



Research Article

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Comparison of post-operative analgesia with transdermal fentanyl patch and epidural fentanyl in lower limb orthopaedic surgeries: a prospective randomised trial

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Abstract

Background. This study aimed to compare post-operative analgesia with transdermal fentanyl patch and epidural fentanyl in lower limb orthopaedic surgeries. **Methods.** An observational study was conducted in Sir Sunderlal Hospital, Banaras Hindu University. The study included ASA I-II patients diagnosed case of knee osteoarthritis undergoing Total Knee Replacement. Patients undergoing regional anaesthesia were included in the study. For Group A Transdermal fentanyl patch 25mcg/hr was applied 14 hours before the starting of surgery, while patients group B received Epidural fentanyl (diluted with normal saline) through LV-5 pump before the surgery. VAS score, MAP and PSS were compared for the 2 groups. Results were given as mean \pm SD. Data collected were analysed using Student's t-test. Differences were considered statistically significant if P values were <0.05 . **Results.** A total of 60 patients were included and 30 patients each were randomly assigned to one of the 2 groups. There was statistically significant variations present in heart rate, VAS score, MAP and PSS between two groups mainly in 8 and 12 hours postoperative using chi-square test and student t-test. ($p < 0.05$) **Conclusion.** We conclude that it is better to give Epidural fentanyl (diluted with normal saline) through LV-5 pump than transdermal opioid (Fentanyl) in terms of better analgesia, less VAS score, more patient satisfaction and of course lesser side effects.

Keywords: Total Knee Replacement, Fentanyl, Mean Arterial Pressure (MAP), VAS (Visual Analog Score), PSS (Patient Satisfaction Score).

INTRODUCTION

Fentanyl is a phenylpiperidine derivative and synthetic opioid agonist. It is administered clinically as a potent analgesic. Also, it is used as an adjunct to inhalation anaesthetics. Our aim is to compare the postoperative analgesic effect of transdermal fentanyl and epidural fentanyl in lower limb surgeries [1]. Transdermal fentanyl patch is available in various formulation e.g; 25,50,75 & 100 mcg/hr. The peak plasma fentanyl concentration is achieved in 18 hrs that tends to remain stable during presence of patch, followed by decrease in the plasma concentration for several hours after removal of the patch[2]. The transdermal fentanyl patch is to be applied 14 hrs before induction of anaesthesia and left in place which decreases the amount the postoperative analgesia [3]. In addition, opioids are also used as an adjunct to local anaesthetics for postoperative analgesia. In modern orthopaedics surgery minimal pain both intraoperatively and postoperatively along with early mobilization is the aim. It is achieved by use of epidural analgesia technique, in which fentanyl in diluted doses is infused in bolus doses or continuous infusions [4]. Keeping the analgesic effect of fentanyl in different routes we did a prospective, randomized double blinded trial study to evaluate the comparison of analgesic effect of transdermal fentanyl patch and epidural fentanyl in lower limb orthopaedics surgery.

MATERIALS AND METHODS

After obtaining departmental institutional ethics committee approval and informed written consent the study was conducted in 60 subjects .

Study Design: Prospective, randomised clinical trial .

Study Location: Sir Sunderlal Hospital, Institute of Medical Sciences (IMS), Banaras Hindu University (BHU), Varanasi.

Study Duration: academic year 2019-2020.

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Sample size: 60 patients.

Subjects & selection method: Patients were randomly selected, informed written consent was obtained and divided into two groups.

Inclusion criteria

1. Patients of age 30-60 years.
2. American Society of Anaesthesiologist (ASA) grade I and II.
3. Diagnosed case of knee osteoarthritis.
4. Exclusion criteria
5. Patients with Diabetes Mellitus, Cardiac disease, Hypertension
6. Patients with Coagulation abnormalities
7. Patients with Spinal deformities
8. Patient allergic to amide type of local anaesthetics

Procedure methodology:

Patients were divided randomly into two groups:

1. Group(A) -Transdermal fentanyl patch 25mcg/hr
2. Group(B) - Epidural fentanyl (diluted with normal saline) through LV-5 pump.

A night before surgery all patients were premedicated with oral ranitidine 150 mg and alprazolam 0.25 mg which was again done 2 hours before on the morning of surgery. Patients were briefly counselled during the pre-operative evaluation and were properly explained about the kind of study before taking the written consent. In the operation room, a good venous access was secured with 18G cannula to all the patients and were preloaded with 10 ml/kg of Ringer's lactate solution. All the baseline parameters were observed and recorded which included electrocardiography (ECG), heart rate (HR), non-invasive blood pressure (NIBP), pulse oximetry (SpO₂).

In group A transdermal fentanyl patch 25 mcg/hr was applied to the skin 14 hrs before the sub arachnoid block was given.

In group B Lumbar epidural anaesthesia was given using 18G Tuohy needle with patients in the sitting position in L3-L4 interspace and

location of epidural space was confirmed by hanging drop technique. 3 ml of 2% lignocaine with adrenaline was administered into epidural space as a test dose for confirmation and thereafter epidural catheter was secured 4-6 cm into the epidural space which was followed by sub arachnoid block and patients were placed supine. The study solutions were prepared by an anaesthesia technician who was given written instructions and was completely unaware of the study design. Injection with bupivacaine 0.125% and fentanyl 600 mcg (2mcg/ml diluted with bupivacaine and normal saline) total volume 300 ml was infused in continuous infusion through LV-5 pump.

Postoperative analgesia was assessed by VAS (Visual Analog Score) scoring and patient satisfaction score in both the groups.

Statistical Analysis

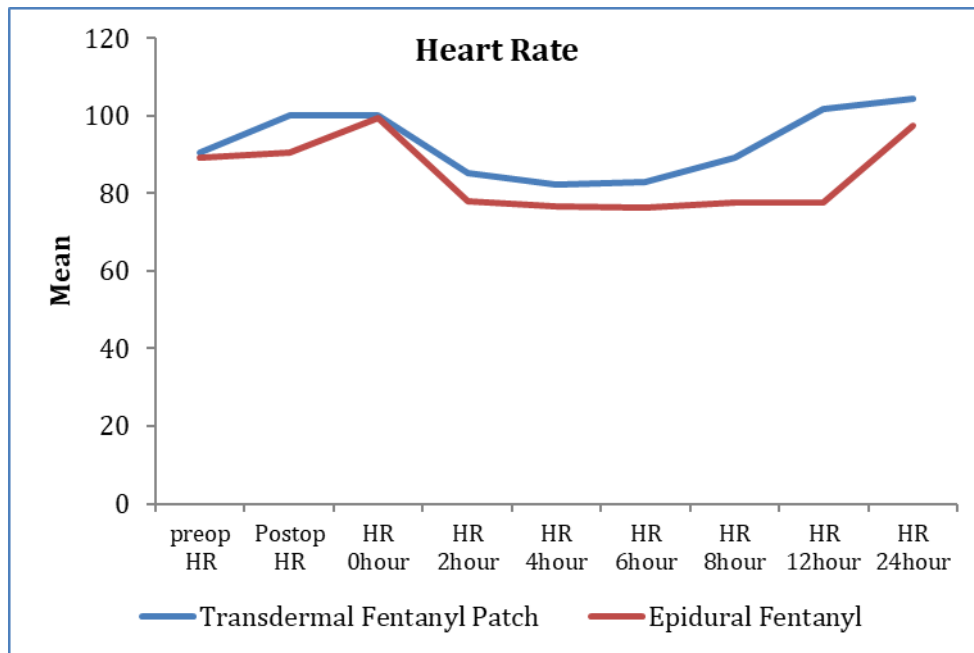
A clinically significant decrease in postoperative pain was noted over period of 24 hours. With a two-sided significance of 0.05, power of study 90% and pooled standard deviation of 0.58, a total of 60 subjects were to be included. We recruited 60 subjects to compensate for lost to follow up cases (5%). Statistical testing was conducted with the statistical package for the social science system SPSS version 21.0. Continuous variables were presented as mean±SD or median (IQR) for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables was performed using paired Student's t-test. Non normally distributed continuous variables were compared using Wilcoxon test. Nominal categorical data was compared using McNemar's Chi-square test. For all statistical tests, a p-value less than 0.05 was taken to indicate a significant difference.

RESULTS

The present study was conducted in Department of Anaesthesiology, IMS, BHU, Varanasi, during the period of March 2018 to May 2019. 60 patients were included in the study with 30 in each group, but 2 patients of group Transdermal Fentanyl Patch dropped out because of the unsatisfactory surgical analgesia by TAP block procedure. Thus data of 58 patients were included in result analysis. The following observations were made.

Table 1: Comparison of heart rate (HR) among two groups

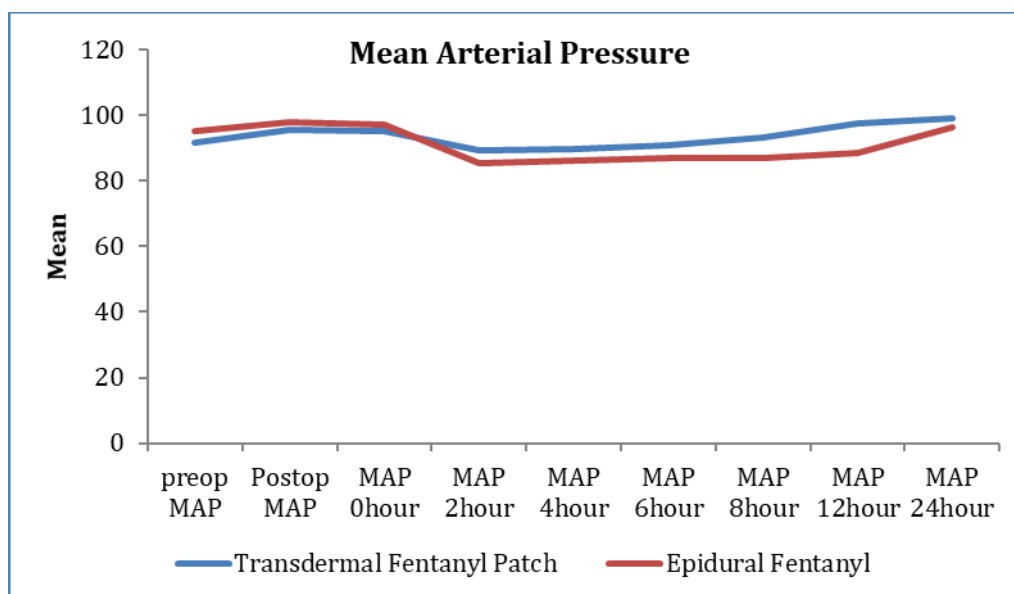
Heart Rate	Group Transdermal Fentanyl Patch Mean±SD N=28	Group Epidural Fentanyl Mean±SD N=30	t-value	p-value
Preop HR	90.53±6.404	89.33±6.789	0.704	0.484
HR 0hour	100.10±10.111	99.37±9.246	0.293	0.770
HR 2hour	85.13±8.609	78.00±13.209	2.478	0.056
HR 4hour	82.30±9.308	76.70±14.561	1.775	0.081
HR 6hour	82.97±9.640	76.23±13.693	2.202	0.052
HR 8hour	89.23±9.576	77.50±15.596	3.512	0.001
HR 12hour	101.77±8.811	77.70±14.245	7.870	<0.001
HR 18hour	102.89±8.856	97.0±7.591	7.113	0.092
HR 24hour	104.30±6.204	97.37±7.476	3.909	0.078



There was statistically significant variations present in heart rate at 8 and 12 hours between two groups using chi square test and student t test. ($p < 0.05$)

Table 2: Comparison of mean arterial pressure (MAP) among study groups

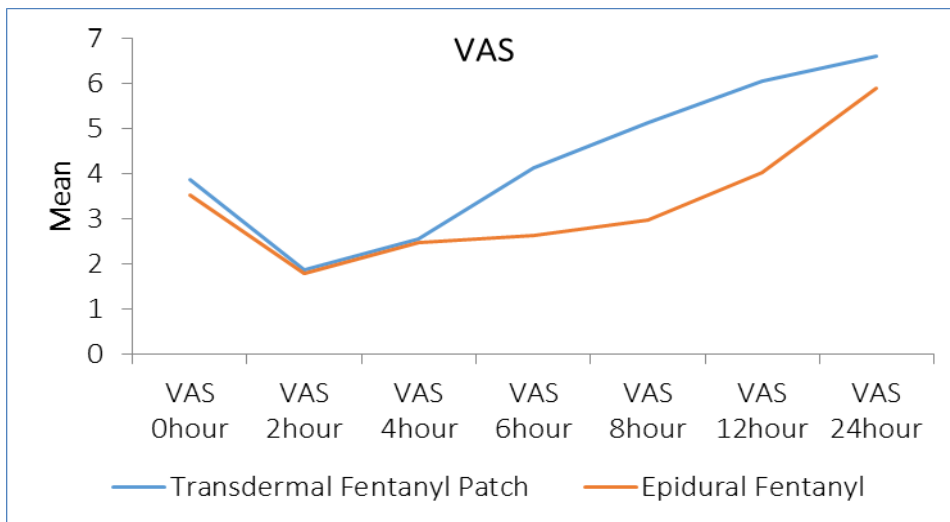
Mean arterial Pressure	Group Transdermal Fentanyl Patch Mean±SD N=28	Group Epidural Fentanyl Mean±SD N=30	t-value	p-value
Preop MAP	91.8556±11.51667	95.3778±12.74349	-1.123	0.266
MAP 0hour	95.0889±10.02599	97.2889±11.70248	-0.782	0.437
MAP 2hour	89.1333±9.40881	85.3778±10.21296	1.481	0.144
MAP 4hour	89.8111±9.36599	86.1556±10.64032	1.412	0.163
MAP 6hour	91.0333±8.90837	87.0889±10.61263	1.559	0.124
MAP 8hour	93.4222±8.60497	87.1111±10.48017	2.549	0.013
MAP 12hour	97.6889±8.78824	88.5556±10.93076	3.567	0.001
MAP 18hour	98.2334±8.94224	96.0022±9.63018	4.760	0.132
MAP 24hour	99.2778±8.99940	96.4889±10.68523	1.093	0.279



There was statistically significant variations present in mean arterial pressure at 8 and 12 hours between two groups using chi square test and student t test. ($p < 0.05$)

Table 3: Comparison of Visual Analog Score (VAS) among study groups

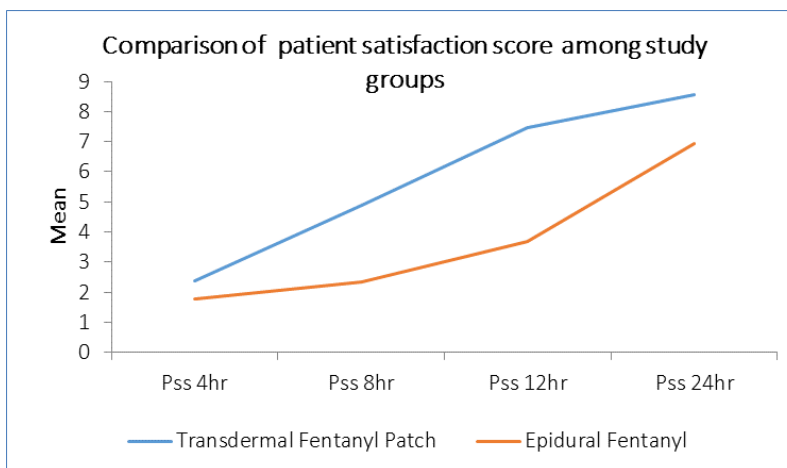
	Group Transdermal Fentanyl Patch Mean±SD N=28	Group Epidural Fentanyl Mean±SD N=30	t-value	p-value
VAS 0hour	3.87±0.973	3.53±0.776	1.467	0.148
VAS 2hour	1.87±1.306	1.80±1.215	0.205	0.839
VAS 4hour	2.57±1.357	2.47±1.196	0.303	0.763
VAS 6hour	4.13±1.252	2.63±0.964	5.199	<0.001
VAS 8hour	5.13±1.167	2.97±1.189	7.126	<0.001
VAS 12hour	6.07±0.740	4.03±1.066	8.582	<0.001
VAS 18hour	6.41±0.728	5.71±1.913	7.981	0.062
VAS 24hour	6.60±0.770	5.90±0.845	3.354	0.781



There was statistically significant variations present in visual analogue score at 6, 8 and 12 hours between two groups using chi square test and student t test. ($p < 0.05$)

Table 4: Comparison of patient satisfaction score (PSS) among study groups

	Group Transdermal Fentanyl Patch Mean±SD N=28	Group Epidural Fentanyl Mean±SD N=30	t-value	p-value
PSS 4hr	2.42±1.691	1.77±1.305	1.528	0.129
PSS 8hr	4.31±2.209	2.33±1.539	5.160	<0.001
PSS 12hr	7.47±1.358	3.67±1.826	9.148	<0.001
PSS 18hr	8.21±1.271	6.71±1.098	7.532	0.071
PSS 24hr	8.57±0.504	6.93±1.112	7.327	0.052



There was statistically significant difference ($p < 0.05$) between two groups in on comparing patient satisfaction score at 8 and 12 hours using chi square test and student t test.

DISCUSSION

The comparative evaluation of epidural and transdermal fentanyl was done. In one group, transdermal fentanyl patch 25mcg/hr was put and in group B epidural fentanyl (diluted with normal saline) through LV-5 pump was given. Datas were analyzed using VAS scoring and patient satisfaction score. Whether or not pain scores given supplemental postoperative analgesia were included, there remains an overall significant difference between the two groups. Patients in the epidural fentanyl group were experiencing significantly less pain than in the transdermal fentanyl group (p less than 0.05). Individual not familiar with the method of pain scoring and concerned about the postoperative recovery of immediately administered analgesics. Plasma concentrations of premedication would be negligible after surgery, and in combination with anaesthetic recovery and the degree of surgical manipulation, all probably contributed to the observed pain scores. The present study found results which may explain the variability in pain score in the early postoperative period. Scott LJ *et al* [5] also recommend that supplemental opioids be given prior to recovery from anaesthesia that have received transdermal fentanyl who have undergone major orthopaedic procedures. The opioid dosage should be adjusted depending on the anaesthetic protocol and the degree of arousal at the time of administration of additional drug. Transdermal fentanyl patches which deliver 25 μg of fentanyl per hour were chosen for this study. Mean pain scores as compared between the epidural fentanyl and transdermal fentanyl groups. Table 1 shows the comparison of heart rate between groups. Table 2 shows the comparison of mean arterial pressure between groups. Table 3 and 4 shows the comparison of VAS score and patient satisfaction score respectively.

Regarding group A, the patches were applied in a uniform manner to the interscapular region. No problems with patch application were noted. From clinical experience, the patches are more conveniently held in place if a six-inch adherent bandage is applied over them. Prior to placing the transdermal fentanyl patch, the site of application should be clipped closely, cleaned, and dried to assure optimal skin adherence. The 25 μg per hour transdermal fentanyl patch yields a maximum serum concentration of 0.9 to 1.8 ng/ml in 24 to 72 hours. The effective analgesic plasma concentration has been reported to be 0.9 to 2.0 ng/ml [6]. However, D.J.R.Duthie [3] *et al* indicates analgesia is achieved with plasma fentanyl concentrations of 0.95 ng/ml. Fentanyl was selected over morphine and other opioid analgesics by nature of its physicochemical properties. Fentanyl is a synthetic opioid analgesic. It is estimated to be 80 to 300 times more potent than morphine [5], depending on species, and has an analgesic therapeutic index approximately four times that of Morphine [7]. Fentanyl has a low molecular weight and is highly lipid soluble. Additionally, fentanyl was found to be non-irritating on direct contact with skin and did not promote long-term hypersensitivity in humans. All of these factors make fentanyl an ideal narcotic for incorporation into a transdermal delivery system. Fentanyl interacts strongly with μ -opioid receptors which are located throughout the central nervous system (CNS). The primary therapeutic effects of fentanyl are sedation and analgesia [8]. In humans, pain tolerance and pain perception are altered; however, pain still may be recognized. Like other narcotics, fentanyl can cause respiratory depression. Approximately 4% of human patients treated for postoperative pain with transdermal fentanyl exhibited respiratory depression; hence, transdermal fentanyl is not recommended currently for control of postoperatively. Although respiratory function was not investigated specifically, no apparent outward clinical signs of respiratory depression were noted in any group. Its cost, variable distribution from skin surface and less efficacy does not make it an excellent option for postoperative pain control. Dose requirements using transdermal fentanyl are difficult to match to individual patients or types of surgery.

While on the other side, epidural infusion rates range from 0.5-2.5 μg kg^{-1} h^{-1} . Epidural bolus opioid supplementation may be used to attain

or maintain good analgesia, especially with the fixed infusion rates [4]. Variability in dose requirements, particularly in the first 24 h after operation, may be associated with differences in anaesthetic technique (e.g., epidural vs. general anaesthesia), intraoperative opioid administration, the magnitude of postoperative pain after different surgical procedures, or all of these [9]. Analgesic Efficacy using continuous epidural fentanyl infusion, PCEA, or both provide an excellent analgesia and overcome the limitations to the duration of action associated with epidural bolus administration. Epidural administration of fentanyl provides a good to excellent postoperative analgesia [10]. Bolus administration produces a rapid onset but short duration of effect. A continuous infusion was therefore more common in the postoperative setting. Compared with transdermal administration, the analgesic efficacy, dose requirement, respiratory and non-respiratory side effects of epidural is good which is indicating an advantage of using epidural rather than transdermal fentanyl patches alone for postoperative analgesia.

CONCLUSION

Since fentanyl is commonly used during many operations, we studied the efficacy of transdermal fentanyl and epidural fentanyl in lower limb surgeries. The analgesic effects of epidural fentanyl were observed to be better than transdermal route. Also epidural route has option of continuous infusion as patient controlled analgesia, can be dose adjusted, less hemodynamic variabilities and good patient satisfaction score. On the other hand its observed that transdermal route is less efficacious in providing analgesia, costly, more visual analog score and less patient satisfaction. Thus the present study concludes that the epidural route of fentanyl administration provides better and more complete analgesia than transdermal fentanyl.

Acknowledgement

At the very outset I would like to pay the homage to founder of Banaras Hindu University, Mahamana Pandit Madan Mohan Malviyaji, who made this glorious temple of training. ideas better and more complete.

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Conflict of Interest

The author has declared no conflict of interest.

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