Changes in Pulmonary Function during Continuous Epidural Bupivacaine with or without Morphine Following Upper Abdominal Surgery

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To assess the effect of postoperative continuous thoracic epidural infusion of bupivacaine on pulmonary function, a prospective randomized study was conducted in patients undergoing upper abdominal surgery (UAS). Sixteen patients, divided into two treatment groups, received continuous epidural infusion of 0.25% bupivacaine at a rate of 2–5 $ml \cdot hr^{-1}$, or that of a combination of 0.125% or 0.25% bupivacaine and 0.0025% or 0.005% morphine at a rate of 2–4 $ml \cdot hr^{-1}$. One, 4, 10, 16, 24 and 40 hr postoperatively, the following indices were measured: visual analogue scale score, modified Prince Henry pain scale score, arterial Pa_{O_2} and Pa_{CO_2}, functional residual capacity (FRC), and tidal volume (TV). There was no difference in pain scores between the two groups except for significantly less pain at 40 hr in the combination group. Postoperative measurements of pulmonary function revealed a significant fall in Pa_{O_2}, FRC and TV, indicating a reduction of 15–25% as compared with the preoperative values, and no significant differences between the two groups. The authors conclude that postoperative continuous epidural infusion of bupivacaine combined with morphine is highly effective in alleviating pain and improving pulmonary function in patients following UAS.
(Key words: pulmonary function, postoperative, epidural, bupivacaine, morphine)

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Following upper abdominal surgery (UAS), a restrictive pulmonary dysfunction with a reduction in functional residual capacity (FRC) and accompanying hypoxemia are frequently seen[1–5]. It has been shown that, although the reduction in vital capacity is evident in the immediate postoperative period, there is a delay of 16 hr before a significant fall in FRC, which decreases to about 70% of preoperative levels by 24 hr following UAS[1]. This suggests the possibility of postoperative therapeutic treatments that could limit the FRC changes and, hence, the usefulness of the measurement of FRC for the evaluation of these treatments.

Mankikian et al.[6] has demonstrated that diaphragmatic dysfunction is a major determinant of the decrease in lung volumes, and that this dysfunction is only reversed by a thoracic epidural block. However, the beneficial effect of a bolus epidural administration of local anesthetics is transitory.

At our hospital, postoperative continuous epidural infusion of local anesthetics, of

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which bupivacaine is usually employed because of its weak muscle relaxant effect[7], has been in use for several years. In addition, our practice has evolved to combine morphine with a more dilute solution of bupivacaine to provide better analgesia and prevent excessive blood concentration of bupivacaine[8]. Although this appears to be useful for attenuating the postoperative pulmonary dysfunction, it is not clear whether continuous epidural infusion technique prevents the reduction in FRC.

The aim of this study was to demonstrate the effects of continuous epidural infusion of bupivacaine with or without morphine on the postoperative pulmonary function, measuring lung volumes and arterial blood gases in patients undergoing gastrectomy.

Methods

Subjects

Sixteen ASA Physical Status 1 and 2 patients, who were scheduled for gastrectomy for cancer, were enrolled in the study. None of the patients were obese, nor had clinical evidence of cardiorespiratory problems. The study was approved by our institution's human research review committee and consent was obtained from each patient.

Premedication comprised 50 mg of hydroxyzine and 0.5 mg of atropine given intramuscularly 1 hr before arrival in the operating room. Before induction of general anesthesia, an epidural catheter (Portex) was introduced into the Th8–9 or Th9–10 intervertebral space. The epidural space was identified by the hanging drop technique. Intraoperatively, all the patients were maintained with light levels of general anesthesia, which was induced with 4 $mg \cdot kg^{-1}$ of thiamylal followed by 1 $mg \cdot kg^{-1}$ of succinylcholin to facilitate tracheal intubation, and received intermittent injections of plain mepivacaine in the epidural catheter to achieve and maintain surgical anesthesia and muscle relaxation. Light general anesthesia was usually nitrous oxide, oxygen, and halothane or enflurane. No muscle relaxants were used for control of ventilation. After completion of surgery, all the patients were extubated and taken to an intensive care unit.

Postoperative analgesia

A continuous epidural infusion was started immediately after the operation with a volumetric infusion pump. All the patients were randomly assigned to one of two groups to receive postoperative pain treatment for a 48 hr period. Patients in group A received continuous epidural infusion of 0.25% bupivacaine at a rate of 2–5 $ml \cdot hr^{-1}$. Patients in group B received continuous epidural infusion of a combination of 0.25% bupivacaine and 0.005% morphine at a rate of 2–4 $ml \cdot hr^{-1}$ until the solution amounted to 40 ml. Then the concentration of bupivacaine was decreased to 0.125%, while that of morphine was kept unchanged or decreased to 0.0025%. The use of narcotics being regulated in Japan, the study was not double-blinded, but patients did not know which solutions were being used. In both groups, if pain relief was insufficient, a bolus injection of 4 ml of the solution was allowed only twice in succession. Every patient in both groups received postoperative pulmonary therapy, including chest physiotherapy, incentive spirometry and voluntary deep breathing, several times a day.

Measurements

On the day before surgery, pulmonary function was assessed by measurement of tidal volume (TV) and functional residual capacity (FRC), using a Gould Godart spirometer and computer, with the patient in a supine position. FRC was measured by the closed circuit helium dilution technique. Arterial blood gases were also measured preoperatively.

Postoperatively, the degree of pain relief was evaluated using a 10-point visual analogue scale (VAS) (0 = no pain, 10 = worst pain) and a modification of the Prince Henry pain scale (mPHPS)[9], which used a five-point rating system: 1 = no pain on coughing; 2 = pain on coughing but not on deep breathing; 3 = pain on deep breathing but not at rest; 4 = slight pain at rest; 5 = severe pain at rest. Arterial blood gases and the degree of pain relief were measured at 1, 4, 10, 16, 24 and 40 hr postoperatively.

Table 1. Patient characteristics

	Group A (n = 6)	Group B (n = 10)
Sex F/M	4/2	3/7
Age (yr)	63.0 ± 11.1	65.1 ± 6.5
Height (cm)	151.6 ± 9.9	157.5 ± 10.0
Weight (kg)	49.9 ± 13.4	54.9 ± 9.5
Duration of operation (min)	355.8 ± 105.0	336.5 ± 83.3
Bleeding (ml)	806.7 ± 428.2	757.0 ± 257.7
Smokers	1 (16.7%)	3 (30%)

No significant difference between the two groups.

Table 2. Preoperative values of pulmonary function variables

	Group A (n = 6)	Group B (n = 10)
% VC (%)	110.3 ± 21.1	110.0 ± 23.4
$FEV_{1.0}/FVC$ (%)	85.8 ± 21.7	77.3 ± 7.8
TV (ml)	460.7 ± 81.7	492.7 ± 45.2
FRC (ml)	1505 ± 279	1796 ± 441
Pa_{O_2} (mmHg)	87.6 ± 8.1	79.6 ± 7.9
Pa_{CO_2} (mmHg)	41.2 ± 3.3	42.8 ± 2.8

% VC, vital capacity as a percent of the predicted value; $FEV_{1.0}/FVC$, forced expiratory volume in 1 sec as a percent of the actual forced vital capacity; TV, tidal volume; FRC, functional residual capacity. No significant difference between the two groups.

Arterial blood gases were obtained after patients had been breathing room air for 30 min. Pulmonary function was also measured at every study period but 1 hr, at which time the possibility of overestimating FRC existed, due to the influence of nitrous oxide remaining in the patient's exhalations.

Postoperative monitoring of electrocardiogram, rectal temperature, urinary volume, and respiratory frequency followed the routines of the ICU. Arterial pressure was measured throughout this study.

Statistical Analysis

All results are presented as mean ± SD. In regard to pulmonary function, each variable at 1, 4, 10, 16, 24 and 40 hr postoperatively was expressed as a percent of the patient's own preoperative value. Statistical analysis consisted of two-way ANOVA, Student's t-test and Wilcoxon's rank sum test. A significant level of $P < 0.05$ was chosen.

Results

Six patients received continuous epidural infusion of bupivacaine (group A) and 10 received that of a combination of bupivacaine and morphine (group B). No significant differences were noted between the groups with respect to sex, age, height, weight, duration of surgery, preoperative blood loss, or incidence of cigarette smoking (table 1). Preoperative arterial blood gas tensions, vital capacity (expressed as a percent of the predicted value), forced expiratory volume in 1 sec (as a percent of the actual forced vital capacity), TV, and FRC were also comparable between the groups (table 2). No one developed such hypotension as required va-

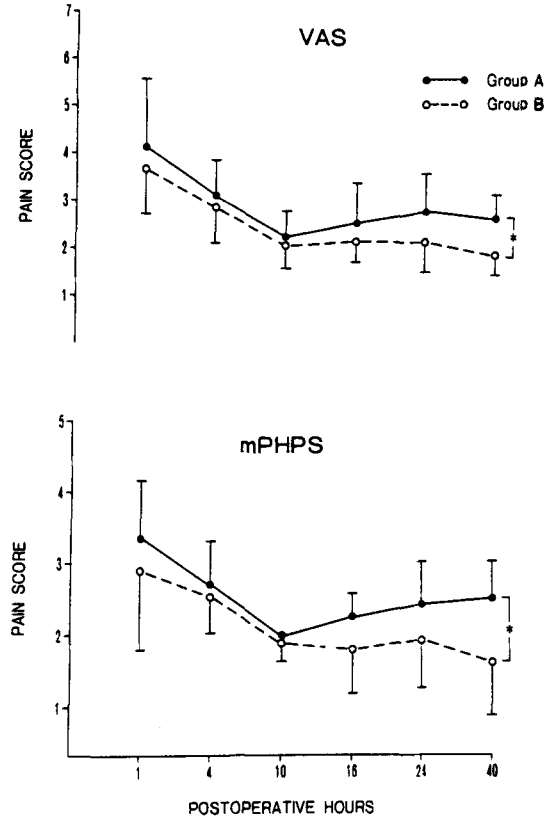

Fig. 1. Visual analogue pain scale (VAS) scores and modified Prince Henry pain scale (mPHPS) scores during continuous epidural infusion. Each value is given as the mean ± DS. Group A, epidural bupivacaine group; Group B, epidural combination group. $*P < 0.05$, statistical significance of intergroup comparisons of mean values.

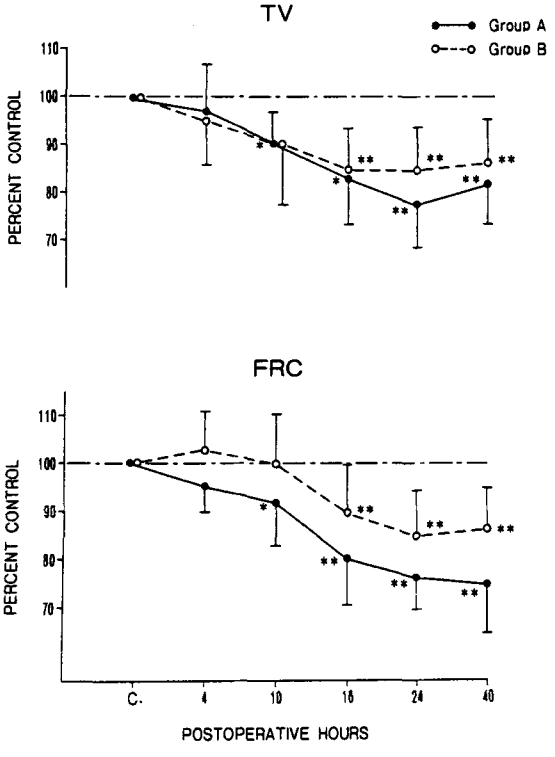

Fig. 2. Time-related changes in tidal volume (TV) and functional residual capacity (FRC) during continuous epidural infusion. Each value is expressed as a percent of the control value given in table 2 and is given as the mean ± SD. Group A, epidural bupivacaine group; Group B, epidural combination group; C., control value. $*P < 0.05$ and $**P < 0.01$, significant differences from preoperative values in each group.

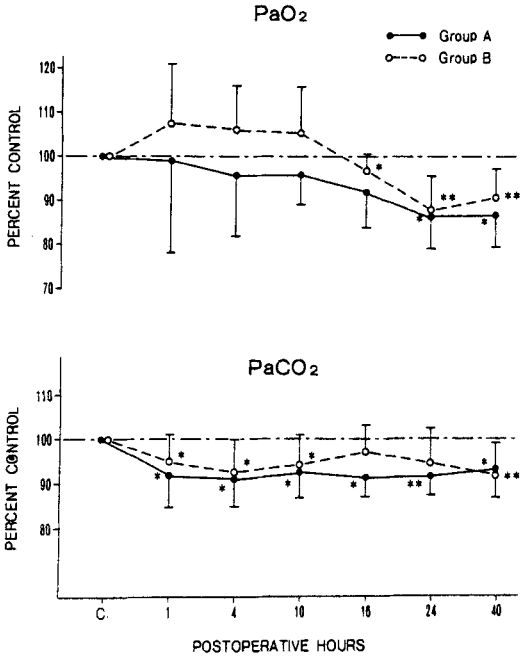

Fig. 3. Time-related changes in blood gas analysis during continuous epidural infusion. Each value is expressed as a percent of the control value given in table 2 and is given as the mean ± SD. Group A, epidural bupivacaine group; Group B, epidural combination group; C., control value. $*P < 0.05$ and $**P < 0.01$, significant differences from preoperative values in each group.

sopressors, which might have influenced the results.

Postoperative analgesia

As illustrated in figure 1, statistical analysis of VAS and mPHPS showed that satisfactory analgesia was achieved by 4 hr after surgery in both groups. These scores then remained below 3 by both scales in the course of the study period. There was no significant difference between pain relief in the two groups until 24 hr. The scores in group A gradually became higher, however, indicating significantly less pain relief at 40 hr.

The mean bupivacaine infusion rate over 48 hr was 0.21 ± 0.05 $mg \cdot kg^{-1} \cdot hr^{-1}$ in group A and 0.10 ± 0.02 $mg \cdot kg^{-1} \cdot hr^{-1}$ in group B. This difference was statistically significant ($P < 0.01$). In group B, the mean morphine consumption and the rate of morphine infusion was, respectively, 6.4 ± 0.8 mg and 2.5 ± 0.4 $\mu g \cdot kg^{-1} \cdot hr^{-1}$. The number of additional bolus injections required for analgesia was significantly different in the two groups ($P < 0.05$). Group A required 3.0 ± 2.3 injections/48 hr and group B 0.2 ± 0.4. No patients requested other supplemental analgesics or sedatives in this study period.

Postoperative pulmonary function

Postoperative sequential measurements of TV and FRC showed a marked reduction in both groups (fig. 2). In group A, there was a delay of 10 hr before a significant decrease in TV and FRC ($P < 0.05$). This decrease in TV and FRC reached a maximum at 24 and 40 postoperative hr, respectively. On the other hand, in group B, a significant fall in TV and FRC did not occur until 16 hr ($P < 0.01$). The maximum decrease in TV and FRC was seen at 16 and 24 hr after surgery, respectively. The most marked reduction in postoperative TV as compared with the preoperative levels was observed in group A, with a reduction of 20% as compared with 15% in group B. Similarly, the decrease in FRC was more marked in group A, with a reduction of 25% as compared with 15% in group B. However, there were no statistical differences between the groups. Preoperative levels were not regained before 40 hr.

Analysis of arterial blood gases showed postoperative hypoxemia (fig. 3). There was also a delayed decrease in Pa_{O_2} in both groups. A significant fall did not occur until 24 hr in group A and until 16 hr in group B. The most marked reduction in Pa_{O_2} was seen at 24 hr postoperatively with a reduction of only 15% ($P < 0.05$), and gradual improvement was observed. In contrast, there was a tendency to hypocapnia in both groups ($P < 0.05$). Nor did significant differences in arterial blood gases occur between the groups.

Discussion

The results obtained in the present study show that continuous epidural infusion of bupivacaine with or without morphine reduced pulmonary dysfunction following UAS,

when compared with studies using conventional systemic analgesia[1,2] and epidural morphine regimens[10,11]. Although either regimen used in this study also offered excellent analgesia, neither restored pulmonary function to preoperative values completely, and there was a delay of 10–24 hr before a significant fall in FRC and Pa_{O_2}.

UAS is responsible for postoperative pulmonary dysfunction, characterized by a restrictive pattern with rapid and shallow breathing, reduced vital capacity and FRC, associated with hypoxemia and atelectasis[1–5]. Although the pathophysiology of the dysfunction is poorly understood, the provision of near perfect analgesia has previously shown an incomplete restoration of spirometric values, suggesting that pain is not the most important mechanism of impairment in pulmonary function[10,12]. In contrast, the importance of diaphragmatic contractility has recently been emphasized[13,14] as well as expiratory abdominal and lower intercostal muscle activity[15] and thoracoabdominal blood volume[16]. The diaphragmatic dysfunction has been reported to be due to a decrease not in the contractile properties of the diaphragm per se[14] but in phrenic nerve activity. Animal studies[17] have demonstrated inhibitory reflexes of phrenic motor output during or after stimulation of visceral or somatic afferents. Shannon[18], for example, reported that stimulation of intercostal and abdominal muscle proprioceptor afferents reflexively decreased phrenic motor activity in cats.

Since diaphragmatic dysfunction may be related to a reflex inhibition of the phrenic nerve output, attempts to prevent the dysfunction should include therapeutics that can block the afferent activity of the reflex. The work of Mankikian et al.[6] in this regard is extremely significant. They have revealed that thoracic epidural analgesia with bupivacaine produces a marked improvement in diaphragmatic function associated with an increase in VC. Another study by Wahba et al.[19] has shown an immediate but slight increase in FRC in patients with pain who benefit from epidural analgesia. However, their findings are that the beneficial effects are transitory in cases in which only a bolus administration, rather than a long-term one, is given.

As expected, the maximum decrease in FRC, TV and Pa_{O_2} in this study was small compared with earlier reports following UAS[1–3]. This is in agreement with Hendolin et al.[20] who reported a good maintenance of respiratory function and a reduced incidence of postoperative atelectasis with continuous thoracic epidural analgesia following cholecystectomy. Considering that epidural analgesia with morphine, as reported in our previous study[11] or in others[10], fails to improve pulmonary or diaphragmatic function following UAS in spite of its excellent analgesic effect, this improvement appears to be the result of the partial prevention of diaphragmatic dysfunction.

A noteworthy finding in our study was that the postoperative course of FRC paralleled that of TV and Pa_{O_2}. In either group, there was a delay of 10–24 hr prior to a significant fall in these variables. These figures are in close keeping with that of Ali et al.[1], who report that postoperative changes in FRC are seen in patients undergoing cholecystectomy under general anesthesia followed by a conventional analgesic technique postoperatively. Of additional interest is the discrepancy between the postoperative changes in the pulmonary variables and those of pain relief. These facts emphasize that, although any excellent pain relief can improve the patient's ability to cough and take deep breaths, preventing atelectasis, it is the method of providing pain relief that is important.

The reasons for the incomplete restoration of the postoperative pulmonary dysfunction in this study are complex. One of the possible causes is the multiple afferent nerve pathway involved in the innervation of the upper abdomen. Lund et al.[21] have demonstrated, using somatosensory evoked potentials, that there is incomplete afferent blockade during conventional doses of thoracic epidural bupivacaine, despite sufficient spread of sensory analgesia. To obtain a better effect, either

a larger volume or a higher concentration of bupivacaine may be necessary. This is not recommended, however, because resting ventilation may be impaired by a stronger thoracic epidural block[22]. Furthermore, in the present study, the postoperative course of pulmonary variables obtained in group A was comparable to that in group B, although the bupivacaine consumption in the former was about twice as much as that in the latter.

No data demonstrated any significant differences between the two groups except for those concerning analgesic effect. Although either regimen provided satisfactory analgesia during this study period except for the first 4 hr, there was a slight attenuation of effect with time in group A, suggesting that morphine combined with bupivacaine circumvented the tachyphylaxis[23], as shown in previous studies[24].

In conclusion, this study confirms that postoperative pulmonary dysfunction following UAS is considerably prevented by the continuous epidural infusion of bupivacaine, which can block the afferent limb of the inhibitor reflex of the diaphragm. The addition of morphine to epidural bupivacaine improves postoperative analgesia and circumvents tachyphylaxis of bupivacaine, but does not give rise to ventilatory depression, nor attenuate the beneficial effect on postoperative pulmonary function despite the smaller consumption of bupivacaine.

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References

1. Ali J, Weisel RD, Layug AB, Kripke BJ, Hechtman HB: Consequences of postoperative alterations in respiratory mechanics. Am J Surg 128:376–382, 1974
2. Meyers JR, Lembeck L, O'Kane H, Baue AE: Changes in functional residual capacity of the lung after operation. Arch Surg 110:576–583, 1975
3. Craig DB: Postoperative recovery of pulmonary function. Anesth Analg 60:46–52, 1981
4. Latimer RG, Dickman M, Day WC, Gunn ML, Schmidt CD: Ventilatory patterns and pulmonary complications after upper abdominal surgery by determined preoperative and postoperative computerized spirometry and blood gas analysis. Am J Surg 122:622–632, 1971
5. Alexander JI, Spence AA, Parikh RK, Stuart B: The role of airway closure in postoperative hypoxaemia. Br J Anaesth 45:34–40, 1973
6. Mankikian B, Cantineau JP, Bertrand M, Kieffer E, Sartene R, Viars P: Improvement of diaphragmatic function by a thoracic extradural block after upper abdominal surgery. Anesthesiology 68:379–386, 1988
7. Bromage PR: Epidural analgesia, Drugs and equipment. Philadelphia, W.B. Saunders, 1978, pp. 305
8. Sakura S, Uchida H, Saito Y, Asano M, Kosaka Y: Continuous epidural infusion for postoperative pain relief: A comparison of three regimens. J Anesth 4:138–144, 1990
9. Torda TA, Pybus DA: Extradural administration of morphine and bupivacaine. Br J Anaesth 56:141–146, 1984
10. Bonnet F, Blery C, Zatan M, Simonet O, Brage D, Gaudy J: Effect of epidural morphine on post-operative pulmonary dysfunction. Acta Anaesthesiol Scand 28:147–151, 1984
11. Sakura S, Nakatani T, Kosaka Y, Tanaka A: Effect of continuous epidural morphine on postoperative pulmonary dysfunction. Hiroshima J Anesth 25:33–39, 1989 (in Japanese)
12. Benhamou D, Samii K, Noviant Y: Effect of analgesia on respiratory muscle function after upper abdominal surgery. Acta Anaesthesiol Scand 27:22–25, 1983
13. Simonneau G, Vivien A, Sartene R, Kunstlinger F, Samii K, Noviant Y, Duroux P: Diaphragm dysfunction induced by upper abdominal surgery, role of postoperative pain. Am Rev Respir Dis 128:899–903, 1983
14. Dureuil B, Viires N, Cantineau JP, Aubier M, Desmonts JM: Diaphragmatic contractility after upper abdominal surgery. J Appl Physiol 61:1775–1780, 1986
15. Duggan J, Drummond GB: Activity of lower intercostal and abdominal muscle after upper abdominal surgery. Anesth Analg 66:852–855, 1987
16. Jones JG: Anaesthesia and atelectasis: the role of V_{TAB} and the chest wall. Br J Anaesth 59:949–953, 1987

17. Albano JP, Garnier L: Bulbo-spinal respiratory effects originating from the splanchnic afferents. Respir Physiol 51:229–239, 1983
18. Shannon R: Intercostal and abdominal muscle afferent influence on medullary dorsal respiratory group neurons. Respir Physiol 39:73–94, 1980
19. Wahba WM, Don HF, Craig DB: Postoperative epidural analgesia: effects on lung volumes. Canad Anaesth Soc J 22:519–527, 1975
20. Hendolin H, Lahtinen J, Lansimies E, Tuppurainen T, Partanen K: The effect of thoracic epidural analgesia on repiratory function after cholecystectomy. Acta Anaesthesiol Scand 31:645–651, 1987
21. Lund C, Hansen OB, Mogensen T, Kehlet H: Effect of thoracic epidural bupivacaine on somatosensory evoked potentials after dermatomal stimulation. Anesth Analg 66:731–734, 1987
22. Takasaki M, Takahashi T: Respiratory function during cervical and thoracic extradural analgesia in patients with normal lungs. Br J Anaesth 52:1271–1276, 1980
23. Renck H, Edstrom H, Kinnberger B, Brandt G: Thoracic epidural analgesia-II: prolongation in the early postoperative period by continuous injection of 1.0% bupivacaine. Acta Anaesth Scand 20:47–56, 1976
24. Hjortso NC, Lund C, Mogensen T, Bigler D, Kehlet H: Epidural morphine improves pain relief and maintains sensory analgesia during continuous epidural bupivacaine after abdominal surgery. Anesth Analg 65:1033–1036, 1986