

# Post-thoracotomy Ipsilateral Shoulder Pain: What should be preferred to optimize it - Phrenic Nerve Infiltration or Paracetamol Infusion?

## Abstract

**Background:** Post thoracotomy ipsilateral shoulder pain (PTISP) is a distressing and highly prevalent problem after thoracic surgery and has not received much attention despite the incidence as high as 85%. **Objectives:** To study the effect of phrenic nerve infiltration with Ropivacaine compared to paracetamol infusion on PTISP in thoracotomy patients with epidural analgesia as standard mode of incisional analgesia in both the groups. **Study Design:** Prospective Randomised and Double Blind Study. **Methods:** 126 adult patients were divided randomly into 2 groups, “Group A (Phrenic Nerve Infiltration Group) received 10 mL of 0.2% Ropivacaine close to the diaphragm into the periphrenic fat pad” and “Group B (Paracetamol Infusion Group) received 20mg/kg paracetamol infusion” 30 minutes prior to chest closure respectively. A blinded observer assessed the patients PTISP using the VAS score at 1, 4, 8, 12 and 24 hours (h) postoperatively. The time and number of any rescue analgesic medication were recorded. **Results:** PTISP was relieved significantly in Group A (25.4%) as compared to Group B (61.9%), with significantly higher mean duration of analgesia in Group A. The mean time for first rescue analgesia was significantly higher in Group A ( $11.1 \pm 7.47$  hours) than in Group B ( $7.40 \pm 5.30$  hours). The number of rescue analgesic required was less in Group A  $1.6 \pm 1.16$  as compared to Group B  $2.9 \pm 1.37$  ( $P$  value  $<0.5$ ). **Conclusions:** Phrenic Nerve Infiltration significantly reduced the incidence and delayed the onset of PTISP as compared to paracetamol infusion and was not associated with any adverse effects.

**Keywords:** Paracetamol, phrenic nerve infiltration, post-thoracotomy ipsilateral shoulder pain, post thoracotomy pain, ropivacaine, thoracic epidural analgesia

## Introduction

Postthoracotomy ipsilateral shoulder pain (PTISP) is a distressing problem after thoracic surgery, with the reported incidence as high as 85%.<sup>[1]</sup> Unfortunately, PTISP has not received much attention and is still a highly prevalent problem in thoracic surgery and continues to be a concern for anesthesiologists. PTISP increases the patient suffering, causing pathophysiological changes that can increase the rate of postoperative complications, delaying recovery, and increasing hospital costs. Although etiology of PTISP is unclear proposed etiologies include ligament distraction, referred phrenic nerve pain, transection of bronchi, lateral decubitus positioning, rib retraction, muscle division, nerve injury, and prolonged surgery,<sup>[1-4]</sup> or may be secondary to stimulation of diaphragmatic tendon.<sup>[5,6]</sup>

PTISP is relatively resistant to intravenous (IV) opioids and increased

epidural infusion rates.<sup>[7]</sup> Several methods of alleviating shoulder pain have been investigated with varying results such as intrapleural bupivacaine,<sup>[8]</sup> superficial cervical plexus, or interscalene brachial plexus blocks,<sup>[9]</sup> suprascapular nerve block (SNB),<sup>[10]</sup> phrenic nerve block (local anesthetic infiltration of the periphrenic fat pad),<sup>[11,12]</sup> stellate ganglion block,<sup>[13]</sup> nonsteroidal anti-inflammatory drugs (NSAIDs),<sup>[14]</sup> and acetaminophen.<sup>[15]</sup> NSAIDs in relatively large doses may be effective, at the cost of increased risk of renal failure in dehydrated and elderly population undergoing major surgery.<sup>[16-18]</sup> Thus, an effective and safe solution for the management of postthoracotomy shoulder pain is still lacking. Acetaminophen has shown opioid-sparing effect when used for the management of pain after cardiothoracic surgery<sup>[19]</sup> and has shown efficacy in reducing the incidence of PTISP in patients undergoing thoracic surgery,<sup>[15]</sup> along with

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lower incidence adverse effects.<sup>[20]</sup> Epidural analgesia is considered to be the gold standard for postthoracotomy pain relief.<sup>[21,22]</sup>

No literature is available that compares any two different anesthetic techniques to minimize the incidence and severity of PTISP.

We, therefore, conducted a prospective, randomized study with an objective to evaluate and compare the efficacy of phrenic nerve infiltration (PNI) with 10 mL of 0.2% ropivacaine with 20 mg/kg paracetamol infusion in relieving the PTISP in patients undergoing thoracotomy procedures with epidural as the standard mode of incisional analgesia in both groups.

## Methodology

After approval from the Institutional Review Board, 126 patients of either gender aged 20–60 years with the American Society of Anesthesiology physical status (ASA) of I and II, admitted for elective unilateral thoracotomy were included in the study.

Following patients were excluded as per the exclusion criteria:

1. Contraindications for epidural block (patient refusal, infection at injection site, coagulopathy, septicemia, and hypotension)
2. Patients requiring postoperative elective mechanical ventilation
3. Patients undergoing total pleurectomy
4. Conduction disturbances such as complete heart block, atrioventricular nodal blocks,
5. Allergies to the drugs used in the study
6. Known contralateral paresis of the phrenic nerve, preoperative ipsilateral shoulder pain
7. Pregnancy.

All the patients were informed about the purpose of the study and written informed consent was taken from all the patients. All the patients enrolled were reliable, cooperative, and mentally capable of adhering to the protocol and providing the relevant study information for the whole study period. At the preoperative visit, patients were demonstrated the visual analog scale (VAS) as a method of postoperative pain assessment on a linear scale numbering from 0 to 10, where 0 = no pain and 10 = worst pain. All patients were clinically evaluated, assessed, and investigated a day before surgery. Patients were allocated to two Groups (A and B) as per computer-generated randomization numbers and were unaware of their Group Allocation. Group A patients ( $n = 63$ ) received a total of 10 mL of 0.2% ropivacaine infiltration in the phrenic nerve fat pad 1–2 cm close to the diaphragm in proximity to the beating heart 30 min before the closure of thoracotomy wound. Group B patients ( $n = 63$ ), received 20 mg/kg of paracetamol infusion 30 min before the closure of the thoracotomy wound.

On arrival to the operating room, an IV line was established with 18G cannula and standard monitoring established. Baseline heart rate (HR), noninvasive blood pressure (BP), and pulse oximetry (SpO<sub>2</sub>) were recorded. The patients were kept in a sitting position. Under all aseptic precautions, a 20G epidural catheter was placed in epidural space through midline thoracic approach at the T5–T7 interspace for intra- and post-operative analgesia. The epidural space was identified by the loss of resistance to saline technique. Epidural catheter was inserted and fixed at 4–5 cm inside the space. A test dose of 3 mL xylocaine 2% with epinephrine 1:200,000 was given to rule out intravascular or intrathecal placement of the catheter.

After preoxygenation, general anesthesia was induced using 2–3 mg/kg propofol, 2–3 µg/kg fentanyl, and injection atracurium 0.5 mg/kg (for providing muscle relaxation for laryngoscopy and endotracheal intubation). Anesthesia was maintained with oxygen (50%) in nitrous oxide and isoflurane (1 MAC). Neuromuscular blockade was maintained with further boluses of atracurium. Patients were intubated with an appropriate sized endotracheal tube and proper positioning confirmed by monitoring end-tidal CO<sub>2</sub> and bilateral chest auscultation.

All patients received 0.1 mL/kg epidural bolus dose of 0.2% ropivacaine 15 min before the surgical incision. Intra- and post-operative analgesia was maintained by an epidural infusion of 0.2% ropivacaine at 0.1 mL/kg/h for 24 h.

Patients were placed in the lateral decubitus position, with the operative side kept nondependent, and arm of that side kept flexed by <90° to avoid the excessive distraction of the shoulder joint. Chest tube placement was standardized. A standard surgical technique and retraction were used in all patients. Patients were given ondansetron hydrochloride 0.1 mg/kg 15 min before the completion of surgery. After completion of surgery neuromuscular blockade was reversed with neostigmine 70 µg/kg and glycopyrrolate 10 µg/kg. Patients were extubated when criteria for extubation were met.

A blinded observer assessed patients postoperatively. If at any assessment period, patients complained of severe pain in dermatomes related to the wound, an additional 0.1 mL/kg bolus dose of 0.2% ropivacaine was administered, and the infusion rate of 0.2% ropivacaine was increased. Patients still complaining of incisional pain were withdrawn from the study.

PTISP assessment was done according to VAS scale by a blinded observer in postoperative ward. PTISP score, HR, BP, SpO<sub>2</sub>, respiratory rate (RR), and adverse events (if any) were assessed and recorded at 1, 4, 8, 12, and 24 h of the end of surgery. The patients complaining of shoulder pain (VAS ≥3) received 50 mg IV tramadol as rescue

analgesia. The time to first rescue analgesia and total number of rescue analgesic doses required in 24 h were calculated.

**Statistical analysis**

The data with regard to age, gender, ASA status, postoperative hemodynamic parameters (HR, BP), RR, SpO<sub>2</sub>, quality of postoperative analgesia using VAS score, time to first rescue analgesia, and total number of rescue analgesic doses given was collected. The compiled data were entered into a Microsoft Excel spreadsheet and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Descriptive Statistics of data including the mean and standard deviation for numerical variables and the percentages of different categories for categorical variables was obtained. Frequency distribution tables, bar, and line graphs were used for data presentation. Student’s Independent *t*-test was employed for parametric data and nonparametric data, Chi-square or Fisher’s exact test, whichever appropriate, was used. *P* < 0.05 was considered statistically significant.

**Results**

Mean age in Group A and Group B was 42.29 ± 11.418 years and 40.73 ± 11.890 years, respectively, (*P* = 0.455). Observations with regard to gender distribution, ASA status in each group were statistically insignificant, *P* > 0.05 [Table 1].

Immediately after surgery, 3.2% of patients in Group A experienced PTISP 1 h postoperatively significantly lower as compared to 15.9% patients in Group B (*P* value = 0.03). The reduction in PTISP was significant at all the time intervals of observations in Group A in comparison to Group B [Table 2].

The overall incidence of shoulder pain among the two groups was statistically significant with an incidence of 25.4% in Group A and 61.9% in Group B [Table 2].

The comparison of the pain scores (VAS) among two groups shows statistically significant result; the pain scores at each studied interval in Group A being lower than the pain scores in Group B [Table 3].

The first rescue analgesia was required after a mean time of 11.1 ± 7.47 h in Group A and after 7.40 ± 5.30 h in Group B. Statistically, a significant difference (*P* = 0.031) was observed between the two groups [Table 4].

The average number of rescue analgesic doses required in Group A was 1.6 ± 1.16 and 2.9 ± 1.37 in Group B. Statistically, a significant difference (*P* < 0.001) was observed between the two groups [Table 4].

There was no significant difference in mean HRs (beats/min) between the two groups postoperatively at the studied intervals (*P* > 0.05) [Table 5].

**Table 1: Age, Gender distribution and American Society of Anesthesiology physical status**

	Group A (n=63)	Group B (n=63)	P
Age (years)			
Range	20-60	20-59	0.455
Mean±SD	42.29±11.418	40.73±11.890	
Gender, n (%)			
Male	34 (54.0)	36 (57.1)	0.720
Female	29 (46.0)	27 (42.9)	
ASA, n (%)			
ASA I	46 (73.0)	50 (79.4)	0.403
ASA II	17 (27.0)	13 (20.6)	

*P* value significant if ≤0.05, n: Number of patients, ASA: American Society of Anesthesiology physical status, SD: Standard deviation

**Table 2: Temporal trend of postthoracotomy ipsilateral shoulder pain**

	Group A, n (%)	Group B, n (%)	P
Pain incidence at various time intervals			
1 h			
Present	2 (3.2)	10 (15.9)	0.030
Absent	61 (96.8)	53 (84.1)	
4 h			
Present	3 (4.8)	11 (17.5)	0.044
Absent	60 (95.2)	52 (82.5)	
8 h			
Present	4 (6.3)	14 (22.2)	0.041
Absent	59 (93.7)	49 (77.8)	
12 h			
Present	10 (15.9)	27 (42.9)	0.001
Absent	53 (84.1)	36 (57.1)	
24 h			
Present	13 (20.6)	30 (47.6)	0.002
Absent	50 (79.4)	33 (52.4)	
Over all incidence of pain			
Present	16 (25.4)	39 (61.9)	<0.001
Absent	47 (74.6)	24 (38.1)	

*P* value significant if ≤0.05, n: Number of patients, SD: Standard deviation, h: Time interval in hours

**Table 3: Temporal trend of visual analog pain score**

Time interval	Group A VAS (mean±SD)	Group B VAS (mean±SD)	P
1 h	0.43 (0.73)	1.16 (1.25)	<0.001
4 h	0.63 (0.92)	1.48 (1.31)	<0.001
8 h	0.70 (0.99)	2.01 (0.93)	<0.001
12 h	0.98 (1.30)	2.40 (0.92)	<0.001
24 h	1.00 (1.21)	2.63 (1.21)	<0.001

*P* value significant if ≤0.05, SD: Standard deviation, VAS: Visual analog pain score, h: Time interval in hours

There was no significant difference in mean systolic blood pressures between the two groups postoperatively at the studied intervals (*P* > 0.05) [Table 5].

There was no significant difference in diastolic blood pressures between the two groups postoperatively at the studied intervals ( $P > 0.05$ ) [Table 5].

There was no significant difference in mean oxygen saturation between the two groups at the studied intervals postoperatively ( $P > 0.05$ ). No incidence of hypoxemia (hypoxemia defined as  $SpO_2 \leq 90\%$ ) was noted in either group [Table 5].

There was no significant difference in mean RRs between the two groups at the studied intervals postoperatively ( $P > 0.05$ ). No incidence of hypoventilation (hypoventilation defined as  $RR \leq 10/\text{min}$ ) was noted in either group [Table 5].

**Discussion**

The postthoracotomy shoulder pain is typically ipsilateral, periarticular, diffuse, resistant to treatment, and independent from pain caused by thoracotomy. The shoulder pain is moderate to severe in intensity and dull aching in nature.<sup>[23]</sup>

Various methods have been used to relieve the PTISP but with limited success. Block of the phrenic nerve at the cervical level via an interscalene approach has been reported to relieve ipsilateral shoulder pain following

thoracotomy.<sup>[9]</sup> The interscalene approach would also address the pain resulting from mechanical shoulder distress despite careful positioning. Concerns with this approach are the incidence of phrenic nerve paresis with associated diaphragmatic dysfunction and respiratory depression.<sup>[24,25]</sup> An adequately placed interscalene block is believed to be associated with 100% incidence of phrenic nerve paresis,<sup>[25]</sup> which could result in 25% reduction in vital capacity. Patients with severely reduced pulmonary function, or with contralateral hemidiaphragmatic paresis, would therefore not be appropriate candidates for this block. Other complications such as pneumothorax, Horner’s syndrome, systemic toxicity of local anesthetics may occur. PNI with local anesthetics at the cardiophrenic angle has been shown to significantly reduce the incidence of postthoracotomy shoulder pain.<sup>[11]</sup> Acetaminophen used preemptively reduces early PTISP<sup>[15]</sup> and may be a viable alternative to NSAIDs in high-risk patients because of opioid-sparing effect<sup>[19]</sup> and lower incidence of adverse effects.<sup>[20]</sup> No literature is available that compares two different anesthetic techniques to minimize the incidence and severity of PTISP.

Patients in the study had no difficulty in distinguishing shoulder pain from wound pain in the presence of a functioning epidural. The thoracotomy pain relief at the incisional site provided by the epidural infusion was adequate in all patients. No patient complained of any pain at the incision site. When shoulder pain did occur, it was distressing to the patient, detracting from the benefits of an effective dermatome block with the epidural. When shoulder pain was absent or prevented by PNI, patients reported remarkably little pain. The overall pain score was assessed with a visual analog scale (VAS) showed a statistically significant difference ( $P < 0.05$ ) between the two groups at all the studied intervals (1, 4, 8, 12, 24 h). Overall pain scores were lower in Group A. Furthermore,

**Table 4: First rescue analgesic time in hours and total number of rescue analgesic doses**

	Group A (n=16/63)	Group B (n=39/63)	P
First rescue analgesic time in hours (mean±SD)	11.1±7.47	7.40±5.30	0.031
Total number of rescue analgesic doses (mean±SD)	1.6±1.16	2.9±1.37	0.002

P value significant if  $\leq 0.05$ , n: Number of patients, SD: Standard deviation

**Table 5: Comparison of heart rates, blood pressures, SpO<sub>2</sub>, and respiratory rate**

	1 h	4 h	8 h	12 h	24 h
HR (beats/min), mean±SD					
Group A	77.08±4.194	76.21±3.865	75.41±3.329	76.81±4.497	76.81±4.631
Group B	77.44±4.103	76.30±4.070	75.40±3.343	77.37±4.124	77.03±4.494
SBP (mmHg), mean±SD					
Group A	120.44±2.758	118.81±2.873	119.33±3.059	119.57±2.917	119.86±2.415
Group B	120.08±3.940	119.29±3.103	119.16±3.399	119.89±2.748	120.87±2.904
DBP (mmHg), mean±SD					
Group A	77.22±3.144	77.33±3.090	77.13±2.196	77.67±2.349	76.51±2.539
Group B	77.13±3.245	76.90±2.977	77.01±2.148	77.68±2.213	76.62±2.773
SpO <sub>2</sub> %, mean±SD					
Group A	96.84±0.919	96.81±0.937	96.97±0.967	96.75±0.897	96.78±0.87
Group B	96.48±0.543	96.67±0.753	96.71±0.569	96.69±0.658	96.57±0.617
RR (breaths/min), mean±SD					
Group A	13.17±0.908	13.22±0.991	13.25±0.967	14.06±1.162	13.22±0.991
Group B	13.19±0.895	13.29±0.991	13.32±0.964	14.13±1.184	13.29±0.991

P value significant if  $\leq 0.05$ , SD: Standard deviation, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SpO<sub>2</sub>%, Oxygen saturation, RR: Respiratory rate, h: Time interval in hours

the mean time to first rescue analgesia was lower in Group B than Group A. Group A received less number of rescue analgesic doses compared to Group B indicating that the phrenic nerve infiltrated group had a better relief of PTISP.

Our observations indicate that the incidence of PTISP was reduced in both groups, but it was significantly less in Group A than in Group B (reduced VAS scores at all measured intervals). The PTISP was relieved significantly in Group A for the first 8 h postoperatively. In Group B, the early postthoracotomy shoulder pain was relieved, but the PTISP had an increasing trend with time for 24 h postoperatively. The incidence of PTISP in Group A (PNI with ropivacaine) was much lower being only 25.4% compared to Group B (paracetamol infusion) 61.9%.

No adverse events such as phrenic nerve palsy, respiratory insufficiency, local anesthetic toxicity, and hemodynamic instability were noted in any of the studied patients.

All these observations suggest that the patients receiving PNI with 10 mL ropivacaine 0.2% had a better PTISP relief compared to those receiving paracetamol infusions. PNI with local anesthetic in the periphrenic fat pad at the cardiophrenic angle resulted in significant reduction in PTISP without causing any adverse effects. Thus, the pain referred to ipsilateral shoulder due to irritation of the pericardium or mediastinal and diaphragmatic pleural surfaces was blocked by local anesthetic infiltration of the phrenic nerve.

The technique of PNI, although technically difficult, had a benefit of being cost-effective in terms of one-time administration and requirement of less number of rescue analgesic doses. PNI was free of any side effects and was more effective than paracetamol infusion in relieving PTISP in thoracotomy patients. A minority of patients receiving phrenic nerve block still experienced shoulder pain, possibly because the level of the block may have been too low, with the stimulation of phrenic nerve occurring proximal to the site of local anesthetic infiltration at the level of the diaphragm. A higher block might have been more appropriate in these patients, with care to avoid intraneural injection because there is less periphrenic fat proximally. Second, the technique relies on the retention of local anesthetic by the periphrenic fat pad, which may have been insubstantial in some patients.

Our observations correlate with a study conducted by Cremades *et al.*<sup>[12]</sup> who randomized the patients undergoing thoracotomy into two groups and infiltrated one group with 10 mL of 0.2% ropivacaine around the phrenic nerve fat pad near the pericardium and the diaphragm. Ipsilateral shoulder pain scores at 1, 6, and 24 h were lower in the phrenic nerve infiltrated the group. No diaphragmatic paresis was found in any patient.

Our observations correlate with Martinez-Barenys *et al.*<sup>[26]</sup> who studied the effect of PNI compared with SNB

on PTISP after thoracic surgery and observed that shoulder pain intensity was significantly lower in PNI group.

Our results are also similar to results of Danelli *et al.*<sup>[11]</sup> who also concluded that PNI with ropivacaine 0.2% 10 mL reduced the incidence and delayed the onset of ipsilateral shoulder pain during the first 24 h after open lung resection, with no clinically relevant effects on respiratory function.

Scawn *et al.*<sup>[1]</sup> in their study also found out that the overall pain scores were lower in lidocaine infiltrated group ( $P < 0.05$ ) and concluded that infiltration of the phrenic nerve with local anesthetic significantly and safely reduces this shoulder pain, potentially allowing the ideal goal of a pain-free thoracotomy. The results of this study are also comparable to our study.

Our results are similar to a study conducted by Mac *et al.*<sup>[15]</sup> who in their study assessed the efficacy of acetaminophen in decreasing postoperative shoulder pain after a thoracotomy in a double-blind randomized and placebo-controlled study and concluded that acetaminophen decreases early PTISP in patients with thoracic epidural analgesia.

## Conclusion

PTISP is severe and very frequent with enigmatic etiology but is most probably due to irritation of pericardium and pleura and is transmitted through the phrenic nerve. The PNI significantly reduced the incidence and delayed the onset of PTISP compared to paracetamol infusion, with no clinically relevant effects on respiratory function.

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## Conflicts of interest

There are no conflicts of interest.

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