

Preemptive Epidural Analgesia for Thoracic Surgery

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Abstract

The purpose of this study was to determine if preemptive epidural analgesia performed before thoracotomy incision and during the operation reduces postoperative pain. Patients in the treatment group received 8 mL of 0.25% bupivacaine and 2 mL of fentanyl (50 µg/mL) via the epidural route prior to skin incision, followed by an infusion of bupivacaine 0.1% and fentanyl 10 µg/mL at 6 mL/hr. The control group received saline in the epidural. All patients in both groups were dosed with 8 mL of 0.25% bupivacaine and 2 mL of fentanyl 50 µg/mL via the epidural route at the time of the chest closure. The patients in the treatment group required less isoflurane intraoperatively and had lower maximum pain scores in the first 6 hours postoperatively. No significant differences were noted after the first 6 hours.

Key Words: Preemptive analgesia, epidural analgesia, thoracic surgery.

Introduction

THORACOTOMY OFTEN LEADS TO significant pain postoperatively. There may also be pulmonary dysfunction, which can be due to the removal of lung tissue, poor preoperative lung function, splinting from pain, and respiratory depression from parenteral narcotics (1–3). The pain may reduce the ability to take deep breaths and cough. Intravenous narcotics may depress respiration and also produce side effects such as nausea and vomiting. Epidural analgesia or intrathecal morphine is often used for treatment of post-thoracotomy pain, and reduces the need for systemic narcotics.

There is some evidence that tissue injury leads to nervous system changes that create hypersensitivity to pain postoperatively. This hypersensitivity is thought to be due to a lower threshold to pain in the peripheral nociceptors and an increased excitability of neurons in the spinal cord. There are few data available regarding the use of preemptive analgesia for thoracic surgery. In one report, the administration of fentanyl into the epidural space prior to thoracotomy incision led to reduced postoperative

pain and morphine requirements, compared with patients who received the same dose of epidural fentanyl 15 minutes after skin incision (4). However, no additional analgesics were administered during the surgery, and local anesthetics were not utilized for treatment. The purpose of the present study was to determine if preemptive epidural analgesia that was provided before thoracotomy incision and intraoperatively reduces postoperative pain and postoperative narcotic usage.

Methods

The protocol was approved by the Institutional Review Board, and written informed consent was obtained from all 40 patients who were studied. These patients were scheduled to undergo elective thoracic surgery (thoracotomy, or thoracoscopy with possible thoracotomy). All patients included in the study had a thoracic epidural catheter placed while in the preoperative holding area. A test dose of 3 mL of bupivacaine 0.25% was administered via all of the epidural catheters immediately following placement.

The study was conducted in a double-blind fashion. Patients were assigned to one of two groups, according to a list of random numbers. In Group A, 8 mL of bupivacaine 0.25% and 2 mL of fentanyl (50 µg/mL) were injected into the epidural catheter after induction of general anesthesia and before skin incision. This was followed by an epidural infusion of bupivacaine 0.1% and fentanyl 10 µg/mL at 6 mL/hr that

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was continued throughout the procedure until chest closure was performed.

In Group B, 10 mL of preservative-free normal saline was injected in the epidural catheter after induction of general anesthesia and before skin incision. This was followed by an epidural infusion of normal saline at 6 mL/hr that was continued throughout the procedure until the chest closure.

Intraoperatively, all patients received oxygen, isoflurane, neuromuscular blockers, and a maximum total fentanyl dose of 3 µg/kg intravenously. At the beginning of the chest closure, all patients in both groups received 8 mL of bupivacaine 0.25% and 2 mL of fentanyl (50 µg/mL) through the epidural catheter. Patients were continued in the study protocol only if a thoracotomy incision was performed.

At the conclusion of surgery, patients were extubated if clinical criteria were satisfied. Otherwise, patients were transferred to the Post-Anesthesia Care Unit (PACU) still intubated, and were extubated later when extubation criteria were met. Upon each patient's arrival at the PACU, an epidural infusion of bupivacaine 0.1% with fentanyl 10 µg/mL was begun at 2 mL/hr. This infusion was titrated according to the clinical needs of each patient. The patients graded their pain on a linear analog scale (Visual Analogue Scale — VAS) of 1–10 for 48 hours postoperatively, on an hourly basis while awake. The rate of the epidural infusion was recorded.

The data were analyzed using unpaired Student's t-tests. A $p < 0.05$ was considered statistically significant.

Results

Thirty-two of the 40 patients initially enrolled in the study underwent a thoracotomy incision, and all of these patients completed the study. The demographic data of patients were similar in both groups. The results are summarized in Table 1.

The patients in Group A had a lower intraoperative requirement for isoflurane, compared with Group B ($0.5 \pm 0.5\%$ vs. $0.78 \pm 0.2\%$, respectively, $p < 0.05$). The intraoperative hemodynamics were similar in both groups (Table 1).

Postoperatively, the patients in group A had a lower maximum pain score in the first 6 hours compared with group B; the pain scores were not significantly different after the first 6 hours (Table 2).

TABLE 1
Intraoperative Data

	Preemptive Analgesia	Control	P-value
n	19	13	
Mean end-tidal isoflurane (intraop) (%)	0.5 ± 0.15	0.71 ± 0.23	0.012
Median HR (intraop) (bpm)	74 ± 13	75 ± 5	NS
Median MAP (intraop) (mm Hg)	82 ± 8	88 ± 9	NS

Discussion

In the current randomized, double-blinded, placebo-controlled study, the patients in the treatment group had lower pain scores in the initial 6 hours, but not thereafter. Additionally, the intraoperative requirements for isoflurane were reduced in the treatment group.

Noxious stimuli may induce changes in the central nervous system, even after the original inciting event has ceased (4). Data from animal experiments have demonstrated that these neuroplastic changes can be prevented by pre-treatment with analgesics prior to the injury (5, 6). Preemptive treatment with local anesthetics or opioids has been shown in some an-

TABLE 2
Postoperative Data

	Preemptive Analgesia	Control	P-value
Median epidural infusion rate (mL/hr)	4.1 ± 1.5	4.3 ± 1	NS
Maximum pain score (0–6 hrs, VAS)	4.1 ± 3.0	6.8 ± 3.6	0.009
Maximum pain score (7–12 hrs, VAS)	3.0 ± 2.3	4.5 ± 3.8	NS
Maximum pain score (13–24 hrs, VAS)	4.5 ± 2.8	4.2 ± 3.4	NS
Maximum pain score (25–48 hrs, VAS)	2.5 ± 1.7	4.5 ± 3.8	NS

VAS = Visual Analogue Scale.

imal studies to be more effective than treatment following injury (6, 7). The existence of phantom limb pain following amputations also supports the theory of central nervous system neuroplasticity.

Tverskoy et al. (8) demonstrated a preemptive effect of both fentanyl and ketamine on postoperative pain and wound hyperalgesia. Patients in the fentanyl group or ketamine group had lower pain scores and higher pain thresholds than patients in the control group, at both 24 and 48 hours postoperatively. In another study, the administration of morphine and ketamine was more effective in treatment of postoperative pain when given preoperatively rather than intraoperatively (9).

Regional anesthesia can also be used to prevent the sensation of noxious surgical stimuli from reaching the spinal cord and leading to neuroplastic changes. Spinal anesthesia for lower abdominal surgery has been reported to lead to less postoperative pain and lower postoperative morphine usage, compared with patients receiving general anesthesia (10).

There are also data that do not support the effectiveness of preemptive analgesia. Johansson et al. (11) reported that preoperative local anesthesia infiltration with ropivacaine for postoperative pain relief after cholecystectomy did not have a prolonged postoperative analgesic effect.

Aida et al. (12) reported that the combination of epidural morphine and intravenous ketamine, administered prior to skin incision for gastrectomy and maintained continuously throughout surgery, produced a preemptive analgesic effect that was still present 48 hours after surgery. In another study, a single dose of ketamine 0.4 mg/kg, administered intravenously prior to skin incision for abdominal hysterectomy, did not have a preemptive analgesic effect (13). Preoperative ketamine did not have a preemptive analgesic effect in patients undergoing total mastectomy (14). The effectiveness of preemptive analgesia may also be affected by the presence of preoperative pain (15) or the type of surgery (16).

Local infiltration of 0.5% bupivacaine prior to incision for laparoscopy resulted in less postoperative pain than either infiltration just prior to skin closure or infiltration of only saline (17). Pre-incisional infiltration of bupivacaine also reduced postoperative pain following lower abdominal surgery conducted under epidural anesthesia (18).

Acute postoperative pain may have long-term implications. Early postoperative pain

following thoracic surgery has been reported to be associated with long-term pain 1.5 years postoperatively (19).

In our study, the pain scores differed only during the first 6 hours. This could have been due to a preemptive analgesic effect, but if so, it did not carry forward beyond this initial period. The early reduction in pain in group A could have been due to a better analgesic effect or from using a different dosing technique. These patients had an initial loading dose, followed by an infusion, and then a dose at the conclusion of surgery. The only intraoperative dose that the control group received was at the conclusion of surgery. Group A received a greater amount of local anesthetic and also had lower intraoperative anesthetic requirements, an effect that we had also reported in an earlier study with intrathecal morphine (20).

In conclusion, while there was a beneficial effect of reduced intraoperative anesthetic requirements, any lasting effect of preemptive analgesia did not extend beyond 6 hours after the operation.

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