



PARAVERTEBRAL ROPIVACAINE 0.5 PERCENT VERSUS SALINE INFILTRATION ON POSTOPERATIVE PAIN SCORES AND REQUIREMENT OF RESCUE ANALGESIC

Imran Bhat¹, Farooq Ahmad Ganie², Buch Velayat¹, Asif Maqbool¹, Ayaz Farooqi¹

¹Department of Anesthesiology, SKIMS, Soura, Kashmir, India

²Senior Resident, Department of Cardiovascular and Thoracic Surgery, SKIMS, Soura, Kashmir, India

*Corresponding Author Email: farooq.ganie@ymail.com

DOI: 10.7897/2277-4572.02460

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Received on: 20/07/13 Revised on: 23/08/13 Accepted on: 28/08/13

ABSTRACT

This study was designed to determine whether ropivacaine decreases the severity of acute post-thoracotomy pain scores and whether ropivacaine decreases the dosage and need of rescue analgesics in comparison with placebo. In our study Patients were randomly assigned in a blinded fashion to receive either 0.5 % ropivacaine or placebo. Between March 2012 and march 2013, 63 patients underwent thoracotomy in our hospital. 53 subjects were randomized to receive either 0.5 % ropivacaine (n = 28) or saline (n = 25). Pain scores (at rest, during deep breathing, and coughing), intra-operative opioid requirement, requirement of rescue analgesics and adverse events were assessed for 12 hours. Mean opioid (morphine) requirement in the ropivacaine group was 5.786 mg (SD 1.272), while as the mean requirement of morphine in the saline group was 6.0 mg (SD 1.299), the difference in the intraoperative opioid requirement was statistically insignificant (p value = 0.5472). Mean paracetamol requirement at 6 hours post-procedure was 0.18 g (SD 0.39) in the ropivacaine group and 0.52 g (SD 0.51) in the saline group, the difference between the groups was statistically highly significant (p value = 0.0081). Our study concluded that ropivacaine 0.5 % improves pain scores. It is also concluded that ropivacaine 0.5 % in comparison to placebo decreases the requirement and dosage of rescue analgesics.

Keywords: Ropivacaine, Rescue analgesics, thoracotomy.

INTRODUCTION

Pain is considered a major independent factor responsible for postoperative morbidity and mortality after thoracic operations¹. Open thoracotomy is one of the most painful surgical procedures and post-thoracotomy pain markedly affects post-operative respiratory function and patient recovery². Post-thoracotomy pain belongs to incision, damage of ribs and intercostal nerves, chest wall inflammation, cut of pleura and pulmonary parenchyma and placement of thoracotomy drainage tube³. Acute post-thoracotomy pain functionally results in lung restriction; adequate ventilation and coughing are compromised and a variety of analgesic techniques like systemic opioid, intercostal nerve blockade, intrapleural analgesia, epidural opioid with or without local analgesic, cryoanalgesia, paravertebral nerve blockage, Transcutaneous electrical nerve stimulation (TENS) are used for post-thoracotomy pain management³. Besides these techniques, patient controlled analgesia (PCA) via systemic or epidural route has been used very commonly. Morbidity and mortality rates after pulmonary resection by thoracotomy remain high. Effective analgesia at rest, during deep breathing and on coughing can help reduce postoperative morbidity through early mobilization and rehabilitation⁴. Thoracic paravertebral block (PVB) induces nerve block of multiple contiguous thoracic dermatomes above and below the infusion site⁵. Two alternatives are used to locate the paravertebral space for drug deposition: a blind anesthetic approach (loss of resistance technique) described by Eason and Wyatt⁶ and de visu during surgery⁷. The present placebo-controlled study investigates whether administering the local anesthetic ropivacaine directly into the intercostal spaces by the thoracic surgeon after thoracotomy reduces pain severity during the first 12 hours after surgery and requirement of rescue analgesics. In an attempt to reduce bupivacaine induced side effects and toxicity, ropivacaine was developed and has been

used for the last few years⁸. Ropivacaine is a long- acting amide local anesthetic and has reportedly lower central nervous system and cardiovascular toxicity and less motor block than equivalent doses of bupivacaine^{8,9}.

MATERIALS AND METHODS

This prospective randomized placebo-controlled study was performed between March 2012 and March 2013 at Sher-I-Kashmir institute of medical sciences, Soura, Srinagar, India. The Institutional Review Board approved the study. We included consecutive patients aged 20 - 60 years scheduled for unilateral thoracotomy. Exclusion criteria were the pregnancy and breast-feeding, epilepsy, third-grade atrioventricular block without a pacemaker, hepatic dysfunction, anti-arrhythmic treatment and allergy to local anesthetics. In this randomized double-blind study, the patients were anesthetized using propofol 1-2 mg/kg, atracurium 0.5 mg/kg, morphine 0.1 mg/kg and glycopyrrolate 20 mcg/kg. Anesthesia was maintained with isoflurane 1.15 %, nitrous oxide 67 % in 33 % oxygen. After the induction of anesthesia, we monitored blood pressure by means of an arterial line. Surgery always began after putting the patients in the lateral decubitus position. The thoracic surgeon deposited the intended drug/placebo, after a negative aspiration test for blood, directly (de visu)⁷ into and one space above and below the ICS where incision was made, towards the end of surgery, before closing thoracotomy. The patients were randomly assigned to receive either a 0.1 ml per kg single bolus of 0.5 % ropivacaine (divided equally into three doses to be injected into each space) or saline at the same scheme of administration. After the operation was finished, the patients were extubated using neostigmine 0.005 mg/kg and atropine 20 mcg/kg intravenously. The primary endpoint was pain intensity on a visual analog scale at rest, deep breathing and on coughing. Secondary endpoints were total morphine consumption, requirement of rescue analgesic

and side effects during the first 12 postoperative hours. Surgeons, anesthesiologists, and all the nurses involved in this study were blinded. Solutions of saline and ropivacaine were prepared identically by the theatre technologist in coded syringes in equal amounts so as to render identification of the product impossible. The code was broken at the end of study. The primary endpoint was assessment of pain at rest, deep breathing and on coughing. It was evaluated after 15 minutes, 1, 3, 6, 9, and 12 h using a visual analog scale (VAS) from 0 to 10 (0 = no pain, 10 = worst pain imaginable). Secondary endpoints were total morphine consumption and morphine-related side effects (nausea and vomiting, urinary retention, pruritus and sedation), need and dosage of rescue analgesics, provided in the form of paracetamol (15 mg/kg) administered intravenously when VAS scores were more than 50 %. Heart rate, arterial blood pressure, and oxygen saturation were recorded. The number of intent to treat was a minimum of 20 patients per group for an alpha risk of 0.05 and a beta risk of 0.12 to demonstrate a 30 % difference in VAS score between the two groups. The two groups were compared by unpaired Student's t-test, chi square and Fisher's exact test. A variance analysis was used for repeated measures. A p-value < 0.05 was considered statistically significant. All analyses were performed with SPSS software (version 13.0) and graph pad.

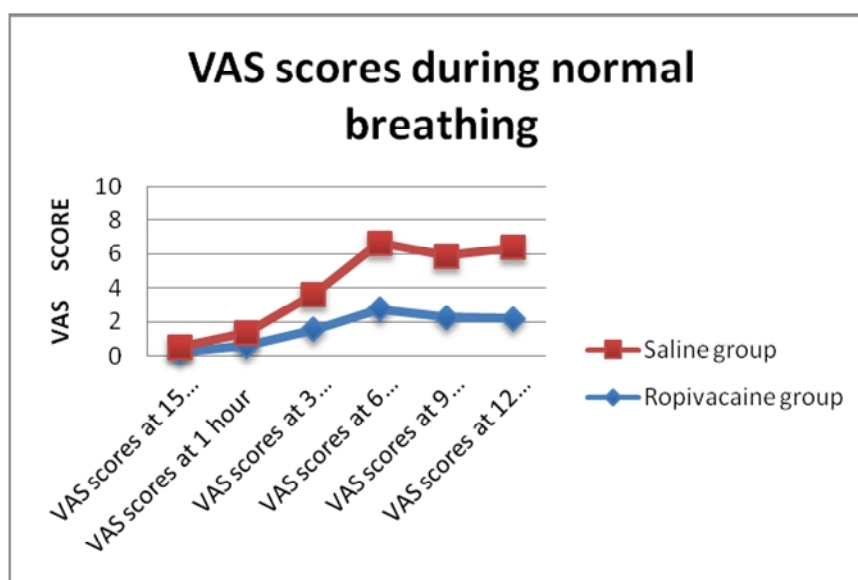
RESULTS

Between March 2012 and march 2013, 63 patients underwent thoracotomy in our hospital. Only 53 patients were enrolled in the study, the rest were below or above the age group to be studied. The type of intervention undergone by the 53 remaining patients was lobectomy (40 %), hydatid cystectomy (35 %), wedge resection (10 %), pneumectomy (5 %), segmentectomy (4 %), exploratory thoracotomy (2 %), and other (4 %). The 53 subjects were randomized to receive either 0.5 % ropivacaine (n = 28) or saline (n = 25). There were no significant differences between the two groups in terms of demographics (except sex), morphometric features,

American Society of Anesthesiologists (ASA) score, vital signs, or in the type of contraindication to paravertebral block or surgical procedure. Mean (SD) age was 40.96 (11.95) years in the placebo group, and 41.48 (12.02) in the ropivacaine group (p value = 0.8735). Mean (SD) weight was 54.561 (10.439) kg in the placebo group, and 56.672 (9.626) kg in the ropivacaine group (p value = 0.4494). There were significantly more males randomized to the placebo group (Mean 0.61, SD 0.50) than to the ropivacaine arm (Mean 0.40, SD 0.50; p = 0.0162). There were no other significant differences in other demographic variables between the control and ropivacaine groups. Pulmonary function testing was available in all patients (100.0 %). There was no statistically significant difference between the two groups. Mean (SD) forced expiratory volume in 1 second (FEV1) for the placebo group was 2.5 (0.9) and 2.2 (0.9) for the ropivacaine group (p = 0.19). Mean (SD) FEV1 % predicted for the placebo group was 82.0 % (24.4) and 76.8 % (21.1) for the ropivacaine group (p = 0.27).

Mean VAS scores at rest

Mean VAS scores at 15 minutes in the ropivacaine group were 0.21 (SD 0.42) and 0.28 (SD 0.54) in the saline group (p value 0.6210). Mean VAS scores at 1 hour in the ropivacaine group were 0.57 (SD 0.63) and 0.76 (SD 0.83) in the saline group (p value 0.3544). Mean VAS scores at 3 hours in the ropivacaine group were 1.54 (SD 0.74) and 2.08 (SD 1.12) in the saline group (p value 0.0397, statistically significant). Mean VAS scores at 6 hours in the ropivacaine group were 2.74 (SD 1.26) and 3.92 (SD 1.15) in the saline group (p value 0.0009, statistically highly significant). Mean VAS scores at 9 hours in the ropivacaine group were 2.25 (SD 1.78) and 3.64 (SD 2.40) in the saline group (p value 0.0193, statistically significant). Mean VAS scores at 12 hours in the ropivacaine group were 2.18 (SD 1.39) and 4.20 (SD 2.00) in the saline group (p value 0.0001, statistically highly significant).



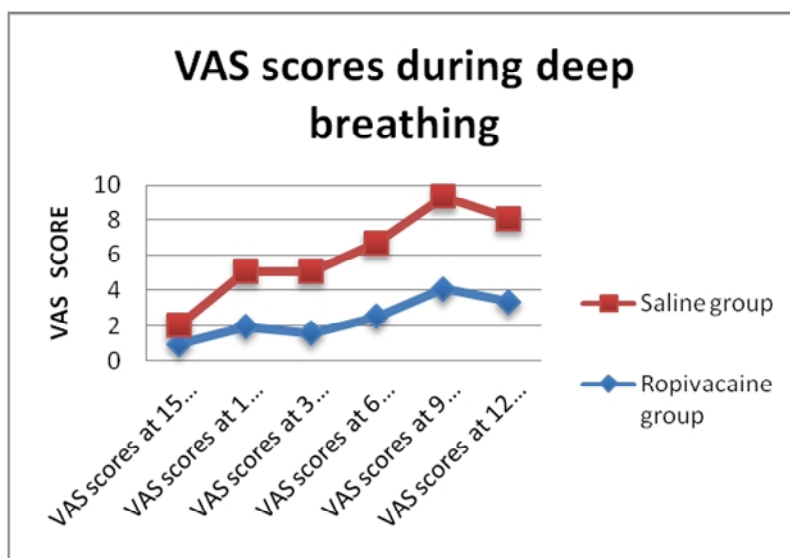
Mean VAS scores during deep breathing

Mean VAS scores at 15 minutes in the ropivacaine group were 0.96 (SD 0.92) and 1.08 (SD 1.08) in the saline group (p value 0.6753). Mean VAS scores at 1 hour in the ropivacaine group were 1.93 (SD 1.18) and 3.12 (SD 1.27) in the saline group (p value 0.0009, highly significant). Mean VAS scores

at 3 hour in the ropivacaine group were 1.56 (SD 1.25) and 3.48 (SD 2.12) in the saline group (p value 0.0002, highly significant). Mean VAS scores at 6 hours in the ropivacaine group were 2.50 (SD 1.69) and 4.20 (SD 2.18) in the saline group (p value 0.0024, statistically highly significant). Mean VAS scores at 9 hours in the ropivacaine group were 4.07

(SD 1.27) and 5.28 (SD 1.28) in the saline group (p value 0.0012, statistically highly significant). Mean VAS scores at 12 hours in the ropivacaine group were 3.32 (SD 1.59) and

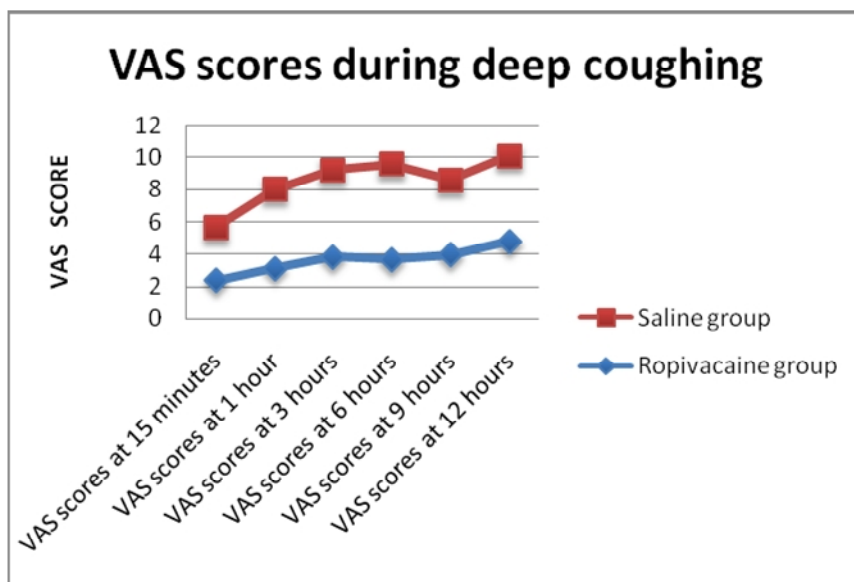
4.76 (SD 1.56) in the saline group (p value 0.0017, statistically highly significant).



Mean VAS scores during deep coughing

Mean VAS scores at 15 minutes in the ropivacaine group were 2.36 (SD 1.13) and 3.28 (SD 1.17) in the saline group (p value 0.0053, highly significant). Mean VAS scores at 1 hour in the ropivacaine group were 3.14 (SD 1.35) and 4.84 (SD 0.94) in the saline group (p value 0.0001, highly significant). Mean VAS scores at 3 hour in the ropivacaine group were 3.82 (SD 1.16) and 5.40 (SD 0.96) in the saline group (p

value 0.0001, highly significant). Mean VAS scores at 6 hour in the ropivacaine group were 3.68 (SD 1.19) and 5.88 (SD 0.78) in the saline group (p value 0.0001, highly significant). Mean VAS scores at 9 hour in the ropivacaine group were 3.96 (SD 1.62) and 4.60 (SD 1.19) in the saline group (p value 0.1135, not significant). Mean VAS scores at 12 hour in the ropivacaine group were 4.79 (SD 1.60) and 5.32 (SD 1.14) in the saline group (p value 0.1719, not significant).



Intraoperative opioid requirement in the two groups

Mean opioid (morphine) requirement in the ropivacaine group was 5.786 mg (SD 1.272), while as the mean requirement of morphine in the saline group was 6.0 mg (SD 1.299), the difference in the intraoperative opioid requirement was statistically insignificant (p value = 0.5472).

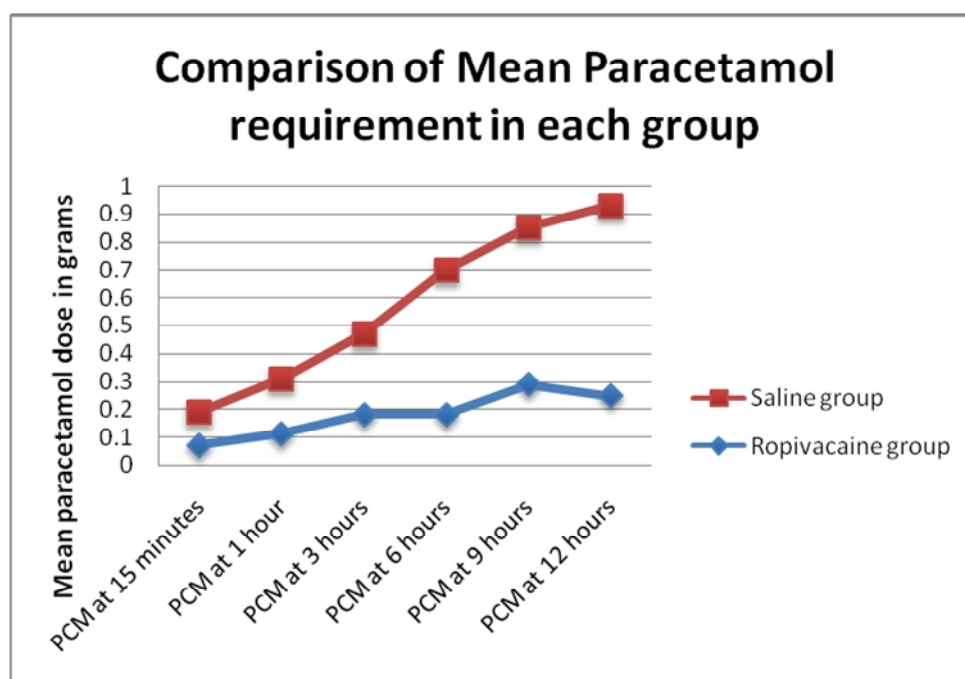
Requirement of rescue analgesics (in the form of paracetamol) in the post-operative period

- Mean paracetamol requirement at 15 minutes post-procedure was 0.07 g (SD 0.26) in the ropivacaine group and 0.12 g (SD 0.33) in the saline group, the difference

between the groups was statistically insignificant (p value = 0.5548).

- Mean paracetamol requirement at 1 hour post-procedure was 0.11 g (SD 0.31) in the ropivacaine group and 0.20 g (SD 0.41) in the saline group, the difference between the groups was statistically insignificant (p value = 0.3554).
- Mean paracetamol requirement at 3 hours post-procedure was 0.18 g (SD 0.39) in the ropivacaine group and 0.29 g (SD 0.46) in the saline group, the difference between the groups was statistically insignificant (p value = 0.3506).

- Mean paracetamol requirement at 6 hours post-procedure was 0.18 g (SD 0.39) in the ropivacaine group and 0.52 g (SD 0.51) in the saline group, the difference between the groups was statistically highly significant (p value = 0.0081).
- Mean paracetamol requirement at 9 hours post-procedure was 0.29 g (SD 0.46) in the ropivacaine group and 0.56 g (SD 0.51) in the saline group, the difference between the groups was statistically significant (p value = 0.0439).
- Mean paracetamol requirement at 12 hours post-procedure was 0.25 g (SD 0.44) in the ropivacaine group and 0.68 g (SD 0.48) in the saline group, the difference between the groups was statistically highly significant (p value = 0.0013).



DISCUSSION

Evidence suggests that the peripheral afferent block is more effective than the central block in preventing nociceptive impulses from entering the central nervous system¹⁰⁻¹². Paravertebral block would also reduce neurogenic inflammation of traumatized tissues that is dependent on efferent functions of peripheral nerves¹³. The results presented here affirm that paravertebral afferent block significantly decreases the intensity of the postoperative pain. We evaluated postoperative pain with VAS scoring during normal breathing, deep breathing and during coughing. VAS scores were significantly lower in the ropivacaine group than saline group during normal, deep breathing. VAS scores, when patients were made to cough, were also significantly lower in the ropivacaine group than saline group during early period (15 minutes, 1 hour, 3 hours and 6 hours), but were insignificant during the later periods (9 and 12 hours) of study. The differences being explained by the waning of ropivacaine effect on peripheral nerves. The typical duration of neural blockade with ropivacaine ranges between 1.5 to 8 hours¹⁴. Postoperative rescue analgesic consumption was less in patients who were given ropivacaine for paravertebral block as compared to saline group. These findings provide further support to the pathophysiological mechanism of pain proposed by Woolf¹⁵ and Woolf and Thompson¹⁶. Small doses of opiates given before incision prevent central sensitization by diminishing the sustained hyperexcitation of the central nervous system caused by intraoperative painful stimuli^{11,17,18} whereas suppression of established neuronal hyperexcitability requires very large doses¹⁷. In our study, opiate premedication was found to minimize the immediate

postoperative pain, though the requirement of opioids between the two groups was statistically insignificant. Suppression of prostaglandin synthesis is probably the basis of the analgesic mechanism of action of NSAIDs¹⁹. Total afferent blockade is not likely to be achieved by prostaglandin synthesis inhibition and thus NSAIDs have a synergistic effect with other analgesics²⁰. Though paracetamol is not considered as NSAID, it has poor inhibitory action on prostaglandin synthesis in peripheral tissues, but more active on COX in brain²⁰. In this study, we used paracetamol for providing rescue analgesia to any patient complaining pain equivalent to or more than 50 % on Visual analogue scale. We observed that differences in the requirement of rescue analgesia in the two groups was statistically insignificant upto 6 hours of study period, but the differences became statistically significant during the later periods of study, patients in the ropivacaine group required less rescue analgesia than the patients in saline group. The difference being explained by the short half life of morphine ($t_{1/2} = 2-3$ hours, effect of parenteral dose lasting for 4-6 hours)²¹, the only intraoperative analgesic administered to the patients in the saline group, while as the patients in the ropivacaine group received morphine as well as paravertebral ropivacaine infiltration.


CONCLUSION

Our study concluded that ropivacaine 0.5 % improves pain scores. It is also concluded that ropivacaine 0.5 % in comparison to placebo decreases the requirement and dosage of rescue analgesics in patients who underwent thoracotomy.

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Source of support: Nil, Conflict of interest: None Declared

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How to cite this article:

Imran Bhat, Farooq Ahmad Ganie, Buch Velayat, Asif Maqbool, Ayaz Farooqi. Paravertebral ropivacaine 0.5 percent versus saline infiltration on postoperative pain scores and requirement of rescue analgesic. *J Pharm Sci Innov.* 2013; 2(4): 82-86.