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Epidural ropivacaine infusion for the treatment of pain following axillary muscle-sparing thoracotomy: a dose-evaluation study

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Abstract
Purpose. We aimed to investigate the optimal dose of continuous epidural ropivacaine for effective analgesia with minimal side effects after axillary muscle-sparing thoracotomy.
Methods. Sixty patients undergoing thoracic surgery via the axillary approach were studied. Patients were given continuous epidural ropivacaine at 6 (group R-6), 9 (group R-9), 12 (group R-12) or 18 $mg \cdot h^{-1}$ (group R-18) in a randomized double-blinded fashion after surgery. All of the patients received nonsteroidal anti-inflammatory drugs (NSAIDs) every 6 h for 24 h postoperatively. Pain intensity was assessed under three conditions (at rest, on moving, and while coughing), at 4, 8, 16, 24, and 48 h after surgery, and the extent of sensory block was evaluated at the same time points. The ability of a patient to walk unaided was assessed at 24 and 48 h after surgery.
Results. Pain intensity at rest and coughing was significantly higher in group R-6 than in the other groups at 16 h after surgery. Pain intensity during moving was significantly greater in group R-6 than in groups R-12 and R-18 at 16 h after surgery. Group R-18 exhibited a significantly greater extent of sensory block than the other groups. The number of patients who were not able to walk unaided 24 h after surgery was significantly greater in group R-18. There were no significant differences in the incidences of side effects among the groups.
Conclusion. Our results showed that epidural analgesia using ropivacaine, at 12 $mg \cdot h^{-1}$, provided the best analgesia with few side effects.

Key words Thoracic surgery · Postoperative pain · Epidural analgesia · Ropivacaine · Ability to walk

Introduction

Posterolateral thoracotomy is very traumatic and is associated with severe postoperative pain [1]. Continuous thoracic epidural analgesia with a combination of ropivacaine and opioid is an effective method for pain relief after posterolateral thoracotomy [2,3]. However, epidural opioids sometimes cause side effects such as nausea, respiratory depression, pruritus, and sedation [4–6].

Axillary muscle-sparing thoracotomy, in contrast to posterolateral thoracotomy, produces less invasion and pain, because of the relatively small skin incision and no resection of muscle [1,7]. Therefore, it is possible that ropivacaine used alone for epidural analgesia, and systemic nonsteroidal anti-inflammatory drugs (NSAIDs), would provide effective analgesia and fewer side effects than epidural anesthesia including an opioid in patients undergoing axillary muscle-sparing thoracotomy. However, very few precise studies have evaluated the effect of epidural ropivacaine on pain relief after axillary muscle-sparing thoracotomy.

The present study was designed to identify the optimal dose of epidural ropivacaine, used along with systemic NSAIDs, for the provision of effective analgesia after axillary muscle-sparing thoracotomy, with a minimal risk of side effects.

Patients, materials, and methods

Sixty patients undergoing elective lung surgery via an axillary thoracic incision were recruited for this prospective, randomized, and double-blinded study, following our obtaining of institutional approval and the patients' written informed consent. Patients were excluded if they had contraindications to epidural anesthesia.

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An epidural catheter was placed in each patient at a level between T4 and T7, according to the site of incision before the induction of general anesthesia. A 4-ml test dose of 1% lidocaine was used to confirm that the catheter had been sited appropriately. General anesthesia was induced with thiamylal (4 mg·kg^{-1} i.v.) and fentanyl (0.1 mg i.v.). Vecuronium was used to facilitate tracheal intubation and maintain muscle relaxation. Anesthesia was maintained with sevoflurane (0.5%–3% end-tidal), 40%–100% oxygen, and intermittent doses of fentanyl (0.1 mg i.v.). Additional boluses of 0.20% ropivacaine (5 ml) were administered when appropriate, such as for indications of inadequate block (e.g., increased heart rate, increased blood pressure). Patients were randomly allocated to one of four groups to receive various continuous doses of epidural ropivacaine (group R-6, 6 mg·h^{-1}; group R-9, 9 mg·h^{-1}; group R-12, 12 mg·h^{-1}; and group R-18, 18 mg·h^{-1}) after surgery, according to a computer-generated table of random numbers. The infusion doses were maintained for 24 h after surgery and then were reduced to a half for the next 24 h. Analgesic solutions were prepared in a double-blind fashion by one of the authors who did not participate in the care of the patients or the data collection. In addition, patients received flurbiprofen (50 mg i.v.), every 6 h for a period of 24 h, followed by oral loxoprofen (60 mg) every 8 h for the next 24-h period.

The intensity of pain at rest, on moving, and while coughing was evaluated, using a verbal rating pain score (VRPS), at 4, 8, 16, 24, and 48 h after surgery. The VRPS was graded on a scale from 0 to 4, in which 0 = no pain and 4 = excruciating pain. The extents of sensory block (assessed by pinprick) and motor block (assessed using the modified Bromage scale from 0 to 3) were also evaluated at 4, 8, 16, 24, and 48 h after surgery. The ability of a patient to walk unaided was also assessed, at 24 and 48 h after surgery.

If patients asked for more analgesia because of pain, buprenorphine (0.1 mg i.v.) was administered, with a 1 h lockout time. Protocols to treat patients' symptoms included metoclopramide (10 mg i.v.) for nausea and naloxone (0.1 mg i.v.) for pruritus. The use of these additional medications was recorded. Hypotension (systolic arterial blood pressure < 90 mmHg) and respiratory depression (respiratory rate < 10 beats·min^{-1}) were also evaluated. Hypotension was treated with intravenous fluid as required. Respiratory depression or deep sedation was treated with naloxone (0.1 mg i.v.). Buprenorphine consumption and associated side effects (hypotension, nausea, pruritus, and respiratory depression) were also recorded during the study. These assessments and treatments were carried out by an anesthesiologist and nurses who were not aware of how patients were assigned to the treatment groups.

Data were analyzed by one-way factorial analysis of variance (ANOVA) along with a multiple comparison test and the Kruskal-Wallis test as applicable. Post-hoc analysis was performed using Fisher's protected least significant difference (PLSD) test and the Mann-Whitney *U*-test when necessary. Values for results were expressed as means ± SD, and $P < 0.05$ was considered statistically significant.

Results

Of the total of 60 patients, 8 patients were excluded due to accidental removal of the epidural catheter (4 patients), change to the posterolateral incision (3 patients), and severe hypotension (1 patient). The remaining 52 patients completed the study. Demographic and perioperative data from this set of patients did not differ significantly among the four groups (Table 1).

Table 1. Demographic and perioperative data

	Group R-6 (n = 13)	Group R-9 (n = 13)	Group R-12 (n = 14)	Group R-18 (n = 12)
Age (years)	60.0 ± 10.1	58.3 ± 8.4	60.0 ± 11.5	61.2 ± 8.4
Sex (M/F)	6/7	6/7	6/8	6/6
Height (cm)	159.7 ± 7.7	159.0 ± 7.5	159.0 ± 8.1	157.0 ± 7.5
Weight (kg)	58.6 ± 12.4	58.6 ± 8.9	56.5 ± 9.1	55.8 ± 10.4
Duration of anesthesia (min)	389 ± 97	386 ± 70	343 ± 104	366 ± 63
Duration of surgery (min)	277 ± 93	274 ± 56	249 ± 102	258 ± 64
Perioperative				
Ropivacaine (ml)	16.7 ± 13.3	15.3 ± 8.7	19.8 ± 11.5	11.5 ± 9.9
Fentanyl (mg)	0.26 ± 0.11	0.19 ± 0.04	0.20 ± 0.10	0.27 ± 0.09
Blood loss (ml)	154 ± 134	119 ± 54	144 ± 205	131 ± 103

Data values are expressed as means ± SD
Group R-6, 6 mg·h^{-1} ropivacaine; group R-9, 9 mg·h^{-1} ropivacaine; group R-12, 12 mg·h^{-1} ropivacine; group R-18, ropivacine 18 mg·h^{-1}. There were no significant differences between the groups

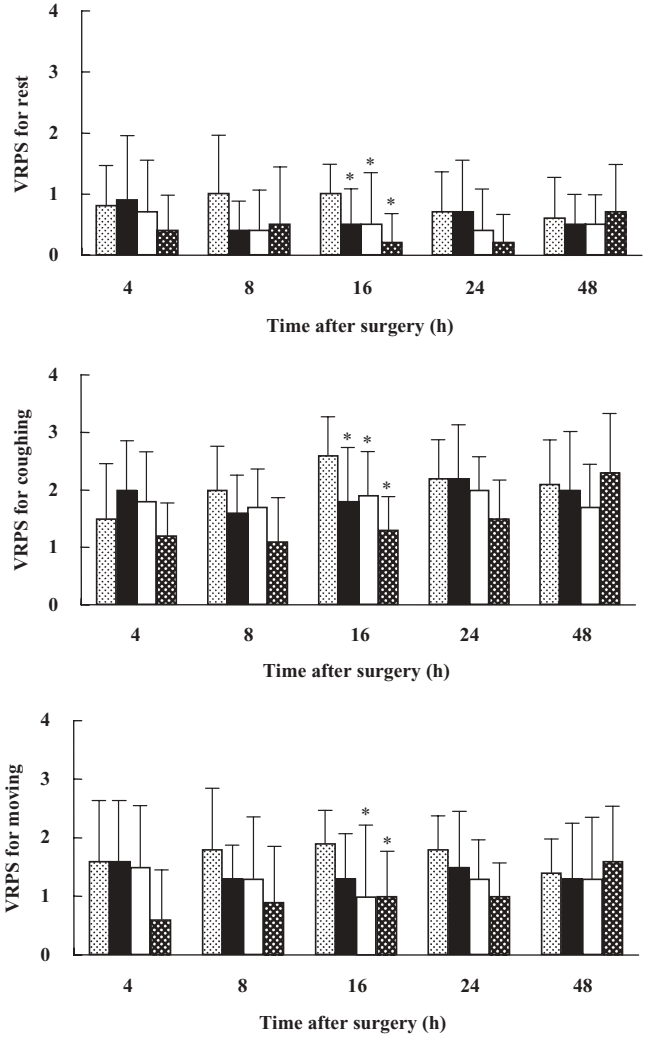

Fig. 1. Effects of a combination of epidural ropivacaine and systemic nonsteroidal anti-inflammatory drugs on postoperative pain at rest, and while coughing and moving. Group R-6 (*black-on-white dotted bars*), 6 mg·h^{-1} ropivacaine; group R-9 (*black bars*), 9 mg·h^{-1} ropivacaine; group R-12 (*white bars*), 12 mg·h^{-1} ropivacaine; group R-18 (*white-on-black dotted bars*), ropivacaine 18 mg·h^{-1}. The infusion dose was maintained for 24 h after surgery and then was reduced to half from 24 to 48 h. *VRPS*, Verbal rating pain score (0 to 4). *$P < 0.05$ compared to group R-6

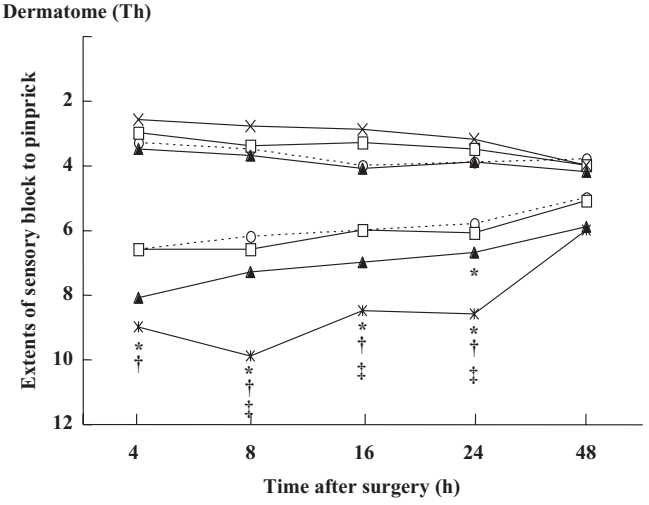

Fig. 2. Effects of thoracic continuous epidural ropivacaine on the extent of sensory block to pinprick after surgery. Group R-6 (*circles*), 6 mg·h^{-1} ropivacaine; group R-9 (*squares*), 9 mg·h^{-1} ropivacaine; group R-12 (*triangles*), 12 mg·h^{-1} ropivacaine; group R-18 (*crosses*), ropivacaine 18 mg·h^{-1}. The infusion dose was maintained for 24 h after surgery and then was reduced to half from 24 to 48 h. *$P < 0.05$ compared to group R-6; †$P < 0.05$ compared to group R-9; ‡$P < 0.05$ compared to group R-12

The VRPS values at 16 h after surgery, both at rest and during coughing, were significantly greater in group R-6 than in the other groups ($P < 0.05$). Furthermore, VRPS during moving was significantly higher in group R-6 than in groups R-12 and R-18 at 16 h after surgery ($P < 0.05$; Fig. 1).

Group R-18 exhibited a significantly greater extent of sensory block than the other groups at any of the time-points (4, 8, 16, and 24 h after surgery; $P < 0.05$), except for group R-12 at 4 h. There were no differences in the extent of sensory block among groups R-6, R-9, and R-12 throughout the time course, except at 24 h (Fig. 2).

No patient showed motor block at any of the assessment times. The number of patients who were not able to walk unaided at 24 h after surgery was significantly greater in group R-18 ($P < 0.05$) than in the other groups (i.e., 2/13, 1/13, 1/14, and 7/12 patients in groups R-6, R-9, R-12, and R-18, respectively). All of our patients were able to walk unaided by 48 h after surgery.

There were no significant differences in postoperative buprenorphine consumption (Table 2). There were no significant differences in the incidence of hypotension, or nausea among the treatment groups. Metoclopramide was administered to all patients who reported nausea. Consequently, none of our patients developed severe nausea. All patients who had hypotension were treated with intravenous fluid, but not with catecholamines. None of our patients had respiratory depression (Table 2) or pruritus.

Discussion

The present results demonstrate that the combination of 12 mg·h^{-1} ropivacaine, used alone for epidural analgesia, and systemic NSAIDs provided effective analgesia and few side effects in patients undergoing axillary muscle-sparing thoracotomy. Although thoracic epidu-

Table 2. Data for postoperative buprenorphine consumption, and data for side effects

	Group R-6 ($n = 13$)	Group R-9 ($n = 13$)	Group R-12 ($n = 14$)	Group R-18 ($n = 12$)
Buprenorphine consumption (mg)				
Time after surgery				
0–24 h	0.13 ± 0.11	0.08 ± 0.08	0.05 ± 0.06	0.04 ± 0.06
24–48 h	0.04 ± 0.06	0.02 ± 0.04	0.01 ± 0.05	0.05 ± 0.06
Cumulative 0–48 h	0.17 ± 0.14	0.10 ± 0.11	0.06 ± 0.09	0.09 ± 0.10
Hypotension (n)	2	3	6	4
Nausea (n)	4	8	4	11
Respiratory depression (n)	0	0	0	0
Disturbance in walking (n)	2	1	1	7*

*$P < 0.05$ Compared to the other groups
Data values are expressed as means ± SD or numbers
Disturbance in walking indicates the number of patients who were not able to walk unaided at 24 h after surgery

ral analgesia with a combination of anesthetics and opioids is the gold standard for pain relief after thoracic surgery [2,3,6,8,9], epidural opioids sometimes cause side effects such as nausea, respiratory depression, pruritus, and sedation [4–6]. Gottschalk et al. [10] demonstrated that a thoracic epidural infusion of 0.375% ropivacaine alone was equivalent to a combination of 0.125% bupivacaine and sufentanil in terms of analgesic effect, without increasing the incidence of side effects. Some dose-finding studies of continuous epidural block with ropivacaine alone for postoperative analgesia after orthopedic and upper abdominal and lower abdominal surgery have been carried out [11–15]. However, there are few studies of postoperative analgesia for thoracic surgery. To our knowledge, our study is the first to evaluate and identify the optimal dose of epidural ropivacaine alone for the provision of effective analgesia and minimal side effects following thoracic surgery.

There are many possible reasons as to why 12 mg·h^{-1} ropivacaine used alone for epidural analgesia after thoracic surgery provided effective analgesia in our study. First, our study included only patients undergoing thoracic surgery via an axillary muscle-sparing thoracic incision and did not include patients undergoing the surgery via a posterolateral incision. Hazelrigg et al. [1] demonstrated that postoperative pain following a muscle-sparing incision was significantly lower than that experienced after a posterolateral incision. Second, all of the patients in our study received NSAIDs every 6 h for 24 h postoperatively. Scott et al. [16] have demonstrated that NSAIDs enhance the analgesic effect produced by a continuous epidural block. However, it is possible that ropivacaine used alone along with systemic NSAIDs may be insufficient for the relief of postoperative pain in patients undergoing thoracic surgery via a posterolateral incision.

Motor block was not observed in any of our patients. This is predominantly due to the fact that we inserted epidural catheters at an upper- to mid-thoracic level and because our infusion dose of ropivacaine was less than that used in previous studies [11–15]. With these particular procedures, the extent of sensory block remained within the thoracic dermatome. However, the results of our study showed that over half of the patients receiving 18 mg·h^{-1} ropivacaine were not able to walk unaided at 24 h after surgery, in spite of being graded as zero on the Bromage scale. In an epidural ropivacaine dose-finding study, Etches et al. [15] observed that the number of patients who were able to stand was lower than the number of patients graded as zero on the Bromage scale after surgery. This implies that evaluation by the Bromage scale alone is unable to reflect the ability to stand or walk. One reason for this discrepancy might be that orthostatic hypotension may have led to the patients being unable to walk. We did not, however, assess orthostatic blood pressure changes in this study.

In the present study, patients receiving 18 mg·h^{-1} ropivacaine experienced a significantly greater extent of sensory block in thoracic segments than patients treated with other doses. An extensive thoracic epidural block interferes with the sympathetic nerves (T1-4) and the splanchnic nerve (T6-L1), which can then produce substantial hypotension [17]. Indeed, Liu et al. [18] have demonstrated that the postoperative thoracic epidural infusion of high-dose bupivacaine was associated with a trend for a higher incidence of orthostatic hypotension following thoracic surgery.

Although the extents of sensory block were similar in the groups who received 9 mg·h^{-1} and 12 mg·h^{-1} ropivacaine in the present study, 12 mg·h^{-1} ropivacaine exhibited better analgesia than 9 mg·h^{-1} ropivacaine. Sakura et al. [19] observed that the epidural administration of a high concentration of lidocaine resulted in a greater intensity of sensory block than a low concentration of lidocaine at the site of injection. In the present study, it is likely that the difference, in terms of analgesia, between 9 mg·h^{-1} and 12 mg·h^{-1} ropivacaine may have

been due to the intensity of sensory blockade at the site of incision.

In conclusion, our study demonstrated that 12 mg·h^{-1} epidural ropivacaine, along with systemic NSAIDs, provided the best analgesia with minimal side effects after axillary muscle-sparing thoracotomy, as compared to 6, 9, and 18 mg·h^{-1} ropivacaine. In contrast, 18 mg·h^{-1} ropivacaine caused inability to walk unaided for 24 h after surgery in over 50% of the patients. Our results indicate that a single dose of 12 mg·h^{-1} ropivacaine, along with systemic NSAIDs, would be appropriate for continuous epidural block after axillary muscle-sparing thoracotomy.

References

1. Hazelrigg SR, Landreneau RJ, Boley TM, Priesmeyer M, Schmaltz RA, Nawarawong W, Johnson JA, Walls JT, Curtis JJ (1991) The effect of muscle-sparing versus standard posterolateral thoracotomy on pulmonary function, muscle strength and postoperative pain. J Thorac Cardiovasc Surg 101:394–400
2. Macias A, Monedero P, Adame M, Torre W, Fidalgo I, Hidalgo F (2002) A randomized, double-blinded comparison of thoracic epidural ropivacaine, ropivacaine/fentanyl, or bupivacaine/fentanyl for postthoracotomy analgesia. Anesth Analg 95: 1344–1350
3. Tuncel G, Ozalp G, Savli S, Canoler O, Kaya M, Kadiogullari N (2005) Epidural ropivacaine infusions for post-thoracotomy pain. Eur J Cardiothorac Surg 28:375–379
4. Scott DA, Blake D, Buckland M, Etches R, Halliwell R, Marsland C, Merridew G, Murphy D, Paech M, Shug SA, Turner G, Walker S, Huizar K, Gustafsson U (1999) A comparison of epidural ropivacaine infusion alone and in combination with 1, 2 and 4 μg/ml fentanyl for 72 hours of postoperative analgesia after major abdominal surgery. Anesth Analg 88:857–864
5. Brodner G, Mertes N, van Aken HV, Mollhoff T, Zahl M, Wirtz S (2000) What concentration of sufentanil should be combined with ropivacaine 0.2% wt/vol for postoperative patient-controlled epidural analgesia. Anesth Analg 90:649–657
6. Tan CN, Guha A, Scawn ND, Pennefather SH, Russel GN (2004) Optimal concentration of epidural fentanyl in bupivacaine 0.1% after thoracotomy. Br J Anaesth 92:670–674
7. Benedetti F, Vighetti S, Ricco C, Amanzio M, Bergamasco L, Casadio C, Cianci R, Giobbe R, Oliaro A, Bergamasco B, Maggi G (1998) Neurophysiologic assessment of nerve impairment in posterolateral and muscle-sparing thoracotomy. J Thorac Cardiovasc Surg 115:841–847
8. Geurts AM, Jessen HJ, Megens JH, Hasenbos MA, Gielen MJ (1995) Continuous high thoracic epidural administration of morphine with bupivacaine after thoracotomy. Reg Anesth 20:27–32
9. Snijdelaar DG, Hasenbos MA, van Egmond J, Wolff AP, Liem TH (1994) High thoracic epidural sufentanil with bupivacaine: continuous infusion of high volume versus low volume. Anesth Analg 78:490–494
10. Gottschalk A, Freitag M, Burmeister MA, Becker C, Horn EP, Standl T (2002) Patient-controlled thoracic epidural infusion with ropivacaine 0.375% provides comparable pain relief as bupivacaine 0.125% plus sufentanil after major abdominal gynecologic tumor surgery. Reg Anesth Pain Med 27:367–373
11. Scott DA, Chamley DM, Mooney PH, Deam RK, Mark AH, Hagglof B (1995) Epidural ropivacaine infusion for postoperative analgesia after major lower abdominal surgery—a dose finding study. Anesth Analg 81:982–986
12. Badner NH, Reid D, Sullivan P, Ganapathy S, Crosby ET, McKenna J, Lui A (1996) Continuous epidural infusion of ropivacaine for the prevention of postoperative pain after major orthopaedic surgery: a dose-finding study. Can J Anesth 43:17–22
13. Schug SA, Scott DA, Payne J, Mooney PH, Hagglof B (1996) Postoperative analgesia by continuous extradural infusion of ropivacaine after upper abdominal surgery. Br J Anaesth 76:487–491
14. Turner G, Blake D, Buckland M, Chamley D, Dawson P, Goodchild C, Mezzatesta J, Scott D, Sultana A, Walker S, Hendrata M, Mooney P, Armstrong M (1996) Continuous extradural infusion of ropivacaine for prevention of postoperative pain after major orthopaedic surgery. Br J Anaesth 76:606–610
15. Etches RC, Writer WD, Ansley D, Nydahl PA, Ong BY, Lui A, Badner N, Kawolski S, Muir H, Shukla R, Beattie WS (1997) Continuous epidural ropivacaine 0.2% for analgesia after lower abdominal surgery. Anesth Analg 84:784–790
16. Scott NB, Forbes DW, Binning AR (1994) The effect of parenteral diclofenac and morphine on duration and height of blockade of continuous epidural infusion of bupivacaine 0.5%. Anaesthesia 49:594–596
17. Veering BT, Cousins MJ (2000) Cardiovascular pulmonary effects of epidural anaesthesia. Anaesth Intensive Care 28:620–635
18. Liu S, Angel JM, Owens BD, Carpenter RL, Isabel L (1995) Effects of epidural bupivacaine after thoractomy. Reg Anesth 20:303–310
19. Sakura S, Sumi M, Yamada Y, Saito Y, Kosaka Y (1998) Quantitative and selective assessment of sensory block during lumbar epidural anaesthesia with 1% or 2% lidocaine. Br J Anaesth 81:718–722