



Comparative study of bupivacaine plus xylocaine with adrenaline versus bupivacaine plus xylocaine with adrenaline plus fentanyl in intrapleural block for post operative analgesia for modified radical mastectomy cases

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Abstract

Background: Postoperative pain plays a significant role in the pathogenesis of postoperative pulmonary complications after upper abdominal and thoracic operations. Diminishing lung volumes due to acute restrictive pulmonary dysfunction due to pain may result in relative hypoxemia, major atelectasis and pulmonary consolidation. Intrapleural analgesia is one of the method for postoperative analgesia.

Methods and Material: After clearance from Institutional Ethics Committee, 80 patients undergoing modified radical mastectomy were selected and divided into two groups randomly. Group B: Intrapleural block was given with inj. Bupivacaine 0.5% (20 ml) with xylocaine adrenaline 10ml. Group BF: Block was given with Bupivacaine 0.5% (20 ml) with xylocaine adrenaline 10 ml with inj. Fentanyl 1 mcg/kg. Total duration of sensory block and analgesia, intraoperative hemodynamics, postoperative pain score and lung volumes and requirement of rescue analgesics were observed.

Results: Hemodynamic parameters were comparable in both the groups. Onset of sensory block in group BF was faster (15.4 ± 2.26) mins than group B (21.925 ± 2.15) mins. Duration of sensory block was significantly higher in group BF (6.45 ± 1.13) hrs than group B (3.5125 ± 0.51) hrs. Total analgesia was significantly prolonged in group BF (11.3 ± 1.0024 hrs) than group B (7.33 ± 2.0153 hrs). Requirement of rescue analgesic dose in group BF was lower (2.05 ± 0.67) than group B (3.025 ± 0.69) Better preservation and earlier recovery of respiratory volumes noted in group BF.

Conclusions: Intrapleural block given with local anaesthetic and fentanyl had faster onset and longer duration of sensory blockade with better preservation of lung volumes.

Keywords: Intrapleural block, , Modified Radical Mastectomy,, Post operative analgesia., regional block

Introduction

Effective postoperative analgesia is a very essential component of the care of the surgical patient. Inadequate pain control may result in increased rate of morbidity or mortality. Evidence suggests that surgery suppresses the immune system proportionate to the invasiveness of the surgery. Good analgesia can effectively reduce this deleterious effect. Various studies available indicate that afferent neural blockade with the help of local anaesthetics is the most effective a technique of analgesia. The advantages

of effective postoperative pain management include patient comfort and therefore satisfaction, earlier mobilization, reduced pulmonary and cardiac complications, a lowered risk of deep vein thrombosis, faster recovery with less likelihood of the development of neuropathic pain, and reduced cost of care [1].

The adverse sequels of postoperative pain are numerous. Patients with significant postoperative pain may demonstrate anxiety, fright, insomnia which often exacerbate their pain perception rendering the postoperative recovery period an

unpleasant and ominous experience. Other pain related stress responses include coagulation system activation, aggregation of platelets and fibrinolytic system alteration which may increase clotting leading to deep venous thrombosis and pulmonary embolism. Pain increases the sympatho-adrenal outflow of catecholamines leading to dysrhythmias, tachycardia and hypertension.

Postoperative pain is one of the major factor in postoperative pulmonary complication especially after upper abdominal and thoracic operations. Reduction of lung volumes due to acute restrictive pulmonary dysfunction secondary to pain may result in relative hypoxemia, major atelectasis and pulmonary consolidation.

Breast cancer surgeries are commonly performed under general anaesthesia which is the standard technique, but is associated with acute post-operative pain further aggravated by the arm and shoulder movements [2,3]. Concomitant use of regional blocks can not only help to minimize pain, but also improves the pulmonary function and reduce narcotic requirement during the perioperative period [4,5].

Among the regional techniques such as intercostal nerve block, thoracic epidural, thoracic paravertebral block (PVB), and inter pleural block (IPB), the last two are commonly being used to provide intra and post-operative analgesia in patient undergoing modified radical mastectomy [6,7]. Perioperative hypertension, tachycardia, headache, nausea, vomiting, and pain are frequently seen following breast surgery. This pain restricts shoulder movement postoperatively and may not be responding except for parenteral narcotics that have an emetogenic effect that needs further observation of these patients [8]. It is widely assumed that when postoperative patients are relatively pain free, their pulmonary functions are improved [9].

Intraleural regional analgesia is a method of postoperative pain relief reported by Reiestad and Stromskug [10]. This technique provides a unique form of regional analgesia that has proven advantageous for upper abdominal surgical interventions and breast surgeries.

Subjects and Methods

After clearance from Institutional Ethics Committee, the study was carried out in patients undergoing Modified Radical Mastectomy (MRM). It was a randomized prospective double blind study. The observer and the patient were blinded for the study drug.

After careful pre-anaesthetic evaluation, 80 female patients diagnosed with Carcinoma of Breast in the age group of 20-69 years, American Society of Anaesthesiologist (ASA) physical status I, II or III who required MRM were included in the study.

Inclusion criteria

All the cases undergoing radical mastectomy of ASA grade I, II, III.

Exclusion criteria

- Coagulation abnormalities

- Known Allergy reaction to drug
- Patient refusal
- Systemic sepsis or local infection at the puncture point
- Thoracic infection within the past 3 months.
- Patients with emphysema and chronic obstructive pulmonary disease (as these respiratory pathologies may have hyper inflated lungs with air filled bullae, injury to which may be difficult to predict and prevent complications).
- Previous or planned pleurectomy

Informed consent for General anaesthesia as well as Intraleural block (IPB) was obtained from the patients and care takers in the prescribed format. The patients were randomly allocated into two groups by computer generated random number sequence in 40 patients each. Odd numbers were given to group B (control group) and the even numbers were given to Group BF.

Group B: Control group

Intraleural block was given with Inj Bupivacaine 0.5% (20 ml) with xylocaine adrenaline (1:200000) 10ml and 5 ml 0.9% saline.

Group BF: Study group

Intraleural block was given with Inj. Bupivacaine 0.5% (20 ml) with xylocaine adrenaline (1:200000) 10 ml and 5 ml saline 0.9% with inj. Fentanyl 1 microgram/kg.

In this study, we use a posterior approach for giving interpleural block and perform injections with the patient in lateral position with affected side upwards before giving general anaesthesia. Consent for the procedure was obtained as per Institution protocol. The block was performed inside the Operation Theatre with an appropriate area which offered privacy, good lighting and ensures sterility, and with oxygen, monitoring and resuscitation drugs and equipment available readily. A senior anaesthetic assistant was always present to watch for procedure and full aseptic precautions observed (Photos 1-3).

The following parameters were noted

1. Time taken for onset of sensory blockade
2. Maximum level of sensory blockade attained
3. Intraoperative Hemodynamics.
4. Duration of sensory block
5. Duration of analgesia
6. Postoperative sedation
7. Postoperative pain score- Verbal Rating Scale (VRS) and Visual Analog Scale (VAS).
8. Postoperative Lung volumes and Peak Expiratory Flow Rate (PEFR)
9. No. of rescue analgesia required in 24 hours.
10. Adverse effects

Onset of sensory blockade was taken as a time taken from the complete injection of study drug till the patient does not feel the pin prick at T4 level.

Duration of analgesia was considered as the time taken



Photo 1. Marking for Intrapleural block.

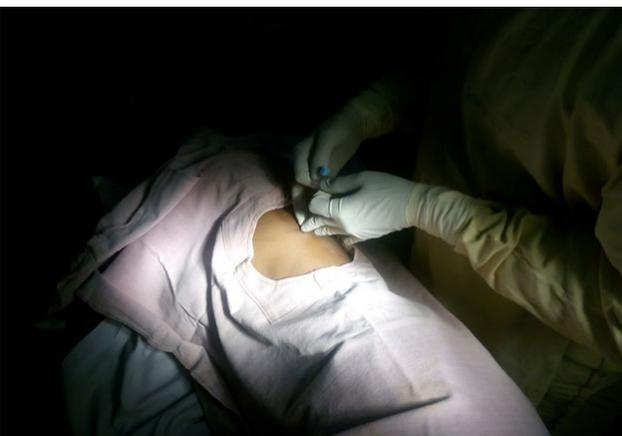


Photo 2. Technique of giving Intrapleural block.

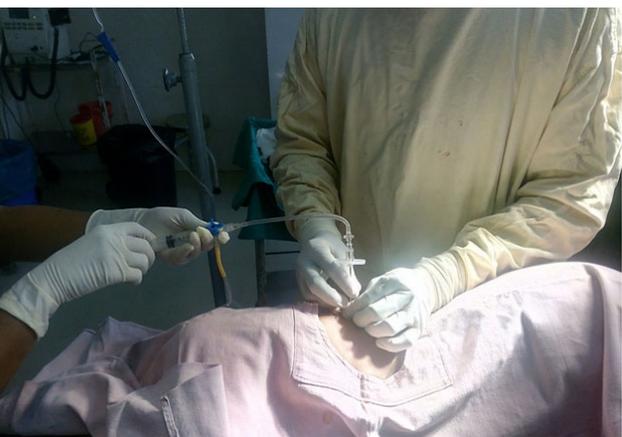


Photo 3. Confirmation of intrapleural space and administration of drugs.

from the completion of the injection of the study drug till the patient requests for analgesic in the post-operative period. Intravenous Diclofenac sodium 75mg was given as the rescue analgesic if the VAS pain score was ≥ 4 . Same dose was repeated whenever patient complained pain afterwards and number of doses counted for 24 hours.

Statistical analysis

Data analysis has been done using the Microsoft excel software 2007.

Sample size was calculated on assuming 80% statistical power and 5% α error. Sample size calculation was based on the presumption that post-operative requirement of inj. Diclofenac sodium as an analgesic drug as per VAS score and VRS taking the difference of 50 mg [among the total requirement] in 24 hours in both the group as (d) and Standard Deviation was taken 76.8 from the previous study. Considering dropouts total 40 patients in each group will be enrolled.

An unpaired t test was used to compare demographic variables, intra operative hemodynamic variables (heart rate, systolic blood pressure) oxygen saturation, and onset and duration of sensory and motor block between the groups. Sedation scores and pain scores were compared, while rescue analgesic requirements in both groups were compared by Chi square test. Inspiratory reserve volume, expiratory reserve volume, tidal volume and peak expiratory flow rate (PEFR) were also assessed. Intergroup comparison was done, using unpaired "t" Test and comparing mean and standard deviation.

A "p" value <0.05 was taken as significant and "p" value <0.001 was taken as highly significant. All the values were presented as Mean \pm SD. Confidence Interval were calculated using Microsoft excel software 2007.

Results

Eighty patients were recruited. All the patients underwent radical mastectomy and received their allocated study drug. No assigned patients dropped out of the study. Demographic profile and surgical data were statistically comparable in both the groups (**Tables 1 and 2**). Mean Arterial pressure in group B and group BF before and after giving intrapleural block as well as intraoperatively and postoperatively were recorded. There were no statistical significant difference in both the groups throughout the procedure (**Figure 1**). Mean time of onset of sensory block in group B was higher (21.925 ± 2.15 minutes) than in group BF (15.4 ± 2.26 minutes) which was statistically significant $\{p < 0.01\}$ (**Figure 2**). Confidence interval of 95% cases of Group B is 22.592 to 21.258 min and Group BF is 16.10 to 14.69 min. Mean duration of sensory block in group B was 3.5125 ± 0.51 hours and in group BF it was 6.45 ± 1.13 hours which was significantly higher $\{p < 0.01\}$ in group BF than group B (**Figure 3**). Confidence interval of 95% cases of Group B is 7.95 to 6.70 hours and Group BF is 11.61 to 10.99 hours. Mean duration of analgesia was significantly higher in group BF (11.3 ± 1.00 hours) than group B (7.95 to 6.70 hours)

Table 1. Patient characteristics and operative data.
 Data expressed as Mean (SD).

	Group B n=40	Group BF n=40	P value
Age (years)	46±8.75	47.95±7.98	0.30
Weight (kg)	58.8±5.78	59.77±7.17	0.79
Duration of Surgery (minutes)	127.25±21.15	122.62±21.18	0.33
ASA Status	I/ II/ III	I/ II/ III	--

Table 2. Complications noted during the procedure and postoperatively.

Complication	Group B	Group BF
Nausea-vomiting	2	3
Chest pain	2	1
Coughing	5	4
Convulsions	0	0
Hypotension	0	0
Bradycardia	0	0
Pneumothorax	0	0
Respiratory depression	0	0
Pruritus	0	2

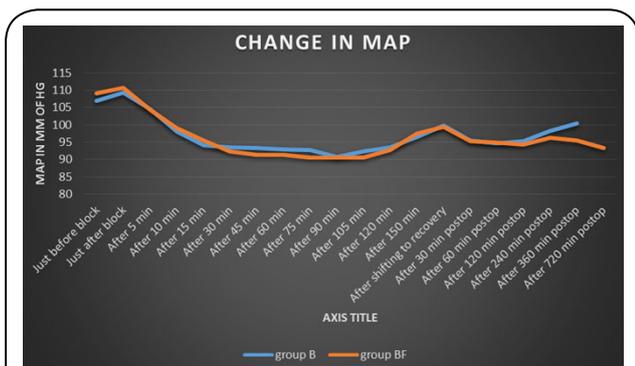


Figure 1. Changes in mean arterial pressure over a period of time. Data expressed as Mean (SD).

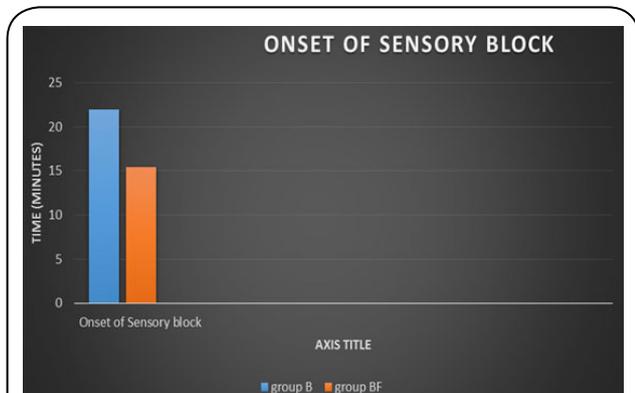


Figure 2. Onset of sensory block. Time '0' start after complete injection of drug in IPB. Data expressed as Mean (SD).

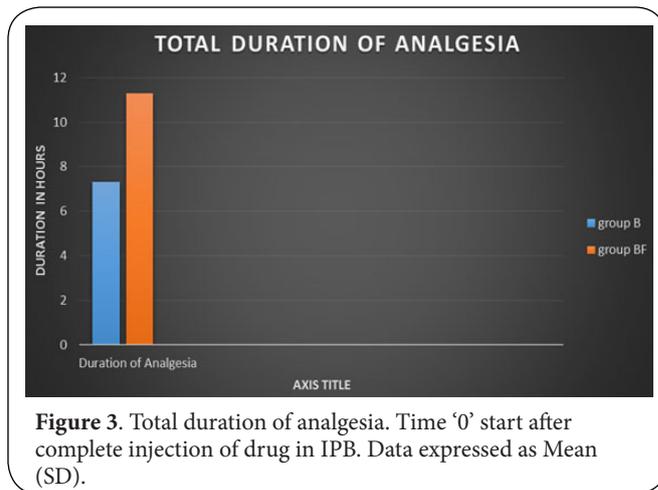


Figure 3. Total duration of analgesia. Time '0' start after complete injection of drug in IPB. Data expressed as Mean (SD).

Figure 4 { $p < 0.05$ }. Confidence interval of 95% cases of Group B is 7.95 to 6.70 hours and Group BF is 11.61 to 10.99 hours.

Figures 5 and 6 shows mean VRS and VAS pain score in group B and group BF in postoperative period. There was no statistical significant difference in both the groups initially upto 240 minutes postoperatively. But after 240 minutes, the mean VRS and VAS score was consistently high in group B than group BF which was statistically significant { $p > 0.05$ }, which shows that addition of fentanyl had prolonged the duration of analgesia beyond 240 min.

More rescue analgesic doses required in group B (3.025 ± 0.69) than in group BF (2.05 ± 0.67) { $p < 0.05$ } (**Figure 7**).

Mean Peak Expiratory Flow Rate was comparable in both the groups preoperatively { $p > 0.05$ }. In postoperative period there was reduction in PEFR in both the groups in immediate postoperative period followed by gradual improvement in PEFR. The difference in both the groups was statistically not significant till 4 hrs postoperatively. But after 4 hr postoperatively there was statistically significant difference in PEFR in both the groups { $p < 0.05$ }. More improvement in PEFR was noted in group BF, suggesting early improvement in PEFR than group B. We noticed nausea, vomiting, chest

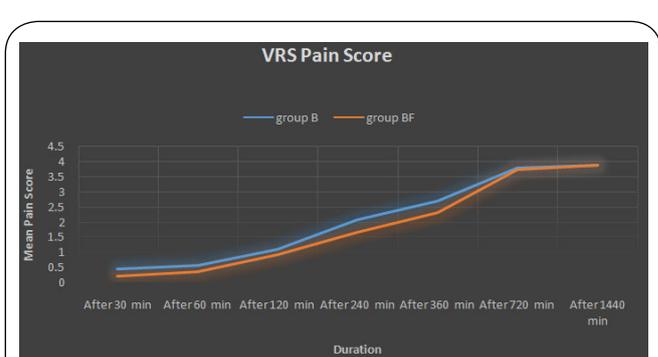


Figure 4. Changes in Verbal Response Scale pain score. Time '0' start postoperatively after shifting the patient in recovery area. Data expressed as Mean (SD).

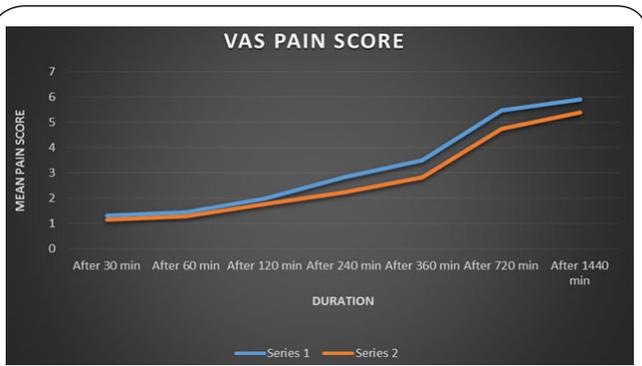


Figure 5. Changes in Visual Analog Scale pain score. Time '0' start postoperatively after shifting the patient in recovery area. Data expressed as Mean (SD).

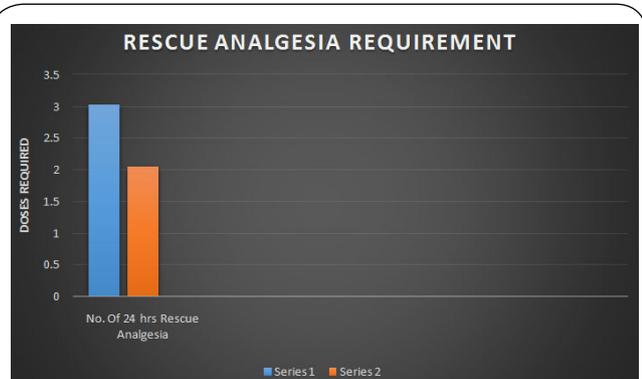


Figure 6. Rescue analgesics. Data expressed as Mean (SD).

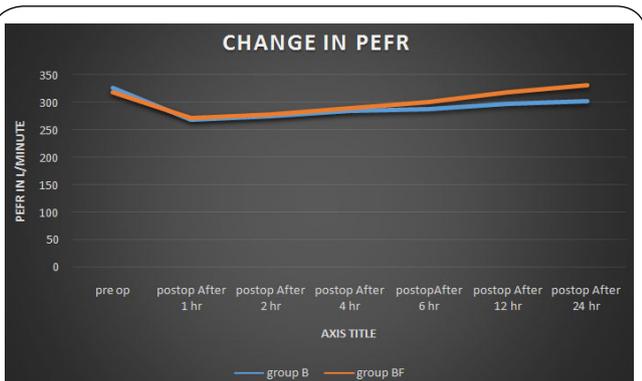


Figure 7. Changes in Peak expiratory flow rate over a period of time. Data expressed as Mean (SD).

pain, coughing during procedure, pruritus in patients of both the groups. There was no incidence of any intra-operative or post-operative complications like convulsion, hypotension, bradycardia, pneumothorax and respiratory depression.

Discussion

Intraleural analgesia consists of the injection of a local

anaesthetic into the pleural space. Intraleural blockade is the technique of giving local anaesthetic in between two pleurae (parietal and visceral) to produce ipsilateral somatic block of various thoracic dermatomes. It also helps to reduce the pain by spread of local anaesthetic bilaterally to block both the splanchnic nerves and the sympathetic chains. It is effective in treating unilateral surgical as well as non-surgical pain from upper abdomen and chest in both the acute and chronic settings. Local anaesthetic solutions can be given as single or intermittent doses, or as continuous infusions via an indwelling intraleural catheter.

Intraleural analgesia has gained popularity because of its low rate of complications. Local anaesthetics as well as opioid agents administered via a catheter placed inside the pleural cavity have been used to anesthetize intercostal nerves to relieve pain.

Opioids administered by various routes are still the mainstay of analgesia for various upper abdomen surgeries pain management. However, systemic opioids have the potential for good pain relief at rest with a lack of effective pain reduction when coughing or breathing deeply. In addition, opioids may cause adverse effects such as respiratory depression, somnolence, prolonged nausea or vomiting and pruritus, when administered via a systemic or epidural route. Patients receiving epidural narcotics may also need care in a setting that monitors their respiration. Adverse effects seen with systemic and epidural opioids may be avoided when using opioids intraleurally [11].

Various authors have observed that, addition of adjuvant to local anaesthetic for IPB not only provides excellent analgesia but also reduces the hemodynamic response to surgery and the intraoperative anaesthetics and analgesic requirements with better emergence from anaesthesia with fewer side effects, a prolonged pain-free period, improving the respiratory performance and giving a rapid mobilization and overall better quality of postoperative recovery which is essential in the reduction of immediate postoperative complications.

Early onset of analgesia by addition of fentanyl is also supported by a study done by B. Rastogi, M. Jain (2009) [12], where in a comparative clinical study of Intraleural Bupivacaine And Intraleural Bupivacaine With Morphine for Post-Operative analgesia for Laparoscopic Cholecystectomy (n=45), they have concluded that mean time of onset of analgesia was 30min in B group and 15 min in group BM.

Prolongation of total duration of analgesia after addition of fentanyl in local anaesthetics is also suggested by Darshna D Patel, Varsha N Swadia [13] (2013) who studied "fentanyl versus sodium bicarbonate in axillary brachial plexus block" scheduled for elective hand and forearm orthopedic surgeries (n=50) and concluded that, the duration of analgesia was 816.2±87.49 minutes in Group F while it was 429±86.45 minutes in Group SB, the p value being <0.001 i.e. highly significant.

Sarita Gohiya and Vineet Gohiya [14] (2013) also concluded that, duration of analgesia is significantly prolonged after

addition of fentanyl in bupivacaine for brachial block for upper limb surgeries (i.e. 11.45+/-1.50 hours in Group I and 21.9+/-2.25 hours in Group II).

There was no statistical significant difference in heart rate ($p>0.05$) in both the groups throughout the procedure. It was noted that MAP was maintained at lower side in group BF throughout the procedure as compared to group B though not statistically significant ($p>0.05$). The reason for lower MAP could be the fentanyl induced hemodynamic stability. This findings are in agreement with findings of B. Rastogi, M. Jain [12] (2009), who studied effect of Intrapleural Bupivacaine and Intrapleural Bupivacaine with Morphine for Post-Operative analgesia for Laparoscopic Cholecystectomy. Their study also showed that the perioperative changes in hemodynamic parameters are non-significant in both the groups.

Mostafa Abdel Hamid Abo El Enin, Ismail Ewis Amin et al [15] (2009) in their study "Effect of Fentanyl Addition to Local Anaesthetic in Peribulbar Block" (n=40) concluded that, addition of fentanyl to local anaesthetic mixtures improve quality of postoperative pain. There was statistically significant differences between the two groups as regard the median VAS at 1, 2, 3, 4, 5, 6 hours. Fentanyl group had lower median pain score than Control group.

B. Rastogi, M. Jain et al. [12] (2009), did a comparative clinical study of Intrapleural Bupivacaine And Intrapleural Bupivacaine With Morphine for Postoperative Analgesia for Laparoscopic Cholecystectomy. In their study, they noted that there was gradual improvement of PEFR in both the groups but that has no significant difference with bupivacaine alone group.

Shideh Dabir, MD, Tahereh Parsa, MD et al [11] (2008) findings are also in favour of our findings. In their study "Intrapleural Morphine vs Bupivacaine for Post thoracotomy Pain Relief" (n=36) they came to the conclusion that, the number of patients who received intravenous morphine supplementation was significantly less in the morphine group than the bupivacaine group.

Complications in both the groups were statistically not significant, but few side effects specifically related to fentanyl, like pruritis was noted but needed no treatment, reassurance was sufficient. Bourke DL, Furman WR [16] (1993) studied, postoperative analgesia with morphine added to axillary block solution and concluded that, in study group where patients received morphine 0.1 mg/kg added to their axillary block solution, there were no major complications as compared to control group, who received saline added to their axillary block solution.

Conclusion

From this study we conclude that, when fentanyl was added as an adjuvant in intrapleural block, it fastens the onset of sensory block, prolongs duration of sensory block, extends total duration of analgesia and has better preservation of respiratory functions compared to bupivacaine plus xylocaine-adrenaline alone. Intraoperatively hemodynamic stability was achieved

in both the groups with no statistical significant difference in mean blood pressure and mean heart rate.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	KPR	VAO	VSP	SP
Research concept and design	✓	✓	✓	✓
Collection and/or assembly of data	✓	✓	✓	✓
Data analysis and interpretation	✓	✓	✓	✓
Writing the article	✓	✓	✓	✓
Critical revision of the article	✓	✓	✓	✓
Final approval of article	✓	✓	✓	✓
Statistical analysis	✓	✓	✓	✓

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