Analgesia and Respiratory Function Following Intrapleural Bupivacaine after Cholecystectomy

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Analgesia and pulmonary function following intrapleural bupivacaine were compared with those following intramuscular pethidine in thirty-four patients after cholecystectomy. The patients were randomly allocated to two groups of seventeen patients each to receive either intrapleural bupivacaine or intramuscular pethidine. The positions of seventeen intrapleural catheters inserted were confirmed by chest radiography. Two out of seventeen catheters were found to be located in the extrapleural space. It was also recognized by fluoroscopy that phrenic nerve palsy did not develop on patients given intrapleural bupivacaine. The subjective quality of analgesia following intrapleural bupivacaine was significantly better than that following intramuscular pethidine. The mean duration of analgesia obtained after each injection of bupivacaine was 4.68 hr (range 3.5 ~ 6.1 hr). Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV 1), which decreased markedly in the postoperative period improved significantly after being given bupivacaine or pethidine. But there was no significant difference in the improvement of FVC and FEV 1, between both groups in spite of the higher percentage of pain relief in the intrapleural bupivacaine group. All respiratory function tests studied thirty days after surgery were not significantly different when compared with those before surgery. (Key word: intrapleural bupivacaine, pain relief)

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Postoperative pain relief is still far from ideal in most institutions. Inadequate pain relief after upper abdominal surgery increases the incidence of pulmonary complications as a result of poor coughing and shallow breathing.

Postoperative pain in this institution has been usually treated with intramuscular narcotics. Other methods for postoperative pain relief have been advocated, such as epidural analgesia[1] and intercostal nerve blocks[2,3]. Recently intrapleural administration of bupivacaine to achieve continuous intercostal nerve block has been described[4–6]. However, a number of practical questions remain unanswered[7]; including the phrenic and splanchnic nerves may also be affected by local anaesthetics deposited in the pleural space.

We compared the quality of analgesia and pulmonary function after cholecystectomy following intrapleural bupivacaine with those obtained following intramuscular pethidine. In addition, radiographic study was performed on nine patients in the intrapleural catheter group to explore phrenic nerve palsy.

Patients and Methods

Thirty-four patients (ASA Class 1 and 2) scheduled for elective cholecystectomy via

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a subcostal incision were included in this study after informed consent was obtained. Patients were randomly allocated to two groups of 17 patients each to receive either intrapleural analgesia via a catheter or intermittent intramuscular pethidine in the postoperative period.

The patients were premedicated with pethidine (1 $mg \cdot kg^{-1}$) and atropine (0.6 mg). Anaesthesia was induced with 2.5% sodium thiopentone and the trachea was intubated with suxamethonium chloride. Anaesthesia was maintained with nitrous oxide, oxygen and isoflurane. Alcuronium was used for muscle relaxation, and pethidine was used intraoperatively at the discretion of the anaesthetist. All patients were operated on by the two nominated surgeons. All patients were free from any cardiopulmonary disease as judged by physical examination, preoperative ECG, chest x-ray and detailed respiratory function tests.

An epidural catheter was placed in the right pleural space of seventeen patients at the conclusion of surgery. The right arm of the patients, who were supine, were abducted to ninety degrees. The 4th rib was identified at the mid-axillary line. An 18 gauge Touhy needle attached to a saline-filled glass syringe was inserted until the shaft of the rib was contacted. The respirator was temporarily disconnected from the patient and the needle walked caudally until it was off the rib edge. The direction of the needle was inclined posteriorly and caudally, at an angle of about 70 degrees to the skin, to avoid passing directly beneath the rib edge. The bevel of the needle faced posteriorly during the insertion. Entry into the pleural space was identified by the "clicking" perforation of the parietal pleura and by the loss of resistance to injection of saline. An epidural catheter was then introduced 6 – 8 cm into the pleural space through the needle. Following a negative aspiration to exclude accidental puncture of the lung or a blood vessel, the catheter was fixed to the skin with a transparent dressing. A micropore filter (0.2 μm) was attached to the end of the catheter through which 20 ml of 0.5% bupivacaine with adrenaline (1:200,000) was injected over 2 min into the pleural space. General anaesthesia was then discontinued.

All seventeen patients with intrapleural catheters inserted had antero-posterior (AP) chest x-ray taken in the sitting position within two hours after the insertion of the catheter to exclude pneumothorax. To confirm the position of the intrapleural catheter, 5 ml of contrast medium (Omnipaque, Nyeguard and Co, Norway) was injected into the catheter. Nine randomly selected patients out of seventeen patients had fluoroscopy done to explore phrenic nerve palsy (three patients within two hours, three patients between twenty-four to thirty hours, three patients between forty-eight and fifty-two hours after catheter placement, respectively). Twenty ml of 0.5% bupivacaine with epinephrine (1:200,000) was injected into the catheter over the next forty-eight to sixty hours whenever the patients complained of pain while coughing. The injections were given with the patients lying supine by anaesthetists competent in carrying out cardiopulmonary resuscitation. The patients remained supine for twenty minutes after each injection. The remaining seventeen patients received intramuscular pethidine (1 $mg \cdot kg^{-1}$) every four hours for analgesia. The intensity of pain was assessed by the patient, using a visual linear analogue scale[8]. This scale consisted of a 100 mm line on which the patient represented the degree of pain he or she was experiencing by placing point somewhere between "no pain" and "the worst pain I have ever experienced." The pain assessment was made immediately before and 30 min after the administration of bupivacaine or pethidine on the first and second morning after surgery. To average and compare the amount of pain relief, we related the intensity of pain after administration of bupivacaine or pethidine to the amount of pain reported before analgesia for each patient.

$$\frac{\text{analogue line representing pain (mm) before analgesic} - \text{analogue line representing pain (mm) after analgesic}}{\text{analogue line representing pain before analgesic (mm)}} \times 100 = \text{percentage of pain relief}$$

Table 1. Physical and clinical characteristics of patients in two groups
IP = intrapleural, i.m. = intramuscular

Data	IP bupivacaine n=17	i.m. pethidine n=17
Sex (M/F)	6/11	7/10
Age (year)	51 ± 12	50 ± 8
Weight (kg)	58.8 ± 7.9	59.9 ± 9
Height (cm)	159.4 ± 8.5	160.8 ± 8.7
Smokers	5	6
FVC % predicted	93.76 ± 11.83	94.29 ± 12.79
FEV 1 % predicted	99.5 ± 14.8	102.46 ± 2.89
TLC % predicted	100.47 ± 10.98	92.87 ± 11.36
FRC % predicted	104.12 ± 27.91	95.78 ± 12.69
DLCO % predicted	107.38 ± 29.44	103.88 ± 20.5
KCO % predicted	119.18 ± 21.24	122.93 ± 19.93
CV % predicted	34.11 ± 30.66	44.18 ± 29.06
Pa_{O_2} (mmHg)	88.42 ± 17.62	82.78 ± 21.83
Pa_{CO_2} (mmHg)	41.04 ± 5.01	38.94 ± 6.04

Values are expressed as means ± SD

Comparison was made using only the percentage of pain relief (the above equation), which represent relative changes in pain relief with each patient serving as his or her own control[9].

Pulmonary Function Tests

All measurements were made in triplicates with the patient seated using the pulmonary function testing system, Chestac 25 (Japan). Spirometry was performed by standardised techniques using a dry rolling seal spirometer[10]; lung volumes such as functional residual capacity (FRC), total lung capacity (TLC) were estimated with the closed circuit dilution method[11], transfer factor (TCO) with a single breath method and closing volume (CV) with the single breath N2 method[12].

FEV 1 and FVC were measured the day before operation and repeated on the first, second, fifth and thirtieth post-operative days. Two sets of measurements were made on the first post-operative day immediately before and 30 min after intrapleural bupivacaine or intramuscular pethidine. FRC, TLC, TCO and CV were measured preoperatively and on the thirtieth postoperative day. Arterial blood gases were estimated before, one day and 30 days after operation.

Statistical analysis was performed using student's paired t-test for intra-group comparison and unpaired t-test for intergroup comparison. $P < 0.05$ indicated a statistical significance.

Results

The physical and clinical characteristics of the patients in the two groups were comparable as shown in table 1.

Radiographic Study of Intrapleural Catheters

Fluoroscopy showed that if the catheter was correctly placed in the pleural space, the injected contrast medium would fan out from the catheter tip and disappear rapidly (fig. 1).

In two patients, the injected contrast medium remained around the catheter tip (figs. 2, 4). The lateral chest films of the two patients showed extrapleural spread of the contrast medium (figs. 3, 5), causing the pleura to be lifted off a few adjacent ribs.

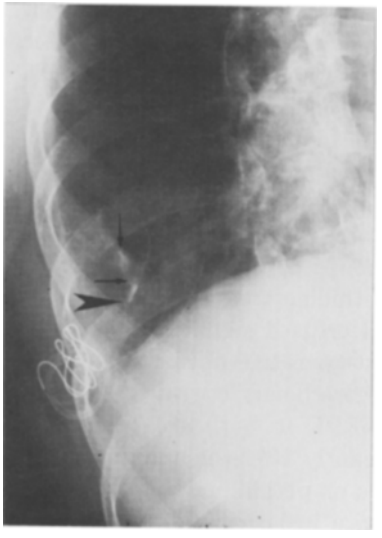

Fig. 1. Supine anteroposterior chest radiograph of a patient. The intrapleural catheter tip is indicated by arrowhead. Contrast medium can be seen to fan out from the catheter tip (small arrows).

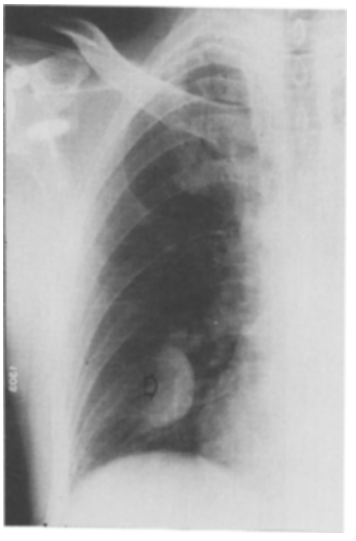

Fig. 2. An erect anteroposterior chest radiograph of a patient following intrapleural catheterization and injection of 5 ml of contrast medium. The catheter tip is surrounded by a discrete mass of contrast medium (arrow).

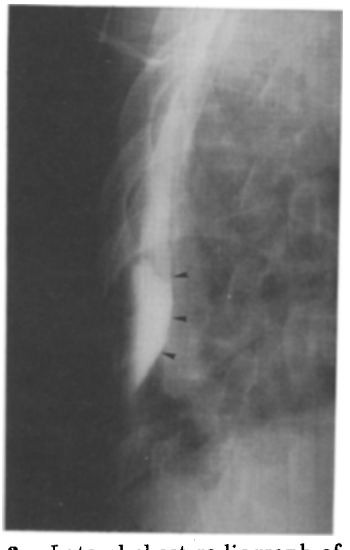

Fig. 3. Lateral chest radiograph of the same subject as in figure 2, showing that the contrast medium is in the extrapleural space separating the pleura from its attachments over a few adjacent ribs (arrowheads).

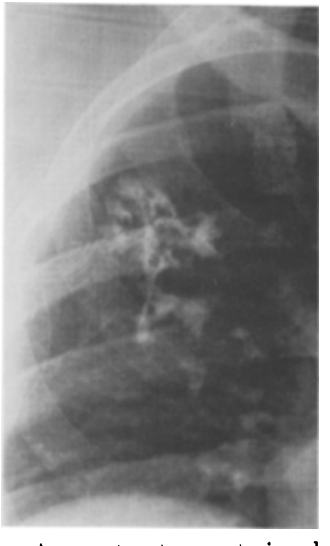

Fig. 4. An erect anteroposterior chest radiograph of a patient following intrapleural catheterization and injection of 5 ml of contrast medium. The catheter tip is surrounded by a discrete mass of contrast medium, the loculated appearance is due to air being inadvertently injected into the catheter together with the contrast medium.

Analgesia resulting from the extrapleural injection of local anaesthetic was obtained in these two patients. However, in order to standardise the results of this study, another catheter was successfully inserted into the pleural space.

Fluoroscopy was done on nine randomly selected patients to explore phrenic nerve

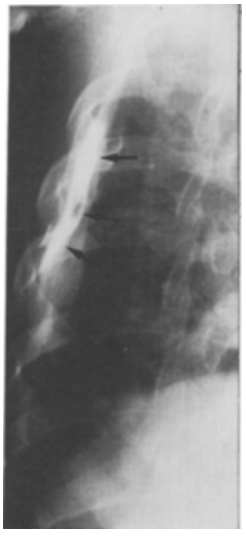

Fig. 5. Lateral chest radiograph of the same subject as in figure 4, showing the contrast medium is in the extrapleural space (arrowheads).

palsy by comparing the movement of the right diaphragm with that of the left. In all the nine patients studied, the right diaphragmatic movement was judged to be normal by two experienced radiologists.

Analgesia

None of the seventeen patients who received intrapleural bupivacaine required any pethidine supplement during the postoperative period. They also had the significantly higher percentage of pain relief as compared to the group of patients who received intramuscular pethidine (table 2). The mean duration of analgesia after each injection of bupivacaine was 4.68 hr with a range of 3.5 hr to 6.1 hr. The onset of analgesia was within 1 to 2 min after injection. Analgesia extended from T4 to T10 dermatomes in fourteen patients and from T5 to T11 dermatomes in three patients.

Respiratory Function Tests

Preoperative baseline pulmonary function tests were not significantly different in the two groups of patients (bupivacaine treated and pethidine treated) (table 1). FEV 1 and FVC decreased significantly in both groups, on post-operative days 1, 2 and 5 compared with those before operation (figs. 6, 7). FEV 1 and FVC in both groups of patients rose significantly after the administration of bupivacaine or pethidine. However, there was no difference in the magnitude of improvement in FEV 1 and FVC after pain relief with either methods (table 3). FEV 1, FVC and all other pulmonary function parameters returned to preoperative baseline levels by the thirtieth post-operative day in both groups (figs. 6, 7).

No significant hypoxaemia (less than 65 mmHg) developed in any of the patient studied.

Complications

Neither pneumothorax nor systemic reaction to bupivacaine was observed.

Discussion

The requirements of postoperative pain relief are as follows: complete pain relief, no detrimental systemic reaction, slight respiratory effects and adequate duration. We investigated intrapleural bupivacaine for postcholecystectomy pain relief with these require-

Table 2. Comparison between the percentage of pain relief obtained by intrapleural bupivacaine (IP) and that obtained by intramuscular (i.m.) pethidine

percentage of pain relief	IP bupivacaine mean ± SD	i.m. pethidine mean ± SD
Day 1 postop	90.43 ± 6.31%	44 ± 14.24%*
Day 2 postop	95.55 ± 6.14%	52.46 ± 13.33%*

*$P < 0.001$

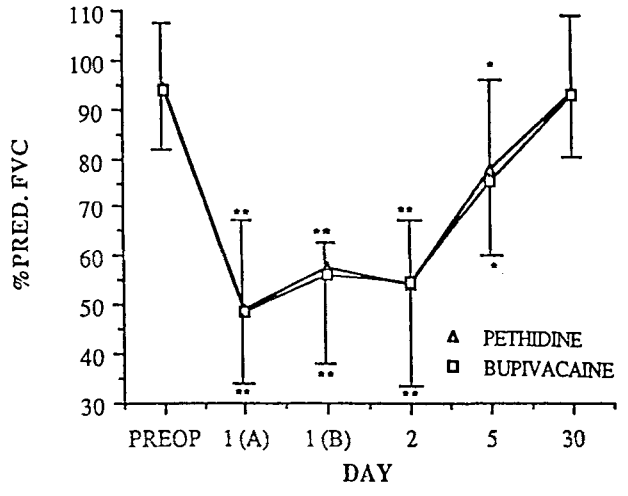

Fig. 6. Percentage predicted forced vital capacity before operation (PREOP), before pain relief (1(A)), after pain relief (1(B)), on days 2, 5, and 30 after operation. Values are means ± SD $^{**}P < 0.001$ $^{*}P < 0.05$.

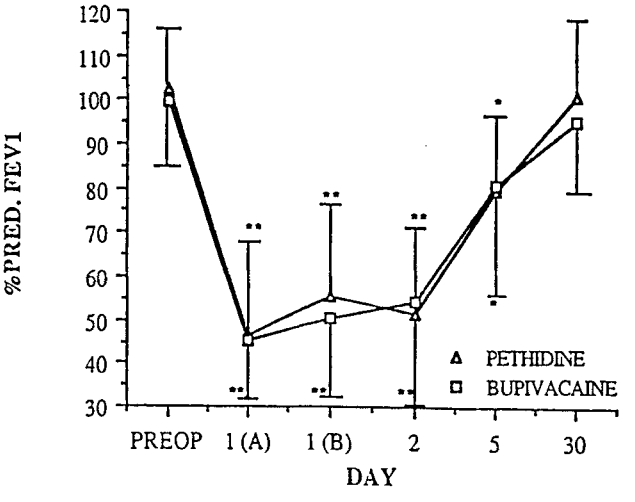

Fig. 7. Percentage predicted forced expiratory volume in one second before operation (PREOP), before pain relief (1(A)), after pain relief (1(B)), on days 2, 5, and 30 after operation. Values are means ± SD $^{**}P < 0.001$ $^{*}P < 0.05$.

Table 3. Improvement in respiratory function tests after pain relief
IP = intrapleural, i.m. = intramuscular

Tests	IP bupivacaine	i.m. pethidine
FVC (% predicted normal)		
before pain relief	51.11 ± 17.23	48.61 ± 13.82
after pain relief	57.45 ± 4.95*	55.95 ± 17.85*
% improvement	14.89 ± 21.39	14.41 ± 12.37
FEV1 (% predicted normal)		
before pain relief	49.47 ± 21.39	45.49 ± 13.64
after pain relief	55.31 ± 19.94*	50.27 ± 18.51*
% improvement	10.45 ± 17.6	15.66 ± 13.78

Values are expressed as means ± SD $^{*}P < 0.001$

ments in mind and compared this method with intramuscular pethidine.

Our results showed that the analgesia obtained by the intrapleural bupivacaine was superior to intramuscular pethidine, as assessed by the patients. No patients in this group required supplementary narcotic and they showed the significantly better percentage of pain relief than the group receiving intramuscular pethidine. The mean duration of analgesia after a single 20 ml dose of 0.5% bupivacaine with epinephrine (1:200,000) was 4.68 hr with a range of 3.5 to 6.1 hr. The duration of analgesia is shorter as compared to other studies. Reiested and Stromskag reported an average of 10 hr, and Seltzer et al reported an average of 7.2–8.6 hr but our results was comparable to that reported by Brismar et al. (less than 6 hr)[4–6].

Onset of analgesia in our patients after bupivacaine injection was within one to two minutes as was also reported by others[4–6]. During fluoroscopy we noticed very rapid disappearance (within seconds) of the contrast medium when we injected it into the pleural space. Our patients had unilateral analgesia from T4/5 to T10/11 dermatomes.

Of particular interest was the fact that in the two patients whose catheters were found to be placed in the extrapleural space there was indistinguishable analgesia as compared to those with properly placed catheters. In effect this would be similar to the single catheter intercostal nerve block technique investigated by Murphy[13]. This brings up two points. One is that it supports the mechanism of analgesia is due to reverse diffusion of the local anaesthetic from the pleural space into the intercostal spaces, resulting in multiple intercostal nerve blocks[4] and the other is that in the other studies published so far there may be the similar possibility of extrapleural catheter placement. None of them documented the location of the catheter radiologically in every case. Our study suggests that the location of the catheters has little clinical significance because both intrapleural and extrapleural bupivacaine seems to give analgesia.

With regards to the respiratory function tests, the FVC and FEV 1 in both groups improved significantly after being given bupivacaine or pethidine. However, we found no significant difference in the improvement of FVC and FEV 1 between both groups in spite of better analgesia in the intrapleural bupivacaine group. Two reasons could account for the result that intrapleural bupivacaine was not superior to intramuscular pethidine with respect to pulmonary function tests. First, 0.5% bupivacaine could cause intercostal muscles paralysis and impair ventilation[14]. Second, bupivacaine had been shown to produce contraction in guinea pig tracheal chains at low concentration ($10^{-4} - 3 \times 10^{-4}$M) and relaxation at higher concentration (6×10^{-4}M)[15]. Therefore it is conceivable that in this study bupivacaine absorbed from the pleural space caused an increase in local bronchomotor tone and masked an otherwise greater improvement in FEV 1 and FVC. Such a dissociation between pain relief and pulmonary function was also found by Bonnet and coworkers[16], using extradural morphine after upper abdominal surgery, and Baxter and co-workers[17], using continuous intercostal blockade after cardiac surgery. All respiratory function tests returned to normal by days 30 after surgery in all patients suggesting that intrapleural injections of bupivacaine and adrenaline did not result in long term impairment of intercostal muscles and bronchial trees.

It was shown by our fluoroscopic study that phrenic nerve palsy did not occur. This was true after the first dose of bupivacaine (3 patients), after 24–30 hr with at least four injections (3 patients) and after 48–52 hr with at least eight to nine injections (3 patients). All our patients lay supinely at the time of intrapleural bupivacaine injection and remained in this position for twenty minutes. We are not sure if phrenic nerve palsy would occur if the patients were made to lie on the left lateral position soon after the injection.

No major complications were seen in our study. We consider that a simple method for confirmation of catheter position is injection

of contrast medium through the catheter when the routine A-P chest x-ray is taken to check for pneumothorax. Our experience showed that if the catheter was placed properly, the contrast medium would not be visible in the interpleural space a few minutes later, whereas if it were in the extrapleural space, it would be seen as a blob (figs. 2, 4).

In conclusion, we found that intrapleural injection of bupivacaine was a very good method of pain relief for patients after cholecystectomy via a subcostal incision, and that analgesia could be prolonged as required. However, it only improved respiratory function tests to the same extent as compared to the intramuscular pethidine group inspite of the better pain relief. Although no major complications were seen in our patients, the potential for these remains. We consider that the intrapleural catheter technique for post-operative pain relief deserves further evaluation by larger series so that its safety can be established.

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References

1. Spence AA, Smith G: Postoperative analgesia and lung function; A comparison of morphine with extradural block. Br J Anaesth 43:144–148, 1971
2. Bridenbaugh PO, Dupen SL, Moore DC, Bridenbaugh LD, Thompson GE: Postoperative intercostal nerve block analgesia versus narcotic analgesia. Anesth Analg 52:81–85, 1973
3. Engberg G: Respiratory performance after upper abdominal surgery. A comparison of pain relief with intercostal block and centrally acting analgesics. Acta Anaesthesiol Scand 29:427–433, 1985
4. Reiestad F, Stromskag KE: Intrapleural catheter in the management of postoperative pain. A preliminary report. Regional Anesthesia 89–91, 1986
5. Seltzer JL, Larijani GE, Goldberg ME, Marr AT, Rocci ML: A kinetic and dynamic evaluation of intrapleural bupivacaine for subcostal incisional pain. Anesthesiology 65:A213, 1986
6. Brismar B, Pettersson N, Tokics L, Strandberg A, Hedenstierna G: Postoperative analgesia with intrapleural administration of bupivacaine – adrenaline. Acta Anaesthesiol Scand 31:515–520, 1987
7. Covino BG: Interpleural regional analgesia. Anesth Analg 67:427–429, 1988
8. Scott J, Huskisson EC: Graphic representation of pain. Pain 2:175–184, 1979
9. Rosen MAS, Hughes SC, Shnider SM, Abbound TK, Norton M, Dailey PA, Curtis JD: Epidural morphine for the relief of postoperative pain after cesarean delivery. Anesth Analg 62:666–672, 1983
10. American College of Chest Physicians. Assessment of ventilatory capacity: statement of the committees on environmental health and respiratory physiology. Chest 67:95, 1975
11. Herrald FJ, J McMichael: Determination of lung volume, a constant volume modification of Christie's method. Proc R Soc London Ser B 126:491–501, 1939
12. R Martin, PT Macklem: Suggested standardised procedures for closing volume determinations (Nitrogen Method). Besthesda MD: Natl Heart, Lung, Blood Inst, Div Lung Dis 1973
13. Murphy DF: Continuous intercostal nerve block for pain relief following cholecystectomy. Br J Anaesth 55:521–524, 1983
14. Jakobson S, Ivarsson I: Effects of intercostal nerve blocks (Etidocaine 0.5%) on chest wall mechanics in cholecystectomized patients. Acta Anaesthesiol Scand 21:497–503, 1977
15. Downed H, Loehning RW: Local anesthetic contracture and relaxation of airway somooth muscle. Anesthesiology 47:430–436, 1977
16. Bonnet F, Blery CH, Zatan M, Simonet O, Brage D, Graudy J: Effects of epidural morphine on postoperative pulmonary dysfunction. Acta Anaesthesiol Scand 28:147–151,

1984
17. Baxter AD, Jennings FO, Harris RS, Flynn JF, Way J: Continuous intercostal blockade after cardiac surgery. Br J Anaesth 59:162–166, 1987