ELSEVIER

European Journal of Cardio-thoracic Surgery 24 (2003) 420–424

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

# Early postoperative pain management after thoracic surgery; pre- and postoperative versus postoperative epidural analgesia: a randomised study

Arif Yegin[a,*], Abdullah Erdogan[b], Nurten Kayacan[a], Bilge Karsli[a]

[a]*Department of Anaesthesiology, Akdeniz University Medical Faculty, Antalya, Turkey*
[b]*Department of Thoracic Surgery, Akdeniz University Medical Faculty, Antalya, Turkey*

Received 6 March 2003; received in revised form 18 May 2003; accepted 26 May 2003

**Abstract**

**Objectives**: Effective analgesia and blockade of the perioperative stress response may improve outcome and epidural analgesia plays a role in the reduction of pulmonary complications following thoracic surgery. In this study, we assessed preoperative and postoperative thoracic epidural analgesia (Preop-TEA and Postop-TEA) techniques on post-thoracotomy pain in 61 patients undergoing posterolateral thoracotomy. **Methods**: A thoracic epidural catheter was inserted into all the patients before surgery. In Group I, 8 mL of 0.25% bupivacaine plus fentanyl 50 μg in 2 mL was administered preoperatively. In Group II, no medication was administered via the epidural catheter preoperatively and intraoperatively. Postoperative analgesia was maintained with patient-controlled epidural analgesia with bupivacaine and fentanyl solution in both groups. Pain was evaluated at 2, 4, 8, 12, 24 and 48 h at rest and coughing. **Results**: Preop-TEA Group was associated with decreased pain compared with the Postop-TEA Group. **Conclusions**: In conclusion, preoperative epidural analgesia is an appropriate method for post-thoracotomy pain and is more effective in preventing acute postoperative pain.
© 2003 Elsevier B.V. All rights reserved.

*Keywords:* Analgesia; Epidural; Thoracotomy; Pain; Postoperative

## 1. Introduction

Post-thoracotomy pain is one of the most severe types of postoperative pain. The insufficient treatment of post-thoracotomy pain results in reduced pulmonary compliance, inability to breath deeply or cough forcefully and retention of secretions, atelectasis and pneumonia [1]. Several analgesic techniques, including intercostal, paravertebral, interpleural and epidural blocks with local anaesthetics and opioids have been used to provide pain relief after thoracotomy [2]. Thoracic epidural analgesia (TEA) is one of the most effective methods in post-thoracotomy pain relief. Opioid analgesics with or without local anaesthetics are widely used for TEA. Postoperatively, patient-controlled epidural analgesia (PCEA) presents a high quality analgesia for acute post-thoracotomy pain, allowing patients to titrate analgesic doses in amounts proportional to the level of pain intensity [3].

Although there is limited experience concerning the efficacy and safety of PCEA, initial reports suggest that it may improve analgesia, patient satisfaction and safety compared with conventional epidural infusion or bolus techniques [4,5].

Pre-emptive analgesia reduces acute postoperative pain arising from surgical wounds. It has been reported in previous studies that administration of regional anaesthesia or epidural opioid analgesia before the surgery may block the sensitising effects of surgical stimulation with a resultant reduction in subsequent acute postoperative pain [6,7].

In this study, we compared the analgesic effects of preoperative and postoperative TEA (Preop-TEA and Postop-TEA) versus Postop-TEA alone, in acute post-thoracotomy pain.

## 2. Methods

The study protocol was approved by the medical ethics committee of our faculty and a written informed consent was obtained from each patient. Sixty-one consenting

* Corresponding author. Tel.: +90-242-227-4343; fax: +90-242-227-8836.
*E-mail address:* ayegin@ixir.com (A. Yegin).

1010-7940/03/$ - see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/S1010-7940(03)00345-2

Downloaded from https://academic.oup.com/ejcts/article/24/3/420/608440 by Akdeniz Universitesi user on 20 September 2021

American Society of Anaesthesiologists physical status II–III patients undergoing posterolateral thoracotomy were randomly divided into two groups to evaluate the effects of two different analgesia techniques—Group I ($n = 30$): Preop-TEA and Group II: ($n = 31$) Postop-TEA. Exclusion criteria included general contraindications for epidural anaesthesia or failure in catheter placement, history of allergy to the study medications, renal insufficiency (creatinine $>15$ mg $dL^{-1}$) or liver dysfunction (aspartate aminotransferase, alanine aminotransferase or both $>40$ U $L^{-1}$), preoperative respiratory function tests showing a forced vital capacity of $<60\%$ predicted, forced expiratory volume at 1 s $<60\%$ or both. The patients more than 65 or less than 18 years old were also excluded, as well as those with disorders of homeostasis or thoracic spine abnormalities. Before the operation, postoperative pain methodology during the 48 h period was explained to all patients.

After arrival into the operating room, all the patients were premedicated with midazolam 2 mg IV and were given 10 mL $kg^{-1}$ $h^{-1}$ ringer's lactate solution. Patients were monitored (Envoy; Mennen Medicals, Rehovot, Israel) with electrocardiography, pulse oximetry and non-invasive blood pressure measurements.

An 18-gauge epidural catheter (B. Braun, Melsungen, Germany) was inserted into all patients, through the T6-7 or T7-8 intervertebral space preoperatively by a midline approach with the loss of resistance technique and placed 4–5 cm in the cephalad direction under fluoroscopic control.

In the Preop-TEA Group, 8 mL bolus solution of 0.25% bupivacaine and 2 mL of fentanyl (25 μg $mL^{-1}$) in saline was administered via the epidural catheter at least 30 min before the induction of anaesthesia. In Postop-TEA Group, no epidural medication was applied until the chest closure. All patients in both groups were dosed with 8 mL of 0.25% bupivacaine and 2 mL of fentanyl (25 μg $mL^{-1}$) via the epidural route at the time of the pleural closure.

Postoperative analgesic treatment was similar and obtained with PCEA in both groups (Abbott Pain Management Provider; Abbott Laboratories, Istanbul, Turkey). PCEA was administered after extubation with an analgesic solution of 0.125% bupivacaine plus fentanyl 2 μg $mL^{-1}$ according to the following program: no initial dose, basal infusion rate 4 mL $h^{-1}$, bolus dose 2 mL and a 10 min lock out interval. If visual analogue scale (VAS) score at rest was higher than 4, a rescue analgesia with 5 mL bolus of PCEA solution was applied. No changes were made to the PCEA settings.

Fentanyl 2 μg $kg^{-1}$, propofol 2.5 mg $kg^{-1}$ and vecuronium 0.1 mg $kg^{-1}$ were administered for anaesthesia induction. Patients were also monitored with invasive blood pressure and central venous pressure after the induction of anaesthesia. A double lumen tube was applied for one lung ventilation. Anaesthesia was maintained with 1–2% sevoflurane, 67% nitrous oxide in oxygen. Analgesia and neuromuscular blockade were maintained with incremental doses of fentanyl citrate and vecuronium bromide in the Postop-TEA Group, but fentanyl was stopped 1 h before the end of surgery to eliminate its analgesic effect during the early postoperative period. In the Preop-TEA Group, IV fentanyl was not given since it was not necessary for analgesia after the induction of anaesthesia. Patients were extubated at the end of the operation and transferred to the intensive care unit.

During the first 48 h after the operation, patients used the epidural PCA as described in the protocol and they were questioned about their pain at 2, 4, 8, 12, 24 and 48 h at rest and coughing by an observer blinded to treatment groups, using VAS (0 = no pain and 10 = worst pain imaginable) and the results were recorded [8].

The degree of sedation was also examined by the same observer on a five-point scale (0 = alert, 1 = mildly drowsy, 2 = moderately drowsy, easily rousable, 3 = very drowsy, rousable, 4 = difficult to rouse or 5 = unrousable) [9]. Side effects, including nausea, vomiting, respiratory depression, sedation and pruritus were recorded and treated with appropriate medication.

### 2.1. Statistical analyses

A priori power analysis indicated that a minimum of 28 patients in each group would be required to demonstrate a 10 mm difference in VAS scores for pain with a power of 83% ($\alpha = 0.05$) [13]. Continuous variables were analysed with two way ANOVA for repeated measurements, followed by Bonferroni correction. Differences between the groups were analysed with $\chi^2$ test and Mann–Whitney $U$ test (SPSS 10 for Windows, SPSS Institute, Chicago, IL). All results were presented as mean ± standard deviation (SD). In all the tests, a $p$ value less than 0.05 was regarded as significant.

## 3. Results

There were no statistically significant differences between the two groups with respect to demographic variables and operative data (Table 1).

The data on postoperative acute pain at rest and cough are shown in Fig. 1. Postoperative pain scores at rest were lower at the first 12 h in the Preop-TEA Group than those in the Postop-TEA Group (Fig. 1). Pain at coughing was less well controlled. However, there were statistically significant differences between the Preop-TEA and Postop-TEA Groups at the first 12 h postoperatively (Fig. 1). There were no statistically significant differences in the degree of sedation scores between the two groups ($p < 0.05$).

Total PCA fentanyl consumption over the 24 h period was significantly higher in the Postop-TEA Group (259 ± 20 μg) than the pre-TEA Group (245 ± 14 μg) ($p < 0.05$; Table 2). The number of rescue medication was

Downloaded from https://academic.oup.com/ejcts/article/24/3/420/608440 by Akdeniz Universitesi user on 20 September 2021

Table 1
Patient characteristics and duration and types of operations (expressed as mean ± SD)

| Variable | Preop-TEA ($n = 30$) | Postop-TEA ($n = 31$) |
|---|---|---|
| Sex M/F | 11/19 | 9/22 |
| Age (year) | 51 ± 14 | 53 ± 13 |
| Weight (kg) | 69 ± 8 | 65 ± 10 |
| Height (cm) | 168 ± 8 | 169 ± 4 |
| Duration of operation (min) | 137 ± 53 | 129 ± 62 |
| Intraop. fentanyl consumption (μg) | 136.6 ± 12.7 | 269.7 ± 75.6 |
| Type of surgery | | |
| Wedge resection | 3 | 4 |
| Segmentectomy | 2 | 1 |
| Lobectomy | 19 | 16 |
| Bilobectomy | 1 | 3 |
| Pneumectomy | 5 | 7 |

Table 2
Total PCEA fentanyl consumption ratio over the postoperative 24 h period and the number of rescue analgesic and total PCEA demands of patients (expressed as mean ± SD)

| | Preop-TEA | Postop-TEA | $p$ value |
|---|---|---|---|
| Number of patients | 30 | 31 | |
| Fentanyl consumption (μg) | 245 ± 14 | 259 ± 20 | 0.034 |
| No. of rescue analgesic | 6 | 13 | 0.033 |

also significantly higher in the Postop-TEA Group ($n = 13$) than the Preop-TEA Group ($n = 6$).

Regarding the adverse effects of the acute pain treatment, there was no statistically significant difference between the two groups. The adverse effects were very few: three patients had pruritus, two had nausea in the Preop-TEA Group and two patients pruritus or nausea in the Postop-TEA Group. Vomiting or respiratory depression was not detected in any of the patients.

## 4. Discussion

Pain is often inadequately treated in many surgical procedures. Acute postoperative pain can cause detrimental effects on multiple organ systems, such as cardiovascular stress, autonomic hyperactivity, tissue breakdown (production of a catabolic state with suppression of anabolic hormones), increased metabolic rate, pulmonary dysfunction (most significant after upper abdominal and thoracic surgery), increased blood clotting (hypercoagulability), fluid retention, dysfunction of the immune system, delayed return of bowel function (ileus) and development of chronic pain syndromes after certain surgeries (phantom limb pain after amputation, post-thoracotomy syndrome) [10]. Pre-emptive analgesia may have a potential role in decreasing the postoperative pain, as has been shown in the reduction of post injury pain in animals [11], but studies in humans have provided controversial results [6,7]. Epidural, intravenous and intramuscular opioids have been shown to reduce the severity of postoperative pain when administered before surgical stimuli [7,12]. One of these studies demonstrated that VAS pain scores and morphine requirements were significantly reduced in patients receiving pre-emptive epidural analgesia [6]. On the contrary, some authors reported that pre-emptive analgesia has failed to decrease postoperative analgesic consumption [13]. In another study, Aida et al. [14] reported that pre-emptive analgesia was

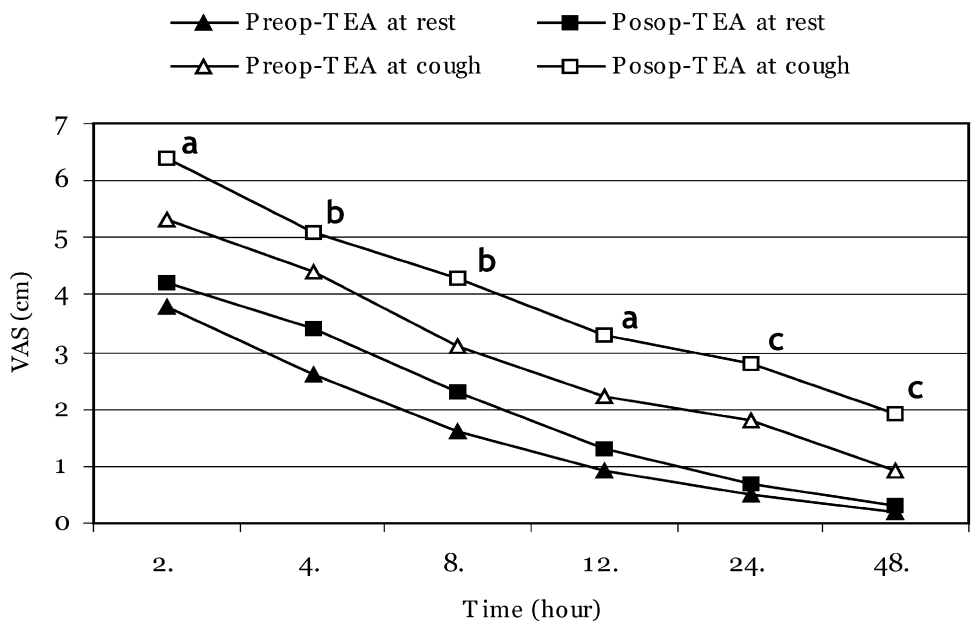



Fig. 1. Median VAS scores during the first 48 h after the operation at rest and coughing ($p < 0.05$ comparison of two groups, $p < 0.05$ comparison of time intervals, $p < 0.05$ comparison of groups and time intervals). (a) $p < 0.05$ according to time, group and time × group for two groups. (b) $p < 0.01$ according to time, group and time × group for two groups. (c) $p > 0.05$ according to time, group and time × group for two groups.

Downloaded from https://academic.oup.com/ejcts/article/24/3/420/608440 by Akdeniz Universitesi user on 20 September 2021

effective in limb surgery and mastectomy, but not in surgeries involving laparotomy (gastrectomy, hysterectomy and appendectomy).

In the literature, there are several studies in which the pre-emptive effect of TEA was used to reduce the post-thoracotomy pain [13,15], but in only one, it has been suggested that pre-emptive thoracic analgesia decreased pain intensity for 2 or 3 days; Obata et al. [15] showed that an epidural block with mepivacaine before surgery reduced long-term post-thoracotomy pain. This study compared the effects of pre- and postoperative initiation of TEA and found a significant clinical efficacy of pre-emptive analgesia for the first 72 h.

In contrast, some studies have found no pre-emptive effect of epidural anaesthesia in post-thoracotomy pain. Aguilar et al. [13] assessed the pre-emptive effect of thoracic epidural bupivacaine in thoracotomy. They gave 8 mL of 0.5% bupivacaine containing 5 μg $mL^{-1}$ of adrenaline through a thoracic extradural catheter 30 min before incision and maintained the anaesthesia with propofol, alfentanil, and atracurium infusions. These authors reported that thoracic epidural block with bupivacaine did not produce a significant pre-emptive effect compared with the placebo group after thoracotomy. Our study has shown that the preoperative administration of bupivacaine plus fentanyl has a marked pre-emptive effect and significantly reduces post-thoracotomy pain for postoperative 12 h.

In a prospective study, Senturk et al. [16] compared the effects of preoperative and postoperative initiation of TEA and IV-PCA on acute and chronic post-thoracotomy pain and they have shown that Preop-TEA was associated with a decreased acute and chronic pain compared with the other groups. They have administered bupivacaine plus morphine in both preoperative and postoperative periods via epidural catheter. In our study, we used bupivacaine and fentanyl for PCEA and similar to Senturk et al.'s study, we found that Preop-TEA administration causes a significant decrease on the post-thoracotomy pain intensity.

Neustein et al. [6] have demonstrated that pre-emptive epidural analgesia provided lower maximum pain scores in the first 6 h postoperatively in post-thoracotomy pain. But they have not found any significant difference in pain scores beyond the first 6 h. In our study, we found that pre-emptive epidural analgesia provided lower maximum pain scores in the first 6 h, similar to Neustein's study and this decrease continued for 12 h in preoperative epidural analgesia group.

PCEA may provide several benefits over conventional epidural continuous infusion or bolus techniques. In our study, use of PCEA with bupivacaine and fentanyl provided good analgesia after thoracotomy. Previous studies have also reported effective postoperative analgesia with continuous epidural infusions of bupivacaine and morphine [17], bupivacaine and fentanyl [9], bupivacaine and sufentanil [18] and boluses of epidural morphine [19].

The ideal combination of local anaesthetic and opioid for PCEA is unknown. We selected fentanyl for its rapid onset and a relatively lower risk of delayed respiratory depression [20,21]. A 2 μg $mL^{-1}$ solution of fentanyl was chosen, because previous studies demonstrated more rapid onset of action and longer duration of analgesia with similar dilution of fentanyl [20]. Other opioids may also have suitable characteristics, but epidural morphine has important disadvantages including a delayed onset of analgesia, long duration and a risk for delayed respiratory depression [22]. We also chose to add 0.125% bupivacaine to our analgesic solution, as previous dose-ranging studies suggest that the addition of approximately 0.125% bupivacaine to fentanyl improves analgesia and reduces epidural fentanyl use [20]. Use of PCEA may provide a lower incidence of side effects, by decreasing the patients requirements for analgesics such as epidural bupivacaine and fentanyl for an equivalent analgesia when compared with continuous epidural infusions [4,9,17]. Decreased use of bupivacaine and fentanyl with PCEA for an equivalent analgesia may be valuable in reducing their side effects. In our study, there was no neurological sequelae due to the thoracic epidural catheterization in the early postoperative period.

Our study has several limitations. First, in the Preop group, we administered the epidural bolus around 30 min before the induction of anaesthesia for consistency. Considering that the surgical incision was started approximately 10 min after the anaesthesia, the time between the epidural bolus and the incision was around 40 min in these patients, which is longer than that reported in the literature, and therefore, might have theoretically caused an increase in the VAS scores of the Preop group. This effect, however, is unfavorable for the Preop group, and thus, does not alter the significance of our results. Second, to eliminate its analgesic effect in the postoperative period, we stopped fentanyl administration in the Postop-TEA Group around 1 h before the end of the surgery. This interval, however, is arbitrary and probably not very consistent in each patient, since it may be difficult to predict the duration of the procedure. Third, we did not perform any testing to determine the level and the depth of the thoracic blockade, which would have been desirable. We believed, however, that because of the premedication performed with 2mg IV midazolam, this testing would not have been very accurate. Fourth, during the operation, we had to employ different analgesia regimens in both groups: in the Preop group, epidural local anaesthetic was continued, since fentanyl was regarded unnecessary and in the Postop group, IV fentanyl was used. This difference, however, is unlikely to have an effect on the postoperative VAS scores, since fentanyl was stopped 1 h before the end of the operation and local anaesthetics were given epidurally at this time simultaneously in both groups. Finally, we preferred a VAS score of 4 as the threshold value for the rescue analgesic administration, since we were concerned about the increased opioid dose after thoracic surgery in both group of patients. It is possible that if a VAS score of 3 or less had been chosen, the number of patients requiring rescue

Downloaded from https://academic.oup.com/ejcts/article/24/3/420/608440 by Akdeniz Universitesi user on 20 September 2021

analgesia would have been different in both groups. Despite these limitations, we believe that our results are still significant, particularly considering the relatively large number of patients recruited in our study compared to those reported in the literature.

## 5. Conclusions

The results of our study suggest that additional use of Preop-TEA besides the postoperative PCEA is an appropriate and effective method for the reduction of early post-thoracotomy pain, and that, the use of bupivacaine plus fentanyl for both types of epidural analgesia is safe and effective.

## References

[1] Perttunen K, Nilsson E, Heinonen J. Exradural paravertebral and intercostal nerve blocks for postthoracotomy pain. Br J Anaesth 1995; 75:541–7.
[2] Guinard JP, Mavrocordatos P, Chiolero R, Carpenter RL. A randomized comparison of intravenous versus lumbar and thoracic epidural fentanyl for analgesia after thoracotomy. Anesthesiology 1992;77:1108–15.
[3] Raj PP. Nerve block: continuous regional analgesia. In: Raj PP, editor. Practical management of pain, 3rd ed. Missouri, MO: Mosby; 2000. p. 710–22.
[4] Ferrante FM, Liu I, Jamison SB, Datta S. Patient controlled epidural analgesia: demand dosing. Anesth Analg 1991;73:547–52.
[5] Owen H, Kluger MT, Ilsley AH, Baldwin AM, Fronsko PRL, Plummer JL. The effects of fentanyl administered epidurally by patient controlled analgesia, continuous infusion or a combined technique on oxyhaemoglobine saturation after abdominal surgery. Anaesthesia 1993;48:20–5.
[6] Neustein S, Kreitzer JM, Krellenstein D, Reich DL, Rapaport E, Cohen E. Pre-emptive epidural analgesia for thoracic surgery. Mt Sinai J Med 2002;69:101–4.
[7] Subramaniam B, Pawar DK, Kashyap L. Preemptive analgesia with epidural morphine or morphine and bupivacaine. Anaesth Intensive Care 2000;28:394–8.
[8] Jewison RN. Clinical measurement of pain. In: Ferrante FM, VadeBoncouer TR, editors. Postoperative pain management. New York, NY: Churchill Livingstone; 1993. p. 120–1.
[9] Scott DA, Beilby DSN, McClaymont C. Postoperative analgesia using epidural infusion of fentanyl with bupivacaine: a prospective analysis of 1014 patients. Anesthesiology 1995;83:727–37.
[10] Grass AJ. The role of epidural anesthesia and analgesia in post-operative outcome. Anesthesiol Clin North Am 2000;18:121–5.
[11] Troncy E, Junot S, Kroack S, Sammut V, Pibarot P, Genevois JP, Cuvelliez S. Results of preemptive epidural administration of morphine with or without bupivacaine in dogs and cats undergoing surgery: 265 cases (1997–1999). J Am Vet Med Assoc 2002;221: 666–72.
[12] Moiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systemic review of preemptive analgesia for postoperative pain relief: the role of timing of analgesia. Anesthesiology 2002;96:725–41.
[13] Aguilar JL, Rincon R, Domingo V, Espachs P, Preciado MJ, Vidal F. Absence of an early pre-emptive effect after thoracic extradural bupivacaine in thoracic surgery. Br J Anaesth 1996;76:72–6.
[14] Aida S, Baba H, Yamakura T, Taga K, Fukuda S, Shimoji K. The effectiveness of preemptive analgesia varies according to the type of surgery: a randomized, double-blind study. Anesth Analg 1999;89: 711–6.
[15] Obata H, Saito S, Fujita N. Epidural block with mepivacaine before surgery reduces long-term postthoracotomy pain. Can J Anaesth 1999; 46:1127–32.
[16] Senturk M, Ozcan PE, Talu GK, Kiyan E, Camci E, Ozyalcin S, Dilege S, Pembeci K. The effects of three different analgesia techniques on long-term postthoracotomy pain. Anesth Analg 2002; 94:11–15.
[17] DeLeon Casasola OA, Parjer B, Lema PJ, Harrison P, Massey J. Postoperative epidural bupivacaine-morphine therapy. Experience with 4227 surgical cancer patients. Anesthesiology 1994;81:368–75.
[18] Broekema A, Gielen MJ, Hennis PJ. Postoperative analgesia with continuous epidural sufentanil and bupivacaine: a prospective study in 614 patients. Anesth Analg 1996;82:754–9.
[19] Ready LB, Loper KA, Nessly M, Wild L. Postoperative epidural morphine is safe on surgical wards. Anesthesiology 1991;75:452–6.
[20] Birnbach DJ, Jonhson MD, Arcario T, Datta S, Naulty JS, Ostheimer GW. Effect of diluent volume on analgesia produced by epidural fentanyl. Anesth Analg 1989;68:808–10.
[21] Coda BA, Brown MC, Schaffer R, Donaldson G, Jacobson R, Hautman B, Shenn DD. Pharmacology of epidural fentanyl, alfentanil and sufentanil in volunteers. Anesthesiology 1994;81:1449–61.
[22] Liu S, Angel JM, Owens BD, Carpenter RL, Isabel L. Effects of epidural bupivacaine after thoracotomy. Reg Anesth 1995;20: 303–10.

Downloaded from https://academic.oup.com/ejcts/article/24/3/420/608440 by Akdeniz Universitesi user on 20 September 2021