**Patient-controlled epidural analgesia with fentanyl and bupivacaine provides better analgesia than intravenous morphine patient-controlled analgesia for early thoracotomy pain**

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**Abstract**

**Background:** Intravenous patient-controlled analgesia (IVPCA) and patient-controlled epidural analgesia (PCEA) were studied in terms of analgesic efficacy, respiratory function and side effects after thoracic surgery for 24h. PCEA using fentanyl and bupivacaine as compared to IVPCA using morphine provides better pain relief both at rest and during coughing and is associated with fewer side effects. **Aims:** To compare IVPCA and PCEA in terms of analgesic efficacy, respiratory function and side effects after thoracic surgery. **Settings and Design:** Tertiary care teaching hospital. Prospective, randomized and open study. **Materials and Methods:** Thirty ASA-I or II patients undergoing thoracotomy were assigned randomly to receive either IVPCA using morphine or PCEA using fentanyl and bupivacaine combination postoperatively. No background infusion was administered in either group. Postoperative evaluation included pain intensity both at rest and during coughing, degree of sedation, arterial blood gas, forced vital capacity (FVC), peak expiratory flow rate (PEFR), presence of side effects such as nausea/vomiting and pruritis at 0, 2, 8, 12 and 24h. The primary outcome of the study was the percentage of patients with analgesia failure defined as VAS>30 despite three consecutive PCA boluses requiring rescue analgesia with intravenous fentanyl. **Statistical Analysis:** Data were analyzed using t-test, χ² test and Mann-Whitney test. **Results:** Significantly less number of patients required rescue analgesia in PCEA group ( \( P<0.05 \)). Pain relief was better both at rest and during coughing ( \( P<0.05 \) ) in PCEA group as compared to IVPCA. Patients in the PCEA group were less sedated and had fewer incidences of side effects, i.e. nausea/vomiting and pruritis. Postoperative FVC and PEFR were reduced significantly compared to baseline only in IVPCA group ( \( P<0.05 \)). Conclusion: After thoracic surgery, PCEA using fentanyl and bupivacaine as compared to IVPCA using morphine provides better pain relief both at rest and during coughing and associated with fewer side effects.
Post-thoracotomy pain is known to be severe and intense as a consequence of tissue damage to the ribs, muscles and peripheral nerves. [1] The role of well-planned pain management has been crucial in decreasing morbidity after major thoracic surgery. [1] Effective pain relief allows post-thoracotomy patients to maintain their functional vital capacity by deep breathing. [2] Ability to cough out secretions and early mobilization lead to quick recovery and shorter hospital length of stay. [3],[4] Moreover, inadequate postoperative pain management may lead to the development of chronic post-thoracotomy syndrome. [5],[6] Various analgesic techniques have been developed to treat postoperative thoracotomy pain. [1],[2],[6],[7] Pain relief using thoracic epidural analgesia has been reported to be associated with lower mortality and respiratory complications and has contributed to improved surgical outcome. [8] In comparison to intravenous patient-controlled analgesia (IVPCA), thoracic epidural analgesia (TEA) using continuous infusion [6],[7] and patient-controlled epidural analgesia (PCEA) [2] have been reported to provide better postoperative analgesia than systemic morphine [2],[6],[7] and TEA with preoperative initiation has been reported to be a preferable method in preventing acute and long-term thoracotomy pain. [6] Although PCEA using opioid (fentanyl or sufentanil) and local anaesthetic (bupivacaine or ropivacaine) mixture has been compared with the IVPCA morphine for surgical procedures other than thoracotomy [9],[10] and reported to provide superior analgesia, reduced rescue analgesic requirement and better patient satisfaction compared to IVPCA; however, there is dearth of information about these two most frequently used analgesic options for postoperative thoracotomy pain. [11] To determine the true analgesic value of epidural analgesia for postoperative pain management, it would be appropriate to compare PCEA with IVPCA. [12] Therefore, we planned this study to compare these two techniques for post-thoracotomy pain in terms of analgesic effects, respiratory function and side effects.

**Materials and Methods**

This was a prospective, randomized, controlled and open study. Thirty-four adult ASA status I or II patients, in the age range 20-70 years and undergoing thoracotomy, were included in the study. Institutional review board clearance and written informed patient consent were obtained. Patients with contraindications to regional anaesthesia (infection at local site, coagulopathy) and those whose ability to communicate was impaired were excluded from the study.

All patients were explained about the use of patient-controlled analgesia (PCA) pump (IVAC Medical system; Welmed Ltd., Hampshire, UK), visual analogue scale (VAS) system, use of Wright's Respirometer (Ferraris Development and Engineering Ltd., Edmonton, London) and Ferraris peak flowmeter (Ferraris Medical Ltd., Hertford, England) a day before surgery. All patients with oral diazepam 0.2mg/kg the night before surgery and at 6 a.m. on the day of surgery.
Patients were randomly allocated (using computer-generated number) to receive either PCEA group with fentanyl and bupivacaine or IVPCA group with morphine for post-thoracotomy pain. In PCEA group patients, an epidural catheter was placed at T4-6 level with 3cm of catheter left in epidural space, before induction of general anaesthesia. After negative aspiration of blood and cerebrospinal fluid, epidural test dose with 3ml of 2% lignocaine added with adrenaline 1:200,000 was administered. No epidural catheter was placed in IVPCA group. Radial artery was cannulated in all patients, under local anaesthesia before induction of anaesthesia.

Anaesthesia was induced with fentanyl 2µg/kg, propofol 2-2.5mg/kg and intubation was facilitated using vecuronium 0.1mg/kg. Anaesthesia was maintained with isoflurane and oxygen. All patients received continuous intravenous infusion of fentanyl 1μg/kg/h intraoperatively along with fentanyl 0.5µg/kg and vecuronium 0.02mg/kg top-ups as and when required. Intraoperative fentanyl infusion was continued up to the patient transfer to postanaesthesia care unit (PACU). No drug was administered through epidural catheter intraoperatively. Intraoperative monitoring included ECG, arterial blood pressure, pulse oximetry, end-tidal carbon dioxide (EtCO₂), end-tidal isoflurane concentration and serial arterial blood gas (ABG) analysis. After completion of surgery, neuromuscular blockade was reversed and trachea was extubated in the operating room and all patients were shifted to the PACU, where they were observed for 24h. All patients in the PACU received humidified O₂ via face mask at FiO₂ 0.4 and were nursed in 30° head-up position.

Patients in PCEA group received mixture of fentanyl 5µg/ml along with bupivacaine 0.125% (i.e. 1.25mg/ml), and patients in IVPCA group received morphine 1mg/ml solution through PCA pump. PCA pump was programmed to deliver 2ml bolus with a lockout interval of 10min in both the groups. No background infusion was used in either group. Rescue analgesia was administered with intravenous fentanyl 0.5µg/kg in both groups whenever the VAS score was >30 at rest despite three consecutive PCA boluses.

Measurements

Preoperative baseline variables, i.e. respiratory rate, heart rate, blood pressure, arterial blood gas, peak expiratory flow rate (PEFR) and forced expiratory vital capacity (FVC) were recorded for each patient. These parameters along with analgesia, sedation, and side effects such as nausea/vomiting, pruritis, hypotension, respiratory depression and desaturation were recorded in the PACU at 0, 2, 8, 12 and 24h. Hypotension was defined as a drop of systolic blood pressure of more than 20% of preoperative value or 2 [13] Sedation was evaluated by a 5-point scoring system: 0 - aware, 1 - drowsy, 2 - asleep/easily respond to verbal command, 3 - asleep/difficulty responding to verbal command and 4 - asleep/no response to verbal command. [14] Spirometry was standardized with each patient in 30° head-up position. At each assessment, spirometry was performed three times, and the best measurement was recorded. All blood samples for ABG analysis were collected from the radial artery cannula.

The primary outcome of the study was the percentage of patients with analgesia failure defined as VAS>30 despite three consecutive PCA boluses.

The other secondary outcomes evaluated were: frequency of rescue analgesia, sec FVC.

Statistical analysis
To determine the number of patients required in each group, a pilot study was conducted with 20 patients (10 in each group). The result of the study suggested the incidence of patient having analgesia failure (VAS>30 at rest in spite of PCA boluses) requiring rescue analgesia was 80% (8/10) in IVPCA group compared to 20% (2/10) in PCEA group (60% reduction in PCEA group). A reduction in the incidence of analgesic failure from 80 to 30% was considered as clinically meaningful reduction justifying comparison of two groups. On the hypothesis, i.e. to detect a difference from 80 to 30% in incidence of analgesic failure, with one-tailed significance level as 5% (α=0.05) and β of 0.2 (power 80%), a sample size of 15 patients was required in each group with Yates continuity correction applied. Sample size was calculated using test of proportions. [15] The sample size calculations were performed on Statistica for Windows software. Thirty-four patients were included in the study for possible dropouts.

Demographic variables, i.e. age, weight, height and duration of surgery, were compared using unpaired Student’s 't' test. Male-to-female ratio and ASA status and other categorical variables were compared using χ2 test. Pain scores, sedation scores, heart rate, respiratory rate, systolic blood pressure, PaO 2 and PaCO 2 at different time intervals as well as frequency of analgesia failure were compared using Mann-Whitney U test. SPSS version 11.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. Postoperative FVC and PEFR at different time intervals were compared with a preoperative baseline values within group using paired t-test. P-value P >0.05). Total mean morphine consumed postoperatively in IVPCA group was 30.09±6.22mg (95% CI: 27.4-33.6) and total mean fentanyl consumed postoperatively in PCEA group was 274.18±104.58μg (95% CI: 211.7-313.0).

The number of patients with analgesic failure was significantly less in PCEA group (five patients) as compared to IVPCA group (12 patients) (P P P =0.002, Mann-Whitney test).

Patients in the IVPCA group were significantly more sedated than those in PCEA group at 8, 12 and 24h assessment time during the study period [Table 3]. However, none of the patients in either group were deeply sedated (sedation score>3) during the study period.

Respiratory rate, heart rate, systolic blood pressure, PaO 2 and PaCO 2 were comparable between the groups during the study period. None of the patients had hypotension during the study period. Oxygenation was satisfactory (PaO 2 >90mmHg) in all patients during the study period. None of the patients had respiratory depression in either group.

Postoperative PEFR and FVC were reduced as compared to baseline values in both the groups at all time intervals; however, statistically significant reduction was observed only in the IVPCA group [Figure 1], [Figure 2].

Incidence of side effects, i.e. nausea/vomiting and pruritis were significantly higher in the IVPCA group. Nausea and vomiting were experienced by 80% patients in IVPCA group and 33% in PCEA group (P =0.01; Chi-square test). Pruritis was experienced by 53% patients in IVPCA group versus 20% patients in PCEA group (P =0.04; Chi-square test).

### Discussion

The present study showed that number of patients with analgesic failure was significantly less in PCEA group compared to IVPCA group. Patients with PCEA using fentanyl and bupivacaine had significantly lower incidence of analgesic failure (80% vs 20%), reflecting greater analgesic efficacy and clinically meaningful reduction in rescue analgesia requirement. No significant difference in demographic variables, including age, weight, height and duration of surgery, was observed between the groups. However, patients in the IVPCA group were significantly more sedated than those in PCEA group at 8, 12 and 24h assessment time during the study period. None of the patients in either group were deeply sedated (sedation score>3). Respiratory rate, heart rate, systolic blood pressure, PaO 2 and PaCO 2 were comparable between the groups during the study period. Oxygenation was satisfactory (PaO 2 >90mmHg) in all patients during the study period. None of the patients had respiratory depression in either group.

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IVPCA using morphine, following thoracic surgery, had better analgesia both at rest and during coughing with lower incidence of side effects, i.e. sedation, nausea/vomiting and pruritis.

The pain score results are in accordance with other studies comparing PCEA using local anaesthetic and fentanyl with IVPCA morphine for other surgeries such as orthopaedic oncology surgery [9] and open colon surgery. [10] However, our pain score results different form results reported by Concha et al. [11] and Grant et al. [16] who compared PCEA with IVPCA for post-thoracotomy pain. Concha et al. [11] compared intercostal blocks plus IVPCA morphine with bupivacaine plus fentanyl thoracic PCEA. Grant et al. [16] compared lumbar PCEA fentanyl solely (boluses combined with a background continuous infusion of fentanyl) with IVPCA morphine. No significant difference between the groups was reported in relation to pain scores, respiratory parameters and side effects. [11],[16] In contrast to the latter study, we did not use a background epidural infusion as this is controversial. [17] Addition of a basal infusion does not improve patient's ability to sleep or rest comfortably and does not alter scores for pain, fatigue and anxiety. [18] In a sedated patient, delivery of continuous opioid at a basal rate may put the patient at higher risk of respiratory depression. [17] We did not use any loading dose of morphine or epidural drug before starting PCA, as intraoperative IV fentanyl infusion was continued till the patients were shifted to PACU.

In our study, the difference in analgesia was evident both while the patients were at rest and on coughing manoeuvres (dynamic pain relief). Better dynamic pain relief in our study is probably explained by the synergistic action of combination of local anaesthetic and opioid. Epidurally administered opioids produce segmental analgesia [19] and improve the quality and duration of sensory block produced by local anaesthetics, [20] which may explain the better pain relief compared to IVPCA.

FVC and PEFR decreased significantly compared to baseline values, in only IVPCA group. This finding is consistent with some studies in the literature where better postoperative vital capacity has been reported with thoracic epidural anaesthesia as compared to systemic opioids, [2] whereas other studies have found no difference with either technique. [21] A cumulative meta-analysis performed by Ballantyne et al. [22] showed that epidurally injected opioids and local anaesthetics significantly improved pulmonary outcome, but failed to demonstrate any benefit of the various pain therapies on pulmonary function. We did not find any difference between the two groups regarding respiratory function probably because our study lacked statistical power to detect a significant difference. Some values of FVC were superior to preoperative value in group PCEA. The type of surgery (removal of mass effect) might have played a role in this along with adequate pain relief.

One limitation of our study is that we have not followed up patients until their discharge from hospital. However, our study clearly supports the superiority of PCEA vs. IVPCA in the first 24h when post-thoracotomy pain is severe. As this was an open labelled study, a potential for patient and investigator bias exists. However, we considered this unnecessary exposure of IVPCA patients to the risks of a sham epidural unethical.

**Conclusion**

PCEA using fentanyl and bupivacaine provides better pain relief both at rest and during coughing manoeuvres (dynamic pain relief). Better dynamic pain relief in our study is probably explained by the synergistic action of combination of local anaesthetic and opioid. Epidurally administered opioids produce segmental analgesia [19] and improve the quality and duration of sensory block produced by local anaesthetics, [20] which may explain the better pain relief compared to IVPCA.

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