Original Research Article

Comparative evaluation of perineural dexamethasone withropivacaine and dexamothasone alone in thoracic paravertebral block for postoperative analgesia in elective thoracotomy: A randomized, double-blind, placebo-controlled trial

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Abstract

Background: Thoracotomy operations generally painful, and poor pain control during the perioperative period can lead to postoperative problems such pneumonia, atelectasis, or respiratory failure. Furthermore, chronic postthoracotomy pain (CPTP), which lasts at least two months following thoracotomy, affects 30%–50% of patients, lowering their quality of life significantly.Because single-dose local anesthetics offer pain reliefof limited duration, adjuvants have been used to provide pro-long analgesia for peripheral nerve block because single-dose local anaesthetics provide only short-term pain relief. **Aim:** The goal of this study was to see if perineural dexamethasone combined with ropivacaine was effective in treating thoracic paravertebral block (TPVB) in patients undergoing elective thoracotomy. **Patients and methods:** In this study, 108 patients undergoing thoracotomy were randomised to one of three groups for TPVB adjuvant therapy: group S (saline), group R (0.5 percent ropivacaine), or group RD (0.5 percent ropivacaine) (5 mg dexamethasone and 0.5 percent ropivacaine). Analgesia after surgery, recuperation time, and chronic discomfort were all recorded. **Results:** In comparison to group S, groups R and RD spent less time in the postanaesthesia care unit, were out of bed earlier, and had shorter postoperative hospital stays. When compared to group S, the RD group regained consciousness sooner, had lower acute pain scores, and utilised less patient-controlled analgesia during the first 72 hours after surgery. 3 months postoperatively, group RD (19.0 percent) had less postthoracotomy pain than group S (47.6 percent), $p \leq 0.050$. **Conclusion:** With an opioid-based anaesthetic regimen, perineural dexamethasone with ropivacaine for TPVB enhances postoperative analgesia quality, lowers recovery time, and may minimize the incidence of chronic pain after thoracotomy.

Keywords: Chronic pain, dexamethasone, nerve block, thoracotomy.

Introduction

Thoracotomy operations generally painful, and poor pain control during the perioperative period can lead to postoperative problems such pneumonia, atelectasis, or respiratory failure. Furthermore, chronic postthoracotomy pain (CPTP), which lasts at least two months following thoracotomy, affects 30%–50% of patients, lowering their quality of life significantly. It has been observed that employing preventive and multimodal methods to treat acute pain following thoracotomy lowers the incidence of chronic pain. As a result, adequately managing pain during any phase of the perioperative operation may help to prevent or lessen the risk of chronic pain after surgery [1,2]. After a thoracotomy, thoracic epidural analgesia (TEA) is a common analgesic method, but it is limited by coagulopathy and other side effects.

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As a result, thoracic paravertebral block (TPVB), an alternative to TEA, may provide equivalent analgesia after thoracotomy with fewer side effects, such as a lower risk of significant neurologic consequences, less hemodynamic difficulties, and better postoperative respiratory function. Preoperative paravertebral blocking has been shown in several studies to reduce neuropathically mediated chronic pain after breast surgery, which has similar underlying processes as CPTP. The role of TPVB in preventing CPTP, on the other hand, is unclear [3-4].Because single-dose local anesthetics offer pain reliefof limited duration, adjuvants have been used to provide pro-long analgesia for peripheral nerve block because single-dose local anaesthetics provide only short-term pain relief. We believe that dexamethasone combined long-acting local ropivacaine for TPVB not only provides effective acute pain control with fewer side effects during the first 72 hours following surgery, but also reduces the incidence of CPTP [5,6]. The goal of this study was to see if perineural dexamethasone combined with ropivacaine was effective in treating thoracic paravertebral block (TPVB) in patients undergoing elective thoracotomy.

Patients and methods

Protocol

This prospective, double-blind, randomised, placebo-controlled clinical trial included 96 patients who were having an elective transthoracic esophagectomy for esophageal carcinoma or open surgery for lung cancer. From August 2020 through January 2021, patients were enrolled. The participants ranged in age from 18 to 80 years old and had an ASA physical status of I–II, according to the American Society of Anesthesiologists. Allergy to local anaesthetics or narcotics, pre-operative chronic opioid medication, coagulopathy, heart disease, central and peripheral neuropathies, severe chronic obstructive pulmonary disease, severe pulmonary emphysema, liver or renal failure, peptic ulcer and a history of previous thoracotomy, or local puncture site infection were all

considered exclusion criteria. In this study, 108 patients undergoing thoracotomy were randomised to one of three groups for TPVB adjuvant therapy: group S (saline), group R (0.5 percent ropivacaine), or group RD (0.5 percent ropivacaine) (5 mg dexamethasone and 0.5 percent ropivacaine). Analgesia after surgery, recuperation time, and chronic discomfort were all recorded. After each patient gave written informed consent, they were randomly assigned to one of three groups using computer-generated random numbers and a 1:1:1 allocation ratio. Randomization was done in sequentially numbered, sealed, opaque envelopes, which were opened after the patient arrived in the operating room. Allocation concealment was done by an assistant who was not participating in the study. Throughout the study, including postoperative follow-ups, research workers were kept blind.

TPVB technique

After induction of anaesthesia, patients were put in a conventional lateral position to administer TPVB. In a 20-mL syringe, an anaesthesia assistant who was not involved in the study, the perioperative period, or the postoperative follow-up produced study medicines. In the paravertebral space, groups received isotonic saline (S), 0.5 percent ropivacaine (R), or 0.5 percent ropivacaine plus 5 mg dexamethasone (RD). An ultrasound-guided parasagittal out-plane approach was used to conduct TPVB. Chlorhexidine in isopropyl alcohol was used to prepare the skin, which was then covered with a sterile sheet. A 22G, 120-mm needle (stimuplex D; B. Braun Melsungen AG, Melsungen, Germany) was guided using a real-time ultrasonic machine (SonoSite M-Turbo, Bothell, WA, USA) equipped with a C60x transducer (2–5 MHz) draped with a sterile cover (3M Tegaderm, St. Paul, MN, USA). With a bolus of 5–7 mL in each interspace region, local anaesthetic or saline was delivered at the paravertebral gaps between T3–T4, T4–T5, and T5–T6 vertebrae. The pleura had migrated southward due to the local anaesthetic, according to ultrasonography.

Anesthesia and perioperative treatment

Peripheral intravenous (iv), right internal jugular vein, and radial artery catheters were put when patients were moved to the operation room. Throughout the procedure, the electrocardiogram (leads II and V5), invasive blood pressure, central venous pressure, heart rate, pulse oximetry, and the bispectral index (BIS) (Vista; Aspect Medical Systems Inc., Norwood, MA, USA) were all monitored. During anaesthetic induction, propofol (Diprivan; AstraZeneca plc, London, UK) was delivered with a target-controlled infusion based on the Marsh model23 (Graseby 3500; Smiths Medical, Watford, UK) pharmacokinetics. Following the achievement of an initial goal concentration of 1.0 g/mL, the concentration was gradually increased by 0.3 g/mL until the BIS value reached 40–60. Then 0.03 mg of midazolam and 0.5 mg of sufentanil were administered into the rats (iv). To enable double-lumen endobronchial intubation, rocuronium bromide (0.9 mg/kg) was employed. The lungs were ventilated with 100 percent oxygen after tracheal intubation, and a volume-cycled ventilator was used with the following settings: tidal volume, 8 mL/kg ideal body weight; inspiratory-to-expiratory ratio, 1:2; and respiratory

frequency, 8 breaths/min. To maintain anaesthesia, propofol and remifentanil were continually administered. andsufentanil and cisatracurium were administered as needed. By adjusting the effect-site concentration of propofol, BIS values were maintained between 40 and 60 during surgery. Before the surgical procedure, the breathing mode was changed to one-lung ventilation, and the frequency and tidal volume were adjusted to maintain pulse oximetry and end-tidal carbon dioxide. At the conclusion of the last skin suture, propofol and remifentanil were no longer used. To reverse residual muscular relaxation after surgery, neostigmine (20 g/kg) and atropine (5–10 g/kg) were given according to tidal volume and frequency. Patients were admitted to the postanaesthesia care unit (PACU) until they were able to regain spontaneous breathing. Patients were extubated in the PACU according to standard extubation criteria and subjects were moved to the ward when a Steward recovery score exceeded 4. Before skin incision, flurbiprofen (50 mg, iv) was injected, and then sufentanil (0.1–0.2 g/kg) and flurbiprofen (50 mg, iv) were given, followed by the use of a patient-controlled analgesia (PCA) pump before the surgery was completed. The PCA contained 7.5 g/kg sufentanil and 250 mg flurbiprofen and had a volume of 250 mL. The infusion rate was kept at 2 mL/h, and the patient-controlled bolus was set at 2 mL with a 15-minute lockout period. Patients were taught to request an additional bolus if their postoperative pain score on a 10-cm visual analogue scale (VAS) exceeded 3. The mean arterial pressure (MAP) was kept between 20% and 20% of the baseline value throughout the procedure. Hypotension was defined as a 20% drop in MAP below baseline or a MAP of 60 mmHg for more than 30 seconds. When fluid therapy was not an option, phenylephrine (40 g, iv) was administered. Atropine (0.3 mg, iv) was given for bradycardia, which was defined as a heart rate of less than 60 beats per minute. Bradycardia and hypotension were treated with ephedrine (3–6 mg, iv).

Study outcomes

PCA use within the first 6 hours after surgery was the primary outcome. Second outcomes were: 1) duration of surgery and one-lung ventilation, sufentanil use, fluid volume (colloid and crystalloid solutions), and phenylephrine consumption during anaesthesia; 2) changes in hemodynamics, such as heart rate and blood pressure, at various time points: baseline (T0), 5 minutes after induction (T1), 5 minutes after paravertebral block (T2), 10 minutes after skin incision (T3), 10 minutes after skin incision (T3) , 10 min after one-lung ventilation (T4), 1 h after one-lung ventilation (T5), 10 min after the end of one-lung ventila- tion (T6), at the end of surgery (T7), at transfer to the PACU (T8), upon awakening (T9), upon extubation (T10), and with transfer from the PACU (T11); 3) PACU recovery data referring to awake time, extubation time, and length of stay;4) a 10 cm VAS for pain (0–10; 0, no pain; 10, worst imagin- able pain); 5) PCA machine use and side effects including postoperative nausea and vomiting (PONV) intensity (0, no nausea and vomiting; 1, mild; 2, moderate; and 3, severe) and the incidence of pruritus at 6, 12, 24, 48 and 72 h after surgery; 6) short-time recovery including major complica- tions, postoperative days for first out-of-bed activity, hospital stay, and hospitalization cost; and 7) CPTP: 3 months after surgery during a telephone interview.

Statistical analysis

SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5.01 were used to analyse the data (GraphPad Software, Inc., La Jolla, CA, USA). The hemodynamics of the patients were studied using a repeated-measure analysis of variance (ANOVA). One-way ANOVA was used to determine quantitative variables, which were given as mean sd, and a least significant difference (LSD) approach was utilised for post hoc comparisons. The Kruskal–Wallis test was used to determine the severity of PONV. When a significant difference between groups was found, Mann–Whitney U tests were used for intergroup comparisons. Categorical variables were compared using the chi-squared or Fisher's exact test (a statistically significant difference between groups was defined as p 0.05). For repeated outcome assessments, p-values were adjusted to 0.017 using the Bonferroni correction method. The effect of confounding factors was determined using analysis of covariance (ANCOVA).

Results

Patient information is listed in Table 1.

Table 1: Patient Characteristics

	GroupS(n=31)	GroupR(n= 32)	GroupRD(n=31)	p-value
Gender,(%)				0.158
Male	(86.96)	(66.67)	(85.71)	
Female	(13.04)	(33.33)	(14.29)	
Age(years)	66.00(6.49)	61.96(7.94)	61.43(7.26)	0.062
ASAstatus				0.970
I	(34.78)	(37.50)	(38.10)	
II	(65.22)	(62.50)	(61.90)	

Weight(kg)	59.91(11.88)	59.54(9.70)	60.76(8.59)	0.920
Height(cm)	167.65(7.24)	165.29(7.47)	166.76(6.03)	0.507
BMI(kg/m^2)	21.19(3.29)	21.79(3.35)	21.77(2.28)	0.751
Heartrate	74.48(10.83)	72.33(9.29)	75.33(15.84)	0.692
Meanarterialpressure(mmHg)	94.00(14.87)	95.96(9.96)	102.24(15.62)	0.122
SBP(mmHg)	137.39(25.84)	135.92(17.36)	146.76(24.79)	0.242
DBP(mmHg)	72.83(11.49)	76.04(9.47)	80.05(13.27)	0.120
Surgicalsite,n(%)				0.099
Esophagus	21 (91.30)	17 (70.83)	19 (90.48)	
Lung	2(8.70)	7(29.17)	2(9.52)	

Except for sufentanil consumption, which was considerably lower in group R compared to group S, there were no significant differences in intraoperative features across groups (Table 2).

Table2: Intraoperative data and characteristics of recovery in PACU

Variables	**Groups**			p-values		
	S	**R**	**RD**	p^1	p^2	p^3
Durationofsurgery(min)	160.96(62.52)	169.79(78.86)	156.71(69.93)	0.669	0.843	0.538
Durationofone-lungventilation(min)	96.52(66.05)	108.04(73.90)	95.95(65.24)	0.567	0.978	0.558
Consumptionofcolloid(mL)	421.74 (328.85)	520.83 (312.05)	576.19 (277.32)	0.274	0.101	0.549
Consumptionofcrystalloid(mL)	1391.30(393.02)	1314.58(467.53)	1576.19(607.38)	0.596	0.219	0.080
Consumptionofsufentanil(μg)	57.17(12.42)	49.58(10.42)	53.10(7.67)	0.015*	0.199	0.264
Consumptionofphenylephrine(μg)	68.70(101.41)	46.96(87.13)	22.86(27.05)	0.355	0.062	0.317
Timeofawaking(min)	68.52(71.31)	45.42(28.76)	35.24(19.26)	0.091	0.020*	0.463
Time of extubation (min)	51.65(43.12)	35.83(18.51)	36.00(19.84)	0.071	0.084	0.985
DurationinPACU(min)	126.70(74.92)	86.58(30.30)	82.43(30.03)	0.008*	0.005*	0.782

There are no variations in heart rate or blood pressure across the three groups, as shown in Figure 2. Table 2 shows that patients in group RD recover faster and spend less time in the PACU than those in group S.

Table 3: Postoperative analgesia and recovery duration

Variables	**Postoperative Time**	**Groups**			p-values		
		S	**R**	**RD**	p^1	p^2	p^3
VAS	6h	0.96(1.19)	0.58(0.83)	0.24(0.44)	0.196	0.193	0.192
	12h	1.09(0.90)	0.50(0.66)	0.48(0.60)	0.914	0.914	0.914
	24h	1.70(1.02)	1.71(1.08)	0.81(0.40)	0.001*	0.001*	0.001*
	48h	2.00(1.09)	1.46(1.18)	1.33(0.66)	0.681	0.681	0.681
	72h	2.00(1.41)	1.29(0.91)	1.10(0.63)	0.531	0.531	0.531
Effectivepressingnumbers	6h	3.96(4.72)	1.83(2.30)	1.62(1.77)	0.825	0.825	0.825
	12h	4.30(4.37)	1.75(2.47)	1.67(1.98)	0.929	0.929	0.929
	24h	6.70(6.06)	8.38(7.37)	3.86(2.95)	0.012*	0.012*	0.012*
	48h	8.35(6.58)	6.42(6.83)	6.71(6.47)	0.881	0.881	0.881
	72h	11.13(9.88)	5.50(5.35)	5.52(4.98)	0.881	0.881	0.881
Sumofpressingnumbers	Day3	32.91(22.11)	23.88(17.09)	19.38(15.02)	0.417	0.417	0.417
Firstout-of-bedactivity	Days	4.57(2.27)	3.33(1.24)	3.19(1.03)	0.765	0.765	0.765
Postoperativestayinhospital	Days	16.61(12.46)	10.88(3.15)	11.62(3.44)	0.748	0.748	0.748
Stayinhospital	Days	23.96(13.08)	18.38(5.30)	20.46(8.76)	0.807	0.807	0.807
Totalhospitalization		62759.70	51870.58	55172.86	0.479	0.479	0.479
expenditures(CNY)		(24554.63)	(8560.51)	(5943.83)			

Table 3 demonstrates that, relative to group S, postoperative VAS scores at all time points and total PCA machine use in group RD fell significantly. PONV intensity did not differ substantially across groups (Table 4).

Table 4: Intensity of PONV 72 h after surgery and chronic postoperative pain incidence

PONV	**Groups**			p-values		
	S	**R**	**RD**	p^1	p^2	p^3
0	23(100)	24(100)	20 (95.24)	0.321	—	—
1	0(0)	0(0)	0(0)	—	—	—
2	0(0)	0(0)	0(0)	—	—	—
3	0(0)	0(0)	1(4.76)	—	—	—
Incidencechronicpain	10(47.6)	7(29.2)	4(19.0)	0.015*	p^1 0.167	p^2 0.050

At the insertion site, no patient reported pruritus, pleural effusion, subjective signs of local anaesthetic toxicity, infection, or hematoma. In comparison to group S, groups R and RD experienced earlier ambulation and a shorter postoperative stay (Table 3). Two of the group S participants developed severe pneumonia and required a tracheostomy. Three months following surgery, the incidence of postthoracotomy pain syndrome was significantly different across the three groups, and persistent pain was reduced in the RD group. Because the difference in age between groups S and R or RD was almost significant (p= 0.062), ANCOVA was used to investigate the effect of age as a confounding factor. Age was just a complicating factor for time of awaking, according to the findings (Table 5).

Table 5: ANCOVA of age factor with time of awaking as a dependent variable

Source	p-values
Modified model	0.005
Group	0.124
Age	0.017
Groupxage	0.106

We assessed all basic data of patients in three groups before loss to follow-up to see if this confounding factor was induced by allocation. The comparison of ages in three groups did not show any significant differences, according to the findings.(Table 6).

Table 6: Basic data of patients in three groups before loss to follow-up

Variables	GroupS(n=36)	GroupR(n= 36)	GroupRD(n=36)	p-value
Gender,(%)				0.435
Gender,n(%)				
Male	24 (75.00)	22 (66.75)	26 (81.25)	
Female	8(25.00)	10 (33.25)	6(18.75)	
Age(years)	62.93(7.98)	60.43(8.78)	60.13(8.02)	0.359
ASAstatus				0.954
I	11 (34.38)	10 (31.25)	10 (31.25)	
II	21 (65.62)	22 (68.75)	22 (68.75)	
BMI(kg/m^2)	21.11(3.11)	21.84(3.44)	21.11(2.58)	0.433
Heartrate	75.24(10.32)	72.63(9.60)	76.27(16.47)	0.512
Meanarterialpressure(mmHg)	93.73(14.92)	95.90(9.77)	100.23(14.71)	0.164
SBP(mmHg)	136.83(26.16)	134.83(17.39)	144.77(23.37)	0.204
DBP(mmHg)	72.47(11.43)	76.53(8.90)	75.65(11.12)	0.139

Discussion

After an open thoracotomy, patients endure extreme discomfort, which makes coughing, deep breathing, and remobilization difficult, leading to atelectasis, bronchospasm, and pneumonia. Because of the multifaceted pathophysiology of postoperative pain, which includes nociceptive and neuropathic causes, a multimodal strategy was required to deliver analgesia. In multimodal analgesia, a complementary analgesic activity should not only provide adequate pain control with few side effects following surgery, but also reduce the incidence and severity of chronic pain [7-10]. By inhibiting thoracic sympathetic and somatic nerves, TPVB can be used for regional anaesthesia to manage initial pain after thoracotomy with fewer side effects, but it does not give complete postoperative analgesia for thoracotomy. By lowering local inflammation and limiting peripheral and central sensitization, flurbiprofenaxetil, a nonselective nonsteroidal anti-inflammatory medication, lowered postoperative opioid use and provided postoperative analgesia. Low-dose opiates combined with flurbiprofen have been shown to minimise postoperative sufentanil consumption and improve analgesic effects [11-14]. Preoperative flurbiprofen injection has been shown to dramatically reduce postoperative pain scores as a preventive analgesia technique. Because the anesthesiologists in charge of the surgery were unaware of the allocation and the response of patients in various interventional groups to the incision and the use of sufentanil could be unpredictable, preoperative sufentanil administration was discretionary rather than mandatory. Sufentanil with flurbiprofen was also given as a loading dosage for PCA at the conclusion of surgery as an alternate multimodal analgesia for postoperative pain control [15-18]. Studies have indicated that opioid combined flurbiprofen postoperative analgesia resulted in reduced pain scores. As a result, this study used a multimodal postoperative analgesia technique. Despite the fact that frequent use of PCA with a back-ground infusion is not suggested, it is appropriate for patients who require significant opioid consumption or who wake up throughout the night owing to acute pain after a thoracotomy. For patients undergoing elective thoracotomy, we found that TPVB plus iv infusions of sufentanil and flurbiprofen for postoperative analgesia lowered PACU stay, postoperative pain scores, required less PCA, recovery time, and expenses [19-22]. Various adjuncts with local anaesthetics were found to be beneficial in clinical trials for single injections, although blockade prolon- gation was inadequate. 39–45 When compared to group S, patients in group RD experienced superior postoperative analgesia and pain intensity at all time points, as well as reduced PCA usage within the first 72 hours after surgery. Furthermore, perineural dexamethasone was found to be superior to a single injection of ropivacaine in terms of reducing acute pain and PCA machine use 24 hours following thoracotomy. Perineural dexamethasone can prolong analgesic duration21,46–48 by lowering nociceptive C fibre activity, according to our findings [23-27]. Our primary outcome and sample size estimation were based on PCA machine use with successful pain control 6 hours after surgery, as early acute postoperative pain has been demonstrated to be a positive and independent predictor of eventual chronic pain49,50. In comparison to group S, CPTP in group RD declined, which was similar to PCA machine use over the first 72 hours postoperatively. As a result, dexamethasone as an adjuvant may not only extend analgesia but also reduce the occurrence of chronic pain. Although the sample size was insufficient to provide sufficient power for a conclusion, analgesic need during the first 72 hours may indicate a lower incidence of CPTP compared with maximum postoperative pain intensity [28-31]. As a result, the cumulative effect of acute postoperative pain following thoracotomy may influence the development of CPTP. In our study, group R participants who got a single-dose local anaesthetic consumed considerably less sufentanil during surgery than group S subjects, which was consistent with prior findings. 53 Furthermore, as compared to group S, the duration of stay and costs in group R dropped, but not in group RD, which could be attributable to diagnostic heterogeneity and surgical locations differences between groups. Due to erroneous or inadequately specific contact information for each patient, 29 percent of patients were lost to follow-up, which could explain the age bias [32-35]. Patients were asked if they had discomfort at the surgery site at rest or during activities of daily life, and follow-up data was gathered from telephone interviews. To create a relationship with respondents in the future, the type, severity, and effects on daily activities should be investigated in a more comprehensive study with well-trained staff [36-39].

Conclusion

When administered as an adjuvant to TPVB with ropivacaine, dexamethasone provides efficient initial pain control, needs less anaesthetic, and minimises complications. For individuals undergoing elective thoracotomy, it also reduces healing time and may lessen chronic discomfort. To completely assess the benefits of TPVB for chronic pain management, more appropriately powered trials are required.

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