ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 03 | March - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON BETWEEN PRE-EMPTIVE THORACIC EPIDURAL ANALGESIA VS CONVENTIONAL THORACIC EPIDURAL ANALGESIA IN PATIENTS UNDERGOING THORACOTOMY IN A TERTIARY CARE CENTRE

Anaesthesiology

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ABSTRACT

Background: Relative effects of timing of providing analgesia, type of surgery of local anaesthetics used for postoperative thoracic epidural analgesia and the possibility of establishment of pre-emptive analgesia as a superior mode for thoracic epidural analgesia are still in grey zone. In this observational study, we evaluated the idea of Pre-emptive thoracic epidural analgesia which can counter the post thoracotomy pain through pain scoring. **Objective:** To find out whether pre-emptive thoracic epidural analgesia is superior to conventional postoperative epidural analgesia for post-thoracotomy pain. **Study Design:** Observational study. Place and Duration of Study: Department of Anesthesiology and Critical Care, Assam Medical College and Hospital, from Januray 2022 to January 2023. **Methodology:** After ethical committee approval and informed consent from patients, 22 patients undergoing thoracotomy were included in study. Preoperatively thoracic epidural catheter was inserted at T8-9 intervertebral space level. Group P was given 0.5ml/kg of 0.125% bupivacaine before induction of anesthesia; whereas group C was administered 0.5 ml 0.125% bupivacaine after closure of wound in supine position. All patients received thoracic epidural analgesia with a bolus dose of 0.1 ml/kg of 0.125% bupivacaine every 6 hourly post operatively .Visual analog scale (VAS) was used to assess pain severity at 1 and 24 hours postoperatively, both at rest and after cough (R1, R24, C1 and C24 respectively). Data were analyzed with SPSS and Microsoft Excel 2010. **Results:** There was no statistical difference in demographic profile of both groups in terms of age, gender, American Society of Anaesthesiologists (ASA) status or type of surgery, complications. Pain was significantly less in group P at 1hour postoperatively (p=0.0001). However, there was no difference in pain severity at rest at 24 hours and with cough at 01 hour or 24 hours postoperatively. **Conclusion:** Pre-emptive thoracic epidural analgesia provides better pain control in immediate post operative period at rest. However, no such differences were observed in pain scores in immediate post operative period on coughing. No differences were observed at 24 hours at rest or coughing in both the groups.

KEYWORDS

INTRODUCTION:

Post thoracotomy pain is widely accepted as one of the most noxious post-surgical pain with debilitating effect and poor outcome of the patient. By facilitation of incentive spirometry, coughing, and deep breathing without splinting, proper dynamic analgesia can help achieve the goal of encouraging ambulation and coughing to lower the risk of postoperative respiratory complications and to enhance postoperative chest care. Major respiratory consequences like shallow and limited inspiration , which leads to reflex contraction of expiratory muscles, and consecutively to diaphragmatic dysfunction (decreased functional residual capacity or FRC and atelectasis, shunting, hypoxemia are witnessed .[1]Increased myocardial oxygen demand, increased afterload, myocardial dysfunction, and arrhythmias are all associated with increased sympathetic tone in response to pain.[2] Adequate analgesia decreases incidence of ICU admissions and decreases incidence of intubation due to inadequate pulmonary secretion removal.

The post-thoracotomy pain syndrome (PTPS), affects about 50% of patients. Since the illness is chronic, 30% of patients may continue to have discomfort 4 to 5 years following surgery. Pain is often minimal in most people and doesn't significantly interfere with everyday activities. Only a small percentage of patients have pain that is so severe that it may be considered a real handicap, rendering the patient incapable. Although the precise pathophysiology of PTPS is still unknown, mounting evidence points to a combination of neuropathic and non-neuropathic (myofascial) pain as the pathogenesis. The most likely cause is a thoracotomy injury to the intercostal nerve. Pre emptive analgesia initiated prior to surgery holds the possibility of reduction in the incidence of PTPS. Scientific evidence is steadily growing but there is still a need for large, prospective, randomized trials evaluating PTPS.[3] There are several factors that can be modified to reduce pain and incidence of PTPS during the perioperative period and the use of multimodal analgesia is suggested for the treatment of PTPS.[4] The idea of pain prevention was first put forth by Crile in 1913[5] and later developed by Wall and Woolf. They suggested that even small changes in treatment timings could affect post-operative pain findings. Woolf later proposed the idea of what is now known as pre emptive analgesia, which involves a central component to post-injury pain. [6] Allodynia and hyperalgesia can be caused by several recognised processes. The concept of sensitization has inspired an increased effort to control acute pain by a more or less total afferent blockage in an effort to prevent the emergence of post-thoracotomy discomfort.

Pre-emptive analgesia aims to stop the development of central sensitization brought on by inflammatory and incisional wounds. Basic research has shown that administering analgesic medications prior to a painful stimulus increases their effectiveness. Clinical investigations have proven that pre-emptive analgesia is beneficial. [7]Pre-emptive analgesia's therapeutic utility, however, has remained debatable[8], in part because of the wide range of study settings, including surgery, medications, doses, routes of administration, and treatment duration, as well as the pain assessment techniques employed in various studies.[1]

According to studies, epidural local anaesthetics improve the segmental bioavailability of opioids in the cerebrospinal fluid, increase the binding of opioids to receptors, and block the release of substance P in the spinal cord's substantia gelatinosa.[2] The present study was carried out to compare the effectiveness between conventional methods of thoracic epidural analgesia versus pre-emptive thoracic epidural analgesia in patients undergoing thoracotomy in our institution.

METHODOLOGY

This hospital based observational study was conducted in the Department of Anaesthesiology, Assam Medical College and Hospital, a tertiary care centre in rural India over the course of one year. Institutional Ethics Committee (H) approval was obtained prior to the commencement of the study and informed written consent were obtained from all the patients. Patients aged 18 to 65 years of all genders, belonging to American Society of Anaesthesiologists (ASA)

grade 1, 2 or 3 physical statuses admitted in the Cardiothoracic and Vascular Surgery ward of Assam Medical College and Hospital and scheduled for elective thoracotomy were included for the purpose of the study. Patients who refused to give consent, those allergic to the drugs used in epidural analgesia or known allergy to local anaesthetics, pregnant or breastfeeding women, morbidly obese patients, those with coagulation disorders, infection at the site of epidural insertion, neurological or neuromuscular or psychiatric illness were excluded from the study.

Over the course of one-year participants were allocated into two groups-group pre-emptive (group P) and group conventional (group C) randomly. Random allocation cards were made for 22 patients by an independent medical officer using computer-generated random numbers and they were divided into two equal groups of 11 each. Another independent medical officer used SNOSE (Sequentially Numbered, Opaque, Sealed and Stapled envelopes Method) method to conceal the allocation sequence from the researcher enrolling and assessing participants.

The envelopes were opened sequentially just before the injection by the anaesthesiologist performing the procedure, who then progressed with the procedure as mentioned in the card inside for that patient. Input date, time, patient ID, results after the procedure, etc. were recorded by that anaesthesiologist on the envelope or another sheet inside of the envelope for that patient. The envelope was then sealed and preserved in a secured place for analysis by principal investigating officer and for future references.

Pre-anaesthetic assessment was done on the day before surgery, VAS score was explained to them, and patient was prepared preoperatively as per the departmental protocol. On the day of surgery intravenous access was secured using an 18G cannula. Standard monitoring including ECG, pulse oximetry, NIBP was started. Skin testing was done to determine sensitivity to the local anaesthetic drug before the procedure.

Under complete aseptic conditions, with the patient in sitting position, skin over the site of epidural insertion was infiltrated with 2 ml of Inj Lignocaine 1%. Epidural space was located using the loss of resistance to air method using 18 G Tuhoy needle and epidural catheter was inserted at the T_{8-9} interspace. The catheter was then secured, and the patient was made to lie supine. Test dose of 60 mg 1% Lignocaine and 15ug Adrenaline was then given through the catheter to rule out intravascular or intrathecal placement of the catheter.

If catheter was found to be intrathecal or intravenous, or in the case of inadvertent dural puncture during introduction of the Tuhoy's needle, the patients received only intravenous analgesia with transdermal opioid patches and were subsequently excluded from the study.

Group P then received 0.5 ml/kg of 0.125% bupivacaine through the epidural catheter before induction. Group C received the same i.e., 0.5ml/kg of 0.125% bupivacaine after closure of the wound and before extubation as was conventionally done in our setup.

All patients were premedicated as per institutional protocol with Inj Glycopyrrolate 4ug/kg, Inj Ondansetron 0.1mg/kg, Inj Fentanyl 2ug/kg. Induction of anaesthesia and muscle relaxation were achieved with Inj Propofol 2mg/ kg body weight, titrated as per individual patients, and Inj Atracurium 0.5 mg/kg body weight. Patient was intubated under direct laryngoscopic guidance using cuffed endotracheal tubes of appropriate size. Single lumen endotracheal tubes were used as double lumen tubes are not available in our setup. Anesthesia was maintained with sevoflurane in 50% oxygen and air mixture. Patients were extubated at the end of surgery and shifted to high dependency units for observation.

All patients received thoracic epidural analgesia with a bolus dose of 0.1 ml/kg of 0.125% bupivacaine every 6 hourly post operatively. For breakthrough pain- Infusion paracetamol 1 gram and/or Inj tramadol 100 mg was given as per institutional protocol.

A 10-point Visual Analogue Scale (VAS) was used to assess the severity of post operative pain in which a score of 0 indicated no pain and a score of 10 indicated the worst pain imaginable. The VAS score was recorded at the first hour post extubation and at the 24th hour post extubation, both at rest (R1 and R24) and with cough(C1 and C24). VAS was graded as no pain: 0, mild pain: 1-3, moderate pain: 4-6, severe pain 7-10. This scoring was done by the HDU nurse who was unaware of the group of the patient.

Other side effects such as the incidence of post top up hypotension or bradycardia (systolic blood pressure of less than 90 mm Hg or 20% reduction from baseline and a heart rate of less than 60 beats/min within 20 minutes of the epidural bolus was considered as post top up hypotension and bradycardia respectively), nausea and vomiting were looked for.

Statistical Analysis

A sample size of 22 patients, 11 for each group was calculated setting the power of the study at 80% and confidence interval at 95%. Data was analysed using the computer program SPSS (Statistical Package for Social Sciences version 2.0, Chicago, SPSS Inc.) and Microsoft Excel 2010. Continuous data were presented in terms of Mean ± SD and Categorical data were presented in terms of frequency. Statistical significance was tested using Student's t-test for continuous data and Chi-square test / Fisher's Exact test for categorical data. A p-value of less than 0.05 ($p<0.05$)was considered as statistically significant for all analysis.

RESULTS

A total of 25 patients belonging to ASA physical status 1,2 and 3 were recruited for the purpose of the study, out of which there was inadvertent dural puncture during the procedure in three patients. These patients were subsequently excluded from the study. A total of 22 patients were analysed, 11 in each group.

In group C (conventional group) mean age was found to be 41.9 years compared to 39.5 years for group P (pre-emptive group), a difference that was not found to be statistically significant (p 0.538). There were 7 males and 4 females in both the groups. Other demographic and hemodynamic variables were comparable in both the groups and found to be statistically insignificant.

The mean VAS score in the first post operative hour at rest in the conventional group (Group C) was 3.72 ± 1.009 while it was 1.818 ± 0.873 in the pre-emptive group (Group P), a difference that was found to be statistically significant with a p value of 0.0001.

The mean VAS score in the first post operative hour after coughing in group C was found to be 4.818 ± 0.98 whereas it was 5.090 ± 0.700 for group P. This difference was not found to be statistically significant (p 0.462)

The mean VAS scores in the 24th hour at rest and after cough in both the groups were also found to be not significant as shown in Table 2.

Table 1: Comparision Of Demographic Data

Variables		Group C	Group P	P value	
Gender	Male	7	7	0.196	Not Sig
	Female	4	4		
Age (Years)		41.909 ± 7.54	39.545 ± 9.97	0.538	Not sig
ASA Status	II	8	8	0.229	Not sig
	III	3	3		
Surgery	DECORTICATION	11	11	Not applicable	
COMPLICATIONS	HYPOTENSION	1	0	Not applicable	
	NONE	10	11		

Table 2: Comparision Of Vas Scores Between The Two Groups

Variables	Group C (Mean ± SD)	Group P (Mean ± SD)	p-value
R1	3.72 ± 1.009	1.818 ± 0.873	0.0001
R24	2.727 ± 0.467	2.363 ± 0.504	0.094
C1	4.818 ± 0.98	5.090 ± 0.700	0.462
C24	3.727 ± 0.467	3.636 ± 0.504	0.665

DISCUSSION:

In our study a better pain control was recorded in the immediate post operative period (after 1 hour) in the Pre emptive group(GROUP P)at Rest (R1)as compared to the conventional group (GROUP

C)(p=0.0001).No statistically significant findings in pain score after 24 hours in conventional TEA and pre-emptive TEA at rest(R24) or after coughing(C24)(p>0.05) .

CL Bong et al. (2005)[9] conducted a meta-analysis of Five RCTs (n=355) after searching MEDLINE, EMBASE and the Cochrane CENTRAL Register since its inception. The authors concluded that pre-emptive thoracic epidural analgesia (TEA) appeared to reduce the severity of acute post-operative pain compared with TEA initiated after completion of surgery for patients undergoing unilateral thoracotomy, but did not affect the incidence of chronic post-thoracotomy pain. This study included all cases for 24 hours ,48 hours for acute pain with VAS and Numeric rating scales.

Sun Kyung Park et al.(2020)[10]searched MEDLINE, Embase, and CENTRAL databases for randomised controlled trials contrasting epidural analgesia started before to (pre-emptive group) and following (control group) thoracotomy incision in people. The main results were the degree of pain experienced during rest and coughing 72 hours after surgery, as well as the frequency of pain 1–6 months after surgery. Meta-analyses with random effects were used to analyse the data. They found that the pain intensity was significantly lower at rest within 72 hours after surgery (19 studies, n=1062) and during coughing within 48 hours after surgery (11 studies, n=638), and the incidence of pain was significantly lower 1 to 6 months after surgery (6 studies, n=276) in the pre-emptive group than in the control group.

Pre-emptive epidural analgesia for acute and chronic post-thoracotomy pain in adults: a systematic review and meta-analysis was conducted by Yifeng Ren et al.(2021)[11] to find similar outcomes establishing superiority of pre-emptive group in acute post thoracotomy pain.

Yasser Mohamed Amr et al.(2009)[12]compared forty patients undergoing posterolateral thoracotomy received TEA either before (preoperative-TEA group) or after (postoperative-TEA group) surgery. Pain scores, pulmonary functions, arterial blood gases, plasma glucose, cortisol levels and epidural fentanyl consumption were compared for 48 hours after surgery. They found that the preoperative-TEA group demonstrated significantly reduced pain scores at 2, 4, 8, 12, 24, and 48 hours at rest and on coughing and a significant reduction in epidural fentanyl .The preoperative-TEA group showed significant improvement in pulmonary functions as compared with the postoperative-TEA group .The postoperative-TEA treated patients were more likely to have a higher arterial carbon dioxide pressure at 4, 8, 12, and 24 hours respectively. However, they could not demonstrate a statistical difference in oxygenation, cortisol, or glucose level. They concluded that although preventive TEA appeared to lessen acute pain intensity, maintain pulmonary function, and minimise analgesic doses, a clinically significant difference between groups could not be drawn from these statistically significant changes.

In a similar study conducted by Liaquat Ali et al.(2020) [13] pain was found to be significantly less in group P at 1hour postoperatively. However, there was no difference in pain severity at rest at 24 hours and with cough at 01 hour or 24 hours postoperatively. They found that pre-emptive thoracic epidural analgesia provides better pain control in immediate postoperative period at rest. However, its efficacy is like conventional epidural analgesia in immediate post op period with cough and at 24 hours with cough and at rest.

In a study conducted by Erturk et al.[14](2014) Forty-four patients were randomized in to two groups (pre-emptive: Group P, control: Group C). Postoperative patient controlled epidural analgesia infusion pumps were prepared for all patients. Respiratory rates (RR) were recorded. Patient's analgesia was evaluated with visual analogue scale at rest (VASr) and coughing (VASc). Number of patient's demands from the pump, pump's delivery, and additional analgesic requirement were also recorded. RR in Group C was higher than in Group P at postoperative 1st and 2nd hours. Both VASr and VASc scores in Group P were lower than in Group C at postoperative 1st, 2nd, and 4th hours. Patient's demand and pump's delivery count for bolus dose and post operative analgesic dose in Group P were lower than in Group C in all measurement times. It was considered that pre-emptive TEA may offer better analgesia after thoracotomy. However, in this study the maintenance anaesthesia was performed by TIVA which could have altered the results for the pre-emptive group. In our study TIVA was not used.

A total of 45 patients who were scheduled for posterolateral thoracotomy were included in the study conducted by Barut et al. (2018)[15]. A combination of epidural levobupivacaine and morphine was administered as a bolus before incision (Group 1; n=15), after incision (Group 2; n=15), or at the end of surgery (Group 3; n=15). Additionally, infusion was used in Group 1 and Group 2 during operation. Postoperative patient-controlled epidural analgesia infusion pumps were connected to all patients. Visual analogue scale (VAS) scores and morphine consumption were recorded during the postoperative 48 h. Glucose, insulin, cortisol, and C-reactive protein (CRP) levels were compared before surgery and at 4, 24, and 48 h after the operation and no significant difference was found in all the three groups for surgical pain, rescue analgesic doses and surgical stress. They have used opioids in epidural unlike our study.

Our study had certain limitations as we had used bolus dosages and no infusion for the local anaesthetics, no evaluation of post operative pain after the 24 hour window, evaluation of respiratory functions post-surgical insult in immediate post operative scenario. The sample size was limited by number of thoracotomies carried out in our institution. Anti-inflammatory effects of pre-emptive analgesia were not evaluated with inflammatory markers. Thus, every aspect of thoracic analgesia could be better evaluated after taking up a larger scale study with parameters highlighted above.

CONCLUSION:

Pre-emptive thoracic epidural analgesia provides better pain control in immediate post operative period at rest. However, no such differences were observed in pain scores in immediate post operative period on coughing. No differences were observed at 24 hours at rest or coughing in both the groups.

Ethical Consideration:

Institutional Ethics Committee(H) permission obtained prior to study commencement.

Other Informations

Protocol:
Passed by Institutional Ethics Committee(H) NO.AMC/EC/PG2487

Funding: No external funding obtained

Conflict of Interest: None

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