



## Comparative administration of continuous paravertebral infusion of ropivacaine with and without fentanyl for pain relief in unilateral multiple fractured ribs patients

Dr. Shailesh Prasad<sup>1</sup>, Dr. Bhagwan Das<sup>2\*</sup>

<sup>1</sup> Assistant Professor, Department of Anesthesia, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India

<sup>2</sup> Senior Resident, Department of Anesthesia, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India

\* Corresponding Author: Dr. Bhagwan Das

### Abstract

Paravertebral block, both single injection and continuous infusion, has been reported to be comparable to thoracic epidural with regard to analgesia while avoiding the possibility of hypotension and urinary retention in the postoperative period. Despite these advantages, it should be noted that percutaneous paravertebral catheter placement carries the same contraindications with regard to anticoagulation as epidural analgesia. The use of elastomeric infusion devices with larger volumes of local anesthetic has been demonstrated in a recent retrospective review comparing patients receiving continuous local anesthetic infusion both subcutaneously in the wound and at the intercostal nerves with patients receiving epidural analgesia. Hence the present study was planned for Comparative Administration of Continuous Paravertebral Infusion of Ropivacaine with and Without Fentanyl for Pain Relief in Unilateral Multiple Fractured Ribs Patients.

The present study was planned in Department of Anesthesia, Anugrah Narayan Magadh Medical College, Gaya, Bihar. The study was conducted from August 2013 to April 2014. Total 20 patients with unilateral fractured ribs and visual analogue scale (VAS) pain score greater than 30 mm were enrolled in the present study. The 10 cases were enrolled in Group A patients received infusion of Ropivacaine 0.375% with adrenaline 5 µg/ml. The Group B patients received the infusion of Ropivacaine 0.2 % with adrenaline 5 µg/ml and fentanyl 2 µg/ml.

The data generated from the present study concludes that Both drug combinations used for paravertebral infusion in the present study, i.e., ropivacaine 0.375% with adrenaline 5 µg/ml and ropivacaine 0.2% with adrenaline 5 µg/ml and fentanyl 2 µg/ml, provided good analgesia with minimal side effects in patients with unilateral MFR. Addition of fentanyl in low concentration i.e., 2 µg/ml to the combination of ropivacaine and adrenaline allowed reduction of ropivacaine requirement without affecting the analgesic efficacy or the incidence of opioid-induced side-effects.

**Keywords:** continuous paravertebral infusion, ropivacaine, fentanyl, unilateral multiple fractured ribs patients, etc

### Introduction

A rib fracture is a break in a rib bone. This typically results in chest pain that is worse with breathing in. Bruising may occur at the site of the break. When several ribs are broken in several places a flail chest results. Potential complications include a pneumothorax, pulmonary contusion, and pneumonia. Rib fractures usually occur from a direct blows to the chest such as during a motor vehicle collision or from a crush injury. Coughing or metastatic cancer may also result in a broken rib. The middle ribs are most commonly fractured. Fractures of the first or second ribs are more likely to be associated with complications. Diagnosis can be made based on symptoms and supported by medical imaging. Pain control is an important part of treatment. This may include the use of paracetamol (acetaminophen), NSAIDs, or opioids. A nerve block may be another option. While fractured ribs have been wrapped, this may increase complications. In those with a flail chest, surgery may improve outcomes. They are a common injury following trauma [1].

The paravertebral block is versatile and can be used for various surgeries depending on the vertebral level it is done. A block at the neck in the cervical region is useful for thyroid gland and carotid artery surgery. At the chest and abdomen in the thoracic region, blocks are used for breast,

thoracic, and abdominal surgery. A block at the hip in the lumbar region is indicated for hip, knee, and anterior thigh surgeries. The paravertebral block provides unilateral analgesia, but bilateral blocks can be performed for abdominal surgeries. Since it is a unilateral block, it may be chosen over epidurals for patients who can't tolerate the hypotension that follows bilateral sympathectomy. The paravertebral space is located a couple centimeters lateral to the spinous process and is bounded posteriorly by the superior costotransverse ligament and anteriorly by the parietal pleura. Complications include pneumothorax, vascular puncture, hypotension, and pleural puncture [2].

Paravertebral nerve block was a popular technique in the early 20th century. However, for some reason, paravertebral nerve block lost popularity and was almost extinct until the late 1970s, when there was a renewed interest in the technique. Recently, this technique was reviewed and found to be safe and efficacious [3].

A paravertebral block is essentially a unilateral block of the spinal nerve, including the dorsal and ventral rami, as well as the sympathetic chain ganglion. These blocks can be performed at any vertebral level. However, they are most commonly performed at the thoracic level because of anatomic considerations. Therefore, this topic primarily focuses on thoracic paravertebral blockade.

Paravertebral nerve blocks are indicated for surgical procedures requiring unilateral analgesia or anesthesia. Common cases benefitting from unilateral paravertebral blocks are breast surgery, thoracotomy, herniorrhaphy, open cholecystectomy, and open nephrectomy. Bilateral paravertebral blocks can be a viable option for midline abdominal surgery<sup>[4]</sup>.

The clinician may consider thoracic paravertebral blockade over thoracic epidural analgesia in patients for whom bilateral sympathectomy and subsequent hypotension would be especially detrimental<sup>[5, 7]</sup>. For example, the use of thoracic paravertebral blockade in a patient with severe aortic stenosis has been reported<sup>[8]</sup>. In another study, thoracic paravertebral blockade resulted in more stable hemodynamics and equivalent analgesia when compared to thoracic epidural analgesia in thoracotomy patients<sup>[9]</sup>. However, because bilateral spread can occur<sup>[10]</sup>, which may cause hemodynamic compromise similar to epidural blockade.

Another unique feature of thoracic paravertebral blockade compared with thoracic epidural analgesia is the relative safety when performing these blocks on patients with a marginal coagulation cascade. This does not mean, however, that thoracic paravertebral blockade can be performed on patients with coagulopathy without caution. According to the American Society of Regional Anesthesia and Pain Medicine's evidence-based guidelines, in the patient receiving antithrombotic or thrombolytic therapy, the exact same precautions should be taken when placing thoracic paravertebral blockade as when placing an epidural. However, if bleeding occurs in the thoracic paravertebral space, significant blood loss will be the likely complication rather than epidural hematoma and neurologic deficit<sup>[11]</sup>.

The thoracic paravertebral space (TPVS) is a wedge-shaped space that lies on either side of the vertebral column. It is wider on the left than on the right. The parietal pleura forms the anterolateral boundary, while the base is formed by the posterolateral aspect of the vertebral body, the intervertebral disc, the intervertebral foramen and its contents. The superior costotransverse ligament, which extends from the lower border of the transverse process above to the upper border of the transverse process below, forms the posterior wall of the TPVS. The apex of the space is continuous, with the intercostal space lateral to the tips of the transverse processes. Interposed between the parietal pleura and the superior costotransverse ligament is a fibroelastic structure, the endothoracic fascia, which is the deep fascia of the thorax and lines the inside of the thoracic cage. In the paravertebral location, the endothoracic fascia is closely applied to the ribs and fuses medially with the periosteum at the midpoint of the vertebral body. An intervening layer of loose connective tissue, the "subserous fascia," is found between the parietal pleura and the endothoracic fascia. The endothoracic fascia thus divides the TPVS into two potential fascial compartments, the anterior "extrapleural paravertebral compartment" and the posterior "subendothoracic paravertebral compartment". The TPVS contains fatty tissue, within which lies the intercostal (spinal) nerve, the dorsal ramus, the intercostal vessels, the rami communicantes, and, anteriorly, the sympathetic chain. The spinal nerves in the TPVS are segmented into small bundles lying freely among the fat and devoid of a fascial sheath, which makes them exceptionally susceptible to local anesthetic block. The intercostal nerve and vessels are

located behind the endothoracic fascia, while the sympathetic trunk is located anterior to it in the TPVS<sup>[12]</sup>.

The TPVS is continuous with the intercostal space laterally, the epidural space medially via the intervertebral foramen, and the contralateral paravertebral space via the prevertebral and epidural space. The cranial extension of the TPVS is still not defined, but we have observed radiologic spread of contrast medium into the cervical region after thoracic paravertebral injection. The origin of the psoas major muscle forms the caudal boundary, and inferior (lumbar) spread through the TPVS is thought to be unlikely. Ipsilateral thoracolumbar anesthesia, radiologic spread of contrast below the diaphragm, and thoracolumbar spread of colored dye in cadavers have been described, and there is disagreement about the caudal limit of spread. The endothoracic fascia is continuous inferiorly with the fascia transversalis of the abdomen dorsal to the diaphragm through the medial and lateral arcuate ligaments and the aortic hiatus. An injection in the lower TPVS posterior to the endothoracic fascia can spread inferiorly through the medial and lateral arcuate ligaments to the retroperitoneal space behind the fascia transversalis, where the lumbar spinal nerves lie, and is the anatomic basis of the technique of "extended unilateral anesthesia"<sup>[13]</sup>.

Several different techniques exist for TPVB. It can be performed with the patient in the sitting, lateral, or prone position. The sitting position allows easy identification of landmarks, and the patients are often more comfortable. The classical technique, which is most commonly used, involves eliciting loss of resistance. At the appropriate dermatome under aseptic precautions, the needle (22-gauge, 8–10-cm short beveled spinal needle, or a Tuohy needle if a catheter is to be placed) is inserted 2.5–3 cm lateral to the most cephalad aspect of the spinous process and advanced perpendicular to the skin in all planes to contact the transverse process of the vertebra below at a variable depth (2–4 cm) depending on the build of the individual. If bone is not encountered at this depth, it is possible that the needle tip is lying between adjacent transverse processes. It is imperative to locate the transverse process before advancing the needle any further to prevent inadvertent deep insertion and possible pleural puncture. This is accomplished by withdrawing the needle to the subcutaneous plane and redirecting it cephalad and caudad to the same depth until bone is encountered. If bone is still not encountered, the needle is advanced a further centimeter and the above process repeated until the transverse process is contacted. The needle is then walked above the transverse process and gradually advanced until a loss of resistance to air or saline, or a subtle "pop" is felt as the needle tip traverses the thin superior costotransverse ligament, usually within 1–1.5 cm from the superior edge of the transverse process.

After gentle aspiration, local anesthetic is injected in small aliquots or a catheter is inserted so that 1–3 cm of the distal end of the catheter lies within the TPVS. The same technique is used with modification in children, and two simple equations help predict the lateral distance for needle insertion and the skin-to-TPVS depth (both in millimeters):  $[10.2 + (0.12 \times \text{weight in kilograms})]$  and  $[21.2 + 0.53 \times (\text{weight in kilograms})]$ , respectively. 53 Various investigators also redirect their needle medially 29 to contact the vertebra, advance caudal to the transverse process, 26, 46, 54 or elicit paresthesia. Medial redirection is not recommended because of the potential for epidural or

intrathecal injection [14, 15].

Unlike epidural space location, where a definite give is felt as the needle tip traverses the firm ligamentum flavum, TPVS location using loss of resistance is subjective and indefinite and may not be appreciated as a definite give. Difficulty is also commonly encountered during catheter insertion and may require manipulation of the needle or injection of saline to create a saline-filled cavity before passing a catheter. Very easy passage of the catheter may indicate interpleural placement [16].

The needle may be advanced by a fixed predetermined distance (1–2 cm) once the needle is walked off the transverse process without eliciting loss of resistance. This variation has been used very effectively with low risk of complication, including pneumothorax. The use of a depth marker is recommended if a nongraduated needle is used to avoid pleural or pulmonary puncture. Fluoroscopy and contrast chest radiography are often used as supplementary methods to confirm the position of the needle or catheter. Contrast injected into the TPVS produces either a longitudinal or a cloud-like spread localized to the paravertebral region as depicted on frontal chest radiograph. Radiologic images are not always readily identifiable, and spread can vary in the same patient having repeated injections [17].

A “pressure measurement technique” was recently advocated. Pressure in the erector spinae muscle is higher during inspiration than during expiration. Once the superior costotransverse ligament is traversed and the TPVS entered, there is a sudden lowering of pressure, and expiratory pressure then exceeds inspiratory pressure: “pressure inversion.” These objective signs are described as an easy and reproducible method of locating the TPVS. Negative pressure during both phases of respiration would indicate interpleural placement. 58

A modification of the classical approach is the medial approach in which the needle is inserted 1 cm from the midline and advanced perpendicularly to contact the lamina rather than the transverse process followed by lateral redirection to slip off the lamina into the TPVS. Developed initially to avoid intrathecal injection by directing the needle away from the intervertebral foramen, this approach has been associated with complications relating to dural puncture. A recent variation of the medial approach is the “paravertebral–peridural block,” in which the needle is inserted 3–4 cm lateral to the midline and advanced at a 45° angle to the coronal plane with medial direction to contact the lamina. The needle is then redirected laterally by gradual increments in the angle of entry to the coronal plane until the needle is walked off the lamina into the TPVS. Retrospective analyses using the paravertebral–peridural block technique report a high success rate and low incidence of complications [18].

Thoracic paravertebral catheters can also be safely, accurately, and easily placed under direct vision during thoracic surgery from within the chest. The original description by Sabanathan *et al.* [19] involves reflecting the parietal pleura from the posterior wound margin on to the vertebral bodies to create an extrapleural paravertebral pocket into which a percutaneously inserted catheter is placed against the angles of the exposed ribs. This method has been refined to ensure accurate placement of the catheter in the TPVS by tunneling the tip through a small defect created by the surgeon in the extrapleural fascia [20],

rather than laying it adjacent to the vertebral bodies. The anatomy of the extrapleural fascia is not clear, and the endothoracic fascia may have been referred to as the extrapleural fascia. This method, which requires an open chest, has been combined very effectively with preincisional percutaneous thoracic paravertebral injection to provide both intraoperative and postoperative analgesia after thoracic surgery. Video-assisted placement of a paravertebral catheter under direct vision during thoracoscopic surgery has also been described.

Paravertebral block, both single injection and continuous infusion, has been reported to be comparable to thoracic epidural with regard to analgesia while avoiding the possibility of hypotension and urinary retention in the postoperative period. Despite these advantages, it should be noted that percutaneous paravertebral catheter placement carries the same contraindications with regard to anticoagulation as epidural analgesia. The use of elastomeric infusion devices with larger volumes of local anesthetic has been demonstrated in a recent retrospective review comparing patients receiving continuous local anesthetic infusion both subcutaneously in the wound and at the intercostal nerves with patients receiving epidural analgesia. Hence the present study was planned for Comparative Administration of Continuous Paravertebral Infusion of Ropivacaine with and Without Fentanyl for Pain Relief in Unilateral Multiple Fractured Ribs Patients.

### Methodology

The present study was planned in Department of Anesthesia, Anugrah Narayan Magadh Medical College, Gaya, Bihar. The study was conducted from August 2013 to April 2014. Total 20 patients with unilateral fractured ribs and visual analogue scale (VAS) pain score greater than 30 mm were enrolled in the present study. The 10 cases were enrolled in Group A patients received infusion of Ropivacaine 0.375% with adrenaline 5 µg/ml. The Group B patients received the infusion of Ropivacaine 0.2 % with adrenaline 5 µg/ml and fentanyl 2 µg/ml.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Cardiovascular stability was achieved and surgical procedures e.g., drainage of pneumothorax or haemothorax, if required, were performed. Patients' demographic data, injury data and haemodynamic status on admission were recorded. Selected patients were shifted to ICU and written informed consent was taken. Monitoring during and after TPVB included non-invasive blood pressure, electrocardiogram and arterial oxygen saturation (SpO<sub>2</sub>).

TPVB was performed under aseptic conditions with the patient in sitting position, using the classical technique eliciting loss of resistance, at a spinal level midway between the uppermost and the lowest fractured ribs. In case of involvement of more than four ribs, one level higher than the middle level was chosen. Following test dose of 2% lignocaine with adrenaline (1:2, 00,000) 3 ml to rule out intravascular or subarachnoid injection, the bolus dose was administered. Non-invasive blood pressure and heart rate were recorded every 5 minutes until 30 minutes after drug injection. Bradycardia was defined as heart rate <50 beats/minute and hypotension as a fall of >30% from baseline readings or an absolute value of <80 mmHg

systolic blood pressure. Any episodes of bradycardia or hypotension were recorded and managed with atropine, fluids and vasopressors as required.

Continuous paravertebral infusion was started according to group allocation 30 minutes after administration of bolus dose. Initial rate of infusion was 0.1 ml/kg/hr in all patients which was gradually increased in steps of 1-2 ml/hr up to a maximum of 0.2 ml/kg/hr, in case adequate pain relief was not achieved. If, despite the maximum rate of paravertebral infusion, VAS score exceeded 40 mm or if the patient requested additional analgesia at any time during the study period, rescue analgesia was provided by intravenous morphine in increments of 1.5 mg. All the patients received diclofenac 1 mg/kg 12 hourly intramuscularly. The patients having any contraindication to diclofenac administration were to receive intravenous tramadol 1 mg/kg along with an antiemetic.

Following was the inclusion and exclusion criteria for the present study.

**Inclusion Criteria:** Patients with unilateral fractured ribs and visual analogue scale (VAS) pain score greater than 30 mm.

**Exclusion Criteria:** Cases of Bilateral rib fractures, significant trauma outside chest wall, Unconsciousness. Unconscious patients, patients having unstable cardiac or severely altered mental status, known liver/kidney disease, known allergy to LA drugs, infection at site of needle insertion, pre-existing spinal deformity and those with significant trauma outside chest wall, (e.g., acute spine or pelvic fracture, severe fracture, severe traumatic brain or spinal cord injury or abdominal visceral injuries) were excluded.

## Results & Discussion

Seventy percent of post-thoracotomy patients have too much pain in the early postoperative period. The pain that is caused by stretching costovertebral, costotransverse

ligaments and posterior spinal muscles, causes many complications such as weak coughing, decrease in tidal volume and atelectasia, hypoxemia, postoperative pulmonary infection and dyspnea. These complications increase according to age, smoking, obesity and other illnesses.

Post-thoracotomy pain is one of the most painful procedures and various methods have been used and new studies are being done for better methods. The effective methods for post-thoracotomy pain management and lowering systemic opioid dose are continuous intercostal block, paravertebral block, epidural opioid and/or local anesthetic techniques.

In Navlet *et al.* study<sup>[21]</sup>, a continuous paravertebral infusion of ropivacaine/fentanyl, or bupivacaine/fentanyl, in 60 patients undergoing elective thoracotomy was done and authors concluded that both bupivacaine, 0.25%, and ropivacaine, 0.3%, with fentanyl are equally effective for post-thoracotomy pain control when used via continuous paravertebral blockade. In another study, Awwad *et al.*<sup>[22]</sup> assessed paravertebral block using bupivacaine 0.5% or normal saline in 44 patients undergoing renal surgery and reported that paravertebral blockade using bupivacaine is an effective and safe method for pain relief following renal surgery through loin incision. Also, Bhuvanewari *et al.*<sup>[23]</sup> concluded that paravertebral block using bupivacaine and fentanyl in patients scheduled for surgery for breast cancer reduce analgesic consumption as well as cumulative pain scores at rest and on movement. Naja *et al.*<sup>[24]</sup> used as a complement to general anesthesia, bilateral nerve-stimulator guided paravertebral blockade with lidocaine, bupivacaine, fentanyl and clonidine, in laparoscopic cholecystectomy and show that mean pain scores visual analog scale were significantly less with active compared with control; also, they concluded that this regimen may improve postoperative pain relief.

**Table 1:** Injury Data

Group	Group A	Group B
<b>Medication</b>	<b>Ropivacaine 0.375% with adrenaline 5 µg/ml</b>	<b>Ropivacaine 0.2 % with adrenaline 5 µg/ml and fentanyl 2 µg/ml</b>
<b>No. of Cases</b>	<b>10</b>	<b>10</b>
Mean number of fractured ribs	3 – 6	3 – 7
Mean chest Abbreviated injury score	2 – 3	2 – 4
Mean Injury severity score	6 – 28	5 – 22
Patients with flail segment	3	4
Patients with pulmonary contusion	2	2
Patients with haemothorax	5	4
Patients with pneumothorax	5	6
Patients with chest tube	6	6
Patients with S/C emphysema	3	4

**Table 2:** Operative Parameters

Group	Group A	Group B
<b>Medication</b>	<b>Ropivacaine 0.375% with adrenaline 5 µg/ml</b>	<b>Ropivacaine 0.2 % with adrenaline 5 µg/ml and fentanyl 2 µg/ml</b>
<b>No. of Cases</b>	<b>10</b>	<b>10</b>
Ropivacaine requirement	830 – 2290	615 – 1260
ICU Stay	3 – 5 days	3 – 4 days
Length of Hospital stay	4 – 11 days	3 – 13 days
<b>Complications</b>		
Delayed haemothorax	0	1
Fever	0	1
Nausea	1	1

Vomiting	1	0
Pruritis	1	0

Kavanagh *et al.* [25] have made a meta-analysis of current techniques for post-thoracotomy pain management. They compared the use of opioids, NSAIDs, ketamine and regional analgesia. They concluded that the combination of thoracic epidural local anesthetics and opioids could essentially abolish postthoracotomy pain but possible complications and cost-benefit issues should be considered.

Macias *et al.* [26] performed a double-blinded randomized study with 80 patients under elective thoracotomy procedure and, as a result, found epidural ropivacaine-fentanyl and epidural bupivacaine-fentanyl groups to be similar. We added morphine to bupivacaine and ropivacaine in our study as well and observed no significant difference.

Cassady *et al.* [27] compared continuous thoracic epidural analgesia with bupivacaine-fentanyl combination and PCA with morphine in adolescents undergoing posterior spinal fusion and found the two groups comparable in terms of effectiveness and safety.

As mentioned above, there are several techniques for postoperative pain management and the choice depends on several factors such as anesthetist's experience, preference, duration of local and systemic pain management, contraindications of some analgesic drugs and techniques and patient's preference [28]. For this reason, many studies are under way to find the ideal postoperative pain management technique.

With regard to post-thoracotomy epidural analgesia, Joshi *et al.* [29] suggested that the combination of lipophilic opioid with local anesthetic was superior to opioid alone. It recently has been suggested that analgesia with lipophilic opioids administered via the epidural route may be primarily from a systemic rather than neuraxial effect. Conversely, hydrophilic opioids, such as morphine and hydromorphone, commonly are used in continuous epidural infusions and may provide more reliable neuraxial analgesia than the more lipophilic opioids such as fentanyl and sufentanil [29].

The limitations of this study—sampling bias, selection bias, and recall bias—are usually present in a retrospective case-control study. Regarding sampling bias, there were significant differences in the frequency of three factors in the backgrounds of patients: BMI, the presence of acquired heart disease, and the presence of ischemic cerebrovascular disease. These factors were strongly related to the way in which both groups were chosen, because patients who used anticoagulant or antiplatelet drugs regularly always allocated to the PVB group. As for selection bias, it is difficult to avoid this bias, however, anesthesiologists and surgeons always decided beforehand who would receive thoracic PVB by considering the contraindications for insertion of an epidural catheter. With regard to recall bias, all relevant medical records were used for this retrospective study. However, we acknowledge that, because the completeness of the medical records varied, some patient data were not available.

## Conclusion

The data generated from the present study concludes that Both drug combinations used for paravertebral infusion in the present study, i.e., ropivacaine 0.375% with adrenaline 5 µg/ml and ropivacaine 0.2% with adrenaline 5 µg/ml and fentanyl 2 µg/ml, provided good analgesia with minimal

side effects in patients with unilateral MFR. Addition of fentanyl in low concentration i.e., 2 µg/ml to the combination of ropivacaine and adrenaline allowed reduction of ropivacaine requirement without affecting the analgesic efficacy or the incidence of opioid-induced side-effects.

## References

1. Senekjian L, Nirula R. "Rib Fracture Fixation: Indications and Outcomes". *Critical Care Clinics*. 2017; 33(1):153-65. doi:10.1016/j.ccc.2016.08.009. PMID 27894495.
2. Scott W Byram. "Paravertebral Nerve Block". *Medscape*, 2017. Retrieved 4 August.
3. Eid HEA. Paravertebral block: An overview. *Curr Anaesth Crit Care*, 2009; 20:65-70.
4. Richardson J, Lönnqvist PA, Naja Z. Bilateral thoracic paravertebral block: potential and practice. *Br J Anaesth*. 2011; 106(2):164-71.
5. Bigeleisen PE, Goehner N. Novel approaches in pain management in cardiac surgery. *Curr Opin Anaesthesiol*. 2015; 28(1):89-94.
6. Koyyalamudi VB, Arulkumar S, Yost BR, Fox CJ, Urman RD, Kaye AD, *et al.* Supraclavicular and paravertebral blocks: Are we underutilizing these regional techniques in perioperative analgesia?. *Best Pract Res Clin Anaesthesiol*. 2014; 28 (2):127-38.
7. Baidya DK, Khanna P, Maitra S. Analgesic efficacy and safety of thoracic paravertebral and epidural analgesia for thoracic surgery: a systematic review and meta-analysis. *Interact Cardiovasc Thorac Surg*. 2014; 18(5):626-35.
8. Serpetinis I, Bassiakou E, Xanthos T, Baltatzi L, Kouta A. Paravertebral block for open cholecystectomy in patients with cardiopulmonary pathology. *Acta Anaesthesiol Scand*. 2008; 52(6):872-3.
9. Pintaric T, Potocnik I, Hadzic A, Stupnik T, Pintaric M, Jankovic V, *et al.* Comparison of Continuous Thoracic Epidural With Paravertebral Block on Perioperative Analgesia and Hemodynamic Stability in Patients Having Open Lung Surgery. *Regional Anesthesia and Pain Medicine*. May-June/11. 36:256-60.
10. Karmakar MK, Kwok WH, Kew J. Thoracic paravertebral block: radiological evidence of contralateral spread anterior to the vertebral bodies. *Br J Anaesth*. 2000; 84(2):263-5.
11. Horlocker TT, Wedel DJ, Rowlingson JC, Enneking FK, Kopp SL, Benzon HT, *et al.* Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med*. 2010; 35(1):64-101.
12. Moore DC, Bush WH, Scurlock JE. Intercostal nerve block: A roentgenographic anatomic study of technique and absorption in humans. *Anesth Analg*, 1980; 59:815-25 Moore, DC Bush, WH Scurlock, JE.
13. Saito T, Gallagher ET, Cutler S, Tanuma K, Yamada K, Saito N, Maruyama K, *et al.* Extended unilateral anesthesia: New technique or paravertebral anesthesia? *Reg Anesth*, 1996; 21:304-7.
14. Saito T, Gallagher ET Cutler S, Tanuma K, Yamada K,

- Saito N, *et al.* Thoracic paravertebral nerve, Atlas of Regional Anesthesia. Edited by Katz J. Norwalk, Appleton & Lange, 1994, pp 96-7.
15. Antila H, Kirvela O. Neurolytic thoracic paravertebral block in cancer pain: A clinical report. *Acta Anaesthesiol Scand*, 1998; 42:581-5.
  16. Antila H, Kirvela O, Mowbray A, Wong KK, Murray JM. Intercostal catheterisation: An alternative approach to the paravertebral space. *Anaesthesia*, 1987; 42:958-61.
  17. Mowbray A, Wong KK, Murray JM, Purcell-Jones G, Pither CE, Justins DM, *et al.* Paravertebral somatic nerve block: A clinical, radiographic, and computed tomographic study in chronic pain patients. *Anesth Analg*, 1989; 68:32-9.
  18. Purcell-Jones G, Pither CE, Justins DM, Kawamata M, Omote K, Namiki A, Miyabe M, *et al.* Measurement of intercostal and pleural pressures by epidural catheter. *Anaesthesia*, 1994; 49:208-10.
  19. Kawamata M, Omote K, Namiki A, Miyabe M, Sabanathan S, Smith PJ, *et al.* Continuous intercostal nerve block for pain relief after thoracotomy. *Ann Thorac Surg*, 1988; 46:425-6.
  20. Sabanathan S, Smith PJ, Pradhan GN, Hashimi H, Eng JB, Mearns AJ, *et al.* Direct access to the paravertebral space at thoracotomy (letter). *Ann Thorac Surg*, 1990; 49:854.
  21. Berrisford RG, Sabanathan SS, Navlet MG, Garutti I, Olmedilla L, Pérez-Peña JM, *et al.* Paravertebral ropivacaine, 0.3%, and bupivacaine, 0.25%, provide similar pain relief after thoracotomy. *J Cardiothorac Vasc Anesth*, 2006; 20:644-7.
  22. Awwad ZM, Atiyat BA. Pain relief using continuous bupivacaine infusion in the paravertebral space after loin incision. *Saudi Med J*, 2004; 25:1369-73.
  23. Bhuvanewari V, Wig J, Mathew PJ, Singh G. Post-operative pain and analgesic requirements after paravertebral block for mastectomy: A randomized controlled trial of different concentrations of bupivacaine and fentanyl. *Indian J Anaesth*, 2012; 56:34-9.
  24. Naja MZ, Ziade MF, Lönnqvist PA. General anaesthesia combined with bilateral paravertebral blockade (T5-6) vs. general anaesthesia for laparoscopic cholecystectomy: A prospective, randomized clinical trial. *Eur J Anaesthesiol*, 2004; 21:489-95.
  25. Kavanagh BP, Katz J, Sandler AN - Pain control after thoracic surgery. *Anesthesiology*, 1994; 81:737-759.
  26. Macias A, Monedero P, Adame P - A randomized, double-blinded comparison of thoracic epidural ropivacaine, ropivacaine-fentanyl or bupivacaine-fentanyl for post-thoracotomy analgesia. *Anesth Analg*, 2002; 95:1344-1350.
  27. Cassady JF, Lederhaas G, Cancel DD, Cummings RJ, Loveless EA. - A randomized comparison of the effects of continuous thoracic epidural analgesia and intravenous patient-controlled analgesia after posterior spinal fusion in adolescents. *Reg Anesth Pain Med*, 2000; 25:3246-3253.
  28. Savage C, McQuitty C, Wang D, *et al.* - Postthoracotomy pain management. *Chest Surg Clin N Am*. 2002; 12(2):251-263.
  29. Umenhoffer WC, Arends RH, Shen DD, *et al.* Comparative spinal distribution and clearance kinetics of intrathecally administered morphine, fentanyl, alfentanil and sufentanil. *Anesthesiology*, 2000; 92:739-753.