Journal of Clinical Anesthesia (2005) **17**, 531–536

ELSEVIER

Journal of Clinical Anesthesia

Original contribution

Comparison of 2 concentrations of levobupivacaine in postoperative patient-controlled epidural analgesia☆

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Received 28 October 2003; accepted 4 January 2005

Keywords:
Anesthetic techniques: epidural, patient controlled;
Anesthetics: local, levobupivacaine, dose, concentration;
Pain: acute, postoperative

Abstract

Study objectives: To evaluate the quality of analgesia and the incidence of side effects of 2 different concentrations of levobupivacaine given as an equal milligram–bolus dose (5 mg) via patient-controlled epidural analgesia after abdominal surgery.

Design: Prospective, randomized, blinded study.

Setting: Postanesthesia care unit and surgical wards of a university hospital.

Patients: Forty-nine patients (41 with complete file) undergoing major lower abdominal surgery.

Interventions: The patients were randomly assigned to 2 groups: 1.5 mg/mL (bolus 3.3 mL, lockout 20 minutes, n = 26) and 5 mg/mL (bolus 1 mL, lockout 20 minutes, n = 23). The epidural catheter was inserted in the low thoracic level (T9-T12) before induction of a standardized general anesthesia technique.

Measurements: Demography, upper sensory block, visual analog scale scores at rest and after coughing, levobupivacaine and rescue morphine consumption, motor blockade, hemodynamics, postoperative nausea and vomiting, sedation, and patient satisfaction were recorded within the first 48 hours.

Main results: Both groups were similar with regard to demographics, upper level of sensory blockade (T8), and visual analog scale pain scores at rest and after coughing, as well as levobupivacaine and subcutaneous rescue morphine consumption. Motor blockade in the lower limbs was very low in both groups. Arterial blood pressure was slightly lower in the 5 mg/mL group during the first 24 hours (P = 0.052). Five patients in the 1.5 mg/mL and 7 in the 5 mg/mL group had postoperative nausea and vomiting (P = 0.43). No other side effects were recorded, and all of the patients were satisfied.

Some of this material was presented as a poster at the Congress of the European Society of Anaesthesiologists, which was held in Glasgow, UK, in May 2003.

☆ The research was conducted at the Department of Anesthesiology, University Hospital Center of Charleroi, Belgium, without any financial support.

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0952-8180/$ – see front matter
doi:10.1016/j.jclinane.2005.01.007

Conclusions: Administering the same dose of levobupivacaine in either a low or high concentration via patient-controlled epidural analgesia mode provides an equal quality of analgesia with no difference in the incidence of side effects.

1. Introduction

The relative effects of mass, volume, and concentration of local anesthetic solutions used for epidural anesthesia and analgesia are still subject of debate. In clinical studies [1-5], contradictory results have been reported, probably due to the fact that the total dose of local anesthetic was not taken into consideration. Bromage [6] found that it is the total local anesthetic dose, and not the total volume, which determines the spread and quality of analgesia. Others have confirmed this finding, after both lumbar [7] and midthoracic [8] epidural administration. Nevertheless, it remains unclear in the literature whether the concentration influences the quality of pain relief during epidural analgesia when the total dose is held constant [9-11]. For continuous thoracic epidural administration, Dernedde et al [12,13] demonstrated that a high-concentration/low-volume local anesthetic infusion provided an equal quality of postoperative analgesia as a low-concentration/high-volume infusion and induced less motor blockade as well as less hemodynamic repercussions.

In patient-controlled epidural analgesia (PCEA), to date, only 2 studies have evaluated the influence of volume and concentration of the local anesthetic [14,15]. Both studies highlighted that the quality of analgesia was comparable with either low or high concentrations of the local anesthetic, but with reduced motor blockade [14] and drug consumption [15] using a low-concentration/high-volume approach.

Based on our previous results with continuous thoracic epidural administration of local anesthetics, we designed a prospective, randomized, double-blind study to compare 2 different concentrations of levobupivacaine, 1.5 and 5 mg/mL, given in equal total milligram–bolus doses (ie, 5 mg), via PCEA mode after lower abdominal surgery.

2. Materials and methods

After approval by the University Hospital Center Ethics Committee, written informed consent was obtained from 49 consecutive American Society of Anesthesiologists physical status I, II, and III patients undergoing elective lower abdominal surgery. Patients were enrolled in the study if they were between 18 and 75 years old, were able to read and understand French, had normal mental health, and were being hospitalized for elective surgery. Exclusion criteria were sepsis, allergy to amide-type local anesthetics or morphine, and coagulopathy. At the time of the preoperative visit, patients were familiarized with a 10-cm visual analog scale (VAS) device for pain (0 = no pain at all, 10 = worst imaginable pain) and nausea [16] intensity assessment (0 = no nausea at all, 10 = worst imaginable nausea).

Patients were premedicated with either midazolam 3 to 6 mg administered intramuscularly 1 hour before induction of anesthesia or with alprazolam 0.5 to 0.75 mg orally in the morning of the intervention. In the operating room, after infusion of 500 mL Ringer solution via an intravenous (IV) cannula, a 20-gauge epidural catheter was inserted through an 18-gauge Tuohy needle into the epidural space at a low thoracic level. The epidural catheter was directed cephalad for a distance of 4 cm and fixed to the back of the patient. As soon as the patient was in the supine position, a test dose of 3 mL 5 mg/mL levobupivacaine (Chirocaine, Abbott, Belgium) was injected to exclude subarachnoid positioning of the catheter as proposed by Murdoch et al [17] and Daoud et al [18].

Standardized general anesthesia was maintained with sevoflurane in 50% oxygen in air or nitrous oxide associated with sufentanil and myorelaxant. Based on an antiemetic institutional policy [19], 2 mg tropisetron (Novaban, Novartis, Belgium) was administered to all patients. Three to 6 mL of 5 mg/mL levobupivacaine was injected through the epidural catheter for the surgical procedure. If surgery lasted longer than 2 hours, patients received an additional injection of half of the original volume of the local anesthetic using the same concentration. After completion of the operation and tracheal extubation, patients were transferred to the postanesthesia care unit where they remained under constant observation for approximately 4 hours. The patients received, in a random fashion using a computer-generated randomization schedule, either 1.5 mg/mL levobupivacaine as a 3.3-mL bolus on demand, with a lockout interval of 20 minutes (n = 26), or 5 mg/mL levobupivacaine as a 1-mL bolus on demand, with a similar lockout interval (n = 23) via a PCEA pump (Abbott aim plus, Abbott Laboratories, North Chicago, Ill). No additional bolus injections were allowed. Patients received multimodal analgesia consisting of every 6-hour IV propacetamol (2 g) and ketorolac (60 mg daily) for postoperative pain relief. Rescue medication with morphine was provided via subcutaneous injections after each 4-hour evaluation of the VAS scale. Subcutaneous morphine consumption during the 48-hour study period was recorded by the nurses who administered the drug. After 48 hours, PCEA was discontinued, and alternative analgesia was provided.

On arrival in the postanesthesia care unit, patients were asked to rate their pain experience on the VAS device. This process was repeated every 2 hours for the first 4 hours and continued every 4 hours for 48 hours after the patient was

Table 1 Demographic and type of surgery in the 2 groups

Variable	1.5 mg/mL (n = 21)	5 mg/mL (n = 20)	*P*
Sex (male/female)	7/14	9/11	0.44
Age (y)	54 ± 11	54 ± 13	0.86
Weight (kg)	73 ± 14	75 ± 16	0.67
Height (cm)	167 ± 10	168 ± 9	0.72
BMI (kg/m^2)	26 ± 4	27 ± 5	0.64
ASA class			0.40
I	4 (19%)	2 (10%)	
II	13 (62%)	16 (80%)	
III	4 (19%)	2 (10%)	
Type of surgery			0.54
Urological (n)	2	4	
Gynecologic (n)	12	10	
Visceral (n)	7	6	

Concentration (mg/mL) refers to levobupivacaine. BMI indicates body mass index; ASA, American Society of Anesthesiologists.

moved to the general surgical ward. Pain at rest, defined as the pain experienced by the patient while lying in bed, and pain while coughing were assessed. The pain threshold was set at 3 cm on the VAS scale [20]. Nausea intensity was evaluated using a VAS device, and vomiting was recorded as either present or absent by direct observation or by spontaneous complaint of the patient. Nausea was defined as a patient's rating score superior to 4 cm on the VAS [16]. Rescue medications given for nausea and/or vomiting were recorded. Motor blockade in the lower limbs was assessed according to a modified Bromage scale [21] (0 = no motor block, 1 = inability to flex hips, 2 = inability to flex knees, and 3 = inability to flex ankle joints). The cephalad level of sensory block was evaluated by loss of sensation to cold using ether swabs. If the levels of sensory block on the right and left sides were different, the most-cephalad level was recorded. The anesthetist and the nurse investigators were blinded to the type of epidural solution administered.

Hypotension was defined as a 20% decrease of systolic blood pressure (SBP) compared with baseline and an SBP less than 90 mm Hg [22]. Bradycardia was defined as a heart rate less than 50 beats per minute, and bradypnea as a respiratory rate less than 10 breaths per minute. Sedation was recorded on a 4-point scale (0 = no signs of sedation, 1 = mild sedation, 2 = moderate sedation, and 3 = severe sedation).

During the first 48 hours, the patients were visited by a pain nurse from the Acute Pain Service, who interviewed each patient regarding satisfaction with postoperative analgesia. The quality of pain management was judged by the patient on a 4-point scale (1 = very dissatisfied, 2 = dissatisfied, 3 = satisfied, and 4 = very satisfied).

2.1. Statistical analysis

Results were expressed as means ± SD for quantitative variables and as frequencies for categorical findings. Time-related VAS measurements were summarized using different pain indicators as described elsewhere [12,13,20]: AUC, area under the VAS-time curve (cm^2); mean VAS (cm); VAS_{max}, peak of VAS (cm); T_{max}, time of VAS_{max} (hour); PVAS >3, the persistence of VAS more than 3 cm (ie, the period during which VAS was more than the critical threshold [hour]); and Pdur, pain duration (ie, the period during which the patient reported pain [VAS >0]) over the 48 hours (hours). The comparison of mean values was done by Wilcoxon test, whereas proportions were compared by the classical χ^2 test. The general linear mixed model (GLMM) was used to analyze repeated measures of continuous data. The GLMM tests 2 null hypotheses as follows: (1) time has no effect on the variable, which means that the variable mean of the combined groups does not vary over time, and (2) the time patterns are equal between the 2 groups, which means that the difference between the mean of each group is the same at every time point. The Bonferroni test, based on Student *t* statistic, was used for post hoc testing. The number of patients included in the study was based on our previous results and on a power calculation assuming a 20% difference with $\alpha = .05$ and $\beta = .20$ [12,13]. All statistical calculations were carried out by means of the SAS package (SAS Institute, Cary, NC, version 6.12) and always using all available data. Results were considered to be significant at the 5% critical level ($P < 0.05$).

3. Results

In our study, 8 patients were excluded because of protocol deviations, lack of data recording, or accidental removal of the catheter. A total of 41 patients with completed case report forms were included in the study (21 in the 1.5 mg/mL group and 20 in the 5 mg/mL group). For these patients, epidural catheters were functioning until the end of the observation period. Table 1 displays patients'

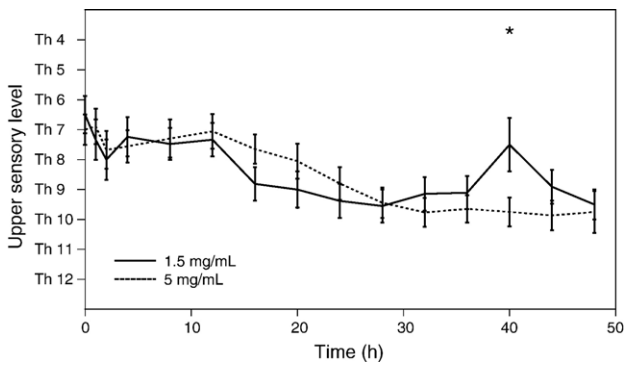

Fig. 1 Evolution of the mean upper sensory dermatomal level in the 2 groups of patients during the 48-hour study period. Concentration (1.5 and 5 mg/mL) refers to levobupivacaine. Error bars indicate SD. Th indicates thoracic. No significant difference between the 2 groups of patients ($P = 0.68$, GLMM statistic). *$P < 0.05$ (Student *t* test).

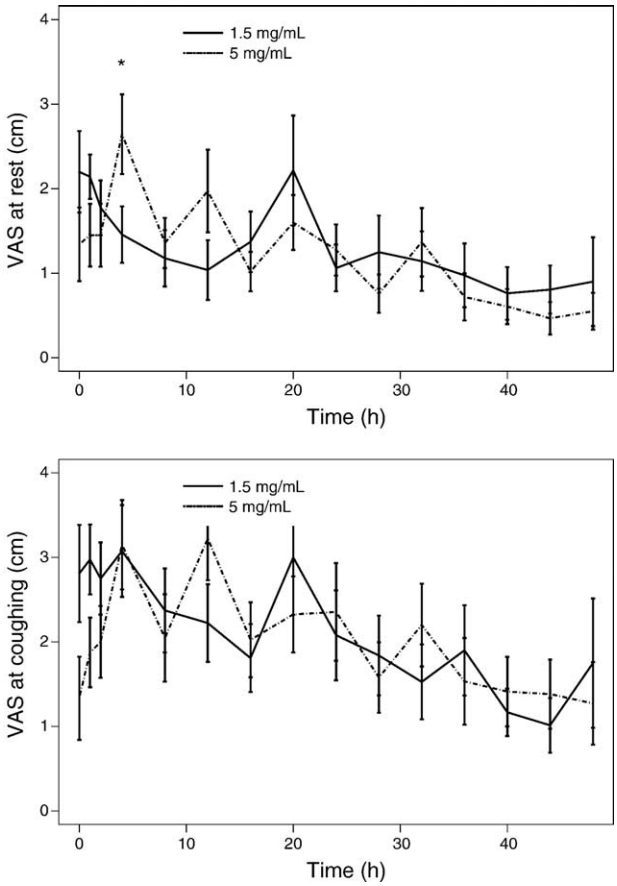

Fig. 2 Evolution of the mean VAS scores at rest and at coughing, expressed in centimeter in the 2 groups of patients during the 48-hour study period. Concentration (1.5 and 5 mg/mL) refers to levobupivacaine. Error bars indicate SD. No significant difference was found between the 2 groups of patients at rest ($P = 0.81$) and at coughing ($P = 0.96$) using the GLMM statistic. *$P < 0.05$ (Student t test).

characteristics and distribution according to the type of surgery. The demographic data baseline recordings and the type of surgery were similar in the 2 groups. Specifically, there was no difference in the age range between groups.

The level of insertion of the epidural catheter was low thoracic (T9-T12), with no differences between the 2 groups ($P = 0.29$). No cases of accidental dural puncture occurred. At the time of surgery, patients received the same amount of IV sufentanil (23 ± 9 μg in the 1.5 mg/mL group and 23 ± 7 μg in the 5 mg/mL group, $P = 0.96$). There was no difference between the groups in the amount of epidural levobupivacaine used for surgery (51 ± 16 mg in the 1.5 mg/mL group and 53 ± 14 mg in the 5 mg/mL, $P = 0.70$). Fig. 1 illustrates the mean upper level of sensory blockade at the different time points after surgery. There was no difference between the 2 groups ($P = 0.68$, GLMM statistics), except at 40 hours, whereupon there was a significantly higher mean upper level in the 1.5 mg/mL group ($P = 0.041$).

Table 2 Pain indicators, at rest and at coughing, in the 2 groups

Variable	1.5 mg/mL (n = 21)	5 mg/mL (n = 20)	P
At rest			
AUC (cm^2)	56.0 ± 52.6	54.0 ± 28.7	0.59
VAS_{max} (cm)	4.3 ± 2.4	3.9 ± 1.9	0.59
VAS mean (cm)	1.2 ± 1.1	1.3 ± 0.8	0.81
PVAS >3 (h)	5.9 ± 10.4	4.3 ± 4.8	0.51
At coughing			
AUC (cm^2)	89.7 ± 59.2	90.6 ± 49.7	0.96
VAS_{max} (cm)	5.6 ± 2.5	5.1 ± 1.9	0.43
VAS mean (cm)	2.1 ± 1.3	2.1 ± 1.1	0.96
PVAS >3 (h)	10.4 ± 11.7	12.1 ± 11.0	0.64

Concentration (mg/mL) refers to levobupivacaine.

Fig. 2 shows VAS pain scores at rest and after coughing during the first 48 postoperative hours in the 2 groups. GLMM statistics of the VAS scores for pain showed no difference between the 2 groups, except that the VAS pain score was significantly superior in the 5 mg/mL group ($P = 0.045$) only at the 4-hour time point. Table 2 displays the values of the pain indicators. We noted that the scores for AUC, VAS_{max}, VAS mean, and PVAS >3 were similar in the 2 groups. Furthermore, we highlight a strong positive relationship between the VAS scores at rest and at coughing ($r = 0.62$, $P < 0.0001$). The type of surgery did not influence the efficacy of pain relief.

Table 3 displays postoperative analgesic consumption. Mean consumption of epidural levobupivacaine during the first 24 hours amounted to 100 ± 47 mg in the 1.5 mg/mL group and 106 ± 46 mg in the 5 mg/mL group ($P = 0.35$). Propacetamol was given to all patients, and ketorolac was administered to 17 patients (81%) in the 1.5 mg/mL group and to 15 (75%) in the 5 mg/mL group ($P = 0.72$). Rescue analgesia, represented by morphine consumption (subcutaneous), was similar in the 2 groups. In the first 24 hours, the mean consumption of morphine was 7.9 ± 10.5 mg in the 1.5 mg/mL group, compared with 6.7 ± 7.0 mg for the 5 mg/mL group ($P = 0.98$). During the second postoperative day, morphine use was reduced to 1.5 ± 5.4 mg in the

Table 3 Postoperative analgesic consumption in the 2 groups

Variable	1.5 mg/mL (n = 21)	5 mg/mL (n = 20)	P
Levobupivacaine 24 h (mg)	100 ± 47	106 ± 46	0.35
Levobupivacaine 48 h (mg)	65 ± 67	72 ± 68	0.14
Morphine 24 h (mg)	7.9 ± 10.5	6.7 ± 7.0	0.98
Morphine 48 h (mg)	1.5 ± 5.4	0.4 ± 1.6	0.63
Propacetamol 24 h (g)	8 ± 0	8 ± 0	>0.99
Propacetamol 48 h (g)	8 ± 0	8 ± 0	>0.99
NSAIDs (n)	17 (81%)	15 (75%)	0.72
Antiemetic drugs (n)	5 (24%)	7 (35%)	0.43

Concentration (mg/mL) refers to levobupivacaine. NSAIDs indicates nonsteroidal anti-inflammatory drugs.

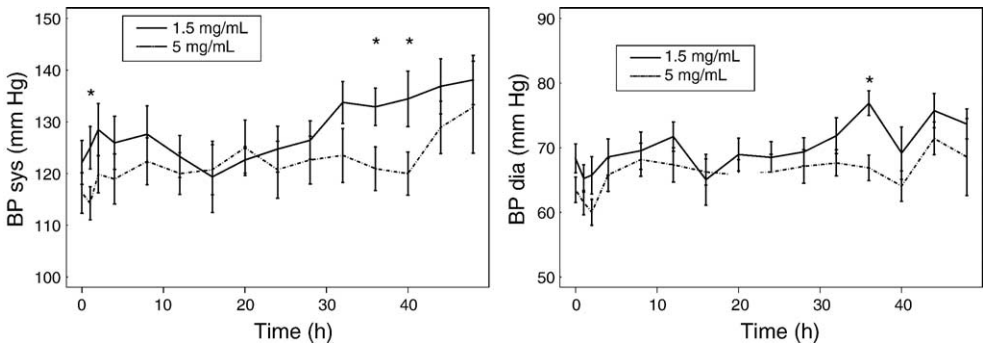

Fig. 3 Evolution of mean SBP and diastolic BP in the 2 groups of patients during the 48-hour study period. Concentration (1.5 and 5 mg/mL) refers to levobupivacaine. Error bars indicate SD. Systolic and diastolic BPs expressed in millimeters of mercury were lightly lower in the 5 mg/mL group during the first 24 hours ($P = 0.05$, GLMM statistic). *$P < 0.05$ (Student t test). Sys indicates systolic; dia, diastolic.

1.5 mg/mL group versus 0.4 ± 1.6 mg in the 5 mg/mL group ($P = 0.63$). No life-threatening respiratory events associated with opioid administration were reported during the study period.

Finally, motor blockade was consistently low in all patients (mean Bromage score <1) without any difference between the 2 groups. Fig. 3 displays the evolution of the SBP and diastolic blood pressure. We note that arterial blood pressure (BP) was slightly lower in the 5 mg/mL group during the first 24 hours ($P = 0.052$, GLMM statistics), which occurred after 1, 36, and 40 hours. During the study period, no vasoconstrictors or atropine was given for treatment of hypotension or bradycardia. We point out that 5 patients (24%) in the 1.5 mg/mL group had nausea compared with 7 (35%) in the 5 mg/mL group ($P = 0.43$). We observed no sedation, respiratory depression, or pruritus in any patient. All patients in the 2 groups were either satisfied or very satisfied regarding the quality of their pain management.

4. Discussion

The results of the present study confirm that altering the concentration and the volume while maintaining equivalent total-milligram doses of levobupivacaine administered via thoracic PCEA resulted in the same quality of analgesia, both at rest and after coughing. Local anesthetic requirements were similar in both groups during the 48-hour study period. We chose to administer a 5-mg-bolus dose with a lockout interval of 20 minutes. This dose corresponds to a maximum of 15 mg/h of the local anesthetic similar to what we have used in previous studies of continuous epidural infusion [12,13]. These results are consistent with previous studies supporting the view that the quality of epidural analgesia depends on the total mass of local anesthetic and not on the volume or concentration [2,6,12-15,23].

We used plain levobupivacaine 5 mg/mL for epidural infusion at a low thoracic level. The concentration was selected to maximize the analgesic effects of the local anesthetic in the thoracoabdominal somatosensory distribution [24]. As proposed by Duggan et al [2], a low volume of a concentrated solution produces the most predictable extradural block. The cephalad extent of the sensory block (T8) was similar in both groups. We recorded only the mean upper sensory block, and therefore, we cannot make any statement about the segmental block (ie, the number of segments blocked).

We placed our epidural catheters in low thoracic vertebral interspaces, which is typical practice for patients undergoing lower abdominal surgery. However, the placement of epidural catheters in such proximity to the lumbar spinal segments, which provide motor innervation to the lower extremities, could increase the risk of motor block when compared with a midthoracic approach, especially in the high-volume group [25]. Nevertheless, lower limb motor block was consistently low in all patients, and we did not observe any difference between the 2 groups.

Although there was no statistically significant difference in hemodynamic parameters, patients in the 5 mg/mL group had a slightly lower BP without any hypotensive episodes. As previously mentioned, Liu et al [14], when using PCEA after lower abdominal surgery, observed that a lower concentration of a similar amount of epidural ropivacaine/fentanyl provides equal analgesia with less motor blockade when compared with higher concentrations of the local anesthetic. Epidural catheters were placed at the T12 to L2 interspace. Placement of catheters in proximity to lumbar spinal segments increases the risk of motor block when compared with a more cephalad approach [26]. Whiteside et al [15] using the same association of drugs after gynecologic surgery showed that a low-concentration/high-volume PCEA appears satisfactory to treat postoperative pain and reduce the dose of the drugs used in comparison with a low volume/high concentration. Our study differs considerably because we did not add any epidural opioids to focus solely on the local anesthetic action. Addition of a high volume of fentanyl to the local anesthetic could produce a more extensive sensory block as a result of greater anatomic spread and interaction with opioid receptors [9,27]. Opioids

also limit the regression of postoperative analgesia observed with local anesthetics alone and improve the quality of pain relief [28,29]. This fact makes a comparison with our results difficult.

The most important limitation related to our study design is that our patients received multimodal analgesia, which might have masked slight differences in the intensity of rest pain between the 2 groups. Nevertheless, as stated by Kehlet and Holte [30], the best quality of postoperative analgesia is achieved by systemic analgesics combined with an epidural approach. We routinely use this analgesic regimen, and we conducted our study in a clinical setting. Further studies should also examine the quality of analgesia with other infusion rate modalities (ie, supplemental night-time infusion in PCEA, as proposed by Komatsu et al [31]).

It should be noted that the plain 5 mg/mL levobupivacaine solution is ready to use. Thus, the risk of administration errors decreases, as well as the nursing time and pharmacy preparation costs.

In conclusion, the 2 concentrations of levobupivacaine (5 and 1.5 mg/mL) given as a 5-mg-bolus dose PCEA induce similar quality of postoperative analgesia without any difference in the frequency of side effects.

References

[1] Scott DB, McClure JH, Giasi RM, Seo J, Covino BG. Effects of concentration of local anaesthetic drugs in extradural block. Br J Anaesth 1980;52:1033-7.

[2] Duggan J, Bowler GM, McClure JH, Wildsmith JA. Extradural block with bupivacaine: influence of dose, volume, concentration and patient characteristics. Br J Anaesth 1988;61:324-31.

[3] Galindo A, Benavides O, De Munos SO, Bonila O, Pena R. Comparison of anesthetic solutions used in lumbar and caudal peridural anesthesia. Anesth Analg 1978;57:175-9.

[4] Liu SS, Ware PD, Rajendram S. Effects of concentration and volume of 2-chloroprocaine on epidural anesthesia in volunteers. Anesthesiology 1997;86:1288-93.

[5] Sakura S, Sumi M, Kushizaki H, Saito Y, Kosaka Y. Concentration of lidocaine affects intensity of sensory block during lumbar epidural anesthesia. Anesth Analg 1999;88:123-7.

[6] Bromage PR. Mechanism of action of extradural analgesia. Br J Anaesth 1975;47(Suppl):199-211.

[7] Pierce ET, Denson DD, Essell SK, Santos DJ, Edstrom HH. The effect of rate of infusion on continuous epidural analgesia for labor and delivery. Reg Anesth 1989;14:31-4.

[8] Renck H, Edström H, Kinnberger B, Brandt G. Thoracic epidural analgesia-II: prolongation in the early postoperative period by continuous injection of 1.0% bupivacaine. Acta Anaesthesiol Scand 1976;20:47-56.

[9] Laveaux MM, Hasenbos MA, Harbers JB, Liem T. Thoracic epidural bupivacaine plus sufentanil: high concentration/low volume versus low concentration/high volume. Reg Anesth 1993;18:39-43.

[10] Mogensen T, Scott NB, Hjortso NC, Lund C, Kehlet H. The influence of volume and concentration of bupivacaine on regression of analgesia during continuous postoperative epidural infusion. Reg Anesth 1988;13:122-5.

[11] Snijdelaar DG, Hasenbos MA, van Egmond J, Wolff AP, Liem TH. High thoracic epidural sufentanil with bupivacaine: continuous infusion of high volume versus low volume. Anesth Analg 1994;78:490-4.

[12] Dernedde M, Stadler M, Bardiau F, Boogaerts JG. Continuous epidural infusion of large concentration/small volume versus small concentration/large volume of levobupivacaine for postoperative analgesia. Anesth Analg 2003;96:796-801.

[13] Dernedde M, Stadler M, Bardiau F, Boogaerts JG. Comparison of different concentrations of levobupivacaine for post-operative epidural analgesia. Acta Anaesthesiol Scand 2003;47:884-90.

[14] Liu SS, Moore JM, Luo AM, Trautman WJ, Carpenter RL. Comparison of three solutions of ropivacaine/fentanyl for postoperative patient controlled epidural analgesia. Anesthesiology 1999;90:727-33.

[15] Whiteside R, Jones D, Bignell S, Lang C, Lo SK. Epidural ropivacaine with fentanyl following major gynaecological surgery: the effect of volume and concentration on pain relief and motor impairment. Br J Anaesth 2000;84:720-4.

[16] Boogaerts JG, Vanacker E, Seidel L, Albert A, Bardiau FM. Assessment of postoperative nausea using a visual analogue scale. Acta Anaesthesiol Scand 2000;44:470-4.

[17] Murdoch JA, Dickson UK, Wilson PA, Berman JS, Gad-Elrab RR, Scott NB. The efficacy and safety of three concentrations of levobupivacaine administered as a continuous epidural infusion in patients undergoing orthopedic surgery. Anesth Analg 2002;94:438-44.

[18] Daoud Z, Collis RE, Ateleanu B, Mapleson WW. Evaluation of S_1 motor block to determine a safe, reliable test dose for epidural analgesia. Br J Anaesth 2002;89:442-5.

[19] Boogaerts JG, Bardiau FM, Seidel L, Albert A, Ickx BE. Tropisetron in the prevention of postoperative nausea and vomiting. J Clin Anesth 2000;12:402-8.

[20] Bardiau FM, Braeckman MM, Seidel L, Albert A, Boogaerts JG. Effectiveness of an acute pain service inception in a general hospital. J Clin Anesth 1999;11:583-9.

[21] Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand Suppl 1965;16:55-69.

[22] Cashman JN, Dolin SJ. Respiratory and haemodynamic effects of acute postoperative pain management: evidence from published data. Br J Anaesth 2004;93:212-23.

[23] Gottschalk A, Freitag M, Burmeister MA, Becker C, Horn EP, Standl T. Patient-controlled thoracic epidural infusion with ropivacaine 0.375% provides comparable pain relief as bupivacaine 0.125% plus sufentanil after major abdominal gynecologic tumor surgery. Reg Anesth Pain Med 2002;27:367-73.

[24] Green R, Dawkins M. Post-operative analgesia. The use of continuous drip epidural block. Anaesthesia 1966;21:372-8.

[25] Kaneko T, Iwama H. The association between injected volume of local anesthetic and spread of epidural anesthesia: a hypothesis. Reg Anesth Pain Med 1999;24:153-7.

[26] Liu SS, Allen HW, Olsson GL. Patient-controlled epidural analgesia with bupivacaine and fentanyl on hospital wards: prospective experience with 1,030 surgical patients. Anesthesiology 1998;88:688-95.

[27] Scott DA, Chamley DM, Mooney PH, Deam RK, Mark AH, Hägglöf B. Epidural ropivacaine infusion for postoperative analgesia after major lower abdominal surgery—a dose finding study. Anesth Analg 1995;81:982-6.

[28] Jorgensen H, Wetterslev J, Moiniche S, Dahl JB. Epidural local anaesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery. Cochrane Database Syst Rev 2000;(4):CD001893.

[29] Pouzeratte Y, Delay JM, Brunat G, et al. Patient-controlled epidural analgesia after abdominal surgery: ropivacaine versus bupivacaine. Anesth Analg 2001;93:1587-92.

[30] Kehlet H, Holte K. Effect of postoperative analgesia on surgical outcome. Br J Anaesth 2001;87:62-72.

[31] Komatsu H, Matsumoto S, Mitsuhata H. Comparison of patient-controlled epidural analgesia with and without night-time infusion following gastrectomy. Br J Anaesth 2001;87:633-5.