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Original Research Article

A comparative study between transdermal patches of Buprenorphine and Fentanyl for postoperative pain relief following orthopaedic surgery under regional anaesthesia

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Abstract: Transdermal buprenorphine and fentanyl is commonly used for chronic pain management. Our aim was to evaluate the efficacy of transdermal buprenorphine and fentanyl patch in postoperative acute pain management. All patients were randomized into two groups (n=30 in each group) using a computer generated random number table. Group B: Buprenorphine (10mcg/h) patch and Group F: Fentanyl (25mcg/h) patch. Both group received patch 12hr prior to surgery. Haemodynamic and analgesic effects were compared by using analysis of variance (ANOVA) followed by Turkey's post hoc test. The side effects were compared using the Chi-square test. Hemodynamic changes were not statistically different in both groups. At the end of surgery VAS score of Group A patients was lower as compared to Group B on day 1, 2 and 3 but not statistically significant. Sedation was more in group A patients in comparison to group B. The transdermal buprenorphine patch was as effective as fentanyl patch in attenuating postoperative pain and maintaining hemodynamic stability.
Keywords: Analgesia, Hemodynamic, Patch, Transdermal delivery system

INTRODUCTION

Transdermal drug delivery has several potential advantages over oral and parenteral administration. These include noninvasive dosing, avoidance of the gastrointestinal tract, and lack of first-pass metabolism and maintaining sustained blood level of drug [1]. Steady and continuous drug delivery can avoid potential side effects associated with repeated doses. Additionally, reduced dose frequency allows for convenience and increased compliance [2]. Opioids are commonly used for chronic pain management in different routes [3]. Buprenorphine is a partial agonist with a very high affinity for opioid receptors for which it has got a long duration of action. It has a ceiling analgesic effect and if given in greater than optimum doses, it may actually reduce the analgesic effect and increase side effects [4]. Fentanyl is a pure agonist and is more potent than morphine [5]. It has a more rapid onset of action; however, it has a short duration of action and generally needs to be given by infusion. Fentanyl does not appear to have any active metabolites and is therefore suitable for patients with renal dysfunction, although dose reduction should be considered [6]. For breakthrough or procedural pain, fentanyl maybe administered as a transmucosal lozenge. For chronic pain it can also be administered transdermally as a patch [7]. This study was designed to study the effect of transdermal patches of buprenorphine and fentanyl for postoperative pain relief in terms of duration of analgesic and complication/side effects.

METHODS

A prospective, randomized double blind study was conducted in the Department of Anaesthesiology, S.C.B Medical College, and Cuttack from June 2014 to October 2016. After approval from Institutional ethical committee, informed written consent was obtained from all the patients. A total of sixty (60) cases of ASA I and II physical status, belonging to either sex; between ages

of 20-60 years and body weight of 30-60 kg undergoing elective orthopaedic surgery under regional anaesthesia were included in the study. Patients with hepatic failure, alcohol abuse, opioid abuse, with any neurological impairment like head injury, stroke, epilepsy, psychiatric disease, compromised cardio respiratory function, pregnancy and history of known allergy to the studied drug were excluded from this study.

Pre anaesthetic checkup was done for all patients the day before the surgery. Routine laboratory investigation like hemoglobin concentration, differential leucocyte count, bleeding time & clotting time, fasting blood sugar, serum urea and creatinine, serum sodium & potassium, liver function test and cardiological evaluation was done. Patients were explained about "Visual analogue scale" (VAS) which is a 10 cm scale. 1-Indicating no pain. 2-Probably no pain, 3-Mild discomfort. 4-Mild pain.5-Mild to moderate pain. 6-Moderate pain, 7-Increased moderate pain. 8-Moderate to severe pain, 9-Severe pain. 10-Severe to excruciating pain. All patients received premedication with oral alprazolam 0.5 mg and oral ranitidine 150 mg on the night before the surgery and all were instructed for 6 hours of fasting.

On the day of surgery, when patients were brought into the operation theatre, preoperative vitals like (pulse rate, blood pressure, respiratory rate, temperature) were checked and IV line was secured with 18 G cannula. The patients were randomly allocated into two groups of thirty patients each to receive following Transdermal patch 12hr before surgery to coincide their peak action in post operative period.

GROUP-B: Patients were given Transdermal Buprenorphine patch Dose -10mg (10mcg/hr),GROUP-F: Patients were given Transdermal Fentanyl Dose -5mg(25mcg/hr). Transdermal patch were prepared and marked by numerical by anaesthesiologist who was not involved in observation. All patches were covered. All the patients were given combined spinal and epidural anaesthesia.

Intra operatively heart rate, noninvasive blood pressure, ECG, SPO_2 were monitored at every 15 mins interval. Post operatively degree of pain were assessed by visual analogue score (VAS) at interval of 4hr up to 24hr postoperatively & at intervals of 12hrly up to 72 hrs after surgery (0 hr- immediately after surgery). If VAS score was 5 or more inj. tramadol 100mg im was given as rescue analgesic. Time for first requirement of rescue analgesic and total dose requirement of rescue analgesic in 72 hours period were noted. Other side effects of opioids like nausea & vomiting, sedation, pruritus & respiratory depression were recorded. Sedation was assessed by Ramsey sedation scale. Data collections were carried out by anaesthesiologist who was unaware of the study groups. Results of the data are scrutinized and subjected to statistical analysis. Unpaired student "t" test was used for inter group comparison. "P' value of less than 0.05 was taken as significant & p value less than 0.001 were taken as highly significant.

RESULTS

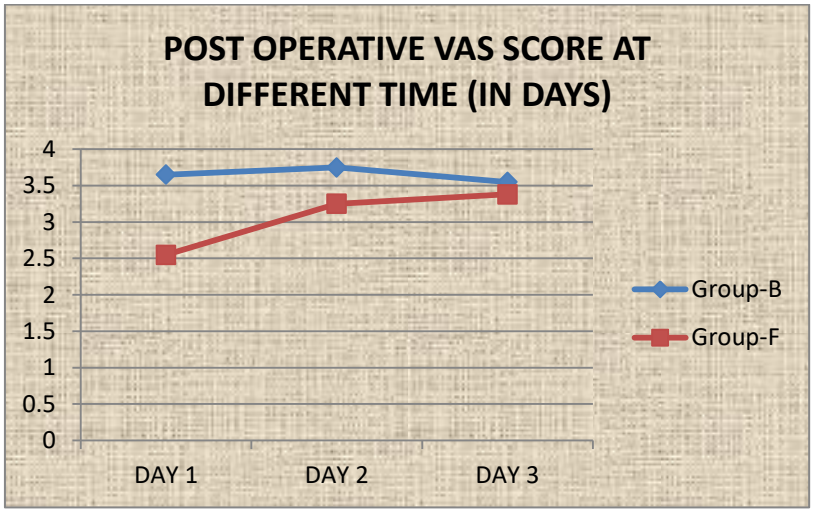
Age, sex and body weight were comparable in both the two groups.

Table-1

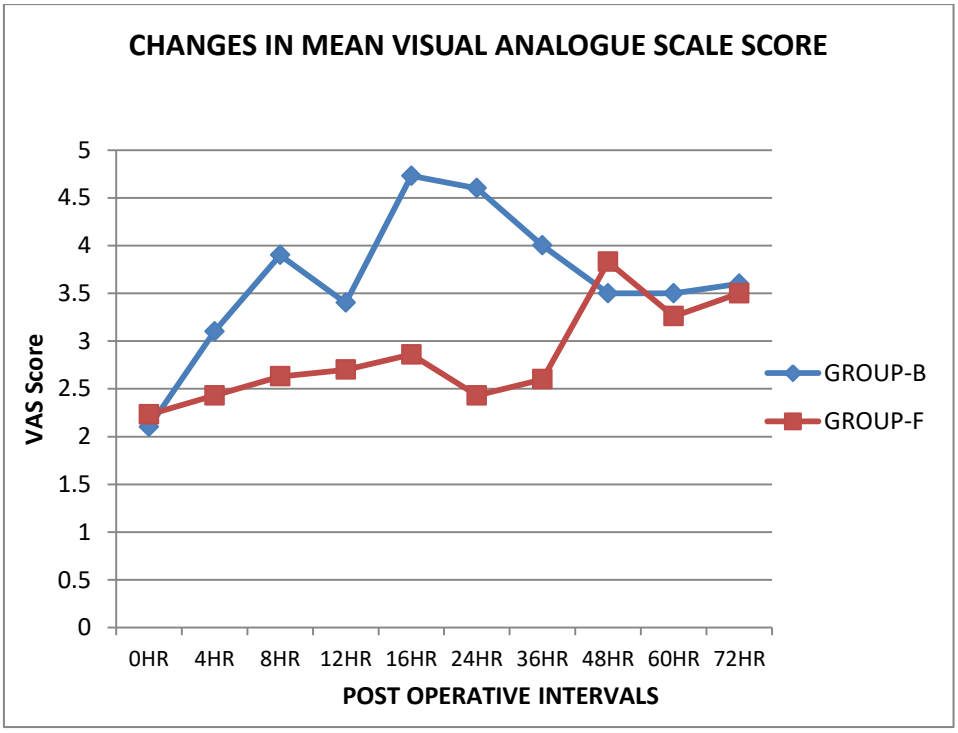
Characteristics	**Group-B Mean ± SD**	**Group-F Mean ± SD**	**P-Value**
Age (years)	39.56±9.5	39.63±10.2	p>0.05
Sex (Male/Female)	20/10	18/12	p>0.05
Weight (kg)	51.06±7.3	48.46±8.1	p>0.05
SBP(mm of Hg)	121.06±11.7	122.2±6.2	p>0.05
Pulse rate(per min)	84.4±6.4	86.2±6.7	p>0.05

Pulse rate and blood pressure are expressed as mean ± standard deviation. There was no significant difference in both parameters among two groups at various intervals during post operatively ($p > 0.05$) (table-1). There was no significant difference in mean VAS score between Group-B & Group-F immediately after surgery (0 hr of surgery) .Then Mean VAS score increased in both the study group but more marked in Group-B than Group-F which was statistically significant. In next 48 hr VAS score in both study group were comparable. Group-F had less VAS score than Group-B, showing better analgesia control and lesser rescue analgesia required but it was not statistically significant.(Graph-1,2)Time of first postoperative analgesic requirement are expressed as mean ± standard deviation. Mean time of first postoperative analgesic

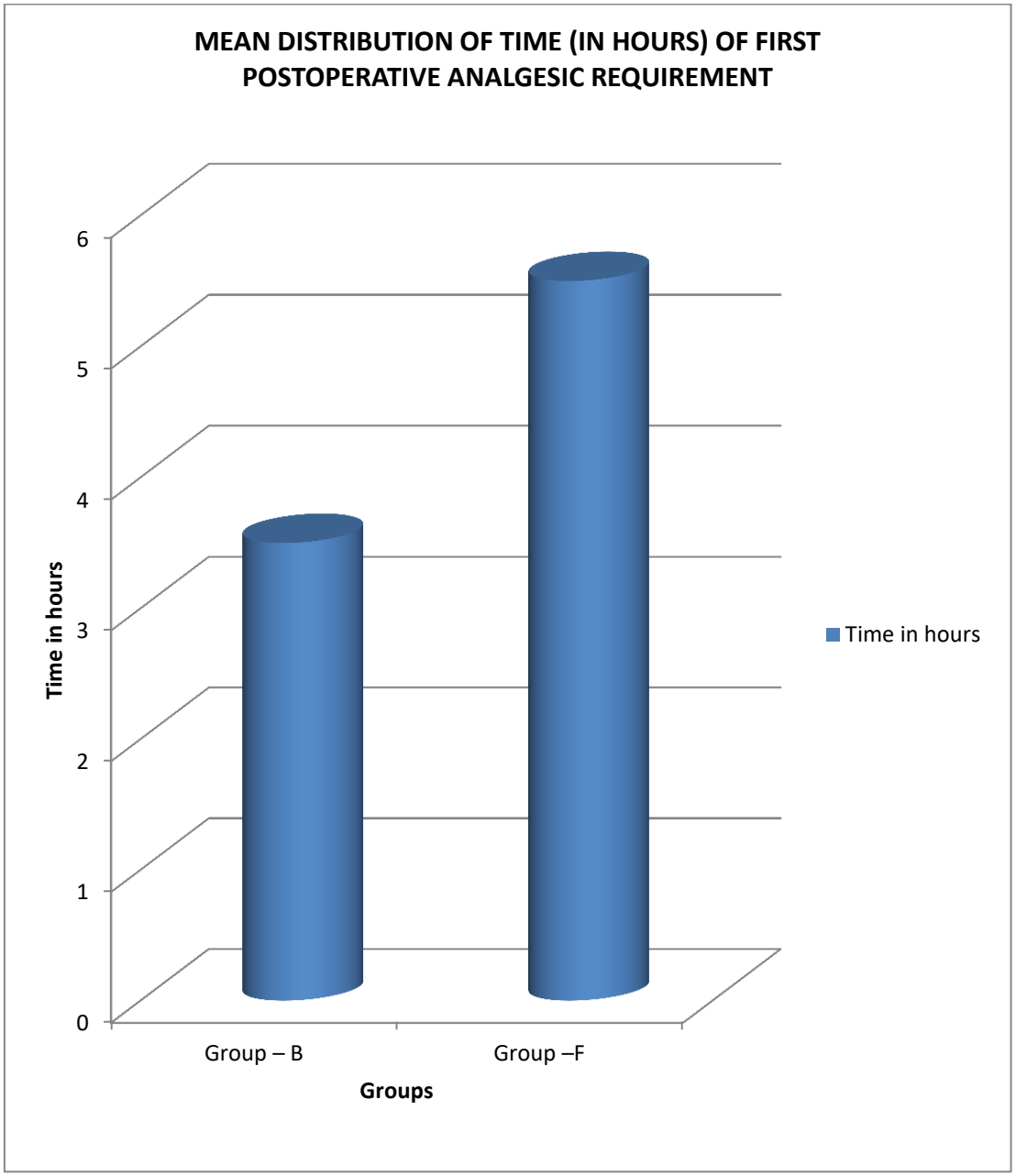
(IM Tramadol) requirement was earlier with group–B, compared to group–F. In Group - F, first rescue analgesic requirement was significantly delayed compared to Group - B ($p < 0.05$).(Graph-3)Sedation score in Group B was significant in comparison to Group F in postoperative period.(Graph-4)Side effects profile like nausea & vomiting ,sedation, G.I discomfort , pruritus, urinary retention & respiratory depression were very not significant in the two groups.



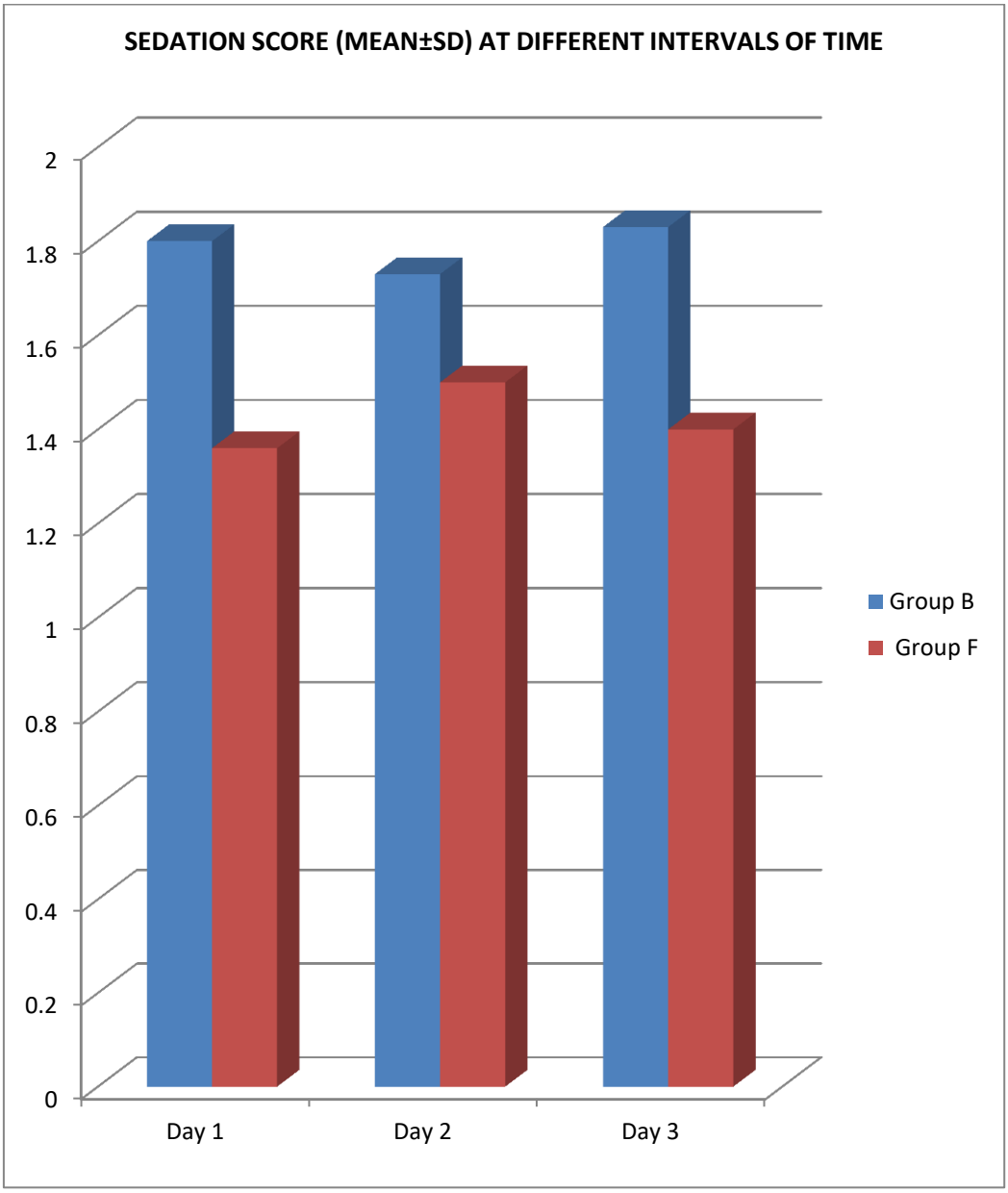
Graph-1(VAS Score-on days)



Graph-2(VAS score-in hours in 1st 24hr)



Graph-3(time of 1st rescue analgesia)



Graph-4(Sedation)

DISCUSSION

Noxious stimuli like surgical incision, produces excitatory changes in central nervous system and sensitize them to subsequent input. Once the sensitization is established, pain response is accentuated and pain is felt following sub noxious stimulation. It has been postulated that if adequate analgesia is given intra-operatively, development of central sensitization is blocked and subsequently post operative analgesia becomes more profound. Patient undergoing elective orthopedic surgery suffers a lot of tissue trauma and intense post-operative pain [8, 9]. Hence pain relief is of utmost importance in these group of patients. Transdermal drug delivery system (TDS) provides safe, convenient and sustained method of drug delivery. It is a preferable alternative to parentral and oral drug delivery methods as it avoids painful skin punctures and multiple dosing. TDS allows sustained delivery of drug to plasma without first pass metabolism. TDS allow continuous drug delivery and sustained plasma levels thereby avoiding peaks and troughs in the plasma levels of the drug. It also decreases the incidence of breakthrough pain by providing sustained pain relief and thereby decreasing the requirement of rescue

analgesics. Due to slow release of drug and avoiding sudden peaks in plasma drug levels, TDS also decreases the incidence of adverse effects associated with drugs [10-13]. However, not all side effects are decreased as shown in some studies that the gastrointestinal side effects associated with oral and transdermal opioids are comparable. TDS are not extensively used to control postoperative pain due to their slower onset (6-24 hours), unpredictable absorption especially during hypothermia as seen in postoperative period, inter patient variability, high cost, availability of limited number of drugs and physician's familiarity with inject able analgesics. Many of the above problems are attenuated by using newer drugs in TDS. Buprenorphine is a semi-synthetic opioid analgesic. It is a partial agonist at the mu opioid receptor. The new buprenorphine TDS appears to be an important new modality for administering analgesia in patients with non-acute pain [14-16]. Fentanyl is a synthetic opioid with potent analgesic activity. Fentanyl has low molecular weight and high lipid solubility therefore it is suitable for delivery via the transdermal therapeutic system (TTS). These systems provide drug at constant rate ranging from 25 to 100 micrograms/hr .At the start of fentanyl TDS treatment, drug first accumulates within skin tissue and then gradually released in systemic circulation which results in a significant delay (12 to 24 hours) before maximum plasma concentration is achieved. Analgesic effect lasts up to three days [17, 18]. In comparison with oral morphine, TDS fentanyl causes fewer gastrointestinal adverse events. High efficacy, tolerability and patient compliance of both buprenorphine and fentanyl make both these two opioid valid therapeutic options for the treatment of postoperative pain in patients following surgery [19]. In our study, no significant difference in pulse rate at various intervals was observed post-operatively in two groups. Systolic blood pressure did not show any significant difference between the two groups at any post-operative intervals the haemodynamic variables in both groups were comparable and did not show any clinically significant deviation from the baseline values. Canneti *et al.;* in his study opined that both transdermal fentanyl and buprenorphine are effective in relieving neuropathic pain in AIDS patients [20]. Kumar *et al.;* in their study concluded that transdermal buprenorphine was effective in relieving postoperative pain after abdominal surgery [21]. In our study there was significant difference in mean VAS score between Group-B & Group-F immediately after surgery . But after that upto 72 hr there was no significant difference in VAS score which was similar to study by Arshad *et al.;* Arshad Z *et al.;* studied Comparison between Transdermal Buprenorphine and Transdermal Fentanyl for Postoperative Pain Relief after Major Abdominal Surgeries .They found VAS score for pain significantly decreased in Fentanyl Group more than Buprenorphine Group from Day 1 to Day 3 [22]. They concluded that both TDS were effective in controlling postoperative pain. However, fentanyl was better in this regard. They found Buprenorphine TDS produces more sedation than Fentanyl TDS. Sedation score were significant between Group-B and Group-F. So use of buprenorphine TDS is as safe and effective as fentanyl TDS in relieving postoperative pain.

CONCLUSION

Both buprenorphine and fentanyl transdermal patch were effective in controlling postoperative pain. However on considering cost-effectiveness, buprenorphine transdermal is better as it is cheaper and can be used for long duration for 7days, but looking at the rescue analgesic requirement and side effect, fentanyl transdermal patch was better than buprenorphine patch.

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