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Continuous Intrapleural Infusion of Bupivacaine for Analgesia after Thoracotomy

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Intrapleural administration of bupivacaine has been reported to produce analgesia following cholecystectomy performed through a subcostal incision, unilateral breast surgery, and renal surgery.[1–4] Perhaps local anesthetic injection into the intrapleural space (pleural cavity) leads to multiple intercostal blockade[4] and block of nerve endings in the pleura. Therefore, we studied whether continuous intrapleural infusion of bupivacaine would be effective in controlling pain after thoracotomy.

MATERIALS AND METHODS

Fourteen consecutive patients (12 men, two women; 55–98 kg; 44–73 yr of age) undergoing thoracotomy were investigated. The study was approved by the Ethical Committee of the hospital, and informed consent was obtained from the patients. The patients were anesthetized using a standardized technique; diazepam and meperidine premedication, thiopental iv for induction of anesthesia, maintenance of anesthesia with N_2O/O_2 (50%), vecuronium iv for muscle relaxation, fentanyl 100 μg/h iv, and inhalation of enflurane as needed. Endotracheal intubation was performed and ventilation was monitored with end-tidal capnometer and analysis of arterial blood-gases.

The surgical procedures were exploratory thoracotomy (five patients), lobectomy (seven patients), and total pneumonectomy (two patients). Before wound closure, the surgeon inserted a 16 radio-opaque nylon epidural catheter (Portex Ltd., Hythe, U.K.) through the thoracic wall, using a Tuohy needle, posteriorly above the incision, which was always at the fifth intercostal space. The catheter tip was approximately 5 cm inside the pleural cavity. The catheter was fixed to the skin with a suture.

When the tracheas had been extubated, and the patients transferred to the recovery room, after 25–45 min, an initial bolus of plain 0.5% bupivacaine (15 ml/51–55 kg, 16 ml/56–60 kg, 17 ml/61–65 kg, 18 ml/66–70 kg, 19 ml/71–75 kg, 20 ml >75 kg of body weight) was injected through a bacterial filter and the catheter. One hour later, an infusion of 0.25% bupivacaine was started. The infusion rate was adjusted according to the same weight division as above, ranging from 5–10 ml/h (0.23–0.33 mg/kg/h). The infusion was continued until the second postoperative morning, *i.e.*, for 40–45 h. After being observed in the recovery room for 2–3 h, the patients were transferred to the ward. Analysis of arterial blood-gases was performed in the recovery room, and capillary blood-gas analyses were performed in the postoperative evening and in the first and second postoperative mornings. A chest radiograph was taken in the recovery room and in the first and second postoperative mornings.

Intramuscular oxycodone (dihydrohydroxycodeinone hydrochloride), approximately 0.14 mg/kg (0.06 mg/kg iv in the recovery room) was ordered to be given to the patients on request. The pain intensity (visual analogue scale, VAS 0–10, 0 = no pain and 10 = unbearable pain) was evaluated before injection of bupivacaine, and, at the same time, blood samples were drawn for plasma bupivacaine concentration assay. The VAS score was given in connection to a deep breath or cough. Plasma bupivacaine concentrations were assayed by gas chromatography.[5] Samples were collected just before the bolus injection and at 5, 15, 30, 45, and 60 min after injection, and in the first and second postoperative mornings (at least 3 h from last im analgesic). In addition, samples were drawn from the pleural drainage tubing during the first hour at similar intervals as the blood samples.

RESULTS

None of the patients managed without oxycodone during the study period. The mean number of oxycodone administrations on the day of surgery (17–20 h postoperatively) was 3.2 (range 0–6) and, in the next 24

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TABLE 1. Mean Bupivacaine Concentrations (μg/ml ± SD) in Plasma and Pleural Drainage Fluid and Mean Visual Analogue Scale (VAS) Pain Scores During the Intrapleural Treatment

	0	5 min	15 min	30 min	45 min	60 min	1st Postop. Morning	2nd Postop. Morning
Bupivacaine plasma concentrations (range)	—	0.59 ± 0.43 (0.19–1.72)	0.76 ± 0.58 (0.25–2.25)	0.82 ± 0.59 (0.22–1.93)	0.76 ± 0.52 (0.19–1.56)	0.73 ± 0.50 (0.24–1.66)	1.64 ± 1.04 (0.37–3.68)	2.29 ± 1.12 (0.72–4.24)
Bupivacaine drainage fluid concentrations* (range)	—	361 ± 568 (0–1725)	197 ± 397 (0–1323)	45 ± 62 (0–196)	37 ± 49 (0–152)	29 ± 38 (0–113)		
Pain scores (VAS) (range)	5.7 ± 3.1 (0–10)	6.0 ± 2.2 (3–8)	5.1 ± 2.9 (2–9)	5.3 ± 2.1 (3–9)	5.0 ± 2.1 (3–8)	5.2 ± 2.4 (2–9)	7.1 ± 2.1 (5–10)	4.8 ± 2.5 (2–10)

* In three patients, there was no drainage fluid in the first hour (n = 11).

h, 4.1 (range 1–7). Mean VAS scores during the first 60 min ranged between 5.0 and 6.0 (table 1). In the first and second postoperative morning, mean VAS scores were 7.1 and 4.8, respectively. Because of rather severe pain and to improve coughing, two patients were given a transcutaneous intercostal block (four nerves, 15–16 ml of 0.5% bupivacaine) in addition to the pleural infusion on the first postoperative day.

The mean bupivacaine plasma concentrations and the mean bupivacaine concentrations in the pleural drainage fluid are shown in table 1. After the initial dose of 0.5% bupivacaine, the mean maximum plasma concentration, 0.82 μg/ml, was found at 30 min. The highest individual concentration in the first hour was 2.25 μg/ml. During the continuous infusion, there was a marked rise in the mean bupivacaine plasma level which was 1.64 μg/ml (individual maximum 3.68 μg/ml) on the first morning and 2.29 μg/ml (maximum 4.24 μg/ml) on the second morning. Symptoms of central nervous toxicity were not evident.

In the pleural drainage samples of four patients (three lobectomy patients, one exploratory thoracotomy patient), the bupivacaine concentrations were quite high during the first hour; at 5 min from injection of the bolus dose, concentrations were 447, 704, 731, and 1725 μg/ml, and, at 60 min, 17, 113, 68, and 68 μg/ml, respectively. In these four patients, the corresponding plasma levels were low; maximally 0.42 μg/ml. In both total pneumonectomy patients, there was no measurable loss of fluid through the drainage (no suction) in the first hour after bupivacaine injection. Their maximal bupivacaine plasma concentrations in the first hour were 0.33 and 0.37 μg/ml.

Slight respiratory depression (*i.e.*, Pa_{CO_2} 51.7 and 52.2 mmHg) was observed in only two patients. This occurred soon after tracheal extubation, *i.e.*, before intrapleural bupivacaine administration. Their Pa_{CO_2} values in subsequent samples during the day were normal or slightly increased (<50 mmHg). The capillary blood-gas analyses on day 1 and day 2 showed normal values in all patients.

During the 2-day bupivacaine infusion period, seven patients had micturition difficulties which required urinary catheterization. All of them had received im oxycodone, at least once before the urinary complication occurred. One patient (lobectomy for a hamartoma) developed interstitial pneumonia in the operated lung. In another patient (exploratory thoracotomy due to lung cancer), the intrapleural catheter broke during the attempts to pull it out after a completed study. The remaining distal 12 cm of the nylon catheter was clearly visible, partially intrapleurally in the cranial direction, attached to the chest wall at the puncture site in subsequent chest radiographs. As the catheter tip could not be extracted through a skin incision, it was left untouched.

DISCUSSION

Intrapleural bupivacaine administration proved unsatisfactory in the management of postoperative pain after thoracotomy. Neither the initial bolus dose of 0.5% bupivacaine, nor the continuous infusion of 0.25% bupivacaine, relieved pain to any great extent. As an operated lung is vulnerable to develop infectious complications, it was deemed unethical to infuse saline intrapleurally for 2 days to control group patients. Bupivacaine, on the other hand, possesses antimicrobial properties.[6] Thus, a control group to be investigated under double-blind principles was not included. Instead, we compared the pain score and im oxycodone administration data with those of a recent postoperative pain study from our department in corresponding types of patients.[7] It was found that the need for im oxycodone (number of injections) and the pain intensity scores were not lower than in those patients who had been given an intercostal blockade by the surgeon before closing the wound and been ordered im oxycodone on request.[7]

The lack of effective pain relief in these patients is in contrast to results when intrapleural bupivacaine administration was used after non-thoracotomy surgery.[1–4] One possible explanation for the difference seems obvious; a major portion of the bupivacaine dose is lost by suction in lobectomy and exploratory thoracotomy patients. Furthermore, the intrapleural distribution of bupivacaine by movements of an operated lung (or lack of a lung) may be restricted. Interestingly, in both total pneumonectomy patients, the plasma levels of bupivacaine remained quite low in spite of no apparent loss through the drainage tubing. The local anesthetic solution was probably sequestered in the posterior space between the diaphragm and the parietal pleura.

An increase in bupivacaine dosage in order to improve analgesia after thoracotomy is not feasible, as the dosage employed here already resulted in marked accumulation of bupivacaine. The plasma concentrations of bupivacaine after the 2-day infusion were at a level regarded as toxic in man (2–4 μg/ml).[8] Generally, the bupivacaine plasma concentrations resulting from the bolus injection were at the same level as those reported by Seltzer *et al.*[2] after injection of 30 ml of 0.5% bupivacaine, but somewhat higher than in the study by Reiestad *et al.*,[3] who injected up to 20 ml of 0.5% bupivacaine. In both studies, the bupivacaine solution contained epinephrine, which probably accounts for delayed absorption and lower plasma levels of bupivacaine. Whether epinephrine improves the analgesic effect of bupivacaine in the intrapleural technique has not been studied.

Perhaps a lack of urinary retention would be an important clinical advantage of the intrapleural catheter analgesia technique.[4] However, half of the thoracotomy patients had micturition problems during the intrapleural treatment period. Intramuscular opiate medication, insufficient pain control, and related immobility probably were the major determinants in the development of this complication.

The cause of the snapping of the intrapleural nylon catheter in one of the patients cannot be established with certainty. Perhaps the catheter was partially cut by the Tuohy needle during the insertion procedure. As nylon is an inert material and the remaining catheter tip did not cause any irritation, a re-thoracotomy was not considered indicated in this patient with an inoperable lung cancer.

Based on this study, we cannot recommend using intrapleural bupivacaine either as a bolus injection of 0.5% (15–20 ml) or continuous infusion of 0.25% (5–10 ml/h) for postoperative pain treatment after thoracotomy.

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