Comparative study of continuous extrapleural intercostal nerve block and lumbar epidural morphine in post-thoracotomy pain

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Objectives: To compare the efficacy of continuous extrapleural intercostal nerve block with bupivacaine 0.5% in 1:200 000 epinephrine and continuous lumbar epidural block with morphine in controlling post-thoracotomy pain and to measure serum bupivacaine concentrations during extrapleural infusion.

Design: A prospective, randomized, controlled trial.

Setting: St. Joseph's Hospital, Hamilton, Ont., a tertiary care teaching centre.

Patients: Sixty-one patients booked for elective thoracotomy were randomized by sealed envelope to two groups.

Interventions: Group A received a continuous extrapleural intercostal nerve block with bupivacaine 0.5% in 1:200 000 epinephrine as a bolus of 0.3 mL/kg followed by an infusion of 0.1 mL/kg every hour for 72 hours. Group B received a continuous lumbar epidural block with morphine as a bolus of 70 g/kg followed by an infusion of 7 g/kg every hour for 72 hours.

Main outcome measures: Pain was assessed by a linear visual analogue scale (VAS) pain score. The cumulative amount of "rescue" intravenous morphine used, and serum bupivacaine concentrations were measured as secondary outcomes.

Results: Pain control was the same in both groups as assessed by linear VAS score ($p = 0.33$). The cumulative dose of intravenous morphine for supplemental analgesia was statistically significant between the groups: group A patients used more morphine than group B ($p < 0.05$). Accumulation of serum bupivacaine was present with no clinical toxicity.

Conclusions: There is no significant difference in the degree of post-thoracotomy pain control measured by the VAS score when analgesia is provided by continuous extrapleural intercostal nerve block with bupivacaine 0.5% in 1:200 000 epinephrine or lumbar epidural block with morphine. Larger amounts of rescue analgesia were used by patients in the continuous extrapleural group with bupivacaine than those in the continuous lumbar epidural block with morphine. Serum bupivacaine concentrations rise without clinical toxicity.

Objectifs : Comparer l'efficacité du blocage continu du nerf intercostal extrapleural avec de la bupivacaïne à 0,5 % dans de l'épinéphrine à 1:200 000 à celle du blocage continu par épidurale lombaire avec de la morphine pour contrôler la douleur consécutive à une thoracotomie et mesurer les taux de bupivacaïne dans le sérum au cours d'une infusion extrapeurale.

Conception : Étude contrôlée randomisée prospective.

Contexte : Hôpital St. Joseph's, Hamilton (Ontario), centre d'enseignement de soins tertiaires.

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PATIENTS : Soixante et un patients devant subir une thoracotomie élective ont été répartis au hasard entre des groupes par enveloppe scellée.

INTERVENTIONS : Les sujets du groupe A ont reçu un blocage continu du nerf intercostal extrapleural à la bupivacaïne à 0,5 % dans de l'épinéphrine à 1:200 000 sous forme de bol de 0,3 mL/kg suivi d'une infusion de 0,1 ml/kg/heure pendant 72 heures. Les sujets du groupe B ont reçu un blocage continu par épidurale lombaire avec de la morphine sous forme de bol de 70 g/kg suivi d'une infusion de 7 g/kg/heure pendant 72 heures.

PRINCIPALES MESURES DES RÉSULTATS : On a évalué la douleur par cotation des douleurs selon l'échelle analogique visuelle linéaire. On a mesuré comme résultats secondaires la quantité cumulative de morphine intraveineuse «de secours» utilisée et les concentrations de bupivacaïne dans le sérum.

RÉSULTATS : Le contrôle de la douleur a été le même chez les sujets des deux groupes selon la cotation des douleurs en fonction de l'échelle analogique visuelle linéaire ($p = 0,33$). La dose cumulative de morphine intraveineuse comme analgésique supplémentaire a été significative sur le plan statistique entre les groupes : les patients du groupe A ont utilisé plus de morphine que ceux du groupe B ($p < 0,05$). Il y a eu accumulation de bupivacaïne dans le sérum sans toxicité clinique.

CONCLUSIONS : La qualité du contrôle de la douleur consécutive à une thoracotomie mesurée par cotation des douleurs selon l'échelle analogique visuelle ne présente aucune différence lorsque l'analgésie est assurée par blocage continu du nerf intercostal extrapleural avec de la bupivacaïne à 0,5 % dans de l'épinéphrine à 1:200 000 ou par blocage par épidurale lombaire avec de la morphine. On a utilisé des volumes plus importants d'analgésiques de secours chez les sujets qui ont subi un blocage continu du nerf extrapeural avec de la bupivacaïne que chez ceux qui ont subi un blocage continu par épidurale lombaire avec de la morphine. Il y a élévation des concentrations de bupivacaïne dans le sérum sans toxicité clinique.

Thoracotomy, for lung, mediastinal and esophageal diseases, is one of the most painful surgical procedures, having a significant negative impact on pulmonary function, postoperative morbidity and mortality.[1,2] Many techniques have been developed to control postoperative pain; of these, narcotic delivered epidurally remains the most favoured.[3–5] Intercostal extrapleural nerve block is a technique proposed as an alternative method of pain control after thoracotomy. It has been used as intermittent boluses and as a continuous infusion.[6–9] The aim of this study, a randomized and controlled trial, was to compare the effectiveness of continuous extrapleural intercostal nerve block with bupivacaine 0.5% in 1:200 000 epinephrine and continuous lumbar epidural infusion with morphine in the management of postoperative thoracotomy pain.

Patients and methods

After approval by the hospital ethics committee and when written consent had been obtained, 61 adults (36 men, 25 women) booked for elective thoracotomy were recruited. Exclusion criteria included the patient's refusal, contraindications to epidural technique and allergy to morphine or local anesthetics. Patients were given instructions in the use of the intravenous patient-controlled analgesia pump, and in filling out a linear visual analogue scale (VAS), graduated from 0 (no pain) to 10 (worst pain ever experienced).

Randomization was by a sealed envelope, allocating the patients to receive postoperatively either extrapleural intercostal bupivacaine (group A) or lumbar epidural morphine (group B). Group A comprised 17 men and 14 women (mean age 61 years) and group B comprised 30 men and 11 women (mean age 62 years).

No preoperative anxiolytic agent was given. Before general anesthesia was induced, patients in group B had an epidural catheter inserted at L2–4, and its safe placement confirmed with 4 mL of a 0.25% bupivacaine solution with 1:200 000 epinephrine. Subsequently, a bolus of epidural morphine 70 g/kg was given, followed by an infusion of 7 g/kg each hour for 3 days at a concentration of 0.1 mg/mL. General anesthesia consisted of a balanced technique: oxygen, nitrous oxide, nondepolarizing muscle relaxants, inhalation agents and narcotic (alfentanil) limited to a maximum dose of 10 g/kg. Before chest closure of patients in group A, the parietal pleura was elevated off the chest wall along the paravertebral space for 2 to 3 cm cephalad to the level of the intercostal incision and 2 to 3 cm caudad to that incision. An epidural catheter was placed in this pocket through a disposable 17 Tuohy needle inserted several intercostal spaces below the incision, and the tip of the catheter was placed in the upper end of the pocket. Whenever possible one suture was used to tack the lateral edge of the pleura down to adjacent intercostal muscle. When the thoracotomy was closed, a bolus of 0.3 mL/kg of 0.5% bupivacaine with 1:200 000 epinephrine was given through the catheter, and a continuous infusion of 0.1 mL/kg per hour was started for 3 days. This dose was determined from previous studies by Sabanathan and colleagues[10] and Richardson and colleagues.[11]

At the end of the procedure, all pa-

tients were extubated and taken to the recovery room. Rescue analgesia with intravenous morphine 2 mg every 10 minutes as needed was made available to the patient through an intravenous PCA pump (Graceby 3330; Graceby Medical, Watford, Herts., UK).

Postoperative measurements

Postoperative pain was assessed by having the patient mark the degree of pain on a linear visual analogue scale (VAS) at 2-hour intervals, beginning in the recovery room, for 10 hours, and subsequently at 4-hour intervals for 72 hours. Pain assessment was independent of the patient's activity such as coughing or chest physiotherapy. Supplemental intravenous morphine needed for control of breakthrough pain was recorded by the intravenous PCA pump.

In 10 patients of group A, serum bupivacaine levels were measured daily by column liquid chromatography using solid phase extraction to determine the degree of bupivacaine accumulation and the possibility of bupivacaine toxicity. All patients were monitored by measurement of the respiratory rate, sedation level, blood pressure, heart rate and rhythm, and continuous pulse oximeter hourly for 24 hours, then every 4 hours for 72 hours.[12]

Statistical analysis

Mean pain scores and the cumulative dose of rescue analgesia used during the first 70 hours postoperatively were compared by the two-tailed *t*-test for unpaired data in both groups. A probability value less than 0.05 was chosen to indicate statistical significance.

Results

Forty-nine of 61 patients completed the study. Ninety percent of patients had carcinoma of the lung. Lobectomy was carried out in 83% of group A patients and 72% of group B patients. Pneumonectomy was performed in 12% of group A patients and 16% of group B patients. The two groups of patients were similar in age, sex and lung function measurements. Mean weight was 74.8 kg in group A and 68.0 kg in group B ($p = 0.13$). Five patients in group B (epidural morphine) were excluded for the following reasons: supraventricular tachycardia with hemodynamic instability, requiring admission to the intensive care unit (1); postoperative confusion (1); severe postoperative drowsiness, requiring discontinuation of epidural morphine (1); accidental removal of the epidural catheter by the surgeon (1); inadequate filling of VAS score because of poor compliance (1). Seven patients in group A (extrapleural bupivacaine) were excluded for the following reasons: intraoperative cardiogenic shock (1), extensive parietal invasion by a lung tumour (2), accidental removal of the extrapleural catheter (1), self-migration of the extrapleural catheter out of the chest (1), incomplete filling of the VAS score because of poor compliance (2).

Comparison of pain scores in the two groups showed no statistically significant difference ($p = 0.33$) (Fig. 1). The amount of intravenous morphine required by patients, measured at 2-hour intervals for the first 10 hours and at 4-hour intervals for 72 hours showed no significant difference (Fig. 2), but the cumulative amount of morphine used for rescue analgesia was greater in the extrapleural bupivacaine group than in the lumbar epidural morphine group, becoming statistically significant ($p < 0.05$) at 14 hours postoperatively (Fig. 3). Serum bupivacaine concentrations measured in 10 patients of group A showed a continuous increase, with values reaching 6 μg/mL without clin-

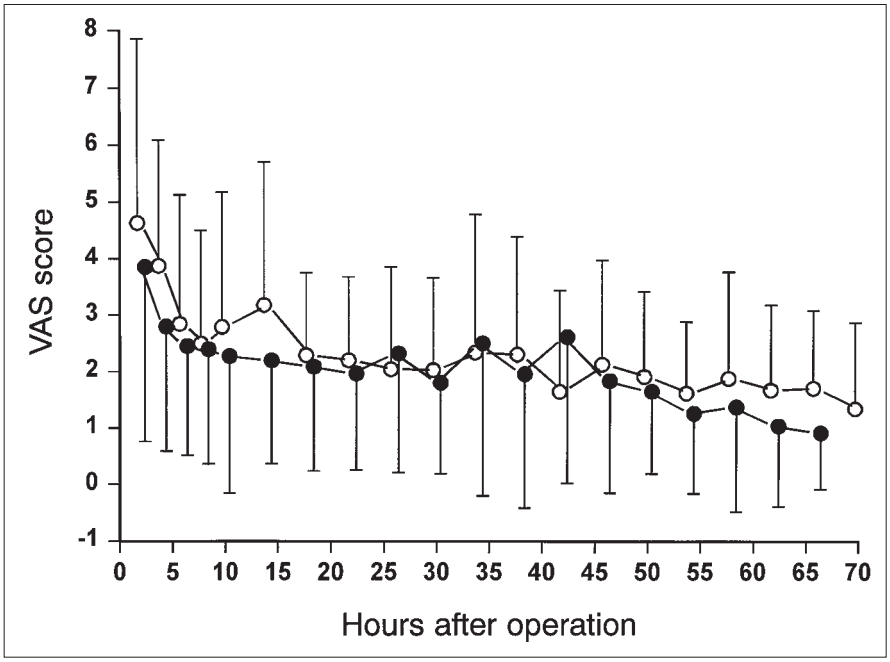

FIG. 1. Mean (and 1 standard deviation) assessment of post-thoracotomy pain score on a linear visual analogue scale (VAS) by patients randomized into 2 groups. Group A (white circles) received extrapleural bupivacaine 0.5% in 1:200 000 epinephrine and group B (black circles) received epidural morphine.

ical signs of toxicity (Fig. 4).

None of the patients in the study had complications arising from the infusion of extrapleural bupivacaine. Two patients (6%) in the epidural group had late respiratory depression requiring naloxone administration. In the extrapleural group, 1 patient suffered atrial fibrillation 8 hours postoperatively and another had congestive heart failure on the second postoperative day. Both cases were related to intrinsic cardiac diseases, and were treated without discontinuing the bupivacaine infusion.

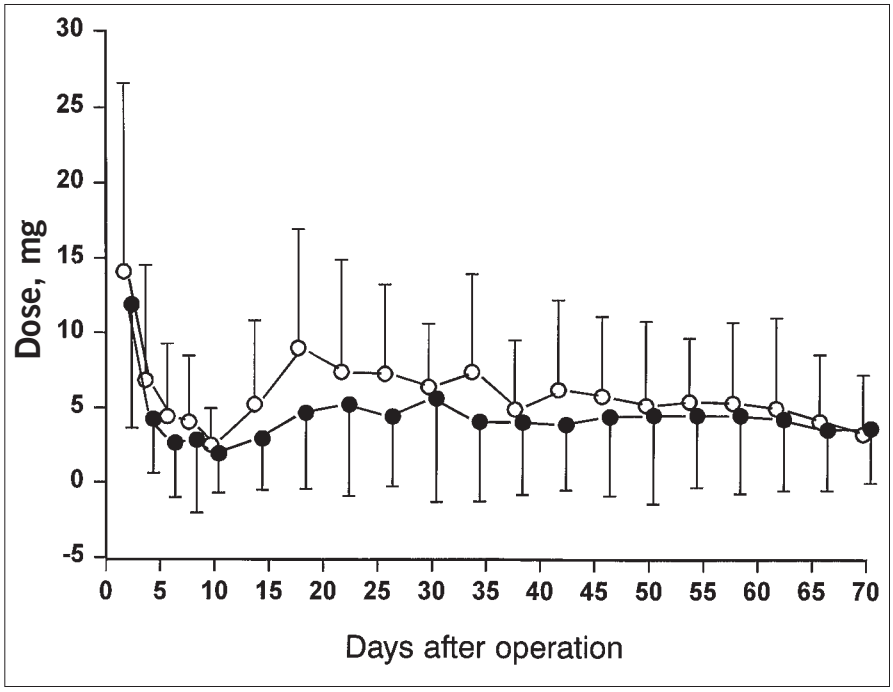

FIG. 2. The mean (and 1 standard deviation) amounts of intravenous morphine required by patients in both groups for rescue analgesia measured at 2-hour intervals for the first 10 hours postoperatively and at 4-hour intervals for 72 hours. Group A = white circles, group B = black circles.

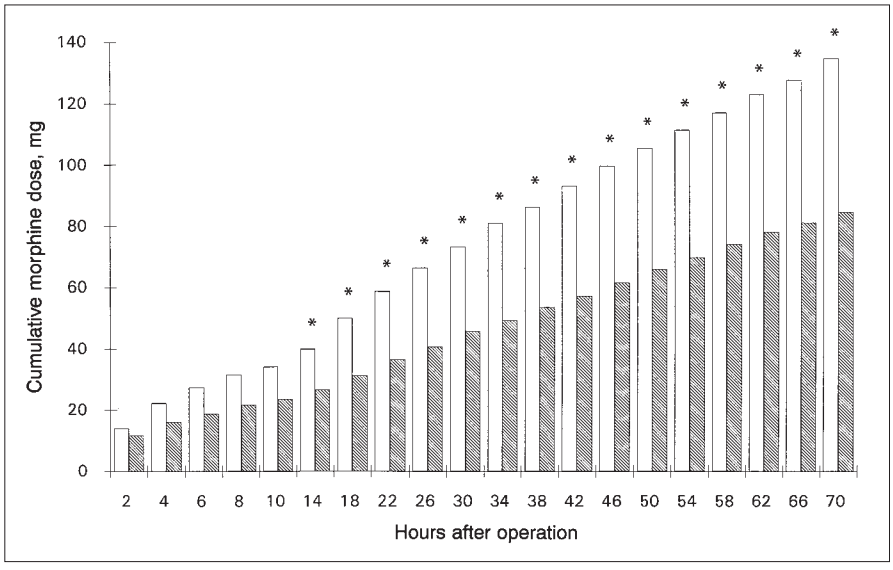

FIG. 3. Comparison of cumulative morphine dose used by patients for rescue analgesia in group A (white bars) and group B (shaded bars). * = $p < 0.05$.

Discussion

The purpose of this study was to compare the effectiveness in controlling post-thoracotomy pain of two different techniques: continuous extrapleural intercostal nerve block with bupivacaine and lumbar epidural nerve block with morphine. The beneficial effect of lumbar and thoracic epidural morphine in postoperative pain management is well described.[3,13,14] Studies have compared the effect of thoracic versus lumbar epidural catheter placement in post-thoracotomy pain management and have found no difference in pain score with the use of epidural morphine,[15] sufentanil,[16] bupivacaine and fentanyl,[4] or fentanyl.[5] However, a decrease in the total amount of narcotic used in the thoracic group was observed. Compared with intravenous administration of morphine, extrapleural infusion of bupivacaine is effective in controlling post-thoracotomy pain.[6,17] Richardson and colleagues[11] reported that the level of post-thoracotomy pain control achieved with extrapleural infusion of bupivacaine was comparable to that with continuous lumbar epidural morphine. However, the amount of epi-

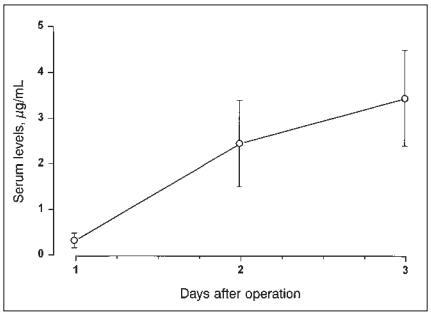

FIG. 4. Mean (and 1 standard deviation) serum bupivacaine levels in 9 patients in group A, measured each day for 3 days postoperatively.

dural morphine used in their study was considered too small, and serum bupivacaine concentrations were not assessed. Furthermore, the cumulative amount of rescue analgesia used was not reported. The advantage of local anesthetics, when used extrapleurally, would be to provide segmental analgesia without the side effects caused by its epidural administration, such as sympathetic blockade, hypotension, urinary bladder retention and muscle weakness.

We found no significant difference between the groups when pain was assessed by a linear VAS pain score, confirming the findings of Richardson and colleagues. The amount of intravenous morphine required for rescue analgesia measured at fixed intervals showed no significant difference (Fig. 2). However, the cumulative amount of intravenous morphine used was greater in the extrapleural bupivacaine group (group A) than in the lumbar epidural morphine group (group B) with statistical significance beginning at 14 hours postoperatively (Fig. 3). This increase in supplemental analgesia may be due to less postoperative pain control obtained with extrapleural bupivacaine or to an increase in activity such as chest physiotherapy and mobilization.

Serum bupivacaine concentrations measured daily during the first 3 days rise continuously without clinical signs of serum bupivacaine toxicity. It reached a value of 6 μg/mL in 1 patient. The pharmacokinetics of bupivacaine during extrapleural infusion are not fully known. The possible explanation for this elevation in bupivacaine concentration without signs of toxicity may lie in the protection acquired by the rise of serum α_1-acid glycoprotein with surgery, thus resulting in increased bupivacaine binding.[18,19]

Despite the evidence that pain control achieved by either intravenous or epidural administration of narcotics does not differ in quality, epidural analgesia, in particular thoracic epidural, is widely favoured in the management of post-thoracotomy pain because of the reduced quantity of supplemental analgesia required.[20–22] Lumbar epidural morphine analgesia is an accepted alternative when thoracic epidural analgesia cannot be achieved. Insertion of the epidural catheter may be technically challenging and associated with complications.[23] The central administration of morphine and other narcotics is not devoid of side effects that require increased nursing surveillance and treatment. These include: early and late respiratory depression, nausea, vomiting, pruritus and urinary retention.[24] The lack of side effects and the absence of complications in patients in our extrapleural group may be of benefit to the postoperative nursing care of those patients who require close monitoring when lumbar or thoracic epidural analgesia is being administered.

Positioning of the extrapleural intercostal catheter is done under direct vision during thoracotomy. Possible contraindications to this technique include parietal tumour invasion, which was present in 2 of our patients (8%) and may not be detected preoperatively. Shredding of the parietal pleura during its elevation may decrease the effectiveness of extrapleural catheterization. This did not happen during our study. Leakage can occur at the insertion site of the extrapleural catheter during administration of the initial local anesthetic bolus. Theoretically, subarachnoid block secondary to extrapleural catheter migration can occur. Infection at the site of catheter placement should also be considered a contraindication.

Conclusions

There is no difference in the quality of post-thoracotomy pain control, as measured by the VAS pain score, when analgesia is provided by extrapleural intercostal nerve block with continuous infusion of bupivacaine 0.5% in 1:200 000 epinephrine or by lumbar epidural block with continuous infusion of morphine. However, the large amounts of rescue analgesia used by patients in both groups signifies that complete analgesia is not achievable with either technique. Patients in the extrapleural bupivacaine group made significantly greater use of rescue intravenous morphine. No side effects were observed in the patients who received continuous extrapleural intercostal bupivacaine infusion, despite high serum bupivacaine levels measured. The absence of any clinical manifestations of bupivacaine toxicity may be due to our small subgroup of 10 patients or to the limited duration of the infusion (3 days). Further investigations are warranted to determine the saturation point of α_1-acid glycoprotein and the pharmacoknetics of bupivacaine when used extrapleurally.

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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* 1974; 128:376-82.

2. Loan WB, Morrison JD. The incidence and severity of postoperative pain. *Br J Anaesth* 1967;39:695-8.

3. Shulman M, Sandler AN, Bradley JW, Young PS, Brebner J. Post-

thoracotomy pain and pulmonary function following epidural and systemic morphine. *Anaesthesiology* 1984;61:569-75.

4. Hurford WE, Dutton RP, Alfille PH, Clement D, Wilson RS. Comparison of thoracic and lumbar epidural infusions of bupivacaine and fentanyl for post-thoracotomy analgesia. *J Cardiothorac Vasc Anesth* 1993;7(5):521-5.

5. Sawchuk CW, Ong B, Unruh HW, Horan TA, Greengrass R. Thoracic versus lumbar epidural fentanyl for post-thoracotomy pain. *Ann Thorac Surg* 1993;55(6):1472-6.

6. Chan VW, Chung F, Cheng DC, Seyone C, Chung A, Kirby TJ. Analgesic and pulmonary effects of continuous intercostal nerve block following thoracotomy [see comment]. *Can J Anaesth* 1991;38(6):733-9. Comment in:*Can J Anaesth* 1992;39 (5 Pt 1):519-20.

7. Mozell EJ, Sabanathan S, Mearns AJ, Bickford-Smith PJ, Majid MR, et al. Continuous extrapleural intercostal nerve block after pleurectomy. *Thorax* 1991;46(1):21-4.

8. Eng J, Sabanathan S. Site of action of continuous intercostal nerve block. *Ann Thorac Surg* 1991;51:387-9.

9. Berrisford RG, Sabanathan SS. Direct access to the paravertebral space at thoracotomy [letter]. *Ann Thorac Surg* 1990;49(5):854.

10. Sabanathan S, Mearns AJ, Bickford Smith PJ, Eng J, Berrisford RG, Bibby SR, et al. Efficacy of continuous extrapleural intercostal nerve block on post-thoracotomy pain and pulmonary mechanics [see comment]. *Br J Surg* 1990;77(2):221-5. Comment in: *Br J Surg* 1990;77(11):1314.

11. Richardson J, Sabanathan S, Eng J, Mearns AJ, Rogers C, Evans CS, et al. Continuous intercostal nerve block versus epidural morphine for postthoracotomy analgesia. *Ann Thorac Surg* 1993;55(2):377-80.

12. Ready LB, Oden R, Chadwick HS, Benedetti C, Rooke GA, Caplan R, et al. Development of an anesthesiology-based postoperative pain management service. *Anesthesiology* 1988;68(1): 100-6.

13. James BC, Kolberg HL, Iwen GW, Gellatly TA. Epidural analgesia for post-thoracotomy patients. *J Thorac Cardiovasc Surg* 1981;82:898-903.

14. Pelton JJ, Fish DJ, Keller SM. Epidural narcotic analgesia after thoracotomy. *South Med J* 1993;86(10): 1106-9.

15. Grant GJ, Zakowski M, Ramanathan S, Boyd A, Turndorf H. Thoracic versus lumbar administration of epidural morphine for postoperative analgesia after thoracotomy. *Reg Anesth* 1993;18(6):351-5.

16. Swenson JD, Hullander RM, Bready RJ, Leivers D. A comparison of patient controlled epidural analgesia with sufentanil by the lumbar versus thoracic route after thoracotomy. *Anesth Analg* 1994;78(2):215-8.

17. Deneuville M, Bisserier A, Regnard JF, Chevalier M, Levasseur P, Herve P, et al. Continuous intercostal analgesia with 0.5% bupivacaine after thoracotomy: a randomized study. *Ann Thorac Surg* 1993;55(2):381-5.

18. Rem J, Saxtry-Nielsen O, Brabdt MR, Kehlet H. Influence of epidural analgesia on postoperative changes in various acute-phase proteins [abstract]. In Rügheimer E, Wawersik J, Zindler M, editors. *Abstracts of the 7th World Congress on Anaesthesia in Hamburg*. Princeton (NJ): Excerpta Medica; 1980. p. 374.

19. Denson DD, Coyle DE, Thompson GA, Santos D, Turner PA, Myers JA, et al. Bupivacaine protein binding in the term parturient: effects of lactic acidosis. *Clin Pharmacol Ther* 1984; 35(5):702-9.

20. Ellis DJ, Millar WL, Reisner LS. A randomized double-blind comparison of epidural versus intravenous fentanyl infusion for analgesia after cesarean section [see comment]. *Anesthesiology* 1990;72(2):981-6. Comment in: *Anesthesiology* 1991; 74(4):795.

21. Glass PS, Estok P, Ginsberg B, Goldberg JS, Sladen RN. Use of patient-controlled analgesia to compare the efficacy of epidural to intravenous fentanyl administration [see comments]. *Anesth Analg* 1992;74(3): 345-51. Comments in: *Anesth Analg* 1992;74(5):865-7; 1993;76(5):1163-4.

22. Loper KA, Ready LB, Downey M, Sandler AN, Nessly M, Rapp S, et al. Epidural and intravenous fentanyl infusions are clinically equivalent after knee surgery [see comment]. *Anesth Analg* 1990;70(1):72-5. Comments in: *Anesth Analg* 1990;71(4):445.

23. Cousins MJ, Bridenbaugh PO, editors. *Neural blockade in clinical anesthesia and management of pain*. 2nd ed. Philadelphia: J.B. Lippincott and Company; 1988.

24. Gustafson LL, Schildt B, Jacobson K. Adverse effects of extradural and intrathecal opiates: reports of a nationwide survey in Sweden. *Br J Anaesth* 1982;54:479-86.