Comparison of analgesic efficacy of ultrasound-guided thoracic paravertebral block versus surgeon-guided serratus anterior plane block for acute postoperative pain in patients undergoing thoracotomy for lung surgery - A prospective randomized study

ABSTRACT

Context: Inadequate pain relief after thoracotomy may lead to postoperative respiratory complications.

Aims: We have compared total morphine consumption in 24 hours following thoracotomy.

Settings and Design: This prospective randomized pilot study involved 50 patients undergoing elective thoracotomy for lung surgery at AIIMS, New Delhi.

Patients and Methods: Fifty patients undergoing elective thoracotomy were randomly allocated into two groups. In Group I patients, ultrasound (USG)-guided paravertebral catheter was inserted preoperatively and in Group II patients, serratus anterior plane (SAP) catheter was inserted by the surgeon before closure. Ropivacaine bolus (group I: 0.2% 0.1 ml/kg and group II: 0.375% 0.4 ml/kg) was given before extubation, followed by its continuous infusion for 24 hours. If the numerical rating scale (NRS) was >3, then patients were given intravenous (i.v.) morphine 3 mg. Total 24-hour morphine consumption, duration of effective analgesia, hemodynamic parameters, side effects, and overall patient satisfaction were recorded.

Statistical Analysis Used: T-test was used to compare the parametric values in both the groups, whereas the Mann–Whitney U-test was performed to compare the nonparametric values.

Results: Postoperative morphine requirement in the ParaVertebral Block (PVB) group (8.65 ± 4.27 mg) was less as compared to the SAP group (11.87 ± 6.22 mg) but that was not statistically significant (p 0.052). Postoperative pain scores at rest and on movement, patient satisfaction, and incidence of chronic post-thoracotomy pain were comparable in both the groups.

Conclusion: SAP block with continuous catheter technique seems to be a safe and effective modality for the management of acute postoperative pain after thoracotomy.

Key words: Paravertebral; postoperative pain; serratus anterior plane block; thoracotomy
Background

Lung cancer is one of the common visceral malignancies among men. Surgical resection for the removal of the primary tumor along with mediastinal lymph node dissection is the mainstay of treatment in stage I and II disease. Severe post-thoracotomy pain may occur in 30-50% of patients.[1] Acute postsurgical pain inhibits pulmonary and immune functions, increases the risk of ileus, thromboembolism and myocardial infarction, prolongs hospital stay and leads to chronic persistent pain. Good pain relief is vital for better postoperative hemodynamic and respiratory profile. Adequate analgesia is known to improve coughing, improve breathing (without splinting), lead to early ambulation, improve physiotherapy compliance, and decrease the duration of hospital stay.

Nociceptive, neuropathic, and central pain processing mechanisms have been responsible for post-thoracotomy pain. Intercostal nerve injury by resection, rib retraction, muscular or costal stretching, and pleural irritation by chest drain placement promotes pain transmission. In addition, neuropathic pain may occur because of the involvement of the phrenic nerve and vagus nerve.[2]

Enhanced recovery after surgery (ERAS) guidelines for thoracic surgery suggests a multimodal approach for pain management with more than one analgesic targeting different sites, reducing opioid usage, and encourages regional anesthesia.

Thoracic epidural with local anesthetics and/or opioids for thoracotomy has been considered as a gold standard technique for thoracotomy surgeries.[3] However, epidural morphine is associated with numerous side effects like sedation, pruritus, respiratory depression, nausea, vomiting, constipation, and urinary retention. Recently, opioids have also been postulated to be responsible for cancer recurrence.[4] In addition, the thoracic epidural may lead to various complications like hypotension, dural puncture, neurological injury, and epidural hematoma.[5] Moreover, the epidural technique may be a contraindication in some conditions like sepsis, coagulation abnormality, spine deformity, or procedure failure.

Various studies have shown paravertebral block (PVB) to be comparable to thoracic epidural block with lesser hemodynamic effects.[6] However, it may also be associated with complications like pneumothorax, vascular injury, epidural or intercostal spread of drugs, and ipsilateral Horner syndrome.[7] Although use of ultrasound (USG)-guided technique has led to a reduction in such complications, still the search continues for easier and better block providing better comfort to the patients.

Serratus anterior plane (SAP) block may have a better side effect profile as compared to thoracic epidural or paravertebral with fewer chances of technique failure and better respiratory outcome. However, limited studies have been done on the effectiveness of SAP block in thoracic surgery.

We have hypothesized that SAP block will provide effective perioperative analgesia which is non inferior to USG-guided PVB with lesser complications in patients undergoing thoracotomy. This is a first study comparing SAP block with PVB with continuous catheter technique in patients undergoing thoracotomy for lung surgeries.

Patients and Methods

This prospective randomized pilot study involved 50 patients undergoing elective thoracotomy for lung surgery in a tertiary care cancer center. The trial was registered before patient enrollment at ctri.nic.in (Clinical Trials Registry-India CTRI Reference No. REF/2017/05/014393, CTRI Reg. No. CTRI/2017/12/010939, Date of registration: 21/12/2017).

All American Society of Anesthesiologists (ASA) physical status I-III, adult patients (18-72 years) of either gender undergoing thoracotomy were included. Patient with infection at the site of injection, coagulopathy, spine deformity, drug addicts or history of opioid dependence, patients with liver disease, cardiac disease or renal failure, those requiring postoperative mechanical ventilation, pregnant patients, patients unable to comprehend numerical rating scale (NRS) and emergency surgery were excluded from the study.

The patients were randomly allocated in one of the two groups using computer-generated random number table and numbers concealed in an opaque envelope, to be opened after recruitment in the study. Group I (PVB group) patients received PVB with ropivacaine along with general anesthesia. Group II (SAP group) patients received SAP block with ropivacaine along with general anesthesia. Ropivacaine bolus was given before extubation in both the groups.

Anesthetic technique

All patients were visited one day prior to the surgery and routine preoperative assessment was done. The patients were kept fasting 8 hours prior to the surgery and premedicated with tablet ranitidine 150 mg and tablet alprazolam 0.25 mg on
the night before the surgery and two hours before the surgery in the morning as per the hospital protocol. After shifting the patient to the operation table, non-invasive oscillometric blood pressure (NIBP), 5-lead electrocardiogram (ECG), and pulse oximetry were attached. A peripheral venous line was secured via 18 gauge cannula and i.v. infusion with plasmalyte was initiated. Oxygen saturation (SpO₂), heart rate (HR), ECG, and end-tidal carbon dioxide tension (EtCO₂) were monitored.

**Procedure to be done in paravertebral group**
- PVB was placed with the patient in the sitting position. Thoracic paravertebral space between T4-T8 depending on surgeon incision was scanned with USG. After local infiltration, a 16/18 G Tuohy epidural needle was introduced lateral to T4-T8 interspinous space. The superior costotransverse ligament was pierced and proper needle placement was confirmed by anterior deflection of the parietal pleura on injection of 3 ml of normal saline. A 21 gauge catheter was inserted via Tuohy needle and fixed to the skin at a mark where it would be 4 cm inside the paravertebral space. Before extubation, a loading dose of 0.1 ml/kg of 0.2% ropivacaine was injected followed by continuous infusion of 0.1 ml/kg/hour of 0.2% preservative-free ropivacaine for 24 hours postoperatively. The catheter was tunneled subcutaneously and secured over skin with adhesive plaster and was labeled to identify from outside.

**Procedure to be done in SAP group**
- Before extubation, a 21 gauge catheter was placed in the plane between serratus anterior and latissimus dorsi muscle at T5 level in the lateral decubitus position by the surgeon percutaneously from the site different from the surgical incision site. In total, 0.4 ml/kg (with a maximum volume of 30 ml) of 0.375% preservative-free ropivacaine was injected followed by continuous infusion of 0.1 ml/kg/hour of 0.2% ropivacaine for 24 hours postoperatively. The catheter was tunneled subcutaneously and secured over skin with adhesive plaster.

**Procedure common to both the groups**
All patients were pre-oxygenated with 100% oxygen for 3 minutes. General anesthesia induction was done using i.v. fentanyl 2 mcg/kg, propofol 2-2.5 mg/kg (titrated to response), and rocuronium bromide 0.6 mg/kg. Anesthesia was maintained with sevoflurane to maintain end-tidal sevoflurane concentration of 1.14 to 1.98% with 50% oxygen in the air at a flow rate of 2 L/minute. During two-lung ventilation, patients were mechanically ventilated using volume-controlled mode with tidal volumes of 6-8 ml/kg, at respiratory rates to maintain a target EtCO₂ of 32-35 mmHg with a positive end-expiratory pressure of 5 cm H₂O. During one-lung ventilation, patients were mechanically ventilated in a volume-controlled mode with tidal volumes of 5 ml/kg, at respiratory rates to maintain a target EtCO₂ of 32-35 mmHg with a positive end-expiratory pressure of 5 cm H₂O. Inspired oxygen fraction (FiO₂) was increased accordingly to maintain SpO₂ more than 95%. Neuromuscular blockade of the patient was reversed and the trachea was extubated at the end of the surgery.

**Postoperative monitoring**
All patients were continuously monitored postoperatively for systolic blood pressure (SBP), diastolic blood pressure (DBP), HR, respiratory rate, SpO₂, NRS score, and side effects at 0, 1, and 2 hours and then every 2 hourly for 24 hours. Arterial blood gas (ABG) was done at baseline, 1 hour and 12 hours after extubation to compare pCO₂ and pO₂/FiO₂ ratio. Patient satisfaction rate ranging from 0% to 100% (very unsatisfied to very satisfied), was evaluated and recorded at 24 hours after the operation.

The pain was evaluated by using NRS. NRS pain score was assessed at rest and during movement (coughing or deep breathing) every 2 hourly in the postoperative period. Intravenous infusion of paracetamol 20 mg/kg (round to 500 mg or 1000 mg) was given during closure of the wound and then every 6 hourly for 24 hours to all the patients in both the groups. Patients received 3 mg i.v. morphine bolus if NRS was >3, which was not repeated unless 10 minutes has elapsed. Maximum 30 mg of i.v. morphine could be given in 4 hours duration. Total 24-hour morphine consumption was recorded by a trained nurse who was not informed about the patient group assignment. The duration of effective analgesia was defined as the time from extubation to the time to reach NRS greater than 3 when patients received 3 mg i.v. morphine.

Rescue analgesic regimen in the form of i.v. 75 mg diclofenac sodium (not to be repeated within 12 hours of receiving rescue dose) was given if the NRS was >3 despite receiving a maximum dose of i.v. morphine. A total dose of rescue analgesic in 24 hours was recorded.

Side effects like hypotension, bradycardia, nausea, vomiting, drowsiness, itching, respiratory depression, sensory, and motor function were noted and treated accordingly.

**Outcome measures**
The primary outcome measure was the total consumption of morphine in 24 hours postoperatively. Secondary outcome measures were NRS pain scores, side effects of block technique, patient satisfaction, and chronic post-thoracotomy pain.
Sample size and statistical methods
We have compared the analgesic efficacy of two regional block techniques for thoracotomy in 50 patients as a pilot study.

To describe patient’s characteristics like demographic parameters, the data were summarized and analyzed using statistical package for social sciences (SPSS, version 24) software. Data were expressed as mean ± standard deviation (SD) or number and percentage as appropriate. Data were tested for normality using the Kolmogorov–Smirnov test. T-test was used to compare the parametric values in both the groups, whereas the Mann–Whitney U-test was performed to compare the nonparametric values wherever required. For comparison of categorical data, Chi-square test/Fisher’s exact test was performed to establish the association between the groups. A value of $P$ less than 0.05 was considered statistically significant.

Results
A total of 63 patients were assessed for eligibility during the study. Out of 63 patients, 5 patients did not meet the inclusion criteria and were excluded from the study. In view of 15% drop out rate due to nonextubation, inoperability or failure of block, we have taken 8 extra patients. Thus, 58 patients were randomized into PVB and SAP groups of 30 and 28 each, respectively. After randomization, 4 patients were excluded from the PVB group and 4 patients were excluded from the SAP group [Figure 1].

Table 1 shows that there was no significant difference in baseline characteristics between the two groups except the requirement of intraoperative intravenous fluids ($P = 0.025$).

The most common type of surgery in the SAP group was lobectomy for carcinoid lung while in the PVB group, it was lobectomy for lung cancer. [Table 2]

Postoperative morphine requirement in the PVB group was less as compared to the SAP block but that was not statistically significant [Table 3]. Postoperative pain scores at rest and on movement were not statistically significant in both the groups at all measuring points [Figures 2 and 3]. As shown in Table 3, the duration of effective analgesia was less in PVB group as compared to the SAP group but was not statistically significant. Since SAP block has a faster onset of sensory block, the duration of effective analgesia was more in the SAP group. Thus, the time to first analgesic request was lesser in the PVB group.

Two (7.69%) patients in the PVB group complained of nausea and 1 (4.16%) patient in the SAP group complained of pruritus.

| Parameters                           | Group S ($n=24$) | Group P ($n=26$) | $P$   |
|--------------------------------------|------------------|------------------|-------|
| Age (years)                          | 40.2±14.43       | 38.34±18.59      | 0.472 |
| Gender (Male: Female)                | 15:9             | 19:7             | 0.423 |
| Weight (Kg)                          | 55.62±9.65       | 56.8±10.02       | 0.668 |
| Height (cm)                          | 163.04±8.64      | 161.53±8.96      | 0.275 |
| BMI (kg/m$^2$)                       | 20.95±3.61       | 21.85±4.00       | 0.795 |
| Duration of surgery (min)            | 207.91±84.66     | 209.61±72.41     | 0.807 |
| Duration of OLV (min)                | 146.35±64.71     | 166.15±64.19     | 0.248 |
| Side of surgery (right: left)        | 11:13            | 13:13            | 0.768 |
| ASA physical status (I/II/III)       | 15:7:2           | 17:7:2           | 0.978 |
| ECOG (1:2)                           | 23:1             | 25:1             | 0.260 |
| Baseline FeV$_1$ (%)                 | 69.91±10.49      | 73.53±18.44      | 0.712 |
| Blood loss (ml)                      | 237±251.35       | 246.9±156.86     | 0.398 |
| Length of skin incision (cm)         | 12.27±3.76       | 12.51±3.38       | 0.596 |
| Number of ribs excised (0:1:2)       | 23:0:1           | 25:1:0           | 0.367 |
| Number of chest drain (0:1:2)        | 2:19:4           | 0:20:6           | 0.297 |
| Chest tube related pain (Yes:No)     | 11:13            | 14:12            | 0.571 |
| Length of hospital stay (days)       | 10.58±5.74       | 9.26±3.35        | 0.578 |

Figure 1: CONSORT (Consolidated Standards of reporting trials) diagram

Figure 2: Pain scores (at rest) in different time points in the postoperative period

Table 1: The comparison between demographic parameters in the two groups (Data are expressed as mean±SD or numbers)
There was no incidence of side effects like vomiting and urinary retention in both groups. Patient satisfaction was comparable in both groups.

The mean SBP, mean DBP, mean HR, respiratory rate, and pulse oximetry in the postoperative period were comparable in both the groups. Both PCO2 and PO2/FiO2 ratio were similar in both the groups at different time points. Technique-related adverse effect was appearance of hematoma formation after opening the chest in the PVB group. The catheter was accidentally removed in 1 patient in both the groups. The catheter was occluded in 1 patient in the PVB group. The incidence of chronic post-thoracotomy pain was comparable in both groups (p 0.727).

Discussion

This study showed that both USG-guided thoracic PVB and surgeon-guided SAP block decreases the amount of postoperative narcotic requirements for 24 hours. SAP block delays the need for first analgesic rescue. Both the regional techniques were hemodynamically safe with minimal side effects.

Regional anesthesia techniques provide effective analgesia, attenuate surgical stress response and decreases opioid use. This along with the direct protective effect of local anesthetic on cancer cell migration may prevent tumor recurrence.[10]

SAP block was first described by Blanco et al. in 2013. This block can be given by injecting the local anesthesia between latissimus dorsi and serratus anterior (superficial plane) or between serratus anterior and intercostal muscles (deep plane).

With regard to hemodynamics, we found no significant differences between the groups. Similar findings were observed in studies by Abdelwahab et al. (2015), Biswas et al. (2016), and Khalil et al. (2017).[11-13] Hemodynamic profile was better in the SAP group as compared to the thoracic epidural group in one study.[13]

Postoperative pain scores at rest and on movement were not statistically significant in both the groups. In our study, in PVB group, median NRS at rest ranged from 2 to 3 and median NRS at deep breathing/coughing ranged from 2 to 5 in PVB group similar to studies by Pipanmekaporn et al. (2012), Ganguly et al. (2015), and Yamauchi et al. (2017).[14-16]
In the SAP group, median NRS at rest ranged from 2 to 3 and the median NRS at deep breathing ranged from 3 to 5. Okmen et al. (2017) found visual analogue score (VAS) scores to be significantly lower at 6, 12, and 24 hours in a retrospective study in patients undergoing thoracotomy in SAP block as compared to patients receiving only i.v. morphine.\cite{17} In a study by Aly et al. (2018), VAS at rest and during coughing was comparable in both SAP and PVB groups except at 12 and 18 hours in postoperative period where VAS on coughing was significantly lower in PVB group.\cite{18} In another study by Saad et al. (2018), the VAS score was similar in both SAP and PVB group up to 9 hours after surgery. However, at 12 and 24 hours, the PVB group had significantly lower VAS score as compared to the SAP group.\cite{19}

In this study, postoperative morphine requirement in the PVB group (8.65 ± 4.27 mg) was less as compared to the SAP group (11.87 ± 6.22 mg) but that was not statistically significant (p 0.052). This finding is similar to the one found in the study by Aly et al. (2018) in which postoperative 24-hour morphine consumption was significantly lower in the PVB group (12.7 ± 2.6 mg) as compared to the SAP group (18.4 ± 1.8 mg) with a P value of 0.025.\cite{18} Similarly, in another study by Saad et al. (2018), 3-6 mg of morphine was required in 23.3% of patients in the PVB group and 96.7% of patients in the SAP group in the first 24 hours and this was statistically significant.\cite{19} Khalil et al. (2017) also found 24-hour morphine consumption to be 10.3 ± 3 mg in the SAP group.\cite{13} Okmen et al. (2017) found 24-hour morphine consumption to be 25.8 mg in the SAP group in patients undergoing thoracotomy.\cite{17} This can be explained by the fact that there is a sparing of posterior cutaneous branches of the intercostal nerves without any autonomic blockade in the SAP block. Painful stimuli from lung and visceral pleura are mediated by sympathetic neurons and thus sparing of the autonomic block will increase pain transmission.\cite{20}

The duration of effective analgesia was less in the PVB group (74.61 ± 155.18 min) as compared to the SAP group (135.83 ± 310.83 min) but was not statistically significant (p=0.451). Since SAP block has a faster onset of sensory block, the duration of effective analgesia was more in the SAP group.\cite{18} Okmen et al. (2016) found 7 hours of analgesia with 20 ml of 0.25% bupivacaine given through SAP catheter in a patient undergoing thoracotomy for lung cancer.\cite{21} Okmen et al. (2017) found the duration of effective analgesia to be 388 ± 38.6 minutes with SAP block in thoracotomy surgeries.\cite{17} The duration of effective analgesia was 57.3 ± 83.1 min in patients undergoing lobectomy for lung cancer patients under the PVB group in the study by Tamura et al. (2017).\cite{21} Aly et al. (2018) found the duration of effective analgesia to be 6.5 ± 1.81 hour in the PVB group and 6.2 ± 1.66 hour in the SAP group (p 0.152).\cite{18}

This wide variation in the duration of the block may be explained by the use of different planes of drug deposition, varying concentration, volume, and type of local anesthetic used. These heterogeneities in technique may explain the wide variation in the time to first rescue analgesia in various studies.

In this study, patient satisfaction was comparable in both the groups (62.5 ± 22.50% in the SAP group and 66.73 ± 15.35% in the PVB group). In a study by Casati et al. (2006), patient satisfaction was 8.5 cm (8-9.8) in the epidural group and 9 cm (7.5-10) in the PVB group.\cite{22}

In our study, the length of hospital stay was 10.58 ± 5.74 days in the SAP group and 9.26 ± 3.35 days in the PVB group. In a study by Casati et al. (2006), the average length of hospital stay was 8 days in the PVB group and 9 days in the epidural group.\cite{23} In another study by Ganguly et al. (2015), the median length of hospital stay was 19 days in both PVB and epidural groups.\cite{15} Aly et al. (2018) found the length of hospital stay to be 3.5 ± 0.8 days in the PVB group and 3.8 ± 1.2 days in the SAP group (p 0.924).\cite{18}

Chest tube related pain occurs because of unblocked afferent fibers from long thoracic nerves, intercostal nerves, phrenic nerve, vagus, and thoracodorsal nerves.\cite{24,25} In our study, chest tube related pain was observed in 44% of patients in the SAP group and 56% of patients in the PVB group. George et al. (2017) reported similar findings and concluded that SAP block with 0.2% ropivacaine at 2-4 ml/hr is more effective in decreasing chest tube related pain in thoracotomy patients as compared to the PVB block.\cite{25} Barbera et al. (2017) found intercostal chest tube related pain in 1 (14.2%) out of 7 patients receiving SAP block in esophagectomy patients.\cite{26}

In our study, both PaCO2 and PaO2/FiO2 ratios were similar in both the groups at different time points signifying adequate ventilation in both the groups. Similarly, in various studies, PaCO2 and P/F ratios were comparable between epidural and PVB groups in patients undergoing thoracotomy surgery.\cite{11,12,15}

SAP block can be used in patients on dual antiplatelet drugs, coagulation disorders, and those receiving thromboprophylaxis with newer anticoagulants. Both PVB and SAP blocks decrease the risk of development of epidural hematoma in such patients. Most of the ERAS protocols are focusing on multimodal analgesia with opioid-free anesthesia.
Thus, SAP block can be a part of the multimodal analgesia technique avoiding or decreasing the dose of opioids and thus may prevent its associated risk and cancer recurrence. Surgeon-guided SAP block can be used in settings where USG machine is not available and it also has an advantage of placing a catheter under direct vision. The plane usually gets disturbed and technically it becomes difficult to do USG-guided SAP block after surgery. Continuous catheter technique can be utilized for prolonged pain relief after thoracic surgeries.

Limitation of the study
There were some limitations in our study. The dermatomal spread of the local anaesthetic drug was not assessed and the time to perform the block was not recorded. The number of patients included in the study may not be enough to prove the efficacy of the SAP block. More studies with a bigger sample size may be needed to further validate our results.

Conclusion
We observed that both SAP block and PVB decrease the amount of postoperative morphine requirements for 24 hours. SAP block maintains hemodynamic stability without any significant side effects and also delays the need for first analgesic rescue. Surgeon-guided SAP block can be used as an alternative to other modalities if there is difficulty placing epidural or PVB block if the patient is on anticoagulants or in case of unplanned thoracotomy.

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Conflicts of interest
There are no conflicts of interest.

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