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Continuous High Thoracic Epidural Administration of Morphine With Bupivacaine After Thoracotomy

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Background and Objectives. The purpose of the study is to determine the ideal concentration of morphine when given with bupivacaine as a continuous high thoracic epidural infusion for postthoracotomy pain. *Methods.* In a prospective study, 60 patients scheduled for thoracic surgery received a high thoracic epidural catheter. Postoperative analgesia was provided by a continuous epidural infusion for 3 days. The patients were randomly divided into two groups: group 1 (loading dose 1 mg morphine epidurally and continuous infusion of bupivacaine 0.75% + 0.2 mg/mL morphine at an infusion rate of 0.8 mL/hr); group 2 (loading dose 0.5 mg morphine epidurally and continuous infusion of bupivacaine 0.75% + 0.1 mg/mL morphine at an infusion rate of 0.8 mL/hr). *Results.* The visual analog scales were not different at rest but with exercise in group 1 there was better pain relief than in group 2. The number of patients requiring supplementation of analgesia in group 2 (n = 42) was six times that of group 1 (n = 7). $PaCO_2$ increased in both groups during the first postoperative day. There was no difference in the incidence of side effects between the two groups. *Conclusions.* Continuous high thoracic epidural administration 0.2 mg/mL morphine in bupivacaine 0.75% at an infusion rate of 0.8 mL/hr with a loading dose of 1 mg morphine is an effective dose for postthoracotomy pain relief in rest, and more important, during exercise. *Reg Anesth 1995: 20: 27–32.*

Key words: analgesic, morphine, anesthetic technique, epidural, pain, postoperative.

Pain after thoracic surgery is associated with shallow breathing and inability to cough effectively. Some of the known relationships between pain and pulmonary function indicate the development of a restrictive pattern of ventilation with reduced lung compliance.[1] An important part of postthoracotomy pain treatment should be that the patient is able to take deep expansive breaths, cough effectively to clear airways, and cooperate with physiotherapy.[1]

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The combination of thoracic epidural anesthesia and light general anesthesia, followed by postoperative epidural analgesia, has been advocated for thoracic surgery in order to provide stable intraoperative haemodynamics and effective postoperative pain relief.[2–3] Epidural administration of the combination of local anesthetics and opioids is an effective method for postoperative pain relief.[2,4–6] Previous studies have shown that epidural administration of morphine provides good pain relief after thoracotomy with a minimum of side effects.[7–12]

Morphine, a widely available and inexpensive opioid, is still the gold standard to which other opioids are compared. Because of the fear for late respiratory

depression, there are only a few studies regarding continuous morphine administration in combination with a local anesthetic through a high thoracic epidural catheter.[8,9,13]

Most studies of morphine for postoperative pain relief used a lumbar epidural catheter for continuous infusion or intermittent bolus injection,[7,9–11] since respiratory depression from epidural morphine is associated with higher vertebral levels of administration.[14] The aim of this prospective study was to evaluate in a randomized double-blind manner two different doses of morphine in combination with bupivacaine used in high thoracic continuous epidural infusion.

Materials and Methods

After informed consent and approval by the hospital ethics committee, 60 patients (ASA class 2 to 4) scheduled for thoracic surgery were randomly divided by into two groups. All patients underwent a lateral thoracotomy by the same surgeon.

All patients received oral diazepam 10 mg, 1 hour before surgery. An intravenous infusion was established with a 16 gauge catheter, and a 20-gauge radial arterial catheter was inserted to allow continuous blood pressure monitoring and arterial sampling blood for blood gas analysis. The epidural catheter was introduced with the patient awake in the sitting position just before surgery. A 16-gauge Tuohy needle was inserted, using a paramedian approach at the T3–T4 or T4–T5 level. The hanging drop technique was used to indicate the entry point of the needle into the epidural space. The needle opening was directed cephalad and a catheter was inserted 4 cm. A test dose of 3 mL lidocaine 2% with epinephrine was given. The patient was then turned into the supine position and sensory block was assessed by response to pinprick 10 minutes later. When bilateral sensory analgesia had been demonstrated, 1 mg morphine (group 1) or 0.5 mg morphine (group 2) was injected epidurally, followed by bupivacaine 0.5% with epinephrine 5 μg/mL 6–8 mL, depending on the size of the patient and extension of the block after the test dose. Immediately thereafter, general anesthesia was induced with intravenous thiopental 5–7 mg/kg, followed by pancuronium 0.1 mg/kg and fentanyl 0.1 mg. After tracheal intubation, anesthesia was maintained with 0.3%–0.5% halothane and a N_2O/O_2 mixture in a ratio of 1 : 1. The patients' lungs were ventilated to keep the end tidal pCO_2 between 33 (mm Hg) and 36 (mm Hg) kPa. Epidural anesthesia during and after surgery was administered as follows:

group 1 (n = 30): bupivacaine 0.75% with morphine 0.2 mg/mL by continuous infusion at 0.8 mL/hr for 3 days.

group 2 (n = 30): bupivacaine 0.75% with morphine 0.1 mg/mL by continuous infusion at 0.8 mL/hr for 3 days.

The infusion was labeled study drug. At surgery completion, all patients were allowed to resume spontaneous breathing, were extubated, and transferred to an adjacent intermediate care unit, where they remained under constant observation for 3 days.

Measured Variables

Blood-gas estimations were made the day before surgery, the day of surgery (day 1), and on the first and second day after surgery (days 2 and 3) at fixed times. During the study, respiration rate was monitored and arterial pressure and electrocardiogram were monitored continuously. If the respiration rate fell below 14/min or the previous arterial blood gas analysis demonstrated substantial (>10%) increase of $PaCO_2$, additional blood samples were taken.

Postoperative Pain Relief

Neither the patient nor the physician evaluator knew which concentration of morphine was being infused. Pain was evaluated every hour using the visual analog scale (VAS), where 0 indicates no pain (optimal pain relief) and 10 indicates the most severe pain (no pain relief). To confirm the effectiveness of analgesic treatment, patients were asked whether they suffered pain during deep expansive breathing, coughing, or physiotherapy. Whenever postoperative pain was experienced, a bolus dose 0.8 mL of the running infusion was administered epidurally.

Side Effects

The incidence of side effects (nausea, vomiting, pruritis, and somnolence) were recorded. Urinary retention was not registered because all patients had urinary bladder catheter.

Data Analysis

Statistical analysis of the data was performed using ANOVA or repeated measures MANOVA, two-tailed Fisher's exact test, Student's *t*-test, and the Wilcoxon's two-sample test, using the SAS statistical package. Values of $P < .05$ were considered significant. Data are expressed as mean values ± SD.

Table 1. Demographic Data

	Group 1 (SD)	Group 2 (SD)
Number	30	30
Male/Female	25/5	23/7
Age (years)	58.1 (14.9)	57.9 (10.8)
Weight (kg)	73.3 (10.6)	73.0 (11.1)
Height (cm)	173.1 (6.5)	172.1 (7.9)
COPD (n)	12	11
$PaCO_2$ (kPa)	40.65(4.35)*	37.65(3.75)*

Group 1: high dose morphine; group 2: low dose morphine. *$P < .05$ (Wilcoxon's two-sample test).

Table 2. Number of Patients Requiring Supplementation of Analgesia in the Postoperative Period

	Group 1 n = 30	Group 2 n = 30	P*
day 1	2	17	<.001
day 2	3	16	<.05
day 3	2	9	<.001

Group 1: high dose morphine; group 2: low dose morphine.
* Two-tailed Fisher's exact test.

Results

Demographic Data

Sixty patients completed this study, 30 patients in group 1 and 30 patients in group 2. There were no differences in demographic data between the two groups except the preoperative $PaCO_2$ in group 1 was higher than in group 2, $P < .05$ (Table 1).

Postoperative Pain Relief

During the 3 days of investigation, all VAS scores remained below the mean level of 3. Between both groups, a significant difference could be demonstrated; group 2 had higher VAS scores than group 1 (Fig. 1). In both groups patients asked for additional pain relief that was accomplished by administering extra bolus doses. On the first day, two patients of group 1 and 17 patients of group 2 were given extra bolus doses. On the second day, three patients of group 1 and 16 patients of group 2 were given extra bolus doses. On the third day, two and nine patients, respectively, were given extra bolus doses (Table 2). Several patients in group 2 had pain on deep breathing compared to zero patients in group 1. Also, a statistically significant number of patients in group 2 had pain on coughing and during physiotherapy on days 1 and 2 (Table 3).

Ventilatory Variables

Postoperative respiratory data are shown in Figures 2 and 3. The mean postoperative $PaCO_2$ was higher in group 1 than in group 2, but there was no statistical difference in mean $PaCO_2$ at any time. The mean $PaCO_2$ on day 1 in both groups was significantly increased compared to the preoperative value, but there was no difference in increase in $PaCO_2$ between group 1 and 2. On days 2 and 3, there was

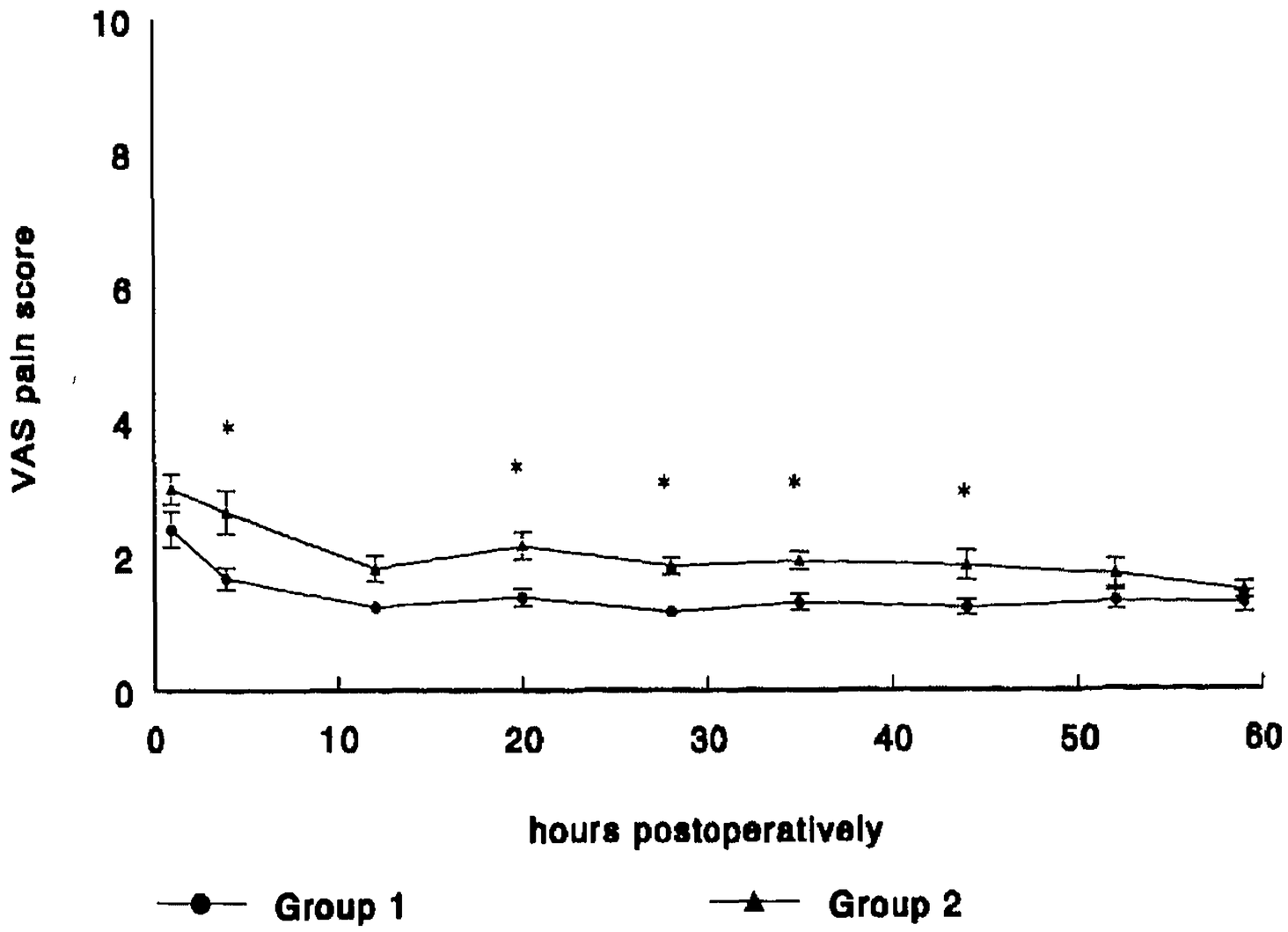

Fig. 1. Visual analog scale scores (±SEM) for postoperative pain relief in both groups, plotted against time (hours), where 0 = no pain and 10 = maximum pain. *$P < .05$ (repeated measures MANOVA).

Table 3. Number of Patients Presenting Pain During Exercise on Each Postoperative Day

	Day 1	Day 2	Day 3
Pain during deep expansive breathing *(n)*			
1	1	—	—
2	5	6 *	3
Pain during coughing *(n)*			
1	3	3	2
2	12 *	14 †	7
Pain during physiotherapy *(n)*			
1	2	1	2
2	10 *	10 †	6

Group 1: high dose morphine; group 2: low dose morphine. *$P < 0.05$, †$P < 0.01$ (two-tailed Fisher's exact test).

no significant increase in $PaCO_2$ compared to the preoperative level of $PaCO_2$.

Hypercapnia (defined as a $PaCO_2$ higher than 52.5 mm Hg) was observed in seven patients in group 1 versus five patients in group 2 in the first postoperative hour. The highest individual $PaCO_2$ 1 hour after the operation was 63 (mm Hg) (group 1) versus 59.3 (mm Hg) (group 2). The mean respiration rate was higher in group 1 at 1 hour after the operation. Thereafter, there was no difference in respiration rate between the two groups.

Side Effects

The incidence of side effects is listed in Table 4. A greater number of patients in group 2 had nausea, vomiting, and pruritus but this did not reach statistical significance.

Discussion

"Thoracotomy pain is generated from several sources, both during and after operation. These include soft tissue injury and inflammation, bone and joint trauma and visceral damage. Pain is exacerbated by movement especially by the obligatory movement of ventilation."[1] Most important for postoperative analgesia after thoracotomy is the possibility for activation, especially deep expansive breathing, coughing, and physiotherapy.[1,2,13]

Continuous thoracic epidural analgesia with a combination of a local anesthetic and an opioid is the most effective method for postthoracotomy pain relief.[2,8] Morphine appears to be an effective adjuvant for thoracic epidural analgesia in combination with bupivacaine despite the possibility of late respiratory depression, because of its water solubility.[8,13,15]

Since morphine is still the gold standard world wide, this study was designed to compare two doses of morphine in combination with bupivacaine by continuous thoracic epidural administration. The onset time of analgesia after epidural injection of morphine is delayed because of its hydrophylic character.[7] Therefore morphine was injected immediately after evaluation of the test dose, followed by bupivacaine 0.5% with epinephrine.

Pain relief during rest was adequate in both groups. There was a difference between the two groups in favor of group 1, but this is clinically irrelevant because the VAS scores remained below 3 in both groups. This was also found by other investigators who administered epidural morphine in combination with bupivacaine after thoracotomy. But in

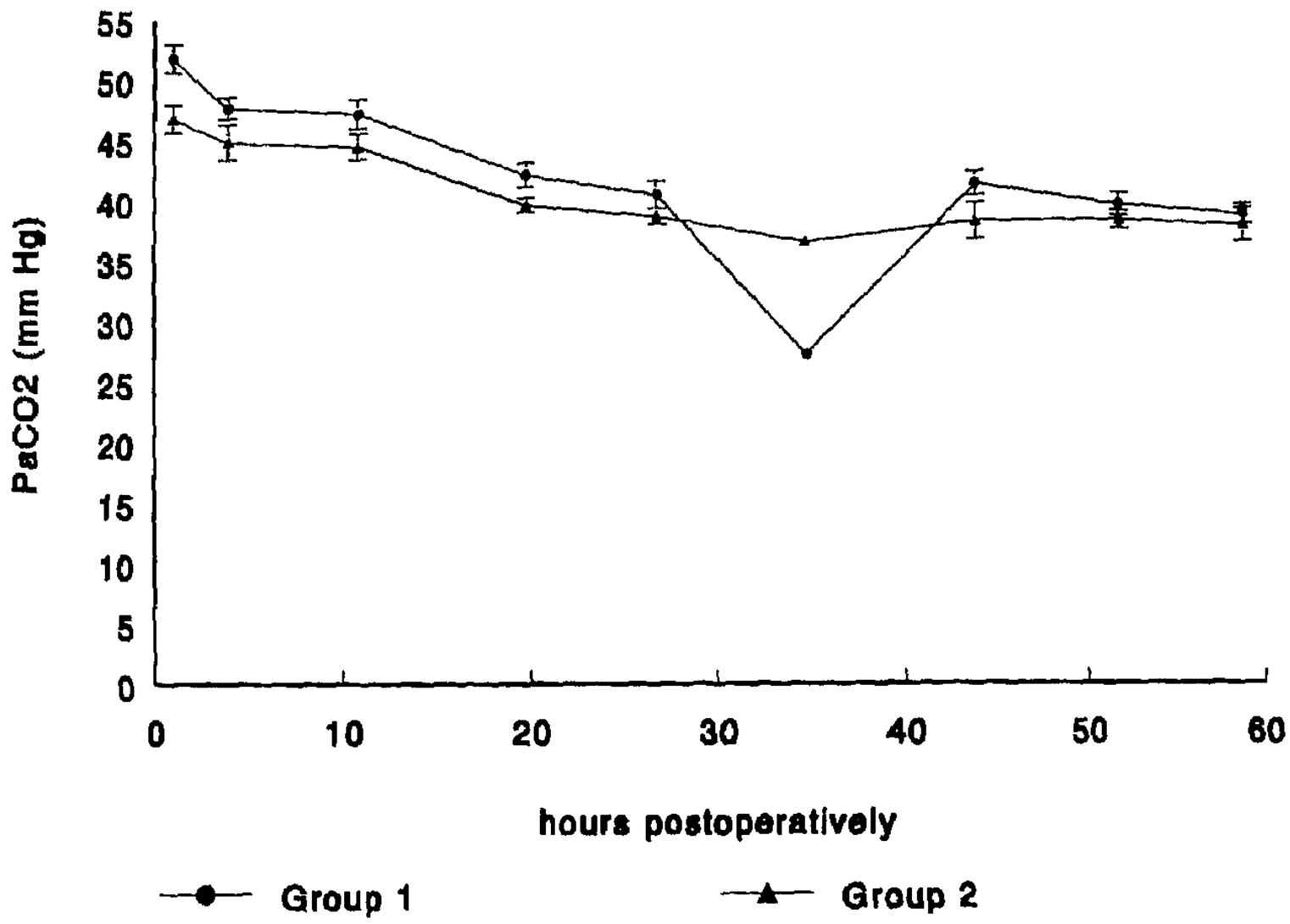

Fig. 2. Average values of postoperative $PaCO_2$ (mm Hg) (±SEM) in both groups, plotted against time (hours). No statistical difference (repeated measures MANOVA).

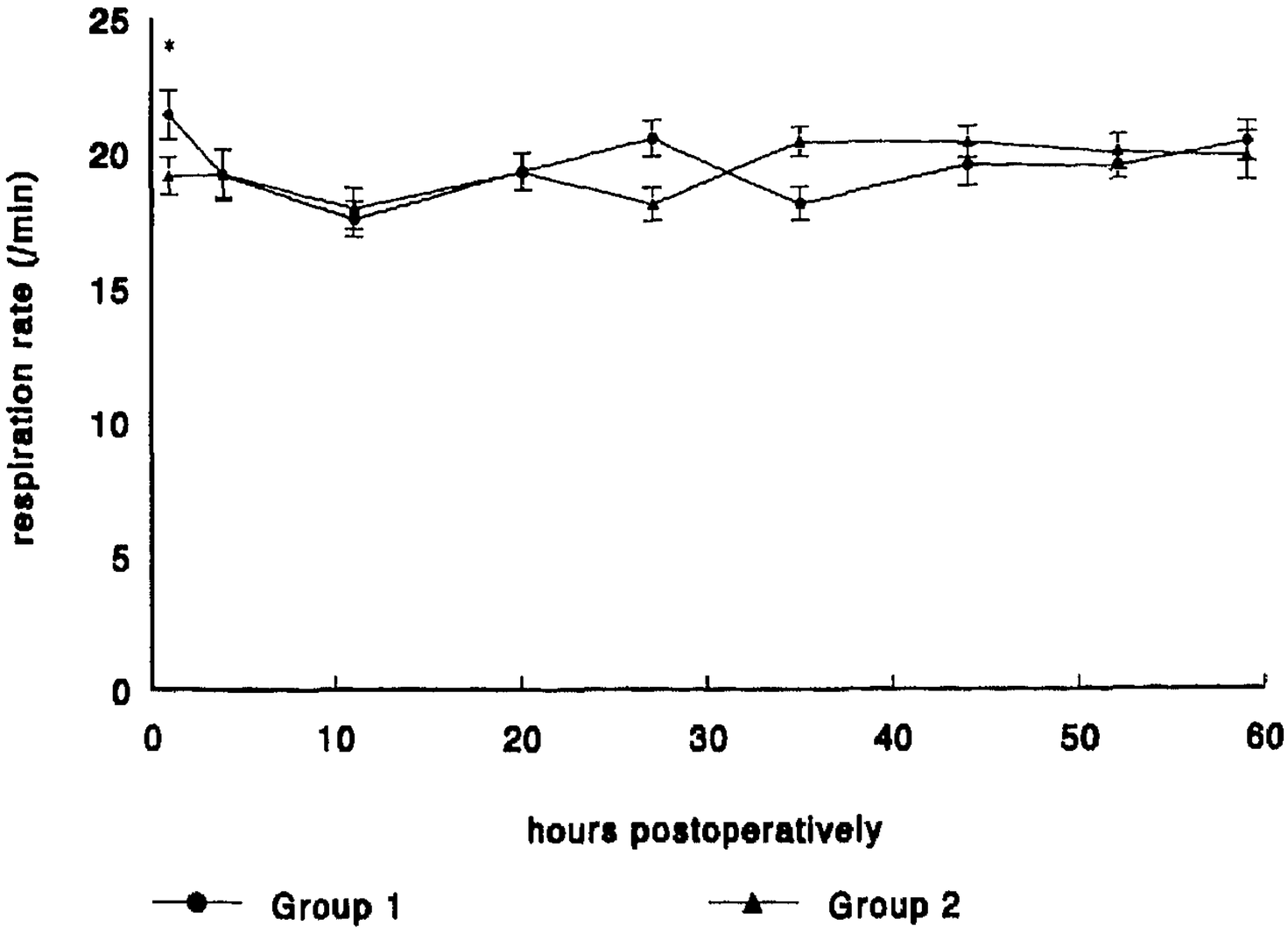

Fig. 3. Respiration rate (min) (±SEM) after the operation in both groups, plotted against time (hours). *$P < .05$ (repeated measures MANOVA).

these studies much more morphine was given epidurally (0.3–1 mg/hr) with different concentrations of bupivacaine, but almost the same amount in milligrams.[8,9,13]

Our study is different from that of Logas et al.[8] who employed 0.1 mg/mL morphine, 0.5% bupivacaine, and higher rates (3–6 mL/hr) of infusion. We showed that the use of higher concentrations of morphine and bupivacaine at low rates of infusion resulted in excellent pain relief after thoracotomy. This low rate of infusion should diminish cephalad spread of morphine, decreasing the risk of respiratory depression.

Pain relief during deep expansive breathing, coughing, and physiotherapy are the most important parameters of adequate analgesia. In only one previous study, postthoracotomy pain relief at rest and during exercise was investigated.[13] In this study, Bigler et al. found no difference in postthoracotomy pain relief at rest and during exercise, although more than 50% of the patients in both groups needed supplemental analgesia.[13] In our study, there was a difference in pain relief during deep expansive breathing, coughing, and physiotherapy in favor of group 1. This adequate pain relief in group 1 is also illustrated by the fact that group 2 needed much more bolus doses during the 72 hours after the operation.

There was a difference in preoperative $PaCO_2$, but this is of no clinical importance. Furthermore, the difference in $PaCO_2$ between the two groups remained during the postoperative period. The increase in $PaCO_2$ between the two groups on the first postoperative day was not significant. Conversely, the increase in $PaCO_2$ in each group was significant. This appears to be a combined anesthetic surgical effect that is also seen in other studies.[13,16] After the first day, the individual $PaCO_2$ returned to the preoperative value in both groups.

During the 72 hours after the operation the respiration rate remained normal without differences. In group 2 (0.1 mg/mL morphine) the incidence of pruritus, nausea, and vomiting was higher than group 1 (0.2 mg/mL morphine). Because of this it is questionable if the side effects are solely due to morphine. The overall incidence of side effects was very low in both groups without any statistical differences.

Table 4. Number of Patients Presenting Side Effects

	Group 1 n = 30	Group 2 n = 30
Pruritus	2	3
Nausea	1	5
Vomiting	1	2
Somnolence	0	0

Group 1: high dose morphine; group 2: low dose morphine. No statistical differences (two-tailed Fisher's exact test).

Conclusion

The continuous high thoracic epidural administration of the combination of morphine and bupivacaine is an effective method for postthoracotomy pain relief. Pain relief during deep expansive breathing, coughing, and physiotherapy was only adequate in group 1. No clinical significant ventilatory depression was demonstrated and no difference in the incidence of side effects were found in both groups.

Therefore, we conclude that 0.2 mg/mL morphine in bupivacaine 0.75% at an infusion rate of 0.8 mL/hr, with a loading dose of 1 mg morphine epidurally, is a very effective dose for postthoracotomy pain relief in rest and, more importantly, during exercise.

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