Intermittent Thoracic Epidural Administration of Ropivacaine-Fentanyl versus Bupivacaine-Fentanyl after Thoracotomy

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Citation

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Abstract

Background: Pain relief after thoracotomy can be achieved with thoracic epidural analgesia. The pharmacodynamic profile of ropivacaine was reported to be superior to that of bupivacaine, especially in clinical settings where motor block is undesired. We aimed to compare intermittent thoracic epidural analgesia after thoracotomy using either bupivacaine – fentanyl or ropivacaine – fentanyl. Hemodynamics, ventilation, analgesia and side effects were compared..

Methods: After general Anesthesia, 30 patients were randomly allocated to receive intermittent epidural bupivacaine 0.25% plus fentanyl 5 µg/ml (n = 15) or ropivacaine 0.25% plus fentanyl 5 µg/ml (n = 15). Heart rate, mean arterial blood pressure, respiratory rate, arterial blood gases were recorded. Motor power, pain score, analgesic requirements and side effects were evaluated over 24 hours postoperatively.

Results: Heart rate, arterial blood pressure, respiratory rate and PaCO2 did not show any between-group differences. At 8 and 12 hours in the recovery room, arterial O2 tension was significantly higher in RF group than in BF group, with respective values of 141 (29) mm Hg vs. 122 (26) mm Hg and 138 (22) mm Hg vs. 116 (19) mm Hg ($P < 0.05$). Analgesia and diclofenac requirements were comparable in both groups. Motor power of the upper limbs was preserved in both groups. The incidence of side effects did not significantly differ between the two groups.

Conclusion: Ropivacaine–fentanyl thoracic epidural analgesia after thoracotomy is comparable to bupivacaine – fentanyl analgesia in terms of pain control and side effects.

INTRODUCTION

Analgesia after thoracic surgery is of utmost importance. Thoracotomy with its noxious insult contributes to postoperative pulmonary dysfunction ([1], [2]). Epidural administration of local anesthetics and opioids has been used for post-thoracotomy pain relief ([2],[3],[4]).

Studies on animals ([5], [6]) and humans ([7], [8]) revealed that ropivacaine produces less motor block and less cerebral and cardiotoxic effects than bupivacaine. Epidural ropivacaine produced comparable motor block with bupivacaine during labor ([8], [9]). However, adding opioid to these local anesthetics demonstrated equal analgesic potency with decreased motor block with ropivacaine-opioid ([10], [11]).

In a clinical setting like thoracotomy, it is pertinent to assure good postoperative analgesia without cardiorespiratory compromise. Epidural ropivacaine-fentanyl may be a better choice than bupivacaine-fentanyl in patients subjected to thoracotomy. To test this hypothesis, we randomly allocated patients subjected to lobectomy to receive intermittent epidural ropivacaine-fentanyl or bupivacaine – fentanyl and blindly observed postoperative analgesia, analgesic requirements, cardio–respiratory variables and side effects.

PATIENTS AND METHODS

This double-blind study was carried out on thirty one adult patients of either sex. Patients undergoing elective lobectomy under posterolateral muscle cutting, rib retraction thoracotomy were the subject of this study. Approval of the Hospital Research Ethics Committee and informed written consent from all patients were obtained. Patients with known

contraindications for epidural analgesia, namely patient refusal, infection at the injection site, bleeding diathesis or neurological disorders, were excluded from the study. Patients with diabetes mellitus and those below 18 years were also excluded. Preoperative evaluation of patients included medical history, clinical examination, routine investigation and chest X-ray. Patients received oral diazepam, 10 mg, and two hours before surgery. After arrival to the operative theatre, an intravenous cannula was inserted and lactated Ringer's solution, 1000 ml, was infused over 30 minutes. Monitoring was established with 3-lead ECG, pulse oximetry and capnography. A radial artery catheter was introduced for serial arterial blood sampling and direct arterial blood pressure monitoring. Perioperative heart rate, mean arterial blood pressure, arterial O_2 saturation and tension were recorded. In addition, respiratory rate and arterial CO_2 tension, the indirect indices of respiratory power, were recorded postoperatively.

Patients were randomly allocated, using the closed envelope method, to receive thoracic epidural ropivacaine plus fentanyl (group RF) or bupivacaine plus fentanyl (group BF). While the patient was in the sitting position, using the paramedian approach and loss of resistance technique at T5–6 or T6–7 interspace, an epidural catheter was threaded 4 cm. Lidocaine 2% (3 ml) was injected via the epidural catheter as a test dose. After confirming correct placement of the catheter, 10 ml of either ropivacaine 0.25% or bupivacaine 0.25% plus fentanyl (5 µg / ml) was injected.

Anesthesia was induced with thiopentone sodium 5 mg/kg and tracheal intubation was facilitated with succinylcholine 1.5 mg/kg. Anesthesia was maintained with halothane, N_2O/O_2 ($FiO_2 = 0.4$) and vecuronium for muscle relaxation. The lungs were ventilated to maintain end-tidal CO_2 between 30–35 mm Hg. At the end of the operation, neuromuscular blockade was appropriately reversed and patients were extubated and O_2 facemask (2 L/min) was applied.

After transfer to the recovery room, either ropivacaine or bupivacaine 0.25% with fentanyl 5 µg/ml in 10 ml solution was injected over 5 minutes via the epidural catheter. One hour later, 5 ml of the same solution were injected every hour for the first 8 hours, every 2 hours for the second 8 hours then every 4 hours for the remaining 8 hours. An observer blinded to the epidural anesthetic solution observed the patients for physiological parameters, analgesia, pain and side effects. Patients were also unaware about the injected epidural solution.

Assessment of postoperative pain was carried out at 4, 8, 12 and 24 hours. Intensity of pain was assessed by using a 5-level pain score as follows: 0 = no pain on coughing; 1 = pain on coughing but not on deep breathing; 2 = pain on deep breathing but not at rest; 3 = slight pain at rest; and 4 = sever pain at rest. Intramuscular diclofenac 75 mg was given When patients requested additional analgesia, usually exceeding score 3.

Motor power of the upper limb was assessed at 12 and 24 hours with a modified Medical Research Council Score (12) for grading muscle strength as follows: 0 = no movement; 1 = flickering or slight movements; 2 = movement against gravity; 3 = movement against resistance; and 4= normal power.

The statistical analyses were carried out using SPSS statistical package. Changes in mean values between the two groups were compared by unpaired Student's t-test and repeated measures analysis of variance. Categorial data (pain and motor scores) were assessed by Mann-Whitney U-test and nominal parameters by Chi-squared test. Statistical significance was assumed when $P < 0.05$.

RESULTS

In this study, 31 patients were involved; one patient was excluded due to postoperative bleeding and disordered epidural injection. The closed envelope randomization assured equal number of 15 patients in each group. Table 1 shows patients' age, weight, height, gender and duration of surgery. These characteristics were similar in both ropivacaine – fentanyl group (RF) and bupivacaine – fentanyl group (BF).

Hemodynamic parameters (heart rate and mean arterial blood pressure) are shown in Figures 1 and 2. There were no significant differences between both groups.

Patients in each group showed an arterial O_2 saturation above 95% and arterial O_2 tension above 110 mm Hg during the postoperative period. At 8 and 12 hours in the recovery room, arterial O_2 tension was significantly higher in RF group than in BF group, with respective values of 141 (29) mm Hg vs. 122 (26) mm Hg and 138 (22) mm Hg vs. 116 (19) mm Hg ($P < 0.05$). Regarding ventilatory parameters, there were no significant changes in the respiratory rate (RR) or arterial carbon dioxide tension ($PaCO_2$) between both groups as shown in Table 2.

Assessment of pain scores at 4, 8, 12 and 24 hours

postoperatively showed no significant differences between both groups. However, more patients in group RF requested analgesics than in group BF, albeit a statistical significance was not reached. Patients who needed analgesics requested the first dose at 4 hours postoperatively (Table 3).

All patients of both groups showed full power of the upper limbs at 12 and 24 hours postoperatively. The incidences of side effects, namely nausea, vomiting and pruritis, were comparable between both groups (Table 3). A couple of patients in each group received rescue treatment (i.v. metoclopramide) for vomiting.

Figure 1

Table 1: Demographic data and duration of anesthesia. Data are means (SD). Ropivacaine – Fentanyl (n = 15) Bupivacaine – Fentanyl (n = 15)

	Ropivacaine-Fentanyl (n = 15)	*Bupivacaine-Fentanyl (n = 15)*
Age (year)	34 (12)	35 (14)
Body weight (kg)	71 (15)	70 (17)
Gender (M/F)	8/7	163.0 (11.8)
Duration of surgery (min)	191 (34)	200 (32)

*Significantly different (P < 0.05).

Figure 2

Table 2: Pre- and postoperative respiratory rate and arterial carbon dioxide tension (PaCO) for the ropivacaine-fentanyl (RF) and the bupivacaine-fentanyl (BF) groups. Data are means (SD).

	Respiratory rate (breaths/min)		*$PaCO_2$ (mm Hg)*	
	RF (n = 15)	BF (n = 15)	RF (n = 15)	BF (n = 15)
Baseline	18 (2)	18 (2)	34.0 (2.7)	36.4 (2.7)
Postoperative				
½ h	24 (4)	24 (5)	31.7 (4.3)	32.6 (5.0)
2 h	24 (4)	24 (4)	32.0 (4.1)	32.1 (3.1)
4 h	23 (4)	23 (4)	33.0 (5.0)	33.8 (4.6)
6 h	22 (3)	23 (4)	31.1 (3.7)	32.6 (3.8)
8 h	21 (3)	22 (3)	33.6 (3.1)	32.9 (3.2)
10 h	21 (2)	21 (4)	34.7 (3.2)	32.4 (3.2)
18 h	20 (3)	21 (4)	34.0 (4.1)	33.1 (3.1)
24 h	20 (2)	20 (3)	34.0 (3.3)	33.9 (2.8)

*Significantly different (P < 0.05).

Figure 3

Table 3: Number of patients eliciting a pain score of 0, 1, 2, 3, and 4; analgesia; and side effects in patients subjected to epidural block with ropivacaine-fentanyl (RF) and bupivacaine-fentanyl (BF). Data are numbers of patients except for time first request of postoperative analgesia.

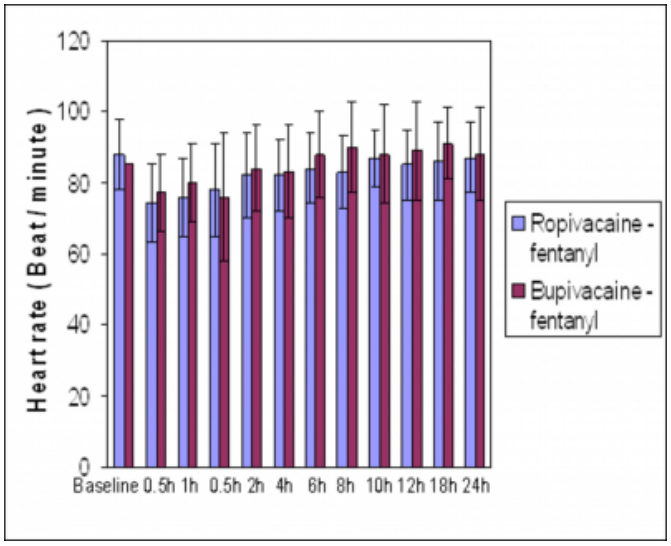
	RF (n = 15)	*BF (n = 15)*
		*Pain score 0 1 2 3 4 **
4 h	0, 5, 7, 3, 0	0, 6, 6, 3, 0
8 h	0, 6, 6, 3, 0	0, 7, 6, 2, 0
12 h	0, 8, 6, 1, 0	0, 9, 6, 0, 0
24 h	0, 9, 5, 1, 0	0, 9, 6, 0, 0
Additional analgesic	6	4
Number of doses	14	10
Time to first request (h)	4	4
Nausea	5	4
Vomiting	2	2
Pruritus	11	9

*0 = no pain; 1 = pain on coughing but not on deep breathing; 3 = pain on deep breathing but not on rest; 4 = slight pain at rest; 4 = severe pain at rest.

*Significantly different ($P < 0.05$).

Figure 4

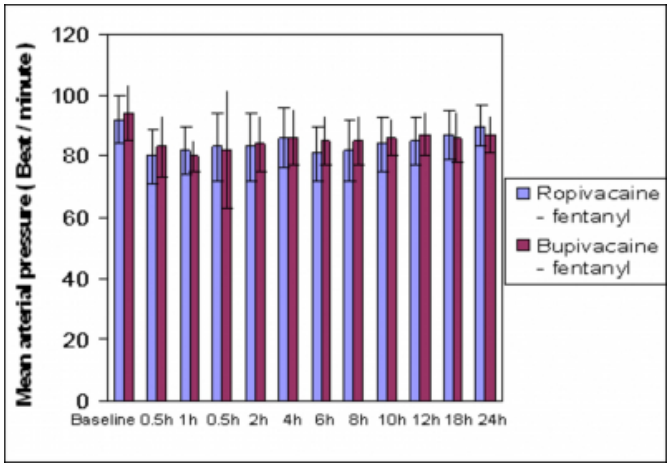
Figure 1: Perioperative heart rate changes during epidural analgesia with ropivacaine – fentanyl or bupivacaine-fentanyl . Values are means ± standard deviation.



*Significantly different ($P < 0.05$).

Figure 5

Figure 2: Perioperative mean arterial blood pressure changes during epidural analgesia with ropivacaine – fentanyl or bupivacaine – fentanyl . Values are means ± standard deviation.



*Significantly different ($P < 0.05$).

DISCUSSION

The results of our study revealed that intermittent epidural injection of ropivacaine – fentanyl is comparable to bupivacaine – fentanyl regarding hemodynamics, motor effects, analgesic profile and the incidence of side effects.

Pain relief after thoracic surgery is pivotal for decreasing postoperative morbidity. Both thoracotomy and pain contribute to postoperative pulmonary dysfunction ([1], [2]). Epidural administration of local anesthetics and opioids has been used for post-thoracotomy pain relief ([2],[3],[4]).

In a recent study, continuous epidural infusion of ropivacaine – fentanyl was comparable to bupivacaine – fentanyl for post-thoracotomy analgesia ([13]). In the same study, larger rescue doses of intravenous morphine were utilized when ropivacaine was infused alone. In our practice, we adopted the intermittent epidural administration of local anesthetics, at predetermined fixed time intervals, for postoperative pain relief. With continuous infusion of epidural local anesthetics and opioids, there may be a need for additional medications (usually an opioid) in as many as 50% of patients ([14]).

Intermittent injections of epidural local anesthetics may provide more reliable analgesia than that obtained by the continuous infusion technique ([15]) and reduces the need for supplementary medications when compared to constant infusions of epidural analgesic mixtures ([16]).

The placement of epidural catheter at the thoracic region for disposition of analgesic drugs at the dermatomal region of incision is thought to reduce the local anesthetic and opioid requirements after thoracotomy. Epidural administration of fentanyl ([17]) and epidural sufentanil-bupivacaine mixtures ([18]), for post-thoracotomy pain, produced good analgesia without remarkable ventilatory impairment when tailored to the site of nociceptive inputs.

In this study, full power of the upper limbs was preserved and the degree of motor blockade – represented by ventilatory indices (respiratory rate and arterial CO_2 tension) – was comparable in both groups. It may reflect lack of motor blocking and ventilatory depressant effects, at least in these volumes/doses. The maintenance of within normal arterial O_2 saturation, arterial O_2 tension, arterial carbon dioxide tension and respiratory rate in both groups indicates the lack of cardio – respiratory compromise as well. Other studies found that epidural fentanyl was better than intravenous fentanyl in terms of stress responses, pain control and respiratory functions ([17], [19]).

Contrary to our results but in another clinical setting (with the use of epidural analgesia during labour) epidural 0.125 % ropivacaine – fentanyl produced significantly less motor block than 0.125 % bupivacaine – fentanyl ([11]). However, other studies comparing ropivacaine with bupivacaine in 0.2–0.25% concentrations demonstrated no differences in motor block between these drugs ([8, 9, 20]).

In this study, analgesia and the need for additional analgesics (NSAID) were statistically comparable between both groups. However, analgesia profile tended to be better with bupivacaine – fentanyl than ropivacaine – fentanyl. We could not obtain a totally pain-free patient scoring 0. The sources of perceived pain are multiple and include the site of surgical incision, disruption of ribs and intercostal nerves, inflammation of the chest wall structures adjacent to incision, crushing of the chest wall parenchyma or pleura and the placement of drainage tubes. In addition, the nociceptive pathways subserving post-thoracotomy pain are poorly understood ([21]).

Recent studies suggest that ropivacaine is less potent than bupivacaine ([22, 23]) and other failed to detect significant difference ([24]). These conflicting results in local anesthetic potencies may be attributed to the addition of epidural opioids, which improves local anesthetic -induced analgesia. Differences in the study designs should also be thought of.

In the present study, postoperative side effects, namely nausea, vomiting and pruritus, were comparable in both groups. In other studies, the incidence and severity of postoperative nausea and vomiting after epidural ropivacaine–fentanyl was similar to that after epidural bupivacaine–fentanyl in patients undergoing lower abdominal ([25]) or thoracic ([13]) surgery. None the patients in this study showed respiratory depression, although epidural fentanyl was apparently large-dose in terms of μg/ml. Dose spacing and the small volume resulted in a total daily dose of approximately 450 μg which is still less than that given by others during epidural continuous infusion ([13]). It is worth mentioning that true incidence of side effects necessitates a larger number of patients.

Bupivacaine is reputed to have more central and cardiotoxic effects compared to ropivacaine ([5,6,7]). We could not detect clinically significant differences in this context. The patients of our study had good physiological parameters and underwent a limited lung resection. We believe that more morbid patients undergoing extensive lung resection are yet to be evaluated with this technique in a further clinical trial. In conclusion, intermittent epidural injection of 0.25% ropivacaine – fentanyl at fixed intervals is comparable to 0.25% bupivacaine – fentanyl for patients undergoing thoracotomy. The intermittent epidural administration of local anesthetics for pain relief seems feasible whenever cost containment is desired and in situations where continuous infusion devices or patient controlled sets can not be afforded. However, our findings can not be extrapolated to more morbid patients.

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