PRE-EMPTIVE VS CONVENTIONAL METHOD OF EPIDURAL ANALGESIA FOR POST THORACOTOMY PAIN: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Objective: To find out whether pre-emptive thoracic epidural analgesia is superior to conventional postoperative epidural analgesia for post-thoracotomy pain.

Study Design: Randomized controlled trial.

Place and Duration of Study: Department of anesthesia and critical care, Combined Military Hospital Rawalpindi, from Apr 2017 to Aug 2017.

Methodology: After ethical committee approval and informed consent from patients, 40 patients undergoing thoracotomy were included in study. Preoperatively thoracic epidural catheter was inserted at T^{7-9} intervertebral space level. Group P was given 0.1ml/kg of 0.125% bupivacaine before induction of anesthesia; whereas group C was administered 5 ml 0.125% bupivacaine after closure of wound in supine position. 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 16.

Results: There was no statistical difference in demographic profile of both groups in terms of age, gender, site of insertion of epidural catheter, American Society of Anaesthesiologists (ASA) status or type of surgery. Pain was significantly less in group P at 1hour postoperatively (p=0.009). However, there was no difference in pain severity at rest at 24 hours and with cough at 01 hour or 24 hours postoperatively.

Conclusion: Preemptive thoracic epidural analgesia provides better pain control in immediate postoperative period at rest. However, its efficacy is similar to conventional epidural analgesia in immediate post op period with cough and at 24 hours with cough and at rest.

Keywords: Postoperative analgesia, Pre-emptive analgesia, Thoracic epidural, Thoracic surgery.

INTRODUCTION

Effective post-thoracotomy analgesia is essential components of care for thoracic surgery patients because thoracotomies are considered to be associated with severe acute postoperative pain. Inadequately treated pain is associated with increased postoperative morbidity with detrimental physiological, psychological, economic and social adverse effects[1]. Severe post-operative pain can cause shallow breathing, atelectasis and increased pulmonary complications which result in prolonged hospital stay and increased mortality. If not treated properly, there is significant risk that post-thoracotomy pain can be converted into chronic pain[2,3]. There are several important strategies to achieve post-operative analgesia. Post thoracotomy pain is countered with systemic analgesics, thoracic epidural, paravertebral blocks, intercostal nerve blocks and intrapleural catheter. In comparison to conventional modalities of analgesia thoracic epidural analgesia (TEA) is most effective and considered as gold standard for post thoracotomypain relief[4-6]. TEA not only reduces pain but also counters stress response of surgery and helps in enhanced recovery after thoracotomy[7]. Studies have shown that TEA provides better analgesia than conventional systemic analgesics both in children and adults[8]. However there are few adverse effects such as hypotension, bradycardia or cardiac arrest associated with use of TEA. These adverse effects are result of inhibition of cardio-accelerator fibers and can be prevented by administration of fluids and vasopressor drugs.

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Received: 18 Jan 2019; revised received: 19 Jun 2019; accepted: 25 Jun 2019

Fortunately the reported incidence of adverse effects with TEA is only 0.1%[9].

At our institute, thoracic epidural analgesia is being employed for postoperative and cancer pain relief as well as analgesic for traumatic rib fracture. Commonly thoracic epidural is inserted pre-operatively in awake, sitting patient and initiated by most thoracic anesthetists at the time of recovery. However, the time for initiation of TEA has lately come under debate. Concept of preemptive analgesia is being introduced in which medication is given before the surgical procedure and initiation of pain. As a result stress response to surgery and pain is minimal. Preemptive analgesia with systemic analgesics is being used in many centers[10,11]. There is a discussion these days that preemptive thoracic epidural analgesia is better than conventional method of starting epidural analgesia in post-operative period. The aim of our study was to find out that whether pre-emptive thoracic epidural analgesia is superior to conventional postoperative initiation of epidural analgesia for post- thoracotomy pain.

METHODOLOGY

This randomized controlled trial was conducted in Department of anesthesiology and critical care department Combined Military Hospital (CMH) Rawalpindi from April to August 2017. Approval was taken from hospital ethical committee. Sample size was calculated with the help of G*Power 3.1.9.2 software by keeping power of 95%, confidence level 95% and effect size 1.219 which was calculated from visual analogue pain scores at 1st hour postoperatively[13]. Total sample size calculated was 38, however we included 40 patients undergoing elective open thoracotomy by consecutive method of sampling. Written informed consent was taken from patients. Patients with ASA >IV, BMI greater than 30kg /m^2, or known allergy to local anesthetics were excluded from our study.

Randomization was done by Sealed envelope method and patients were divided into two equal groups (preemptive: group P, n=20 and conventional: group C, n=20). Pre-anesthesia assessment and preparation were done as per institute protocol and no changes were made for the study. On the day of surgery 18G IV line was inserted and monitoring with ECG, SpO2 and NIBP started. Complete aseptic measures taken and 2 ml of 1% lignocaine injected in skin while patient was in sitting position. Thoracic epidural catheter with help of 18 G Tuohy needle was inserted in T^{7-9} intervertebral space.

After making supine position, group P was given test dose with 60mg lignocaine and 15ug adrenaline to rule out that catheter was not intrathecal or intravascular. 0.1 ml/kg of 0.125% bupivacaine was given to same group. While group T was given test dose and 0.1ml/kg of 0.125% bupivacaine after closure of wound and before extubation as is conventionally done in our setup. Group P was also given a top-up dose of 0.1ml/kg of 0.125% bupivacaine after closure of wound. For induction of anesthesia all patients were pre-medicated with IV dexamethasone 0.1 mg/kg and metoclopramide 0.15mg/kg. IV nalbuphine 0.1mg/kg was administered to all the patients as part of multimodal analgesia. Induction and muscle relaxation was done with IV propofol 1.5 mg/kg and IV atracurium 0.5mg/kg. Double lumen endobronchial tube was inserted under direct laryngoscopy with Macintosh blade. Anesthesia was maintained with isoflurane in 60% oxygen. Extubation was done at end of surgery and patients were shifted to ICU.

All the patients were given thoracic epidural analgesia as bolus of 0.1ml/kg of 0.125% bupivacaine every 6 hour postoperatively. For breakthrough pain rescue analgesia was given with 0.1 mg/kg of Nalbuphine IV. The level of insertion and the dose of local anesthetic; incidence of post top-up hypotension and bradycardia (systolic blood pressure of less than 90 mm Hg or 20% reduction from baseline and heart rate of less than 60 beats per minute within 20 minutes of epidural bolus was considered hypotension and bradycardia respectively) were recorded on the performa. The visual analogue scale (VAS) was used to assess the pain score and severity. Score

was given from 0 to 10 with 0 as no pain and 10 as worst imaginable pain.To characterize the severity of pain VAS points were graded as: no pain (0-4mm), mild pain (5-44mm), moderate (45-74mm) and severe (75-100mm)[12]. VAS at rest was noted at 1 (R1) and 24 hours (R24) post-operatively. VAS after cough was also noted at 1 (C1) and 24 hour (C24) postoperatively. This scoring was done by an ICU nurse who was unaware of the group of patient. The VAS was doneat 1 hour and at 24 hours post extubation.

Data was analyzed by SPSS 16. Quantitative data like pain score and age were presented as means ± SD and were compared by using independent samples t-test. Qualitative data like incidence of hypotension and bradycardia, gender, ASA status and type of surgery were described as frequency and percentage. Chi square test and Fisher's exact test were used to compare these variables. A *p*-values less than or equal to 0.05 were taken as significant.

RESULTS

A total of 40 patients (20 in each group) undergoing elective thoracic surgeries were included in our study. The demographic profile of the study groupsare tabulated as table-I.

The study groups did not have any significant difference in demographic profile. The incidence of hypotension did not differ significantly between two groups. Hypotension occurred in only 1 patient in preemptive analgesia group and *p*-value was 0.5 which was statistically non-significant. None of the patients developed bradycardia. Comparison of VAS between two groups at 1 and 24 postoperative hours are shown in table-II. Difference of pain score between two groups is significant only at 1st hour at rest. While all other results between two groups are statistically non-significant.

Table-I: Demographic profile of the study groups.

Variable		Group C (n=20)	Group P (n=20)	*p*-value
Age (years)	Mean ± SD	44.05 ± 14.37	48.5 ± 17.21	0.38
Gender	Males	15 (75%)	16 (80%)	0.5
	Females	5 (25%)	4 (20%)	
ASA Status	II	16 (80%)	17 (85%)	0.5
	III	4 (20%)	3 (15%)	
Surgery	Pneumonectomy	3 (15%)	2 (10%)	0.875
	Lobectomy	7 (35%)	8 (40%)	
	Decortication	10 (50%)	10 (50%)	
Level of Insertion	T7-8	2 (10%)	5 (25%)	0.485
	T8-9	13 (65%)	11 (55%)	
	T9-10	5 (25%)	4 (20%)	

Table-II: Comparison of VAS between two groups.

Variable	Group C Mean ± SD	Group P Mean ± SD	*p*-value
R1	4.2 ± 1.24	3.2 ± 1.06	0.009*
R24	2.9 ± 1.17	2.55 ± 0.76	0.269
C1	5.05 ± 1.09	4.4 ± 1.09	0.067
C24	4.0 ± 1.12	3.65 ± 1.04	0.313

**p*-value is less than 0.05 and statistically significant.

R1 (VAS at rest at 1st post op hour), R24 (VAS at rest at 24th post op hour), C1 (VAS with cough at 1st post op hour), C24 (VAS with cough at 24th post op hour).

Figure-1 & 2 show frequency of severity of pain in conventional epidural analgesia and pre-emptive epidural analgesia groups respectively.

DISCUSSION

Our study has shown better pain control in the immediate post-operative period (*p*-value

0.009) with pre-emptive TEA but only at rest. However, there was no statistically significant difference in pain score on cough immediate postoperatively (*p*-value 0.067) as well as at rest or cough at 24 hours (*p*-value 0.269 and 0.313). Our results partially correlate with the findings of a study by Erturk *et al*. who studied forty four patient to evaluate the effectiveness of preemptive thoracic epidural[13]. Similar to our study they

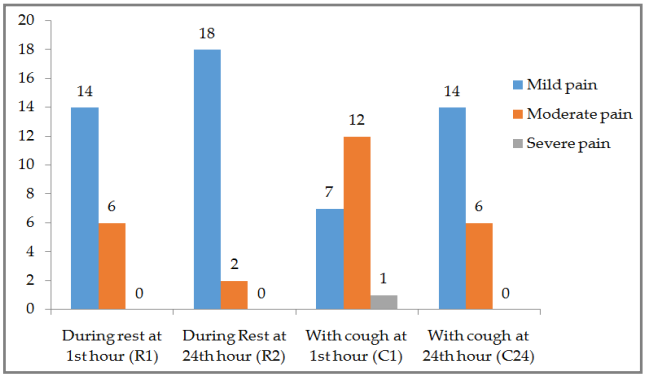

Figure-1: Frequency of severity of pain in conventional epidural analgesia group.

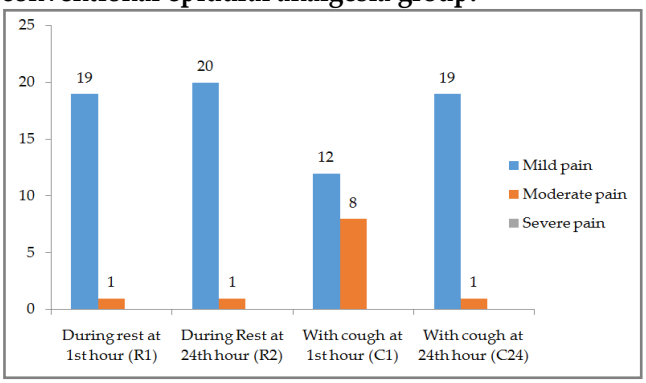

Figure-2: Frequency of severity of pain in preemptive epidural analgesia group.

reported a lower VAS with preemptive epidural analgesia at rest in immediate postoperative period and VAS was not different in both groups at 24 hours postoperatively both at rest and with cough. However in contrast to our study they concluded that preemptive analgesia is also effective in reducing the pain score even with cough in immediate postoperative period[13]. Another study conducted by Amr *et al* showed significantly reduced pain scores at rest as well as with cough at 2, 4, 8, 12, 24 and 48 hours[14].

Erturk *et al*[13] used levobupaivacaine in their study while we and Amr *et al*[14] used bupivacaine in our studies. Erturk *et al* used TIVA with propofol and remifnetanyl for maintenance of anesthesia; whereas we used isoflurane for maintenance of anesthesia and nalbuphine for analgesia. Few other differences among our studies are that both the previous studies had used epidural infusions as compared to our study where we used epidural boluses. And both of these studies used fentanyl in epidural infusions, which might be the reason that they had more significant results than ours.

In another study ninety patients undergoing thoracotomy were equally distributed into three groups. Control group only received patient controlled epidural analgesia (PCEA). 2nd group received routinely used analgesia with 0.125% ropivacaine 6 mL 30 min after surgery and then PCEA postoperatively. Third group received pre emptive analgesia with 0.125% ropivacaine 6 mL 30 min before start of surgery and every 60 min during surgery, then after completion of surgery PCEA. There main outcomes were visual analogue scale scores and cytokine levels. They concluded that pre emptive epidural analgesia produces better analgesia effects, reduced analgesic requirements, less side effects, attenuates surgery induced immune alterations and improves post operative recovery in patients undergoing thoracotomy[15].

In an old study Yegin *et al* also showed that the efficacy of post thoracotomy analgesia had been better in pre-emptive group[16].

Recently a study was conducted by Barut *et al* who used a combination of epidural levobupivacaine and morphine to study the efficacy of preemptive epidural analgesia in 45 patients undergoing thoracotomy. They divided patients in three groups. Group 1 received bolus before incision, group 2 after incision, and Group 3 at the end of surgery. Intraoperatively infusions were used in group 1 and group 2. Postoperative PCEA infusions were used. VAS scores and morphine consumption were recorded during the

postoperative 48h. Glucose, insulin, cortisol, and C-reactive protein (CRP) levels were compared before surgery and at 4, 24, and 48h after the operation. They did not find any significant difference among three groups in terms of analgesia, drug consumption and stress response[17].

Pain should be considered as the 5th vital sign and checked regularly along with the hemodynamic parameters in the perioperative period. Pre-emptive multimodal analgesia has shown some advantage over conventional analgesic technique. Preemptive analgesia acts by blocking nociception before painful stimulus and by modulation of central and peripheral pain pathways[18].

Our study had certain limitations. Firstly, we did not add opioids in epidural analgesia and gave local anesthetic in boluses. Secondly, we did not study the respiratory parameters and functions. We recommend that these limitations should be catered and further studies should be done with larger sample size and in multicenter which should also record the reduction in systemic opioid requirements in post thoracotomy period after the use of preemptive epidural analgesia technique. After these studies any definitive recommendations can be made for routine use of preemptive epidural analgesia.

CONCLUSION

Preemptive thoracic epidural analgesia provides better pain control in immediate postoperative period at rest. However, its efficacy is similar to conventional epidural analgesia in immediate post op period with cough and at 24 hours with cough and at rest.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. White PF, Kehlet H. Improving postoperative pain management: What are the unresolved issues? Anesthesiol 2010; 112(1): 220-25.
2. Bottiger BA, Esper SA, Stafford-Smith M. Pain management strategies for thoracotomy and thoracic pain syndromes. Semin Cardiothorac Vasc Anesth 2014; 18(1): 45-56.
3. Agostini P, Lugg ST, Adams K. Postoperative pulmonary complications and rehabilitation requirements following lobectomy: a propensity score matched study of patients undergoing video-assisted thoracoscopic surgery versus thoracotomy. Interact Cardiovasc Thorac Surg 2017; 24(3): 931-37.
4. Ling XM, Fang F, Zhang XG, Ding M, Liu QA, Cang J. Effect of parecoxib combined with thoracic epidural analgesia on pain after thoracotomy. J Thorac Dis 2016; 8(5): 880–87.
5. Kanazi GE, Ayoub CM, Aouad M. Subpleural block is less effective than thoracic epidural analgesia for post-thoracotomy pain: a randomised controlled study. Eur J Anaesthesiol 2012; 29(4): 186-91.
6. Tezcan AH, Karakurt O, Baskan S, Ornek DH, Baldemir R, et al. Post thoracotomy pain relief with subpleural analgesia or thoracic epidural analgesia: a rondomized clinical trial. Sao Paulo Med J 2016; 134(4): 280-84.
7. Dinic VD, Stojanovic MD, Markovic D, Cvetanovic V, Vukovic AZ, Jankovic RJ. Enhanced recovery in thoracic surgery: a review. Front Med (Lausanne) 2018; 5(1): 14-22.
8. Kotzé A, Hinton W, Crabbe DGC, Carrigan BJ. Audit of epidural analgesia in children undergoing thoracotomy for decortication of empyema. Br J Anaesthesia 2007; 98(5): 662-66.
9. Von Hosslin T, Imboden P, Luthi A, Rozanski MJ, vhnider TW, Filipovic M. Adverse events of post-operative thoracic epidural analgesia: a retrospective analysis of 7273 cases in a tertiary care teaching hospital. Eur J Anaestehsiol 2016; 33(10): 708-14.
10. Steinberg AC, Schimpf MO, White AB. Preemptive analgesia for postoperative hysterectomy pain control: systematic review and clinical practice guidelines. Am J Obstet Gynecol 2017; 217(3): 303-31.
11. Penprase B, Brunetto E, Dahmani E, Forthoffer JJ, Kapoor S. The efficacy of preemptive analgesia for postoperative pain control: a systematic review of the literature. AORN J 2015; 101: 94-105.
12. Jensen MP, Chen C, Brugger AM. Interpretation of visual analog scale ratings and change scores: a reanalysis of two clinical trials of postoperative pain. J Pain 2003; 4(3): 407-14.
13. Erturk E, Kaya FA, Kutanis D, Besir A, Akdogan A, Geze S, Tugcugil E. The effectiveness of preemptive thoracic epidural analgesia in thoracic surgery. Biomed Res Int 2014; 2014: 673682.
14. Amr YM, Yosuef AA, Alzeftawy AE, Messbah WI, Saber AM. Effect of pre-incisional epidural fentanyl and bupivacaine on postthoracotomy pain and Pulmoanry function. Ann Thorac surg 2010; 89(2): 381-85.
15. Yang C, Chang H, Zhang T, Liang C, Li E. Pre-emptive epidural analgesia improves post-operative pain and immune function in patients undergoing thoracotomy. ANZ J Surg 2014; 85(2): 472-77.
16. Yegin A, Erdogan A, Kayacan N, Karsli B. Early postoperative pain management after thoracic surgery; pre- and postoperative versus postoperative epidural analgesia: a randomized control trial. Eur J Cradio-thoracic Surg 2003; 24(3): 420-24.
17. Barut GA, Tunç M, Şahin Ş, Ulus F, Sazak H. Effects of epidural morphine and levobupivacaine combination before incision and after incision and in the postoperative period on thoracotomy pain and stress response. Turk J Med Sci 2018; 48(4): 716-23.
18. Can A, Erdem AF, Atdin Y. The effect of preemptive thoracic epidural analgesia on long term wound pain following major thoracotomy. Turk J Med Sci 2013; 43: 515-20.