobupivakain, göğüs cerrahisi için analjezi, hemodinami ve yan etkiler yönünden benzer bulundu. Torakal epidural fentanil ile kombine edildiğinde levobupivakainin sürekli infüzyonu bupivakaine iyi bir alternatif olabilir.*

ANAHTAR KELİMELER: *Bupivakain, levobupivakain, torakal epidural analjezi*

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INTRODUCTION

Thoracotomy is considered as being one of the most painful surgical procedures (1). Insufficient post-thoracotomy analgesia result in decreased pulmonary compliance, inefficient coughing, retention of bronchial secretions, atelectasis, pneumonia (2). Therefore efficient analgesia would decrease complication rates and improve outcome after thoracotomy.

Post-thoracotomy analgesic treatment regimen includes systemic opioid analgesics, non-steroid anti-inflammatory drugs, and ketamine or regional interventions such as intercostal, intrapleural, paravertebral, and epidural blocks. The regional analgesic protocols are frequently used in combination with the systemic ones (3). Today, thoracic epidural analgesia (TEA) is accepted as the gold standard in postthoracotomy pain treatment (4).

Bupivacaine is the local anesthetic (LA) agent of choice because of its longer duration and prominent sensorial blockage following epidural usage. However levobupivacaine, enantiomer of racemic mixture of bupivacaine, has recently become quite popular as a new LA drug which has similar clinical effect and reduced cardiotoxicity and neurotoxicity. It makes levobupivacaine a favorable drug for epidural infusion in postoperative analgesia (5) nevertheless there are limited number of studies about its epidural usage for postthoracotomy analgesia.

In this study, we aimed to compare the analgesic efficacy, hemodynamia, and side effects of thoracal epidural bupivacaine and levobupivacaine administered preoperative, intraoperative, and postoperative periods of thoracotomy.

MATERIALS AND METHODS

This prospective and randomized study was performed with approval of the institutional human investigation ethics committee and written informed consent obtained from the patients. The study was performed in accordance with the principles of the Declaration of Helsinki. This study was conducted between January 2009 and August 2009. Our study was conducted with 30 patients by modeled previously similar studies. (6, 7) Thirty patients, between the ages of 18 and 64 years, undergoing elective thoracotomy were divided into 2 groups with closed envelope technique. The patients with ASA (American Society of Anesthesiologists) physical status of I-III were enrolled in this study.

Exclusion criteria were existence of chronic pain, regular usage of analgesics, a history of severe endocrine and/or metabolic disorders, coronary artery disease, congestive heart failure, psychiatric disease, allergy to LAs or opioids, and any contraindication to the epidural catheterization. The preoperative visit was performed the day before the operation. All patients were informed about the visual analog scale (VAS; ranging from 0= no pain, to 10= worst pain imaginable), the analgesic and anesthetic protocols.

All patients were premedicated with midazolam (0.07 mg kg^{-1}) and atropine sulphate (0.01 mg kg^{-1}) intramuscularly (I.M.) 30 min before the operation. Electrocardiography, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR), and peripheral oxygen saturation (SpO_2) were monitored and recorded in the operating room. The patients received 7 ml kg^{-1} intravenous (I.V.) crystalloid solution prior to the epidural catheterization. Epidural catheter was inserted at T5–6 or T6–7 intervertebral space using the median approach and hanging drop technique while the patient was in the sitting position. Epidural catheter was advanced 5 cm to the cephalad direction. Epidural lidocaine 2% (3 ml) was administered as a test dose. After 15 min, motor blockage and sensorial block were assessed by means of the Bromage scale and pin-prick test, respectively.

The patients with significant sensorial block, without motor block, were preoxygenated. Propofol (2 mg kg^{-1} I.V.), fentanyl citrate (1 µg kg^{-1} I.V.), and vecuronium bromide (0.1 mg kg^{-1} I.V.) were given for induction of general anesthesia. Anesthesia was maintained with sevoflurane and vecuronium bromide. The mixture of O_2 and N_2O was given during double-lung ventilation whereas 100% O_2 was used in one-lung ventilation (OLV). A routine OLV procedure was performed throughout this study. The arterial blood gases were analyzed hourly during the operation. Incremental I.V. fentanyl citrate was administered in accordance with HR and arterial pressure elevations during intraoperative period. The neuromuscular blockage was reversed by neostigmine (0.03 mg kg^{-1} I.V.) and atropine sulphate (0.01 mg kg^{-1} I.V.) at the end of operation. All patients were uneventfully transferred to the intensive care unit (ICU) following extubation.

Group I (n=15) received bupivacaine (10 cc % 0.25) whereas Group II (n=15) received levobupivacaine (10 cc % 0.25) both 15 min before surgical incision and during the closure of thorax. Continuous epidural infusion of fentanyl (5 µg ml^{-1}) combined with either bupivacaine (0.125%) or levobupivacaine (0.125%) was given at the rate of 5 ml h^{-1} in ICU. In addition, all patients received I.V. morphine bolus with patient controlled analgesia (PCA) device. Morphine bolus dose was adjusted to 1 mg, and 4-hour-limit was 10 mg. The lock-out duration

of PCA device was 10 min. If shoulder pain persisted diclofenac sodium (75 mg I.M.) was also administered at postoperative period. Intercostal blockage was not performed in the two groups patients.

Our study protocol consisted of twelve phases including preoperative period. In all phases SBP, DBP, MAP, HR, RR, SpO_2, and the scores of VAS at rest, and during coughing, sedation, and motor block were recorded. Timing of measurements and records were as follows: before the first dose of epidural LA, 15 min after the first dose of epidural LA, before the second dose of epidural LA, 15 min after the second dose of epidural LA, before the epidural infusion, and 30 min, 1 h, 2 h, 6 h, 12 h, and 24 h after the beginning of epidural infusion in ICU. Besides the doses of intramuscular diclofenac sodium, total amount of I.V. morphine and the number of PCA demands were also recorded.

Respiratory depression (RR < 8 breath min^{-1} or SpO_2 < 90%), hypotension (20% decrease in MAP with respect to basal values), bradycardia (HR < 50 beat min^{-1}), nausea, vomiting, shoulder pain, and other complications were recorded during postoperative 24 hours. In case of nausea or vomiting I.V. metoclopramide was administered. If hypotension was not responsive to crystalloids or colloids, 5 mg I.V. ephedrine was given. If bradycardia existed, atropine sulphate (0.5 mg I.V.) was administered.

Statistical analysis

Statistical analysis was performed using SPSS 15.0 pack program. The results were expressed as mean ± SD. Frequency distributions, averages, standard deviations, percentages, cross-tables were used while evaluating data. Categorical comparisons were performed by chi-square test and or Fisher's exact test. The Student's t-test and Mann-Whitney-U-Test were used in order to detect the significant differences between the groups. Repeated-Measurement Variance Analysis and Kruskal-Wallis Tests were applied to detect the significant differences within the groups. If there were differences between the groups on multi-comparisons, Tukey HSD and Dunnet tests were performed in order to detect which groups have differences. P-values less than 0.05 were considered to be statistically significant in all analyses.

RESULTS

The groups were similar with respect to demographic characteristics. Age, sex, body mass index, and height revealed no significant differences between the groups ($p > 0.05$) (Table 1).

There was no significant difference within and between the groups in terms of SpO_2 and RR ($p > 0.05$). Compared to the basal values decrease in MAP was statistically significant in Group I 15 min after the 1st dose of LA, before the 2nd dose of LA, 15 min after the 2nd dose of LA, before epidural infusion, and 30th min, 1st, 2nd, 6th, 12th, and 24th h of epidural infusion ($p < 0.05$). Compared to the basal values decrease in MAP was statistically significant in Group II 15 min after the 1st dose of LA, before the 2nd dose of LA, 15 min after the 2nd dose of LA, before epidural infusion, and 30th min, and 12th hour of epidural infusion ($p < 0.05$) (Table 2). Compared to the basal values decrease in HR was statistically significant in Group I 15 min after the 1st dose of LA, before the 2nd dose of LA, 15 min after the 2nd dose of LA, before epidural infusion, and 30th min, 1st, and 2nd hour of epidural infusion ($p < 0.05$). Compared to the basal values decrease in HR was statistically significant in Group II before the 2nd dose of LA, 15 min after the 2nd dose of LA, before epidural infusion, and 30th min, and 1st hour of epidural infusion ($p < 0.05$) (Table 3). The difference in MAP and HR was not statistically significant between the groups ($p > 0.05$) (Table 2 and 3).

Compared to the basal values decreases in VAS scores at rest and during coughing were statistically significant in both groups from postoperative 30th min to 24th h ($p < 0.05$). The difference was not significant between the groups with respect to VAS scores at rest and during coughing ($p > 0.05$) (Table 4, Table 6). When screening, median VAS values of all measurements, it was found that, there was no statistically significant difference between two groups ($p > 0.05$) (Table 5, Table 7).

Total iv morphine consumptions were similar between the groups on the first day of the operation ($p > 0.05$) (Table 8). The number of PCA demand were 55,00 ± 11,26 and 56,80 ± 10,79 in the Group 1 and Group 2 at the end of 24h, respectively. There was no significant difference between the groups in the number of PCA demand ($p > 0.05$).

Table 1:Demographic Characteristics (Mean ± SD) (N=15 for both groups)

	Group I	Group II	P
Age (Year)	45.73 ± 10.94	45.87 ± 9.84	0.972
Sex (Male/Female)	8/7	8/7	1.000
Weight (kg)	65.93 ± 7.67	65.67 ± 7.59	0.924
Height (cm)	165.40 ± 5.82	165.53 ± 5.48	0.949

Table2.The mean±standard deviation of arterial pressures (MAP) within and between the groups

MAP (mmHg)	Group 1 (n=15)	Group 2 (n=15)	P
Preoperative Period	93.26±7.68	87.67±10.82	0.113
Before the 1st dose of LA	85.13±11.96	80.33±12.68	0.295
15 min after 1st dose of LA	79.46±11.82*	75.33±11.34*	0.337
Before the 2st dose of LA	81.53±9.78*	77.06±9.65*	0.218
15 min after 2st dose of LA	79.46±9.94*	74.86±9.23*	0.200
Before epidural infusion	66.80±9.63*	72.60±8.30*	0.088
30th minute	68.53±6.89*	73.53±8.06*	0.078
1th hour	72.40±11.66*	79.53±9.50	0.077
2nd hour	75.40±11.27*	78.33±9.30	0.444
6th hour	76.26±8.78*	77.33±6.74	0.712
12th hour	76.46±12.87*	76.20±7.92*	0.946
24th hour	77.13±9.58*	79.80±7.85	0.411

LA: Local Anesthesic, MAP: Mean Arterial Pressure
*Compared to basal values within the groups (p<0.05)

Table 3. The mean±standard deviation of heart rates (HR) within and between the groups.

HR (beat min^{-1})	Grup I (n=15)	Grup II (n=15)	P
Preoperative period	85.60 ± 16.48	82.13 ± 9.13	0.482
Before the 1st dose of LA	77.73 ± 13.17	80.00 ± 11.56	0.620
15 min after the 1st dose of LA	73.13 ± 9.59*	76.40 ± 8.60	0.334
Before the 2nd dose of LA	72.73 ± 9.49*	74.00 ± 6.34*	0.671
15 min after the 2nd dose of LA	73.20 ± 8.43*	74.20 ± 6.20*	0.714
Before epidural infusion	65.60 ± 9.17*	71.33 ± 7.83*	0.076
30th minute	65.60 ± 8.98*	70.33 ± 6.63*	0.112
1st hour	68.73 ± 11.40*	74.20 ± 7.90*	0.138
2nd hour	73.40 ± 11.85*	77.20 ± 8.24	0.317
6th hour	82.13 ± 12.32	83.73 ± 10.11	0.700
12th hour	82.86 ± 12.77	84.53 ± 7.95	0.671
24th hour	83.73 ± 12.61	86.66 ± 8.70	0.465

LA: Local anesthetic, HR: Heart rate.
*Compared to basal values within the groups ($p < 0.05$).

One patient in each group experienced shoulder pain. Postoperative hypotension, responsive to ephedrine, was developed in two and one patient in Group I and II, respectively. Only one patient in Group I had nausea which was sensitive to metoclopramide. None of the patients experienced respiratory depression and itching in our study. Urinary retention could not be evaluated in patients with existing urinary catheter. There was no sedation, and motor block in the patients.

Discussion

Thoracotomy is known to be responsible for pulmonary dysfunction, and severe post-thoracotomy pain may aggravate this circumstances. Thus, post-thoracotomy pain cause serious health problems such as difficulties in breathing and coughing, accumulation of secretions resulting in atelectasis, pneumonia, bronchitis, bronchospasm, hypoxemia, respiratory failure, and extended mechanical ventilation (8, 9).

Although various methods of pain management exist, many studies have suggested that TEA is the most efficient technique for post-thoracotomy analgesia. Currently, TEA is accepted to be the gold standard of post-thoracotomy pain management (9).

Although all LAs induce toxicity by inhibition of voltage-dependent ion channels, and cause side effects on cardiovascular and central nervous system (10) the most widely used method of postoperative epidural

Table 4. Comparison of the visual analog scores at rest (VASr).

VASr	Score	Grup I (n=15)		Grup II (n=15)		P
		n	%	n	%	
Before PCA	4	5	33.33	4	26.67	0.974
	5	4	26.67	5	33.33	
	6	4	26.67	4	26.67	
	7	2	13.33	2	13.33	
30th minute	3	4	26.67*	4	26.67*	0.825
	4	6	40.00*	4	26.67*	
	5	3	20.00*	5	33.33*	
	6	2	13.33*	2	13.33*	
1st hour	3	8	53.33*	5	33.33*	0.542
	4	5	33.33*	7	46.67*	
	5	2	13.33*	3	20.00*	
2nd hour	2	4	26.67*	4	26.67*	0.632
	3	9	60.00*	7	46.67*	
	4	2	13.33*	4	26.67*	
6th hour	2	8	53.33*	10	66.67*	0.519
	3	6	40.00*	5	33.33*	
	4	1	6.67*	0	0.00*	
12th hour	1	6	40.00*	7	46.67*	1.000
	2	9	60.00*	8	53.33*	
24th hour	0	6	40.00*	7	46.67*	1.000
	1	9	60.00*	8	53.33*	

VASr: Visual analogue scale at rest, PCA: Patient-controllled analgesia.
*Compared to basal values within the groups ($p<0.05$).

analgesia is the continous infusion of LA and opioid combination (11). LAs, opioids, or combination of them may be used for TEA. A combination of LA and opioid is increasingly preferred to decrease the side effects (12).

Opioid receptors are mainly found on C-fibers. C-fibers transmit diffuse and slight pain of the chest wall; which can easily be managed by the administration of opioids. However, sharp and severe pain, which is transmitted by A-fibers, cannot be managed by opioids alone. LAs are considered to be quite effective for this type of pain (13).

Multimodal regimens or combinations of LAs and opioids with regional techniques are more often preferred and supply more efficient analgesia. Synergistic analgesic effects can be observed with usage of the

Table 5. Comparison of the median visual analog scores at rest (VASr).

VASr	Group I (n = 15)	Group II (n = 15)	p
Before PCA	5 (4-7)	5 (4-7)	0.846
30th minute	4 (3-6)	4 (3-6)	0.698
1st hour	3 (3-5)	4 (3-5)	0.301
2nd hour	3 (2-4)	3 (2-4)	0.798
6th hour	2 (2-4)	2 (2-3)	0.397
12th hour	2 (1-2)	2 (1-2)	0.717
24th hour	1 (0-1)	1 (0-1)	0.717

VAS: Visual Analog Scores

Table 6. Comparison of the visual analog scores during coughing (VASc).

VASr	Score	Grup I (n=15)		Grup II (n=15)		P
		n	%	n	%	
Before PCA	5	5	33.33	4	26.67	0.974
	6	4	26.67	5	33.33	
	7	4	26.67	4	26.67	
	8	2	13.33	2	13.33	
30th minute	4	4	26.67*	4	26.67*	0.825
	5	6	40.00*	4	26.67*	
	6	3	20.00*	5	33.33*	
	7	2	13.33*	2	13.33*	
1st hour	4	9	60.00*	5	33.33*	0.339
	5	4	26.67*	7	46.67*	
	6	2	13.33*	3	20.00*	
2nd hour	3	5	33.33*	5	33.33*	0.621
	4	8	53.33*	6	40.00*	
	5	2	13.33*	4	26.67*	
6th hour	2	1	6.67*	0	0.00*	0.392
	3	8	53.33*	11	73.33*	
	4	6	40.00*	4	26.67*	
12th hour	2	6	40.00*	8	53.33*	0.714
	3	9	60.00*	7	46.67*	
24th hour	0	6	40.00*	7	46.67*	1.000
	1	9	60.00*	8	53.33*	

VASc: Visual analog scale during coughing, PCA: Patient-controlled analgesia.
*Compared to the other group ($p < 0.05$).

smaller doses which reduce the incidence of side effects and provide early mobilization (9). Wheatley et al. (12) showed that a combination of LAs and opioids was superior to either drug administered alone, especially for pain management after upper abdominal, orthopedic, and thoracic surgeries.

Although there is still no consensus on the ideal epidural analgesic agent or combination, fentanyl with relatively faster onset of action and lower risk of late respiratory depression is used frequently (9, 14, 15). De Cosmo et al. (16) conducted a comparative study on two different concentrations of levobupivacaine in thoracic surgery. Continuous infusion of 0.125% and 0.0625% levobupivacaine combined with sufentanil were compared. They found that 0.125% levobupivacaine had lower VAS scores and fewer side effects due to decreased I.V.

Table 7. Comparison of the median visual analog scores at coughing (VASc).

VASc	Group I (n = 15)	Group II (n = 15)	p
Before PCA	6 (5-8)	6 (5-8)	0.846
30th minute	5 (4-7)	5 (4-7)	0.698
1st hour	4 (4-6)	5 (4-6)	0.191
2nd hour	4 (3-5)	4 (3-5)	0.654
6th hour	3 (2-4)	3 (2-4)	0.502
12th hour	3 (2-3)	2 (2-3)	0.472
24th hour	1 (0-1)	1 (0-1)	.717

VAS: Visual Analog Scores

Table 8. Total morphine consumptions (mg).

Total morphine (mg)	Group I (n = 15)	Group II (n = 15)	P
Before PCA	0.00 ± 0.00	0.00 ± 0.00	NS
30th min	2.26 ± 0.45	2.26 ± 0.45	1.000
1st hour	4.53 ± 0.63	4.60 ± 0.73	0.793
2nd hour	7.73 ± 0.88	8.00 ± 0.92	0.426
6th hour	12.13 ± 1.92	12.53 ± 1.95	0.577
12th hour	17.06 ± 2.25	17.40 ± 2.16	0.682
24th hour	20.26 ± 2.52	20.46 ± 2.55	0.831

PCA: Patient-controlled analgesia

morphine requirement. Similarly, 0.125% epidural bupivacaine or levobupivacaine was combined with fentanyl in our study. Both of these combinations were equally effective in terms of analgesia. We did not observe serious side effects and motor blockage in both groups.

Preemptive analgesic applications are accepted as the new approach for pain management and have been successfully used to manage post-thoracotomy pain. The target of preemptive analgesia is to block pain pathways before the actual pain stimulation. This means pain management is initiated before noxious stimuli. Thus, smaller doses of analgesics provide more effective analgesia. Ong et al. (17) published a meta-analysis of preemptive epidural analgesia for acute postoperative pain. They found consistent improvements in VAS scores, postoperative supplemental analgesic requirements, and time to first rescue analgesic in preemptive epidural analgesia. Furthermore, a loading dose of LA may reduce chronic post-thoracotomy pain if administered before surgical noxious stimuli(18). Likewise, we administered LA before surgical incision in our study.

Mendola et al. (19) compared three different concentrations (0.5%, 0.25%, and 0.15%) of levobupivacaine combined with sufentanil. The study drugs were given in boluses before surgical incision, every 20 min during almost 2 h perioperative period. Approximately 30 min before the end of operation, an epidural infusion was started. Additionally epidural boluses of analgesic mixture were administered using a PCA device in postoperative period. Three different concentrations of a continuous infusion of thoracic epidural levobupivacaine and sufentanil were found to be associated with an equal incidence of side effects, and with a good pain control in post-thoracotomy patients. They demonstrated that levobupivacaine caused a low incidence of hypotension and no bradycardia, without significant difference between three groups.

We administered epidural boluses of levobupivacaine or bupivacaine 15 min before surgery and at closure of the thorax. Epidural infusion of the study drugs was started in postoperative period. There was no severe hemodynamic side effect in both groups during perioperative period.

A multimodal analgesic approach with LAs, intratechal and/or parenteral opioids, and NSAID is considered the best method for post-thoracotomy pain management (9). Parenteral opioids are often preferred as supplementary analgesics for inadequate post-thoracotomy pain relief. De Cosmo et al. (20) compared the continuous epidural infusions of sufentanil combined with levobupivacaine or ropivacaine. They administered I.V. rescue morphine PCA and finally found that both groups have similar analgesic efficacy. In our study, we compared the continuous thoracic epidural infusions of bupivacaine or levobupivacaine combined with fentanyl. All patients received I.V. morphine PCA as an additional analgesic after the operation. The average morphine consumptions were approximately 12 mg and 20 mg for the period of 6 h and 24 h after the operation, respectively. Cücü et al. (21) compared paravertebral with epidural bupivacaine on patients undergoing thoracotomy. They also preferred I.V. morphine PCA as a supplementary analgesia. Total morphine consumption was found as 35 mg for the postoperative day in their trial.

Cox et al. (22) concluded that levobupivacaine and bupivacaine were similarly effective. In addition, there were no significant differences between the groups in arterial pressure and heart rate following the lower limb surgery under extradural anesthesia.

The patients with postoperative intractable shoulder pain received NSAID in both groups. Shoulder pain may be owing to injury of the dorsal primary horn of the intercostal nerve, wide costal resection, and position of the patient during the operation (23). Gerner (24) suggested that the postoperative shoulder pain, resistant to epidural analgesia, might be relieved by NSAID. In our study, one patient in each group had resistant shoulder pain after the operation. This pain was managed by I.M. 75 mg diclofenac sodium.

It is important to prefer analgesics associated with lower side effects, and the incidence of complications in postoperative period. Hypotension and bradycardia are two important hemodynamic side effects of epidural analgesia. Burlacu et al. (25) established that both levobupivacaine and bupivacaine had similar side effects. We did not experience any serious side effects in this study. A total of 3 patients suffered from hypotension. We supposed that hypotension was caused by selective blockage of cardiac sympathetic fibers following TEA. Urinary retention, nausea and itching are the predictable complications of opioids (26). Urinary retention could not be evaluated in patients with existing urinary catheter. Respiratory depression is a serious side effect of opioid usage during postoperative epidural infusion (7). Though, none of the patients had respiratory depression and itching in our study. Only one patient had nausea in bupivacaine group.

In conclusion, bupivacaine and levobupivacaine was similar in the analgesia, hemodynamia, and side effects for thoracic surgery. Both groups showed comparable necessity for additional morphine. In combination with thoracic epidural fentanyl, a continuous infusion of levobupivacaine may be considered as a good alternative to bupivacaine. To achieve efficient analgesia after thorax surgery, epidural analgesia may be insufficient solely so that multimodal procedures must be preferred.

REFERENCES

1. Tiippana E, Nilsson E, Kalso E. Post-thoracotomy pain after thoracic epidural analgesia: a prospective follow-up study. Acta Anaesthesiol Scand 2003; 47: 433-438.
2. Yegin A, Erdogan A, Kayacan N, Karsli B. Early postoperative pain management after thoracic surgery; pre- and postoperative versus postoperative epidural analgesia: a randomized study. Eur J Cardiothorac Surg 2003; 24: 420-424.
3. Debreceni G, Molnár Z, Szélig L, Molnár TF. Continuous epidural or intercostal analgesia following thoracotomy: a prospective randomized double-blind clinical trial. Acta Anaesthesiol Scand 2003; 47: 1091-1095.
4. Sandler AN. Post-thoracotomy analgesia and perioperative outcome. Minerva Anestesiol 1999; 65: 267-274.
5. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anesthetic. Drugs 2000; 59: 551-579.
6. Ganesh A, Adzick NS, Foster T, Cucchiaro G. Efficacy of addition of fentanyl to epidural bupivacaine on postoperative analgesia after thoracotomy for lung resection in infants. Anesthesiology 2008; 109: 890-894.
7. Behera BK, Puri GD, Ghai B. Patient-controlled epidural analgesia with fentanyl and bupivacaine provides better analgesia than intravenous morphine patient-controlled analgesia for early thoracotomy pain. J Postgrad Med 2008; 54: 86-90.
8. Rock P, Rich PB. Postoperative pulmonary complications. Curr Opin Anaesthesiol 2003; 16: 123-131.
9. De Cosmo G, Aceto P, Gualtieri E, Congedo E. Analgesia in thoracic surgey: review. Minerva Anestesiol 2009; 75: 393-400.
10. Akarsu T. Levobupivacaine plus fentanyl versus bupivacaine plus fentanyl in epidural anesthesia for lumbar disc surgery. Turkiye Klinikleri J Med Sci 2011; 31: 100-108.
11. Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA Jr, Wu CL. Efficacy of postoperative epidural analgesia: a meta-analysis. JAMA 2003; 290 : 2455-2463.
12. Wheatley RG, Schug SA, Watson D. Safety and efficacy of postoperative epidural analgesia. Br J Anaesth 2001; 87: 47-61.
13. Dickenson AH. Spinal cord pharmacology of pain. Br J Anaesth 1995; 75: 193-200.
14. Tan CN, Guha A, Scawn ND, Pennefather SH, Russell GN. Optimal concentration of epidural fentanyl in bupivicaine 0,1% after thoracotomy. Br J Anaesth 2004; 92: 670-674.
15. Sanjay OP, Kadam VR, Menezes J, Prashanth P, Tauro DI. Thoracic epidural infusions for post thoracotomy pain relief: a clinical study to compare the efficacy of fentanyl-bupivacaine mixtures versus fentanyl alone. Ind J Thorac Cardiovasc Surg 2003; 19: 113-118.
16. De Cosmo G, Mascia A, Clemente A, Congedo E, Aceto P. Use of levobupivacaine for the treatment of postoperative pain after thoracotomies. Minerva Anesthesiol 2005; 71: 347-351.
17. Ong CK, Lirk P, Seymour RA, Jenkins BJ. The efficacy of preemptive analgesia for acute postoperative pain management: a meta-analysis. Anesth Analg 2005; 100:757-773.
18. Şentürk M, Özcan PE, Talu GK, et al. The effects of three different analgesia techniques on long-term postthoracotomy pain. Anesth Analg 2002; 94: 11-15.
19. Mendola C, Ferrante D, Oldani E, et al. Thoracic epidural analgesia in post-thoracotomy patients: comparison of three different concentrations of levobupivacaine and sufentanil. Br J Anaesth 2009; 102: 418-423.
20. De Cosmo G, Congedo E, Lai C, et al. Ropivacaine vs. levobupivacaine combined with sufentanil for epidural analgesia after lung surgery. Eur J Anaesthesiol 2008; 25: 1020-1025.
21. Cücü O, Karaca P, Enç Y, ve ark. Comprasion of thoracic paravertebral and epidural blocks for pain relief after thoracotomy. Turkish J Thorac Cardiovasc Surg 2006; 14: 42-47.
22. Cox CR, Faccenda KA, Gilhooly C, Bannister J, Scott NB, Morrison LM. Extradural S(-)-bupivacaine: comparison with racemic RS-bupivacaine. Br J Anaesth 1998; 80: 289-293.
23. Berrisford RG, Sabanathan SS, Mearns AJ, Bickford-Smith PJ. Pulmonary complications after lung resection: the effect of continuous extra-pleural intercostal nerve block. Eur J Cardiothorac Surg 1990; 4: 407-411.
24. Gerner P. Postthoracotomy pain management problems. Anesthesiol Clin 2008; 26: 355-367.
25. Burlacu CL, Buggy DJ. Update on local anesthetics: focus on levobupivacaine. Ther Clin Risk Manag 2008; 4: 381-392.
26. Macias A, Monedero P, Adame M, Torre W, Fidalgo I, Hidalgo F. A randomized, double-blinded comparasion of thoracic epidural ropivacaine, ropivacaine/fentanyl, or bupivacaine/fentanyl for postthoracotomy analgesia. Anesth Analg 2002; 95: 1344-1350.