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Comparative Study of Transdermal Patch of Fentanyl with that of Buprenorphine for Postoperative Pain Management in Postthoracotomy Surgery Patients

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Abstract

Background: Pain after thoracotomy is probably the most severe pain experienced by the patient and opioid are one of the most commonly used analgesics for postoperative pain. Hence, the present study was undertaken to compare the efficacy and safety of 25 mcg/hour of fentanyl patch with 20 mcg/hour of buprenorphine patch for postoperative pain management in postthoracotomy patients. *Methods:* Total sixty patients of ASA Grade I, II and III, age between 20 and 60 years, who have undergone thoracotomy surgeries were enrolled in the study and randomly divided into two groups of 30 patients each. Group A received 25 mcg/hour of fentanyl patch and Group B received 20 mcg/ hour of buprenorphine patch immediately after patient was received in critical care unit postsurgery. Patients were followed for three days. *Results:* Demographic profile and baseline characteristics were comparable between two groups. Group A had significantly higher level of mean VAS score as compared to Group B at Day 2 and 3. In the same follow up period, both the groups were comparable in regards to mean level of sedation score and hemodynamic variables (HR, SBP and DBP). In Group A 11 (36.66%) patients and in Group B, 8 (26.66%) patients required single dose of rescue analgesic, (p - value > 0.05). The incidence of nausea and vomiting were 13.33% in Group A and 23.33% in Group B. *Conclusion:* Both the fentanyl and buprenorphine patch are effective and safe in controlling postoperative pain but buprenorphine is better than fentanyl in this respects, as it have longer duration of action and require less rescue analgesic for pain relief.

Keywords: Opioids; Analgesics; Transdermal; Patch; Fentanyl; Buprenorphine; Thoracotomy.

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Introduction

Cardiovascular thoracic surgeries will include thoracotomy or thoracoscopy procedures. Thoracotomy incision will cause impaired pulmonary function and chest pain postoperatively with restricted arm and shoulder movement. This pain originates from pleural and muscular damage, costovertebral joint disruption, intercostal nerve injury during surgery.[1] Thus, postoperative

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pain relief is an essential aspect of critical care management in these patients as it affects the quality of patient recovery and resulting postoperative morbidities. Adequate pain management leads to early mobilization, improves respiratory function and reduces postoperative complications.[2]

At present, various analgesic modalities are available for postthoracotomy pain management including thoracic neuraxial blocks and in dwelling catheters, intercostal nerve blocks, patient controlled analgesia, oral, parenteral and transdermal NSAIDs and parenteral or transdermal opioids. Among these modalities transdermal opioid delivery is advantageous as it avoids the peaks and troughs of intermittent dosage which may lead to various side effects like sedation, nausea, vomiting and respiratory depression.[3]

The fentanyl patch is one of the great commercial successes in transdermal drug delivery. The suitability of this molecule for delivery through skin had been identified in the 1970s, and subsequently, a number of transdermal formulations became available on the market.[4] Buprenorphine is a synthetic opioid analgesic with over twenty-five years of international clinical experience indicating it to be safe and effective in a variety of therapeutic situations for the relief of moderate to severe pain.[5] Hence, the present study was carried out to compare transdermal fentanyl and transdermal buprenorphine for postoperative pain relief.

Materials and Methods

After obtaining approval from Institutional Ethics Committee and informed consent from patients, this prospective randomized study was conducted in 60 patients of ASA Grade I, II and III, having age between 20 and 60 years, weight 40–80 kg and who have undergone thoracotomy surgeries. Patients were divided based on computerized randomization into two groups of 30 patients each. Group A received 25 mcg/hr of fentanyl patch and Group B received 20 mcg/hour of buprenorphine patch immediately after patient received in critical care unit postsurgery. Patients with ASA Grade 4, age < 20 years and > 60 years, known opioid allergy or dependence in the past, skin infection and sensitive skin, patients with impaired pulmonary functions, weight less than 40 kg and more than 80 kg and patients own refusal for participation were excluded from the study. A detailed preanesthetic check-up was done. Patients were taken up for surgery after adequate starvation of 8 hrs. In the operation theatre, intravenous access was established. All noninvasive monitoring was attached including pulse oxymeter, cardioscope; sphygmomanometer. Patients were premedicated with glycopyrrolate 4 μg/kg ondansetron 0.1 mg/kg IV and sedated with midazolam 0.03 mg/kg IV and fentanyl 2 μg/kg IV. After preoxygenation for 5 mins general anesthesia was induced with propofol 2 mg/kg and after ensuring adequate mask ventilation patient was paralyzed with 0.9–1 mg/kg rocuronium and trachea was intubated with portex endotracheal tube of 7.5 mm ID for females and 8.5 mm ID for males. After ensuring correct placement with end tidal CO_2 and proper positioning of the tube positive pressure ventilation was initiated. Anesthesia was maintained with a mixture of 50% O_2 and nitrous oxide mixture and sevoflurane (MAC 1 to 1.2) with 0.3 mg/kg/hr rocuronium infusion. An arterial line was then be secured for invasive arterial blood pressure and heart rate monitoring.

After completion of procedure patient was shifted to critical care unit sedated and paralyzed with assisted ventilation and continuous infusions of the relaxant and other intraoperative drugs required. Patient was put on ventilator, all monitors attached including pulse oximeter, ECG, arterial blood pressure and temperature. After confirming the vital parameters to be normal transdermal opioid patch was applied on clear hair free area of upper arm or chest or back. Along with their routine drugs Inj. Paracetamol TDS and Inj. Tramadol bd was continued for 24 hours postsurgery. As the peak levels of transdermal opioids were attained after 12–24 hours, the analgesia was covered with parenteral NSAIDs and opioids. Patient was gradually weaned over 12 hours and extubated after serial arterial blood gas monitoring and patients response in terms of sensory and motor activity.

After extubation, pain was assessed using visual analog scale whereas sedation scoring was done according to Ramsey Sedation Scale. Continuous hemodynamic monitoring was done. The requirement of rescue analgesics after 24 hours was noted. In case of any side-effects related to the patch, the patch was removed and discontinued. All monitoring and findings were noted for three days postoperatively. In case of any complications were noted and managed accordingly. If not fulfilling the criteria for study, patient was excluded from study.

Statistical Analysis:

The data from both the groups was collected and compared statistically using student *t*-test / Fischer-exact test. Statistically significant differences

between two groups detected by keeping α = 0.05 and power of study 95%.

Observations and Results

Total 60 patients were enrolled in the study, among them 39 (65%) were males and 21 (35%) were females. The demographic profile of the patients and baseline characteristics were comparable between two groups and found no statistically significant difference (p > 0.05) as shown in (Table 1).

Table 1: Demographic profile of the patients and baseline characteristics

Characteristics		Group A	Group B	p - value
Age in years		43.5 ± 10.52	42.73 ± 13.49	0.807
Sex, No. (%)	Male	21 (70%)	18 (60%)	–
	Female	09 (30%)	12 (40%)	–
ASA Grade, No. (%)	I	18 (60%)	17 (56.6%)	–
	II	12 (40%)	13 (43.3%)	–
Heart Rate		87.13 ± 7.46	88.73 ± 8.32	0.436
SBP		126.56 ± 4.87	126.76 ± 8.31	0.909
DBP		82.4 ± 7.07	81.1 ± 7.60	0.495
sPO_2 (%)		98.96 ± 0.96	99 ± 0.98	0.894
VAS		4.4 ± 0.81	4.4 ± 0.81	1
Sedation Score (RSS)		1.96 ± 0.31	1.93 ± 0.25	0.656

Table 2 shows, the mean values of VAS from Day 2 and Day 3 in both groups. Group A had significantly higher level of mean VAS score as compared to Group B during the follow up period. At day 2 and day 3 the difference was highly significant. In Group A, 11 (36.66%) patients and in Group B, 8 (26.66%) patients required single dose of rescue analgesic, The difference in rescue analgesic requirement was not statistically significant (p - value > 0.05).

Table 2: Variation in VAS from day 1 to day 3

Follow-up day	Group A	Group B	p - value
Day 2	1.86 ± 1.16	0.2 ± 0.61	< 0.0001
Day 3	2.2 ± 0.96	0.2 ± .61	< 0.0001

At day 1, 2 and 3, both the groups were comparable in regards to mean level of sedation score, Table 3 and hemodynamic variables (HR, SBP and DBP), Fig. 1. There was no statistically significant difference found between two groups.

The incidence of nausea and vomiting were 13.33% in Group A and 23.33% in Group B. One patient in Group A had itching, (Fig. 2).

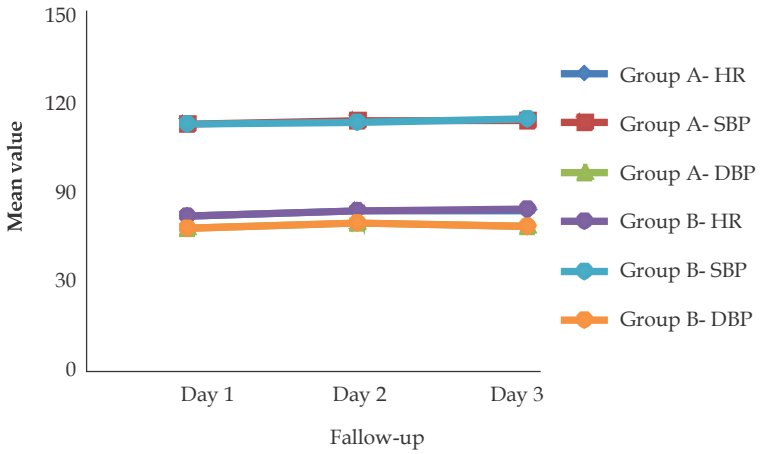

Fig. 1: Comparison of Hemodynamic Parameters between two groups at day 1 to day 3.

Table 3: Variation in Sedation score from day 1 to day 3

Follow-up day	Group A	Group B	*p* - value
Day 1	1.96 ± 0.18	1.96 ± 0.18	1
Day 2	1.96 ± 0.18	2.00 ± 0.00	0.32
Day 3	2.00 ± 0.26	2.00 ± 0.00	1

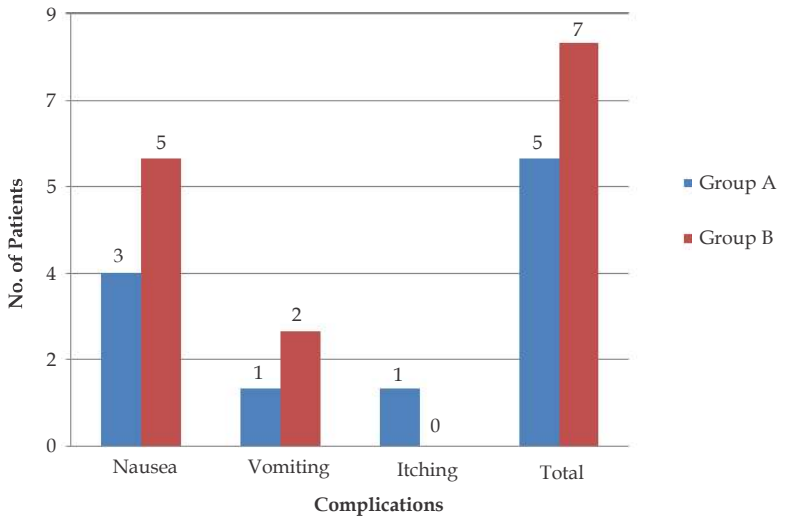

Fig. 2: Complications in both the groups.

Discussion

Thoracotomy is considered the most painful of surgical procedures and providing effective analgesia is the onus for all anesthetists. In postthoracotomy patients analgesia can be administered as boluses or continuous infusion with pharmacokinetic and patient-controlled systems like PCA (Patient Controlled Analgesia),[6] Target Control Infusion (TCI) and a new approach of PMA (Patient Maintained Analgesia). The use of adhesive skin patches (Transdermal Drug Delivery Systems-TDDS) to deliver drugs systemically for postoperative analgesia is a relatively new phenomenon and for that opioids (morphine, fentanyl, pethidine, buprenorphine and tramadol) have been the mainstay of postoperative analgesia.[7]

The first report of fentanyl permeation in human skin samples in the scientific literature appears in the seminal paper by Michaels et al.[8] The suitability of the transdermal route for fentanyl delivery was examined further by Roy and Flynn.[9-11] The first transdermal fentanyl patch was approved by the FDA in the 1990s. Fentanyl patches are designed to deliver fentanyl at four constant rates as 25, 50, 75, and 100 µg/ h^{-1} for a period of 72 h. After initial application, a depot of fentanyl forms in the upper skin layers and serum fentanyl concentrations increase gradually, generally leveling off between 12 and 24 h. The steady-state serum concentration is reached after 24 h and maintained as long as the patch is renewed. However, variations have been found in serum fentanyl concentration during the 72 h period; concentrations tend to be higher in the first 24 h and decrease on the second and third day due to the decreasing concentration gradient between patch and skin. Fentanyl delivery is not affected by local blood supply, but an increase in body temperature up to 40°C can increase absorption rate by about 30%.[7,13]

Similarly, transdermal application of buprenorphine meets all the requirements for successful treatment of chronic pain. Buprenorphine is a partial agonist at the µ receptor and its analgesic efficacy is comparable with the usual doses of other opioids such as pentazocine, morphine and pethidine.[13,14] In India, buprenorphine patches are available in three different strengths as 5, 10, 20 μg/h.[15] Each transdermal patch usually contains 5 mg of buprenorphine in 6.25 cm^2 area releasing 5 µg of buprenorphine per hour over a period of 7 days. Patches with higher strengths have proportionately larger areas. After application, these are usually kept for 7 days. More than one patch may be applied depending on the need, but the total dosage should not exceed 20 μg/h as prescribed by FDA.[16]

In the present study, we compared 25 mcg/hour of fentanyl patch with 20 mcg/hour transdermal buprenorphine patch for postoperative pain relief in postthoracotomy patients. There was no statistically significant difference found between two groups in regards to demographic profile and baseline characteristics as similar to the study done by Arshad et al. [jcdr-9-UC01].

In Group B the VAS score was significantly lowerthan Group A on day 2 and 3. The potency of fentanyl in form of transdermal patch is very good and able to maintain VAS score around 2. As mentioned in previous studies it is comparable. But when compared to the VAS score of buprenorpine patch which is mostly 0, buprenorphine patch 20 mcg/hr seems to be far better. Thus, the result of VAS score in this study suggested that both the patches were effective in controlling postoperative pain but buprenorphine was better in this regard. Fentanyl patch had duration of action of 3 days while buprenorphine patch had duration of action of 7 days. Therefore, buprenorphine provides longer pain relief as compared to fentanyl but the latter is more effective analgesic. In Group A, 11 patients and in Group B, 8 patients were required single dose of rescue analgesic. Further, this finding resolved that buprenorphine patch is better analgesic than fentanyl patch. Arshad et al.[17] reported that fentanyl is better in controlling postoperative pain than buprenorphine, in contrast, it has been observed that in present study the buprenorphine superior than fentanyl, it may be because of double dose of buprenorphine i.e. 20 mcg/hour rather than 10 mcg/hour used in Arshad et al. study.[17]

Sedation scores and hemodynamic variables in both groups were comparable. None of the patient in our study showed excessive sedation or respiratory depression. All patients were calm, comfortable and easily aruosable throughout the study period. The sedation scores were slightly increased in Group B as compared to baseline but in Group A, sedation score were same at day 1, 2, and slightly increased at day three as compared to baseline. Thus, buprenorphine patch provides more sedation than fentanyl patch but this difference was not statistically significant. There are isolated case reports of bradycardia with the use of fentanyl TDS[18] but in current study, we did not found any adverse hemodynamic events in either group.

Nausea and vomiting were main side-effects of the opioid drugs. The incidence of nausea and vomiting were 13.33% in Group A and 23.33% in Group B, this is significantly lower than observed in previous studies.[19,20]

Conclusion

The transdermal fentanyl 25 mcg/h and transdermal buprenorphine 20 mcg/h are safe and effective for postoperative pain relief in postthoracotomy patients but the buprenorphine is better than fentanyl in this respect and can be used for 7 days. However, Fentanyl is more cost-effective and is preferred for postoperative pain management more often but with this study we would like to use buprenorphine patch often however, hope to make it more cost-effective for further studies and clinical use.

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