

Original Research Article

Comparative study of continuous infusions of Ropivacaine v/s Ropivacaine + Fentanyl for post thoracotomy analgesia in 50 patients

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Abstract

Background: Epidural opioids have been widely used for post thoracotomy pain relief. One such drug is Fentanyl, a short acting lipophilic opioid analgesic, structurally related to Pethidine for its opioid activity. Adding Fentanyl, as an adjuvant to Ropivacaine, also reduces total consumption of Ropivacaine and incremental doses of rescue analgesics.

Materials and methods: 50 patients of either sex aged 18-60 year belonging to ASA class II-III scheduled for elective thoracotomy were included in this study and divided into two groups: Group R receiving 0.1 ml/kg/hr of 0.2% Ropivacaine continuous epidural infusion for 24 hour and Group RF receiving 0.1 ml/kg/hr of 0.2% Ropivacaine + 4 µg/ml Fentanyl continuous epidural infusion for 24 hour.

Results: There was no significant difference between two groups regarding to Age, sex, height, weight and ASA grade and preoperative vitals as well as VAS score at rest. There was highly significant difference between groups at 30 minute and 6 hour regarding to this variable with P <0.001. Patients in group RF were more comfortable during PEFR measurement than group R.

Conclusion: A continuous thoracic epidural infusion of 0.1 ml/kg/hr of 0.2% Ropivacaine + Fentanyl 4 µg/ml provided better pain relief than 0.2% Ropivacaine alone after thoracotomy; both at rest and during spirometry. The use of 0.2% Ropivacaine alone was associated with worse pain control during spirometry, larger consumption of IV Diclofenac Sodium and worse performance during spirometry. Addition of Fentanyl to Ropivacaine for continuous epidural analgesia in post thoracotomy patients provides better pain relief and improves spirometry performance.

Key words

Ropivacaine, Fentanyl, Post thoracotomy, Comparison.

Introduction

Postero-lateral thoracotomies are one of the most painful procedures. The source of perceived pain are the surgical incision, disruption of the ribs and inter costal nerves, inflammation of the chest wall structures adjacent to the incision, incision or crushing of the pulmonary parenchyma or pleura, stretching of the shoulder joint and placement of thoracotomy drainage tubes [1]. Patients undergoing thoracotomy may suffer from severe postoperative pain, impaired pulmonary function and chronic pain, incidence of atelectasis and postoperative pneumonia [1, 2]. Patients must be pain free at rest, should be able to breathe deeply, cough effectively and comply with postoperative physiotherapy. Numbers of analgesic techniques like systemic IV opioids, inter costal nerve block, paravertebral block, intrathecal opioids, inter pleural analgesia, epidural analgesia have been tried for post thoracotomy pain relief [3]. Many of these techniques claims to provide good pain control but out of these, continuous thoracic epidural analgesia provides superior analgesia and also the preferred modality. In contrast to systemic IV NSAIDs and opioids, epidural analgesia is associated with fewer systemic side effects and requires less supplementary analgesics. Bupivacaine is one of the most widely used drug for continuous epidural analgesia. However, Ropivacaine is an amino-amide local anesthetic with an efficacy broadly similar to that of Bupivacaine [4]. It may be preferred option because of its reduced central nervous system and cardiotoxic potential, which is because of the replacement of the butyl by a propyl terminal group. Furthermore, its

decreased propensity for motor block helps in improving respiratory therapy. Ropivacaine is the local anesthetic also has the advantage of more differential block allowing for a better separation between sensory and motor block, low toxicity relative to potency and long duration of action, resulting in a low risk of toxicity during continuous infusion. Epidural opioids have been widely used for post thoracotomy pain relief. One such drug is Fentanyl, a short acting lipophilic opioid analgesic, structurally related to Pethidine for its opioid activity [2]. Adding Fentanyl, as an adjuvant to Ropivacaine, also reduces total consumption of Ropivacaine and incremental doses of rescue analgesics.

Hence, this study titled “Comparative study of continuous infusions of Ropivacaine v/s Ropivacaine + Fentanyl for post thoracotomy analgesia in 50 patients” shows the efficacy of continuous Ropivacaine epidural infusion for post thoracotomy analgesia and the advantage of addition of Fentanyl to Ropivacaine epidural infusion.

Objectives

Objectives were to study the efficacy of continuous epidural infusion of 0.2% Ropivacaine for post-operative pain relief after thoracotomy, advantages of addition of Fentanyl to 0.2% Ropivacaine continuous epidural infusion on post-operative pain relief, beneficial effect of post-operative pain relief on pulmonary outcome by spirometric evaluation in both groups and any side effects or complications regarding to procedure.

Materials and methods

This prospective randomized clinical study was carried out after approval from institutional ethical committee. Informed written consent was obtained from each patient and procedure was explained. 50 patients of either sex aged 18-60 year belonging to ASA class II-III scheduled for elective thoracotomy were included in this study and divided into two groups:

Group R receiving 0.1 ml/kg/hr of 0.2% Ropivacaine continuous epidural infusion for 24 hour.

Group RF receiving 0.1 ml/kg/hr of 0.2% Ropivacaine + 4 µg/ml Fentanyl continuous epidural infusion for 24 hour.

Exclusion criteria were age less than 18 year and more than 60 year, allergy to local anaesthesia/opioids, active local infection, abnormal coagulation profile, renal or hepatic failure, patient's refusal.

Pre-operative assessment was done one day before planned surgery. Any significant past, family and personal history were noted. General physical examination was done. Vitals (Temperature, HR, BP, RR, SpO₂) and investigations like CBC, SE, RFT, LFT, ECG, CXR, CT thorax, ABGA, coagulation profile were noted. During this assessment patients were given instructions on how to perform a simple spirometry with a portable monitor device through a mouth piece and pre operative FVC, FEV₁ and PEF_R were obtained. Patients were also given instructions on how to measure pain with VAS 0-10 mark, with 0 representing no pain and 10 representing worst pain.

Patients were explained about procedure and written consent was taken.

Technique: Combined epidural-general anaesthesia

50 patients undergoing elective thoracotomies were randomized into 2 groups. Each group included 25 patients. Group R receiving 0.1 ml/kg/hr of 0.2% Ropivacaine epidural infusion

and Group RF receiving 0.1 ml/kg/hr of 0.2% Ropivacaine + 4 µg/ml Fentanyl epidural infusion.

On the day of surgery, in operating room two wide bore IV canula inserted. ECG monitor, pulse oxymeter and NIBP were attached and data noted. Radial artery cannulation was done for continuous BP monitoring and for frequent blood samples for ABGA. ABGA sample was sent.

Pre medicated with Inj. Ondansetron 4 mg IV, Inj Glycopyrolate 0.2 mg IV, Inj Fentanyl 1 µg/kg IV. In sitting position under strict aseptic precaution with 18 G touhey needle 20 G Epidural catheter was inserted at T₇-T₈ epidural space after confirming epidural space by hanging drop method. An epidural catheter was placed 5 cm into epidural space. Test dose of Lidocaine Hydrochloride with adrenaline (1:200000) 1.5% 3 ml is given through epidural catheter to rule out accidental intrathecal or intravenous placement of epidural catheter.

Patient was preoxygenated with 100% O₂ for 3 min. Induction done with Inj. Sodium Pentothal 6 mg/kg IV, Inj. Lidocaine 1% 1 mg/kg IV, Inj. Succinyl Choline 2 mg/kg IV, Intubation was done with appropriate sized double lumen tube. Anaesthesia was maintained by controlled ventilation with Oxygen (60%) + Air (40%) + Sevoflurane + Inj. Vecuronium Bromide (Loading dose: 0.08 mg/kg IV and maintenance dose: 0.02 mg/kg IV SOS). Bolus dose of 0.2% Ropivacaine 10 ml was given through epidural catheter to all patients after intubation. More than 20% rise in BP or HR was considered as an inadequate depth of anaesthesia and at that time incremental IV doses of Fentanyl 100 µg were given. Duration of surgery was noted. Reversal was done with Inj. Glycopyrolate 0.008 mg/kg IV, Inj. Neostigmine 0.05 mg/kg IV. Extubation was done after return of spontaneous ventilation, adequate tone and power of muscle and protective reflexes. Patients were transferred to ICU. At the time of ICU admission, patients were randomly allocated to group R and group RF for post operative epidural analgesia.

Continuous epidural infusion was started at admission in the ICU after attaching monitors for SpO₂, pulse rate, ECG, IABP and data noted.

All the quantitative data were analyzed using unpaired T test. The results were expressed as mean \pm SD. P value <0.05 – statistically significant, = <0.001 – highly significant, =>0.05 – non significant.

Statistical analysis

The data was collected are reported as Mean \pm Standard deviation. Group comparisons of normally distributed variable were tested by two sample unpaired 't' test. A 'P' value of 0.05 or less was considered to indicate a statistically significant difference for all statistical tests.

Results

There was no significant difference between two groups regarding to Age, sex, height, weight and ASA grade and preoperative vitals as well as VAS score at rest (**Table – 1**).

Table – 1: Demographic data and Perioperative vitals.

Variable	Group R (M \pm SD)	Group RF (M \pm SD)
Age (Years)	40 \pm 14	39 \pm 11
Height (cm)	165 \pm 13	166 \pm 17
Weight (kg)	71 \pm 15	70 \pm 13
Female/Male	9/16	8/17
Duration of surgery (hour)	167 \pm 26	160 \pm 18
ASA Grade (II/III)	10/15	12/13
Pulse rate	88 + 5	90 + 5
SBP	130 + 14	124 + 11
DBP	78 + 8	81 + 9
RR	18 + 2	17 + 3
SpO ₂	95 + 1	96 + 1

VAS score (at PEFR measurement) of both groups was as per **Table – 2**. There was highly significant difference between groups at 30 minute and 6 hour regarding to this variable with

P <0.001. Patients in group RF were more comfortable during PEFR measurement than group R.

As per **Table – 3**, as only 2 patients from group RF required rescue analgesic; better pain control was achieved by Ropivacaine plus Fentanyl continuous epidural infusion than Ropivacaine alone.

Table – 2: VAS score during PEFR measurement.

Post op hour	Group R (Mean)	Group RF (Mean)	P value	Significance
½	5.5	3.3	<0.001	HS
6	5	2.7	<0.001	HS
24	2.5	2.3	0.41	NS

Table – 3: Rescue analgesic requirement.

No. of rescue analgesic dose	Group R (n=25)	Group RF (n=25)
0	6	23
1	3	2
2	16	0

Discussion

Post thoracotomy pain is one of the worst pains, which possesses a unique challenge of controlling pain while keeping the chest wall in motion so as to allow deep breathing and coughing in order to reduce complications like pneumonia and atelectasis which can be detrimental. Currently continuous epidural infusion of local anesthetics with or without opioids is the choice for postoperative pain control. Thoracic Epidural Analgesia plays a pivotal role in multimodal treatment programs, allowing for important advances in recovery from surgery and reductions in overall morbidity and cost [5]. Ropivacaine is a new aminoamide local anesthetic, monohydrate of the hydrochloride salt of 1-propyl-2',6'pipercoloxylidide and has less cardiovascular and central nervous system toxicity than racemic Bupivacaine [6]. Fentanyl, a synthetic opioid,

when added to Ropivacaine infusion, potentiates its analgesic effects and gives better outcome by providing adequate postoperative analgesia in thoracotomy with minimal side effects [7-18].

There was no significant difference in demographic data, duration of surgery; postoperative vitals were comparable in both groups in our study. The mean duration of surgery was 167 ± 26 min in Group R and 160 ± 18 min in Group RF ($P > 0.05$).

Antonio Macias, et al. [19] found in their study that postoperative hemodynamic variables were equivalent between both groups.

Sakai T, et al. [24] conducted a study to investigate the optimal dose of continuous epidural Ropivacaine for effective analgesia with minimal side effects after axillary muscle-sparing thoracotomy. They found that hypotension was seen more frequently with the use of 0.5% Ropivacaine in thoracic epidural in compared to 0.2% Ropivacaine.

VAS Pain Score at rest and during PEFR measurement

In our study, VAS pain score at rest was comparable in both groups with P value > 0.05 . Patients in group R experienced more pain as compared to patients in group RF at time of PEFR measurement at 30 minutes and 6 hours after ICU admission with P value < 0.001 and < 0.05 respectively. Our study showed better pain control especially during spirometry in group RF.

Antonio Macias, et al. [19] demonstrated in their study that VAS pain score at rest was comparable between group R receiving 0.2% Ropivacaine alone and group RF receiving 0.15% Ropivacaine + Fentanyl 5 $\mu\text{g/ml}$. But there was significant difference in VAS pain score during PEFR measurement at 2 and 12 hours after ICU admission with $P < 0.05$ indicating that analgesia was better in group RF.

Gonca Tuncel, et al. [22] demonstrated in their study that there was significant difference in

VAS pain score at rest and during movement between group R receiving 0.2 % Ropivacaine alone and group RS receiving 0.2% Ropivacaine-Sufentanil 0.75 $\mu\text{g/ml}$ with $P < 0.05$ indicating better analgesia was achieved in group RS.

One study conducted a randomized double blinded comparison of different concentrations of Fentanyl with 0.2% Ropivacaine through thoracic epidural for post thoracotomy analgesia. In conclusion, they found that thoracic epidural Fentanyl 5 $\mu\text{g/ml}$ or 7.5 $\mu\text{g/ml}$ are associated with superior postoperative analgesia after thoracotomy compared with Fentanyl 2.5 $\mu\text{g/ml}$, when used in conjunction with Ropivacaine 0.2% [20, 21, 23].

Logas WG, et al. [7] conducted a randomized prospective study for comparison of continuous thoracic epidural infusion of Morphine, Bupivacaine and combination of Morphine + Bupivacaine for postoperative pain relief after thoracotomy. In conclusion they found that epidural combination group tended to have lower self assessed pain score compared to other group.

Mahon SV, et al. [16] concluded in their study that VAS pain score during rest and during movement were higher in the Fentanyl only group at 2 hour assessment than Fentanyl-Bupivacaine group.

Our study showed better pain control especially during motion/spirometry in group RF. In group R pain control was worse during spirometry despite IV Diclofenac to obtain similar VAS pain score at rest.

Need for rescue analgesic

Most of the patients receiving Ropivacaine infusion alone experienced inadequate analgesia and needed boluses and dose arrangements or rescue analgesics like IV Morphine, IV Diclofenac, IV Tramadol or NSAIDS.

In our study we used Inj. Diclofenac Sodium as a rescue analgesic whenever VAS pain score > 4 at rest or during PEFR measurement. As we wanted

to make patient feel pain free during deep breathing, coughing and chest physiotherapy, we considered >4 VAS score during PEFR as ineffective pain control in our study and supplemented with rescue analgesic even though patient had VAS score <4 during rest.

We found that IV Diclofenac supplement was more frequent in group R at 30 minutes and 6 hour after ICU admission. In contrast to only 2 patients from group RF, 19 patients from group R required rescue analgesic at 30 minutes after ICU admission. At 6 hour 16 patients from group R was supplemented with rescue analgesic as they had VAS score >4 during PEFR. At 12 and 24 hour none of the patients from both groups required rescue analgesic as effective pain control was achieved by epidural infusion.

Antonio Macias, et al. [19] found similar result in their study and more IV Morphine as rescue analgesic was required in Ropivacaine epidural infusion group in compare to Ropivacaine + Fentanyl epidural infusion group.

Gonca Tuncel, et al. [22] demonstrated in their study that the need for additional boluses and subsequent increase of infusion rate was high in Group Ropivacaine ($P<0.05$). Twenty percent of patients in Group Sufentanil-Ropivacaine received additional boluses while the rate was 83% in Group Ropivacaine.

Pulmonary function test

In our study, respiratory variables like FVC, PEFR, FEV₁ were comparable in both groups with P value >0.05 . Though there was no significant difference between both groups regarding this, performance of group R was slightly inferior in spirometry during FVC, PEFR and FEV₁ measurement. Though the performance was inferior, the statistical difference was minor as we had administered rescue analgesics of patients in group R to control their pain and hence their performance. We did not find any significant difference in motor block which would affect spirometry values in both groups. Though the basal mean values of spirometry variables obtained by preoperative spirometry

were almost same, there was better improvement seen in group RF patients in terms of FVC, FEV₁, PEFR in compare to group R.

Antonio Macias, et al. [19] in their study used Ropivacaine v/s Ropivacaine + Fentanyl epidural infusion for post thoracotomy analgesia and demonstrated similar observations during spirometry. The group, received Ropivacaine + Fentanyl, was more efficient in performing spirometry.

Ballantyne JC, et al. [13] in their study used spirometry variables (FEV₁, FVC, PEFR) for comparison of pulmonary outcome due to post operative analgesic therapies. They concluded that despite of different post operative analgesic therapies like systemic opioid, epidural opioid, epidural local anesthetic, epidural local anesthetic + opioid, paravertebral block, inter costal block, there were no significant difference in respiratory variables. Though it is not related to our study but this study demonstrated that effective pain control, by whichever modality, is best predictor for pulmonary outcome. It might not necessarily mean control by exclusive single route. Multiple routes like IV and epidural can be combined to get the needed results.

ABGA

In our study we did arterial blood gas analysis at frequent intervals to evaluate efficacy of effective pain control on pulmonary gas exchange. PaO₂ and PaCO₂ both were comparable between two groups as minor difference was because of the pain had already been taken care of by IV Diclofenac in group R.

Side effects

In our study, the incidence of pruritus, frequently seen with Fentanyl, was more in group RF. The degree of sedation in the two groups was similar over the 24 hour study period. There were no severely sedated patients in any group. As we used lower concentration of Ropivacaine (0.2%) in our study, no case of hypotension was observed in any group which is most common side effect of 0.5% Ropivacaine. No case of

vomiting, bradycardia and respiratory depression was observed. One patient in both group had nauseating feeling which was relieved by Inj. Ondansetron 4 mg IV. We did not find any motor block in both groups that makes patient uncomfortable during spirometry.

Antonio Macias, et al. [19] found in their study that PONV was more frequent in Group receiving Ropivacaine epidural infusion alone. The degree of sedation in the two groups was similar over the 48 hours study period. There were no severely sedated patients in any group and no case of respiratory depression was observed.

Conclusion

A continuous thoracic epidural infusion of 0.1 ml/kg/hr of 0.2% Ropivacaine + Fentanyl 4 µg/ml provided better pain relief than 0.2% Ropivacaine alone after thoracotomy; both at rest and during spirometry. The use of 0.2% Ropivacaine alone was associated with worse pain control during spirometry, larger consumption of IV Diclofenac Sodium and worse performance during spirometry. Addition of Fentanyl to Ropivacaine for continuous epidural analgesia in post thoracotomy patients provides better pain relief and improves spirometry performance.

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