Anesthesiology 2006; 104:1047–53

Efficacy of Single-dose, Multilevel Paravertebral Nerve Blockade for Analgesia after Thoracoscopic Procedures

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Background: **Although video-assisted thoracoscopic surgery for pulmonary resection is increasingly chosen over thoracotomy, the optimal analgesia regimen for thoracoscopy is unknown. The purpose of this trial was to compare the efficacy of analgesia from preoperative bupivacaine paravertebral nerve blockade with that from placebo injections.**

Methods: **Eighty adult patients undergoing unilateral thoracoscopic procedures were enrolled in a prospective, double-blinded, randomized clinical trial of preoperative, multilevel, single-dose paravertebral nerve blockade. Patients received six paravertebral injections with 5 ml of either 0.5% bupivacaine with 0.0005% epinephrine (treated, n = 40) or preservative-free saline (control, n = 40). Cumulative weight-adjusted intraoperative fentanyl and postoperative patient-controlled morphine usage, visual analog pain scores, and spirometry were used to compare efficacy of analgesia between groups.**

Results: **The treated group received significantly less intraoperative fentanyl compared with the control group ($P = 0.003$) and had a 31% smaller cumulative patient-controlled morphine dose ($P = 0.03$) in the 6 h after block placement. Within 6 h, treated patients also reported lower maximum pain scores ($P = 0.02$) and demonstrated less pain score variability ($P = 0.01$). No statistically significant difference in cumulative morphine usage existed at 12 or 18 h after block placement. No significant difference in spirometry, cortisol levels, or cytokine production was found between treatments.**

Conclusions: **Single-dose paravertebral nerve blockade with bupivacaine is effective in reducing pain after thoracoscopic surgery, but only during the first 6 h after nerve blockade. Because of the limited duration of effect with currently available local anesthetic agents, the current data suggest that, at present, this technique is not indicated in the setting of thoracoscopic surgery.**

AFTER pulmonary resection, decreased lung capacity and incisional pain further compromise pulmonary function in a group of patients often already presenting with limited pulmonary reserve.[1] The incidence of complications after lung surgery, including atelectasis, respiratory insufficiency, pulmonary infection, and postthoracotomy neuralgia, is significant.[1–3] Video-assisted thoracoscopic surgery (VATS) patients have a diminution in forced vital capacity and the forced expiratory volume in 1 s on the first postoperative day.[1] The value of preemptive analgesia in reducing postoperative pulmonary dysfunction has been suggested by previous studies.[2,4,5] Although perioperative continuous thoracic epidural analgesia as well as paravertebral infusion of local anesthetic have been reported to be effective for postoperative analgesia in thoracotomy patients,[2,6] these techniques have not been studied extensively in VATS patients. However, benefits of unilateral paravertebral nerve blockade (PVB) for thoracic surgery and bilateral PVB for upper abdominal procedures have been reported, including ease of performance, decreased postoperative narcotic requirement, improved pulmonary mechanics, increased patient satisfaction, decreased pain scores, and a blunting in the increase of cortisol and glucose in the perioperative period.[3,6,7] Unfortunately, most randomized clinical trials in thoracic surgical patient groups to date have been comparisons between PVB and other regional techniques, such as epidural analgesia or intercostal nerve blockade, without blinding or placebo control, and have not included thoracoscopy patients. The ideal postoperative analgesia regimen for the short-duration but intense pain associated with VATS procedures has not been elucidated. The purpose of this study was to determine whether preoperative, unilateral PVB with bupivacaine is efficacious compared with a placebo-control group of patients injected with preservative-free normal saline in the paravertebral space. The primary efficacy end point of the study was comparison of postoperative patient-controlled morphine requirement between treatment and control groups. In addition, we postulated that preoperative PVB would decrease postoperative visual analog pain scores, reduce the decrement in postoperative pulmonary function, and blunt the perioperative inflammatory response compared with placebo.

Materials and Methods

Patient Population

With Duke University Institutional Review Board approval (Durham, North Carolina), 84 consenting adult patients undergoing elective unilateral thoracoscopic procedures were enrolled in the study. Exclusion criteria were (1) procedures involving neural tissue; (2) procedures for drainage of empyema or patients displaying signs and symptoms of systemic infection; (3) patients with a significant bleeding history as determined by the attending anesthesiologist or with prothrombin time greater than 14.0 s, partial thromboplastin time greater

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Received from the Departments of Anesthesiology and Surgery, Duke University Medical Center, Durham, North Carolina. Submitted for publication September 20, 2005. Accepted for publication February 9, 2006. Supported in part by a grant (New Investigator Award–Clinical; July 2001 to June 2003) from the Foundation for Anesthesia Education and Research, Rochester, Minnesota. The Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina, provided the remainder of the funding for this trial.

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than 40 s, or platelet count less than 50,000/μl; (4) severe spine or chest wall deformity; (5) preexisting motor or sensory deficit; (6) serum creatinine greater than 1.5 mg/dl; and (7) hypersensitivity to ketorolac, morphine, or bupivacaine. Postenrollment exclusion was permitted if the pulmonary resection became more extensive than thoracoscopy with lobectomy, the surgeon was forced to extend any incision beyond 6 cm, or additional thoracic incisions were required beyond the dermatomes affected by PVB as judged by the attending anesthesiologist.

Data Collection

Data collected for each patient included preoperative demographics, hospital duration of stay, and final pathologic diagnosis. Handheld spirometer measurements (Micro Spirometer; Micro Direct, Inc., Auburn, ME) of forced vital capacity and forced expiratory volume in 1 s (best of three attempts) were recorded before paravertebral injections as well as 2 and 8 h after skin closure and on postoperative day 1. Blood was collected for analysis of cytokine levels (interleukin 6, interleukin 8, interleukin 10, and interleukin 1ra) and cortisol levels at the following time points: (1) before paravertebral injection, (2) after induction of anesthesia, (3) upon lung reexpansion after pulmonary resection, (4) before discharge from the recovery room, and (5) on the morning of the first postoperative day. Serum samples were frozen at −80°C. Cytokine levels were determined by enzyme-linked immunosorbent assay (Searchlight Multiplex Assay; Pierce Biotechnology, Woburn, MA). Cortisol levels were measured using a competitive binding enzyme immunoassay (Cortisol EIA; Alpco Diagnostics, Salem, NH). Fentanyl and midazolam use from the starting time of paravertebral injection procedure through the operative period as well as operative time were collected for analysis from the electronic anesthetic record (Saturn; Draeger Medical, Inc., Telford, PA). Postoperatively, the amount of morphine delivered by patient-controlled analgesia (PCA) device (Lifecare® 4100 PCA Plus; Abbott Laboratories, North Chicago, IL) and perceived pain levels at rest (0–10 visual analog score) were monitored and recorded every 2 h by nursing personnel in accordance with institutional PCA protocol.

Sample Size Estimation

Pilot study data from 26 patients (13 per group) receiving paravertebral injections with bupivacaine or placebo found cumulative, postoperative PCA morphine usage (± SEM) of 0.31 ± 0.027 mg/kg in the treated group *versus* 0.41 ± 0.031 mg/kg in the placebo group. According to these data, a sample size of 25 patients per group would provide greater than 95% power to detect a 10% difference in the primary end point of postoperative morphine usage. To enhance clinical significance of the results, sample size was increased to allow assessment of the secondary end point of improved pulmonary function. We assumed a 25% improvement of forced vital capacity in the treatment group (decline of 27% compared with anticipated decline of 36%) with an SD of 14%. These estimates were based on results from a previous study of thoracoscopy patients by Furrer *et al.*[1] A sample size of 40 patients per group would provide 80% power to detect this difference.

PVB Procedure

Patients were randomly assigned to two equal groups. After written informed consent, an order for study drug preparation was faxed to the Duke University Investigational Drug Service (Durham, North Carolina). The treatment group was determined by a random number table generated before study initiation, and the blinded study medication was prepared and released to the operating room pharmacy on the day of surgery to be dispensed to the study coordinator. The double blinding was maintained, and records of group assignment were not released by the Investigational Drug Service until enrollment was complete. The treatment group of patients received PVB injections of 0.5% bupivacaine containing 0.0005% epinephrine, whereas the control group received paravertebral injection of an equivalent volume of preservative-free normal saline. The total dose of bupivacaine did not exceed 3 mg/kg. Injections were performed using 5 ml of the study solution deposited into the paravertebral space on the operative side from level T4 through T9. The injections were performed according to the technique described by Weltz *et al.*[8] After applying nasal cannula oxygen and administering intravenous sedation of midazolam and propofol, the location of the vertebral transverse process at each level was identified by bony landmarks, and a skin wheal of 1% lidocaine was placed over the transverse processes of T4 through T9 on the operative side. A 22-gauge Tuohy needle was then inserted until the tip of the needle touched the transverse process. The needle was then partially withdrawn and redirected caudally to slide under the transverse process and advanced 0.5 cm (small-framed individuals) up to 1.0 cm (large-framed individuals) past the depth of the transverse process into the paravertebral space. After negative aspiration, 5 ml of the study solution was injected slowly into the paravertebral space. A group of three attending anesthesiologists performed the injections to minimize variation in technique.

Intraoperative Management

Standardized anesthetic technique and uniform monitoring were used. Before anesthesia induction, a BIS® monitor (Aspect Medical Systems, Newton, MA) was placed to gauge depth of anesthesia. Patients received a standardized anesthetic technique consisting of propofol

(2 mg/kg) and fentanyl (3 μg/kg) for induction. Muscle relaxation was achieved initially with succinylcholine (1.5 mg/kg) or vecuronium (0.1 mg/kg) at induction followed by vecuronium titrated to maintain a single twitch response to train-of-four peripheral nerve stimulation of the ulnar nerve. Comparable depth of anesthesia was maintained in all patients by using the Bispectral Index with a target range of 50–60 during the surgical procedure; depth of anesthesia was adjusted using isoflurane or sevoflurane. Fifty-microgram doses of fentanyl were administered for hypertension or tachycardia at the discretion of the blinded anesthesia team.

After induction of general anesthesia, patients were placed in the lateral position. Isolated ventilation of the nonoperative lung was established, and the operative lung was allowed to deflate. Two thoracoscopy ports were inserted as described by Burfeind and D'Amico.[9] A 1.5-cm incision was made in the seventh or eighth intercostal space for camera insertion, and a 2- to 6-cm access incision was made for insertion of surgical instruments in the fourth or fifth intercostal space without rib spreading. Excised lung tissue from pulmonary resection was removed through the existing access incision using a specimen bag. If extension of the access incision was required, the patient was excluded from analysis as per protocol. Chest tube placement after completion of surgical resection was performed through the existing camera port incision with the chest tube directed posteriorly and inserted up to the apex of the operative lung.

All patients received 30 mg intravenous ketorolac tromethamine just before emergence and received 15 mg intravenous ketorolac every 6 h for the next 24 h. Each patient received demand-only, intravenous morphine by PCA at a dose of 0.02 mg/kg with an 8-min dosing interval that was initiated at the time of arrival at the postoperative recovery unit. Up to three loading doses of 0.04 mg/kg morphine were allowed after initiation of PCA at the discretion of blinded recovery room providers. For nausea or emesis, all patients had a standing order for 4 mg intravenous ondansetron every 4 h as needed. No other sedatives or analgesics were administered to research participants. Hospital discharge criteria included adequate oral intake, pain controlled by oral analgesics, assessment of patient well-being by the attending surgeon, and minimal chest drainage or air leak allowing tube thoracostomy removal. Absence of pneumothorax was confirmed by chest radiograph before discharge.

Statistical Analysis

The demographic and physical characteristics of the two groups were compared using a *t* test for normally distributed continuous measures, a Wilcoxon rank sum test for nonnormally distributed measures, and a Fisher exact contingency table test for categorical measures. The duration of surgery was annotated in minutes as duration from the start of the block placement procedure (noted as treatment) to recovery room admission time. For the primary end point of analgesic efficacy, morphine usage was cumulated at 6, 12, and 18 h after PVB placement from a review of the Duke standard nursing PCA assessment record. Use spanning two intervals was divided between intervals by interpolation. The value for each interval was cumulative, including the total morphine from previous monitoring intervals. Group comparisons were made at each of the three intervals separately. Serial visual analog pain scores from the first 18 h after PVB placement were also divided into the same three 6-h intervals. The worst pain score, pain score range, and median pain score over each of the three intervals were all compared separately. For the secondary end point of pulmonary function, proportional decrement from baseline was calculated for forced expiratory volume in 1 s and forced vital capacity at each measurement time (postoperative hour 2, postoperative hour 8, and postoperative day 1) with the formula [(measured − baseline)/baseline] × 100%. Percentage decrement from baseline at each time point was compared between treatments. To deal with nonnormal distributions, the Wilcoxon rank sum test was used for group comparisons of duration of surgery, intraoperative fentanyl usage, perioperative midazolam usage, cytokine and cortisol levels, and all continuous end point measures including PCA morphine usage and visual analog pain scores. A P value less than 0.05 was considered to be significant, except for the three representations of visual analog pain scores, where a Bonferroni-adjusted α of 0.0167 was applied for the multiple comparisons.

Results

Eighty-four patients were enrolled in the trial. Four patients were randomized and received PVB but were dropped from analysis as dictated by the protocol for conversion of the surgical procedure from VATS to thoracotomy. Three patients completed the trial but could not be analyzed because of incomplete data. A total of 77 out of 80 patients (38 treated, 39 placebo) had analyzable data with regard to the primary end point of morphine use. There were no differences in demographic characteristics between the two groups with regard to patient weight or sex (table 1). Neither the duration of surgery from time of block placement to arrival in the postoperative recovery area nor the duration of recovery room stay was different between the two groups (table 1). Hospital duration of stay was similar between the groups, with a median value of 2 days and a mode of 1 day. The dose of perioperative midazolam administered was similar between groups (fig. 1). The amount of intraoperative fentanyl administered was significantly less in the treated group compared with the placebo group ($P = 0.003$; fig. 1).

Table 1. Demographic Variables, Operative Duration, and Recovery Time

Measure	Treatment	n	Count	%	Mean	SD	*P* Value*
Female sex	Bupivacaine	40	18	45			0.359
	Placebo	40	13	33			
African-American	Bupivacaine	40	10	25			0.252
	Placebo	40	5	12			
Smoker	Bupivacaine	40	21	52			0.990
	Placebo	40	22	55			
Malignancy present	Bupivacaine	40	24	60			0.821
	Placebo	40	22	55			
Diabetes present	Bupivacaine	40	6	15			0.263
	Placebo	40	2	5			
Hypertension present	Bupivacaine	40	15	38			1.00
	Placebo	40	15	38			
			Min	Max			
Age, yr	Bupivacaine	40	21	78	55.5	16.7	0.525
	Placebo	40	24	80	54.8	12.8	
Weight, kg	Bupivacaine	40	61	113	87.6	14.3	0.400
	Placebo	40	55.7	151	86.2	20.9	
Treatment to recovery room time, min	Bupivacaine	40	45	295	147.6	65.5	0.708
	Placebo	40	55	320	139.1	57.3	
Recovery room stay, h	Bupivacaine	40	0.6	10	2.8	1.9	0.266
	Placebo	40	1.2	13	2.5	1.9	
Hospital duration of stay, days	Bupivacaine	40	1	15	2.6	2.5	0.401
	Placebo	40	1	5	1.8	1.0	

* *P* value from Wilcoxon rank sum or Fisher exact test comparing treatment groups.

With regard to the primary end point of PCA morphine usage, the treatment group used 31% less morphine during the first 6 postoperative hours compared with the placebo group. Median cumulative morphine use in the treatment group at 6 h after paravertebral injection was 0.11 mg/kg compared with 0.17 mg/kg in the placebo group ($P = 0.029$; fig. 2). The difference in cumulative morphine use dissipated at the 12-h ($P = 0.41$) and 18-h ($P = 0.49$) time points (fig. 2). Visual analog pain score data showed a statistically significant smaller range of pain score variability and a lower maximum pain score in the treatment group for the first 6 postoperative hours compared with the placebo group ($P = 0.0098$ and 0.0165, respectively, for adjusted $\alpha = 0.0167$; table 2). These findings did not persist for the 6–12 h or 12–18 h postoperative time periods. No difference between treatment groups was identified with regard to perioperative pulmonary function (fig. 3) or markers of inflammation (table 3). No serious adverse events related to the study procedure were identified during this trial.

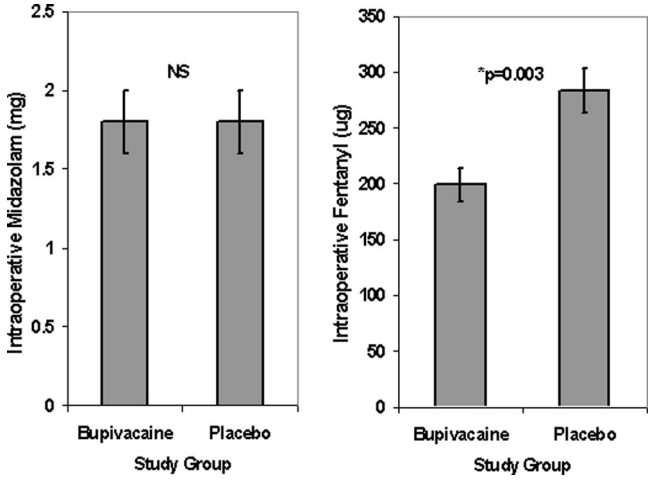

Fig. 1. Intraoperative intravenous analgesic and amnestic dosing, by treatment. *Error bars* represent SEMs. Treatment groups were compared using the Wilcoxon two-sample test with a *P* value less than 0.05 considered to be significant. NS = not significant.

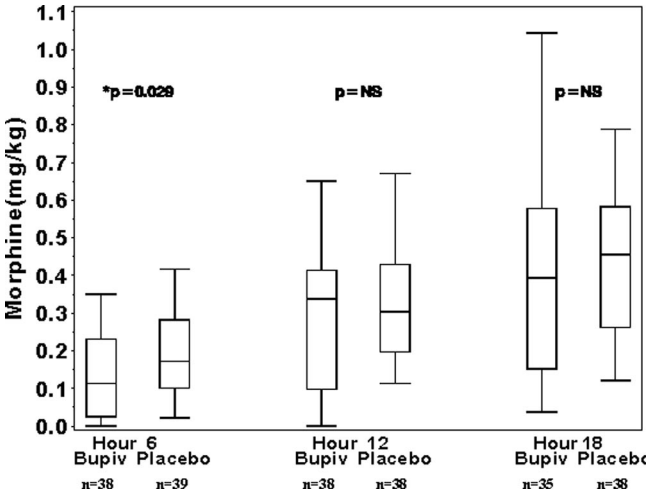

Fig. 2. Cumulative weight-adjusted morphine use over time after paravertebral injection, by treatment. The *horizontal lines* in the center of each box are drawn at the 50th percentile (median). The *bottom and top edges* are located at the sample 25th and 75th percentiles, and the *vertical lines* extend to the 5th and 95th percentiles. Bupiv = bupivacaine; n = number of subjects; NS = not significant.

Table 2. Visual Analog Pain Scores by Time from Treatment

Time	Treatment	Min	Max	Mean	SD	*P* Value*
0–6 h						
Median	Bupivacaine	0	9	3.4	3	0.0863
	Placebo	0	10	4.7	2.9	
Worst	Bupivacaine	0	10	3.9	3.2	0.0165
	Placebo	0	10	5.8	3.3	
Range	Bupivacaine	0	7	1.1	1.7	0.0098
	Placebo	0	7	2.3	2.1	
6–12 h						
Median	Bupivacaine	0	8	2.7	2.5	0.9916
	Placebo	0	8	2.6	2.1	
Worst	Bupivacaine	0	9	3.1	2.9	0.8450
	Placebo	0	9	2.8	2.4	
Range	Bupivacaine	0	5	1	1.3	0.0599
	Placebo	0	5	0.6	1.1	
12–18 h						
Median	Bupivacaine	0	8	1.9	2.2	0.4713
	Placebo	0	7	2	1.8	
Worst	Bupivacaine	0	8	2.2	2.6	0.5170
	Placebo	0	8	2.2	2.1	
Range	Bupivacaine	0	7	0.6	1.4	0.8669
	Placebo	0	6	0.5	1.2	

* *P* value from Wilcoxon rank sum test comparing treatments.

Discussion

In this prospective, randomized, double-blinded, placebo-controlled trial of preoperative, unilateral, multilevel, single-dose paravertebral nerve blockade for thoracoscopic surgery, a significant decrease in intraoperative and postoperative narcotic use was observed for up to 6 h after block placement in the treatment group. This finding was accompanied by a decrease in maximum reported pain score as well as reduced pain score variability in the treatment group compared with placebo. The findings failed to persist past 6 h.

A previous study of breast cancer patients undergoing surgery with analgesia from an identical PVB technique suggested effective pain relief for up to 23 h after block placement at more cephalad paravertebral levels.[8] Previous investigators have reported improved pain control and improved postoperative respiratory function in patients receiving continuous epidural local anesthetic or opioid infusion compared with intravenous narcotic analgesia for patients undergoing thoracotomy.[2] The disadvantages of continuous thoracic epidural infusion for patients undergoing VATS procedures include the risk of central neuraxial needle placement, neuraxial opioid side effects in short-stay surgery patients, and more intensive postoperative monitoring requirements. The potential disadvantage of paravertebral infusion of local anesthetic *via* a catheter placed at a single level in VATS patients is the variable and often limited extent of local anesthetic spread within the paravertebral space for a procedure in which small incisions are made for access or scope insertion at multiple levels.[10,11] When a randomized, double-blinded trial was performed comparing continuous infusion of local anesthetic *via* a paravertebral catheter with local anesthetic plus low-dose morphine infusion *via* an epidural catheter for cholecystectomy patients, the paravertebral infusion was found to be significantly less effective than the epidural infusion and insufficient as the sole postoperative analgesic.[12] A single-dose technique capable of providing adequate analgesia for patients would have a distinct advantage over more invasive catheter-based techniques for patients anticipating hospital discharge within 24 h after the surgical procedure (32 of 80 patients in this trial). Although our results support a benefit from the single-dose paravertebral bupivacaine injections within the first 6 h after block placement, a lasting benefit from preoperative nerve blockade was not apparent in this study. Patients receiving the bupivacaine initially showed less PCA morphine use. However, cumulative PCA morphine use by the treatment and control groups were indistinguishable at 12 and 18 h after PVB. Anticipated duration of bupivacaine-induced analgesia is from 2 to 5 h in the epidural space and from 4 to 12 h when used for peripheral nerve blockade.[13] Results from this study show an analgesic effect that resolves after 6 h. Therefore, unlike the results reported in the breast cancer patients, superior analgesia seems to be present only while the bupivacaine is present in therapeutic concentrations in the paravertebral space. No obvious benefit from preoperative analgesia in preventing late-onset discomfort was observed in this trial. The differing results compared with those reported in breast cancer surgery may be due to the persistence of tube thoracostomy in VATS patients or the more invasive nature of VATS procedures with stimulation of visceral pain fibers unaffected by paravertebral nerve blockade.

Although patients may have had more effective analgesia for the first 6 h after bupivacaine PVB compared

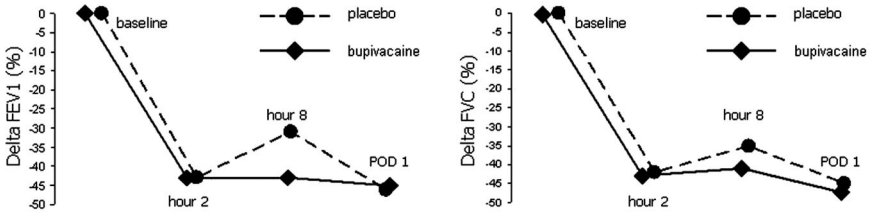

Fig. 3. Postoperative pulmonary function change, by treatment. Delta FEV_1 and delta FVC represent the percentage change calculated as [(measured − baseline)/baseline] × 100% with the median values for each group graphed at the protocol-defined measurement points. Groups were compared at each time point using the Wilcoxon rank sum test with a *P* value less than 0.05 considered to be significant. FEV_1 = forced expiratory volume in 1 s; FVC = forced vital capacity; hour 2 = 2 h after paravertebral injection; hour 8 = 8 h after paravertebral injection; POD 1 = postoperative day 1.

Table 3. Markers of Inflammation

Marker	Baseline	After Induction	After Resection	Recovery Room	Postoperative Day 1
IL-6 (25th, 75th percentiles), pg/ml					
Bupivacaine	5 (2, 22)	5 (2, 19)	6 (4, 28)	20 (12, 48)	24 (15, 47)
Placebo	4 (1, 9)	4 (2, 10)	7 (3, 16)	18 (9, 36)	24 (14, 48)
P value*	0.33	0.51	0.41	0.50	0.88
IL-8 (25th, 75th percentiles), pg/ml					
Bupivacaine	5 (0, 13)	4 (2, 12)	5 (2, 8)	7 (3, 16)	7 (4, 14)
Placebo	3 (2, 8)	4 (0, 9)	3 (0, 7)	6 (3, 12)	7 (3, 14)
P value	0.56	0.54	0.20	0.49	0.78
IL-10 (25th, 75th percentiles), pg/ml					
Bupivacaine	2 (0, 5)	2 (0, 4)	2 (0, 5)	3 (1, 7)	2 (2, 7)
Placebo	1 (0, 3)	1 (0, 3)	2 (0, 4)	5 (2, 12)	3 (2, 7)
P value	0.19	0.42	0.42	0.12	0.45
IL-1ra (25th, 75th percentiles), pg/ml					
Bupivacaine	75 (39, 152)	65 (33, 169)	69 (34, 138)	64 (39, 235)	102 (60, 215)
Placebo	54 (33, 89)	55 (28, 102)	54 (26, 84)	75 (44, 139)	95 (62, 164)
P value	0.14	0.36	0.11	0.57	0.49
Cortisol (25th, 75th percentiles), μg/ml					
Bupivacaine	10 (8, 15)	9 (7, 15)	28 (21, 36)	26 (17, 42)	15 (8, 21)
Placebo	13 (8, 20)	16 (7, 21)	29 (20, 37)	25 (21, 39)	15 (8, 25)
P value	0.12	0.05	0.66	0.91	0.64

* *P* value from Wilcoxon rank sum test comparing treatments.

IL = interleukin.

with patients receiving placebo injections, no significant difference in markers of inflammation was observed between treatment and control patients at any measured time point. Inflammatory markers were measured at three time points in the first 6 h after PVB (after induction, after resection of the surgical specimen, and in the recovery room), with no apparent trend in levels of either proinflammatory or antiinflammatory cytokines or cortisol related to the study treatment. This finding suggests that the pattern of cortisol and the cytokines measured in this trial may be a function of surgical tissue trauma or some other factor, such as the presence of a malignancy, rather than the effectiveness of analgesia. A larger sample size and measurement of a more extensive array of inflammatory markers at more time points would be required to further study this question.

In a recent trial by Vogt *et al.*,[14] 20 patients receiving a single injection of 0.4 ml/kg of 0.375% bupivacaine with 0.0005% epinephrine into the paravertebral space below the fifth rib attachment on the operative side were compared with 20 control patients undergoing needle puncture of the back but no injection. The authors found significantly improved visual analog pain scores at rest and with coughing for 48 h after thoracoscopic surgery and concluded that this technique improved postoperative pain treatment in a clinically significant fashion. However, there was no difference between treatment and control patients with respect to cumulative PCA morphine consumption, patient satisfaction, peak expiratory flow rate, or duration of hospital stay.[14] A single-injection technique was used in this trial, and sensory level testing showed that only 30% of the treated patients would have adequate spread of the local anesthetic to cover pain sensation from the fourth to the ninth intercostal space as required for the procedure described by Burfeind and D'Amico.[9] Although selection of visual analog pain scores as the primary end point resulted in different conclusions from our study, the results of the two trials are quite similar. Neither trial found evidence of extended benefit from paravertebral nerve blockade with respect to PCA narcotic usage, pulmonary function, or hospital duration of stay. In the current study, treated patients used less intraoperative narcotic, used less PCA morphine for the first 6 h, and reported less severe pain on emergence from anesthesia than control patients. However, the lack of extended benefit renders this technique ineffective as a sole analgesic regimen. Without additional objective evidence to support the finding of improved visual analog pain scores, it is difficult to justify this technique over PCA morphine for postoperative analgesia. Although small, the risk of complication from PVB placement and the additional costs of the procedure are not warranted according to the findings of our study.

The most likely cause for failure of persistent benefit is the duration of bupivacaine's local anesthetic properties. Resolution of the nerve blockade was simply too quick for this patient group. This limitation might be eliminated by the development of longer acting agents. If the nerve blockade were able to persist until removal of the patient's chest tube (usually the morning of the first postoperative day), sustained benefit could be achieved, and the necessity for PCA could be eliminated. Slow-release, encapsulated local anesthetic agents that might prolong the efficacy of this single-dose technique are

currently in human trials and may serve to optimize this technique in the future.[15,16]

One major limitation of this trial was the inability to accurately identify failed blocks. Ineffective local anesthetic deposition at any of the six levels could have negatively impacted the difference between groups. Although the blocks were placed by a select group of attending physicians with extensive thoracic analgesia experience, definitive identification of failed block placement was problematic. After block placement, patients underwent induction of anesthesia within 5–10 min, leaving inadequate time for maximal nerve blockade to develop and rendering preoperative testing of sensory levels unreliable. In a subgroup of 34 patients in this study, dermatomal sensation to cold was tested with an ice water–filled glove after recovery from anesthesia by blinded research personnel. Almost all subgroup patients who received bupivacaine (17 of 18, 94%) had a demonstrable change in sensation to cold on the side of the block when checked in the postoperative period. However, 50% (8 of 16) of subgroup patients receiving placebo injections also reported alteration in cold sensation postoperatively. This result likely represents acute change in sensation around the surgical site, resulting in an unreliable test. Use of a technique such as thermography reported by Cheema *et al.*[17] might provide a better assessment of block efficacy.

An additional limitation of this trial was discontinuation of the PCA device in four of the subjects before the 18-h end point. Although the device was removed in each case because the subject no longer required intravenous narcotic therapy, the possibility existed that including these subjects (three treated, one control) in the primary outcome analysis might skew the results because they no longer had access to PCA morphine. Therefore, a subgroup analysis of the primary end point was performed with exclusion of these four subjects. PCA morphine usage remained significantly less in the treatment group compared with the control group ($P = 0.029$) at 6 h after paravertebral injection. Cumulative morphine usage at 12 and 18 h remained similar ($P > 0.5$).

While significantly improved analgesia was not observed past 6 h in this trial, the potential benefit of preemptive analgesia has not been ruled out. Patients received significantly less intraoperative fentanyl from blinded anesthesia providers and awoke with less pain. Comparison of long-term outcome parameters such as incidence of postthoracoscopy neuralgia, decreased functional status, and neurocognitive decline might reveal a benefit from PVB not apparent at the time of this analysis.

Conclusion

Despite a significant improvement in analgesia as demonstrated by a decrease in narcotic requirement and severity of reported pain for the first 6 h after paravertebral nerve blockade, the benefit failed to persist. These results suggest that common use of this technique as the sole postoperative analgesic regimen is not indicated for thoracoscopic surgical patients.

The authors thank Lindsay E. Kuhn, B.S. (Research Coordinator, Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina), for her assistance in the conduct and analysis of the study.

References

1. Furrer M, Rechsteiner R, Eigenmann V, Signer C, Althaus U, Ris HB: Thoracotomy and thoracoscopy: Postoperative pulmonary function, pain and chest wall complaints. Eur J Cardiothorac Surg 1997; 12:82–7

2. Ballantyne JC, Carr DB, deFerranti S, Suarez T, Lau J, Chalmers TC, Angelillo IF, Mosteller F: The comparative effects of postoperative analgesic therapies on pulmonary outcome: Cumulative meta-analyses of randomized, controlled trials. Anesth Analg 1998; 86:598–612

3. Richardson J, Sabanathan S: Thoracic paravertebral analgesia. Acta Anaesthesiol Scand 1995; 39:1005–15

4. Richardson J, Sabanathan S: Pain management in video assisted thoracic surgery: Evaluation of localised partial rib resection. A new technique. J Cardiovasc Surg 1995; 36:505–9

5. Richardson J, Sabanathan S, Mearns AJ, Evans CS, Bembridge J, Fairbrass M: Efficacy of pre-emptive analgesia and continuous extrapleural intercostal nerve block on post-thoracotomy pain and pulmonary mechanics. J Cardiovasc Surg 1994; 35:219–28

6. Richardson J, Sabanathan S, Jones J, Shah RD, Cheema S, Mearns AJ: A prospective, randomized comparison of preoperative and continuous balanced epidural or paravertebral bupivacaine on post-thoracotomy pain, pulmonary function and stress responses. Br J Anaesth 1999; 83:387–92

7. Richardson J, Jones J, Atkinson R: The effect of thoracic paravertebral blockade on intercostal somatosensory evoked potentials. Anesth Analg 1998; 87:373–6

8. Weltz CR, Greengrass RA, Lyerly HK: Ambulatory surgical management of breast carcinoma using paravertebral block. Ann Surg 1995; 222:19–26

9. Burfeind WR, D'Amico TA: Thoracoscopic lobectomy. Operative Techniques Thorac Cardiovasc Surg 2004; 9:98–114

10. Naja MZ, Ziade MF, El Rajab M, El Tayara K, Lonnqvist PA: Varying anatomical injection points within the thoracic paravertebral space: Effect on spread of solution and nerve blockade. Anaesthesia 2004; 59:459–63

11. Cheema S, Richardson J, McGurgan P: Factors affecting the spread of bupivacaine in the adult thoracic paravertebral space. Anaesthesia 2003; 58: 684–7

12. Bigler D, Dirkes W, Hansen R, Rosenberg J, Kehlet H: Effects of thoracic paravertebral block with bupivacaine *versus* combined thoracic epidural block with bupivacaine and morphine on pain and pulmonary function after cholecystectomy. Acta Anaesthesiol Scand 1989; 33:561–4

13. Covino BG, Wilksmith JAW: Clinical pharmacology of local anesthetic agents, Neural Blockade in Clinical Anesthesia and Management of Pain. Edited by Cousins MJ, Bridenbaugh PO. Philadelphia, Lippincott–Raven, 1998, pp 97–128

14. Vogt A, Stieger DS, Theurillat C, Curatolo M: Single-injection thoracic paravertebral block for postoperative pain treatment after thoracoscopic surgery. Br J Anaesth 2005; 95:816–21

15. Kopacz DJ, Bernards CM, Allen HW, Landau C, Nandy P, Wu D, Lacouture PG: A model to evaluate the pharmacokinetic and pharmacodynamic variables of extended-release products using *in vivo* tissue microdialysis in humans: Bupivacaine-loaded microcapsules. Anesth Analg 2003; 97:124–31

16. Grant GJ, Barenholz Y, Bolotin EM, Bansinath M, Turndorf H, Piskoun B, Davidson EM: A novel liposomal bupivacaine formulation to produce ultralong-acting analgesia. ANESTHESIOLOGY 2004; 101:133–7

17. Cheema SP, Ilsley D, Richardson J, Sabanathan S: A thermographic study of paravertebral analgesia. Anaesthesia 1995; 50:118–21