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Original Research Article

A prospective randomized study to compare the efficacy of 0.125% Bupivacaine with fentanyl or with Dexmedetomidine via extrapleural paravertebral catheter for postoperative analgesia in thoracic surgeries

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Abstract: Background: Postoperative pain is a major problem associated with any surgery. Thoracic surgeries result in excessive breakthrough pain which should be countered appropriately to decrease postoperative poor ventilation. Extrapleural paravertebral catheter is one such modality effective for postoperative pain caused by thoracic surgeries, comparable to thoracic epidural. Adjuvants like fentanyl or dexmedetomidine not only reduce the total local anesthetic dose but also provide superior and profound analgesia.
Aims and Objectives: To compare the effect of bupivacaine with fentanyl or with dexmedetomidine via extrapleural paravertebral catheter for continuous postoperative analgesia.
Materials and Methods: Our study was a prospective, randomized, and comparative study conducted in the Department of Anesthesiology, M.Y. Hospital and M.G.M. Medical College, Indore. A total of 40 patients (taking the COVID era into consideration) aged between 18 to 65 years with ASA Grade I, II & III undergoing thoracic surgeries were included. Patients were divided into two groups of 20 each: Group (B+F) who received 0.125& Bupivacaine along with Fentanyl 2 mcg/ml @ 0.15ml/kg/hr and Group (B+D) who received 0.125& Bupivacaine with Dexmedetomidine 0.2 mcg/kg/hr @ 0.1ml/kg/hr via extrapleural paravertebral catheter.
Results: The mean PEFR was comparable between the two groups at 12 hours (P=0.198), 24 hours (P=0.058), 48 hours (P=0.15), and 72 hours (P=0.10). Improvement in PEFR was observed in both groups from 12 hours to 72 hours, with group 1 (B+F) showing 348.00 $\pm$ 18.317 L/min at 12 hours and 521.50 $\pm$ 24.468 L/min at 72 hours, while group 2 (B+D) showed 355.50 $\pm$ 15.39 L/min at 12 hours and 535.00 $\pm$ 28.562 L/min at 72 hours, indicating improvement in lung function. The mean time taken for the request to first analgesia in Group 1 (B+F) was 259.15 $\pm$ 11.536 minutes and in Group 2 (B+D) was 360.2 $\pm$ 13.671 minutes, and this mean time was found to be statistically significant between the two groups (P=0.000*).
Conclusion: The mean VAS score (visual analog scale) noted at 72 hours with coughing was better with dexmedetomidine than with fentanyl. The mean time taken for the request to first rescue analgesia in group B+F was 259.15 $\pm$ 11.536 minutes, and in group B+D, it was 360.20 $\pm$ 13.671 minutes, which was significantly higher in the dexmedetomidine-containing group. A more stable hemodynamic profile was observed in the B+D group.

Keywords: Fentanyl; Dexmedetomidine; Extrapleural paravertebral; Postoperative pain.

1. Introduction

Postoperative pain is the most common problem associated with any surgical intervention, which requires appropriate analgesia. According to the International Association for the Study of Pain, pain is defined as an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage [1].

Thoracotomy surgery can crush the intercostal nerve, especially as the nerve is quite exposed on the caudal side of the rib. Moreover, incidental rib fractures may damage the intercostal nerve immediately or entrap an intercostal nerve during healing, leading to neuropathic pain symptoms. This extensive pain leads to respiratory function compromise, and patients stay in the hospital for a long time. There are many drugs and techniques for relieving postoperative pain, with regional techniques or systemic analgesics being common. Systemic opioids carry the risk of respiratory depression, and NSAIDs are poor analgesics for thoracotomy incisions [2].

Extrapleural paravertebral catheter is an alternative technique to decrease pain in thoracotomy [3]. Analgesia after thoracotomy needs to be effective for the patient's comfort and because it improves compliance with coughing and deep breathing, thereby decreasing the risk of pulmonary atelectasis and ventilation perfusion abnormalities [4].

Thoracic epidural analgesia is considered the gold standard for treating post-thoracotomy pain. However, it may result in devastating complications like spinal hematoma, epidural abscess, and paraplegia. Continuous infusion of bupivacaine through an indwelling epidural catheter placed extrapleurally at thoracotomy overcomes the need for repeated intercostal block and complications due to thoracic epidural analgesia.

Traditionally, opioids like Fentanyl have been used as an adjunct for epidural administration in combination with a lower dose of local anesthetic to achieve the desired anesthetic effect. The addition of opioids provides a dose-sparing effect of local anesthetic and superior analgesia.

Dexmedetomidine is a highly selective $\alpha 2$ adrenergic agonist. It acts on both pre- and post-synaptic sympathetic nerve terminals and the central nervous system, thereby decreasing the sympathetic outflow and norepinephrine release, causing sedative, anti-anxiety, analgesic, sympatholytic, and hemodynamic effects. Additionally, dexmedetomidine lacks most of the side effects of opioids.

In this technique, the catheter is placed in the extrapleural space by the surgeon under direct vision. For the placement of extrapleural catheters, an 18-gauge Tuohy needle is placed through the chest wall at a convenient site two interspaces below the thoracotomy incision and a few centimeters away from the chest tube site. The needle's stylet is removed, and an epidural catheter is passed through the needle and placed inside the extrapleural space. We carried out this study to prospectively compare the effect of 0.125% Bupivacaine with Fentanyl or with dexmedetomidine via extrapleural paravertebral catheter insertion for continuous postoperative analgesia in patients undergoing thoracic surgeries.

2. Materials and Methods

This is a prospective, randomized, comparative study that was conducted for a period of one year in the Department of Anaesthesiology, M.Y. Hospital and M.G.M. Medical College, Indore.

2.1. Sample size

The study comprised 40 patients divided into two groups of 20 each scheduled for thoracic surgery under general anesthesia. The sample size was calculated using G* power software version 3.1.9.2 with a 95% confidence level and 80% power for two groups using a "t" test (mean difference between two independent groups) for large effective size "d" (0.8).

2.2. Inclusion criteria

1. Patients scheduled for thoracic surgery.
2. Age between 18-65 years.
3. ASA grade I, II, III.

2.3. Exclusion criteria

1. Patient refusal.
2. ASA grade IV.
3. Hypersensitivity to local anesthetics.
4. Coagulation profile derangement.
5. Platelet count < 50000.
6. Non-intact pleura at paravertebral space.
7. Adhesion, infection, tumor, scarring in paravertebral space.

2.4. Ethical clearance

The study was approved by the institutional ethics and scientific review committee of M.G.M. Medical College and M.Y. Hospital, Indore prior to commencement.

2.5. Randomization

Patients were randomly allocated into 2 groups (Group B+F or Group B+D) by chit method just before the surgery.

2.6. Procedure

After obtaining written informed consent and recording vitals and nil by mouth status as per institutional protocol, all patients were started on intravenous fluids. Routine monitors were attached (pulse oximeter for Spo2, heart rate (HR), non-invasive blood pressure, and ECG). General anesthesia was given as per the standard institutional protocol. Intubation was done with an appropriate size double-lumen endotracheal tube after giving a muscle relaxant. Thoracotomy was done under general anesthesia. An extrapleural catheter was inserted by the surgeon under direct vision external to the parietal pleura just before thoracotomy closure. Then an infusion of 0.125% Bupivacaine with fentanyl 2mcg/ml @ 0.15 ml/kg/hr in Group B+F was started, and 0.125% Bupivacaine with dexmedetomidine 0.2 mcg/kg/hr @ 0.1ml/kg/hr in Group B+D. Then the dose or rate of infusion was decreased after 2 days or chest drain removal, as pain subsided.

Assessment of Postoperative Pain & Management

The pain score using a visual analog scale was assessed at 1, 6, 12, 18, 24, 48, and 72 hours after the surgery. Patients who complained of pain with a VAS score of more than or equal to 4 were given IM Inj. Tramadol 1mg/kg (rescue analgesia). The peak expiratory flow rate was assessed at 12, 24, 48, and 72 hours. The hemodynamic changes and adverse events including hypoxia, hypotension, hypertension, nausea, vomiting, pruritus, etc. were assessed in all the patients at 1, 6, 12, 18, 24, 48, and 72 hours.

2.7. Statistical analysis

Data was initially collected in the customized proforma designed for the purpose of the study. Then this data transferred to Microsoft Excel for analysis and online statistical software graph pad and Epi info was used for calculating p value. Association between two non-parametric variable was seen using Pearson Chi-square test, comparison of means between the two group was done using unpaired 't' test. A p value of <0.05 was considered as statistically significant. The final data was presented in the form of graphs. Observations were thoroughly discussed and reviewed with available literature.

3. Observations & Results

Distribution of patients according to group is represented in a pie diagram (Figure 1). Distribution of patients according to age, gender, and ASA grade is presented in bar diagrams (Figures 2, 3, and 4, respectively).

Comparison of mean heart rate, systolic blood pressure, diastolic blood pressure, SpO2, VAS during rest, VAS during cough, and peak expiratory flow rate (PEFR) between the two groups are presented in line diagrams (Figures 5-11).

The mean time to request for first rescue analgesia is presented in a bar diagram (Figure 12). The complications observed in both groups are presented in a bar diagram (Figure 13).

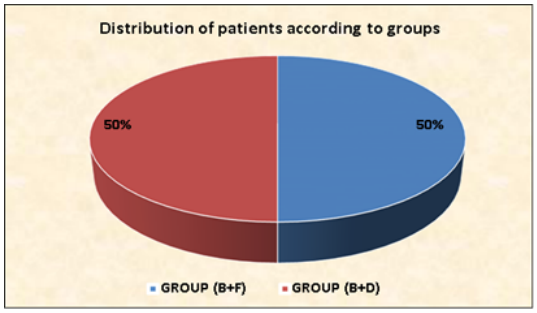

Figure 1. Pie diagram showing distribution according to group

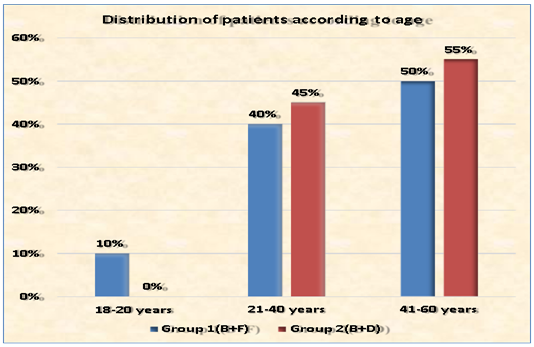

Figure 2. Bar diagram showing distribution according to age

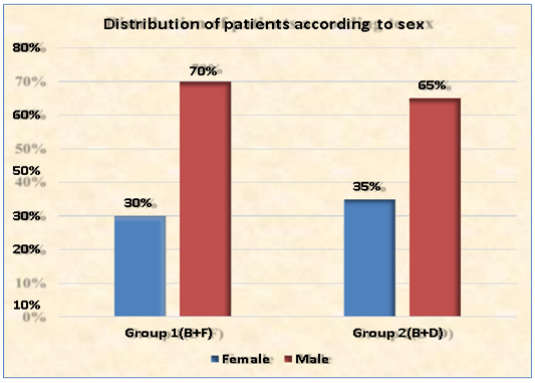

Figure 3. Bar diagram showing distribution according to gender

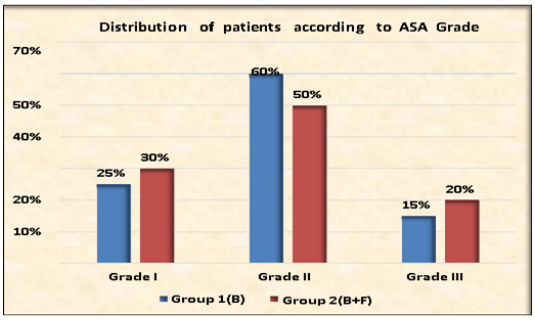

Figure 4. Bar diagram showing distribution according to ASA Grade

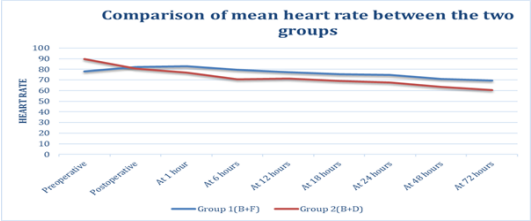

Figure 5. Line diagram showing comparison of mean heart rate between two groups

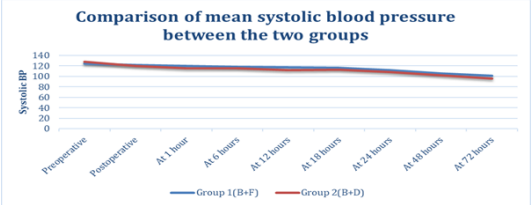

Figure 6. Line diagram showing comparison of mean systolic blood pressure between the two groups

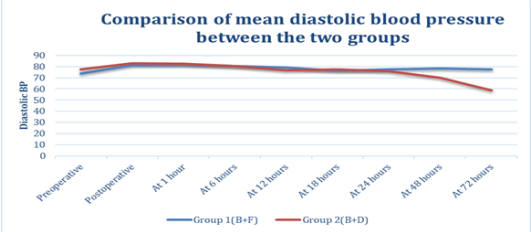

Figure 7. Line diagram showing comparison of mean diastolic blood pressure between the two groups

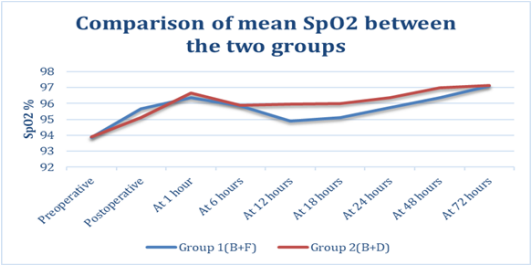

Figure 8. Line diagram showing comparison of mean SpO2 between the two groups

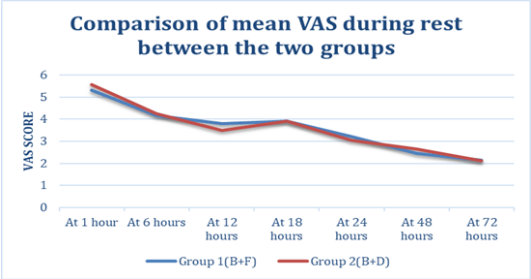

Figure 9. Line diagram showing comparison of mean VAS during rest between the two groups

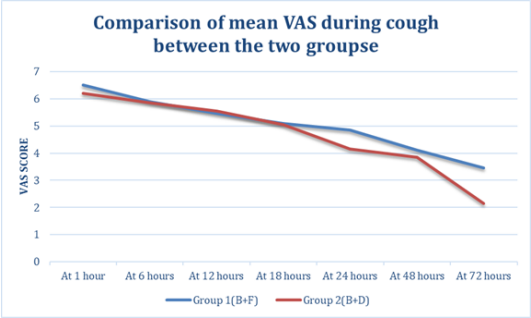

Figure 10. Line diagram showing comparison of mean VAS during Cough between the two groups

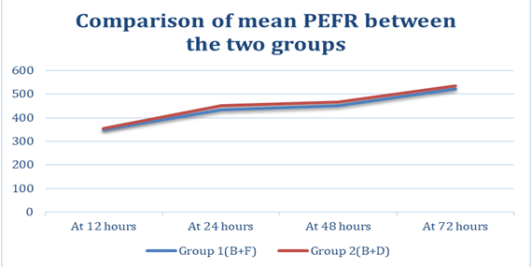

Figure 11. Line diagram showing comparison of mean PEFR between the two groups

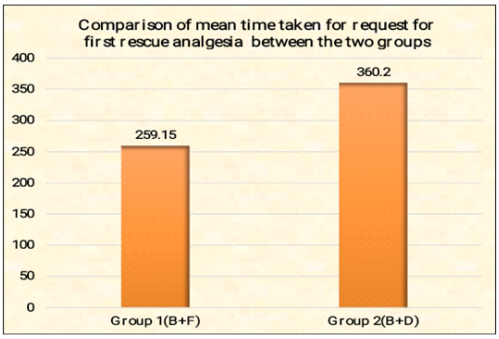

Figure 12. Bar diagram showing comparison of mean time to request for first rescue analgesia

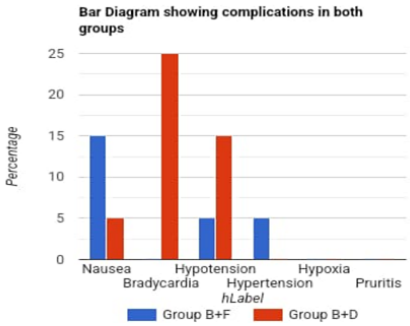

Figure 13. Bar diagram showing complications observed in both the groups

4. Discussion

Thoracic surgeries can cause severe pain, discomfort, and respiratory complications such as atelectasis, diaphragmatic dysfunction, respiratory failure, splinting, and ineffective cough resulting in pneumonia. Proper management of this pain is crucial to reduce such complications and shorten the patient's hospital stay. This study aimed to evaluate and compare the effect of 0.125% bupivacaine with fentanyl or with

dexmedetomidine via extrapleural paravertebral catheter for continuous postoperative analgesia in 40 patients undergoing thoracic surgeries. The patients were randomized into two groups: Group 1 (B+F) received bupivacaine + fentanyl, and Group 2 (B+D) received bupivacaine + dexmedetomidine.

The mean age in Group 1(B+F) was 42.2 ± 14.57 years and in Group 2(B+D) was 40.3 ± 9.953 years, with a male predominance in both groups, with 70% males in Group (B+F) and 65% in Group (B+D). Most of the patients in both groups were in ASA Grade II, with 15% of ASA Grade III in Group (B+F) and 20% of ASA Grade III in Group (B+D). The patients in both groups were comparable in terms of age-wise distribution and demographic profile. The mean preoperative heart rate was 78 ± 4.91 per minute in Group 1(B+F) and 89.65 ± 4.891 per minute in Group 2(B+D). The mean heart rate was comparable between the two groups at postoperative ($P > 0.05$). However, the mean heart rate was significantly lower in Group 2(B+D) at 6 hours, 12 hours, 18 hours, 24 hours, and at 72 hours postoperatively ($P < 0.05$) compared to Group 1(B+F).

The mean systolic blood pressure and mean diastolic blood pressure both showed a decrease in dexmedetomidine containing group compared to group.Mean oxygen saturation and pain score (VAS) - both during rest were comparable between the two groups at all the time intervals ($P>0.05$), but VAS score of 72 hours at cough shows slight improvement in dexmedetomidine containing group . The mean VAS during rest at 1 hour postoperatively was 5.3 ± 0.553 in Group 1(B+F), and 5.55± 0.51 in Group 2(B+D), The mean oxygen saturation and pain score (VAS) at rest was comparable in both the groups in all time intervals. However the pain is controlled in both the groups effectively. This is in concordance with the study of Bharti et al. [5] , Selim et al. [6], Alansary et al. [7], and Kiran et al. [9], which too demonstrated lower mean pain score with the addition of adjuvant fentanyl or dexmedetomidine with that of just bupivacaine. Elhakim et al. [10] evaluated effects of administration of dexmedetomidine in thoracic epidural in patients undergoing thoracic surgeries found that there was significant decreases in intraoperative fentanyl consumption in patients receiving dexmedetomidine as compared with bupivacaine only. Bajwa et al. [11] reported that dexmedetomidine provided superior post- operative analgesia compared with fentanyl in patients who were undergoing orthopedic procedures under regional anaesthesia (Lumbar epidural anaesthesia). Reddy et al. [12] in their study concluded that dexmedetomidine containing group had superior post-operative pulmonary functions and less post-operative morphine requirements in patients undergoing thoracic surgeries in ultrasonography-guided paravertebral blocks which too is in accordance to our study. Dutta et al. [13] in their study observed that dexmedetomidine reduces post-operative pain scores , longer median time to first rescue analgesia and lower morphine requirements in thoracic surgery for post thoracotomy pain syndrome.

In the present study we noticed that a significant decrease in the heart rate in both the groups as compared to baseline. In group 1 (B+F) it was 78 ± 4.91per minute and group 2 it was 89.65 ± 4.891 per minute which after 72 hours came to be 69.45 ± 1.234 per minute and 60.4 ±1.501 per minute respectively. The heart rate was significantly lower in the dexmedetomidine group compared to fentanyl group . The finding is similar to what observed by Bharti et al. [5] , Bajwa et al. [11], Elhakim et al. [10]. The mean systolic and diastolic blood pressure was slightly lower in dexmedetomidine group than that of with fentanyl group , this is in accordance with study done by Bajwa et al. [11] , Kiran et al. [9] . But Bharti et al. [5] observed no changes in blood pressures in both the groups.

The mean PEFR was also comparable between the two groups at 12 hours ($P=0.198$), at 24 hours ($P=0.058$), at 48 hours ($P=0.15$) and at 72 hours ($P=0.10$). In both the groups, we have noticed, improvement in PEFR from 12 hours to 72 hours that is in group1(B+F) 348.00 ± 18.317 L/min at 12 hours and 521.50 ± 24.468 L/min at 72 hours while in group 2(B+D) 355.50 ± 15.39 L/min at 12 hours and535.00 ± 28.562 L/min at 72 hours . From above values, we observed improvement in lung function. Reddy et al. [12] , Hassan et al. [14] in their study reported improvement in PEFR in dexmedetomidine group than that of bupivacaine only group which is in accordance to our study.

The mean time taken for request to first analgesia in Group 1(B+F) was259.15 ± 11.536 minutes and in Group 2(B+D) was 360.2 ± 13.671 minutes and this mean time was found to be statistically significant between the two groups ($P=0.000^*$). Our study was in accordance with study done by Bharti et al. [5] , Reddy et al. [12], Alansary et al. [7], which also showed lower requirement of opioids. The analgesic effect of dexmedetomidine is mediated by it's action at the brain, brainstem, spinal cord and peripheral tissues. dexmedetomidine causes hyperpolarisation of nerve tissue by altering transmembrane action potential and ion conductance at the brainstem locus ceruleus. In the spinal cord, the analgesic effect is related to the activation of the descending medullospinal noradrenergic pathway or to the reduction of spinal sympathetic outflow at

presynaptic ganglionic sites. Epidural opioids are believed to act as pre- and postsynaptic receptors in the spinal cord dorsal horn to achieve a selective block of nociceptive pathways. In the study it was observed that nausea was seen in 15% cases in (B+F) group that of 5 % in (B+D) group . In (B+D) group bradycardia was more than that in (B+F) group. The hemodynamic stability was observed in both the groups.

5. Conclusion

From our study, it can be concluded that Dexmedetomidine used as adjuvant with bupivacaine in the extrapleural paravertebral catheter is better with that of fentanyl used as adjuvant for continuous postoperative analgesia in thoracic surgeries. Mean VAS score (visual analog scale) noted at 72 hours with coughing was better with dexmedetomidine than that of with fentanyl. Also mean time taken for request to first rescue analgesia in group B+F was 259.15 ± 11.536 minutes and in B+D group was 360.20 ± 13.671 minutes which was significantly higher in dexmedetomidine containing group.There was more stable hemodynamic profile observed in B+D group.

6. Limitation Of Study

Although this study has tried to meet its aims and objectives in all aspects,there are few limitations to it. We conducted a single-centre study, we did not compare the efficacy of extrapleural catheter with thoracic epidural and inter pleural analgesia in our study, the total sample size 40 (20 in each group), if sample size was larger then the result would be more precise.

To overcome these limitations, a multicentric study with large sample size is needed to obtain more conclusive results.

Author Contributions: MG-Concept and design of the study, prepared first draft of manuscript; GT- Interpreted the results; reviewed the literature and manuscript preparation; SS- Concept, coordination, statistical analysis and interpretation, preparation of manuscript and revision of the manuscript; AA- Concept, coordination, statistical analysis and interpretation, preparation of manuscript and revision of the manuscript; KKA;Guidance.

Conflicts of Interest: "The authors declare that they do not have any conflict of interests."

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