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Research Article

Postoperative Pain Management in Lower Limb Surgery Patients using Transdermal Buprenorphine and Diclofenac Formulation

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ABSTRACT

Background: The present study was carried out to determine the difference in the effectiveness of buprenorphine and diclofenac transdermal patches in attenuating postoperative pain, following lower limb orthopedic surgeries in a tertiary care teaching hospital in Kerala, South India.

Methods: 88 patients who underwent lower limb orthopedic surgeries under spinal anesthesia were included in this simple randomized single-blind study. Group A received transdermal Buprenorphine 10 mcg/h patch and Group B received transdermal Diclofenac 200 mg patch. Both patches were, applied 30 minutes before spinal anesthesia and the intensity of pain was determined using, Visual Analog Scale (VAS) and Faces Pain Scale (FPS-R). The pain scores at every 4th hour for 24 hours were measured and recorded for all patients. Side-effects and patient satisfaction were checked and evaluated.

Results: 39 patients (44.31%) out of a total of 88 patients required rescue analgesia. Mean and maximum VAS and FPS scores of patients in the Diclofenac group were higher. Adverse effect: Buprenorphine group complained of nausea (22.7%), headache (15.9%), and dizziness (13.6%) while Diclofenac group complained of nausea (18.2%). Majority of patients in both groups expressed their satisfaction with transdermal patch therapy as good (93.18%).

Conclusion: Transdermal Buprenorphine patch was more effective in attenuating postoperative pain than transdermal Diclofenac patch, following lower limb orthopedic surgeries.

Keywords: Orthopedic surgeries; Spinal anesthesia; Transdermal diclofenac patch; Transdermal Buprenorphine patch

INTRODUCTION

The International Association for the Study of Pain (IASP) has defined pain as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage'. Effective pain management facilitates easy recovery from injury or surgery and aids rapid recovery of functions. Surgery results in damage to local tissue with consequent release of prostaglandins, histamine, serotonin, bradykinin, 5-hydroxytryptamine, substance P and leads to the generation of noxious stimuli that are transduced by nociceptors and transmission to the neuraxis by A-delta and C nerve fibers [1].

Patients undergoing surgeries experience acute postoperative pain and less than half report post-operative pain relief [2]. Postoperative pain management is a necessary component of patients undergoing major surgery as the postoperative pain hamper the normal recovery process, cause the extended length of hospital days, patient dissatisfaction, negative perception of hospital performance and increased healthcare utilization costs [3].

Transdermal drug delivery has several potential advantages over oral and parenteral administration as they are noninvasive, avoids gastrointestinal tract, lack the first-pass metabolism and maintain a sustained blood level of the drugs. Steady and continuous drug delivery avoids potential side-effects associated

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with repeated doses [4]. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) exert anti-inflammatory and analgesic effects through the inhibition of prostaglandin synthesis, by blocking the activity of cyclo-oxygenase. The non-selective NSAID diclofenac transdermal patch is a newly introduced Transdermal Delivery System (TDS) that provides continuous and systemic release of diclofenac and is designed to remain at the site of application for 24 hours. Since the oral bioavailability of diclofenac is about 50%, to avoid first-pass metabolism, the transdermal route is an alternative choice [1]. Opioid analgesics are prescribed for moderate to severe pain, especially of visceral origin. The opioid patch is a drug reservoir separated from the skin by a membrane and the drug is released over a specific period of time. Buprenorphine is a semi-synthetic, centrally acting opium alkaloid derived from the baine and belongs to the 6,14-endo-ethano-tetrahydro-oripavine. It is a partial μ-receptor agonist and κ and δ receptor antagonist. After the removal of the patch, plasma concentration is reduced by ~50% in the first 12 hours [4].

This study is designed to find the effect of transdermal patches of buprenorphine and diclofenac for postoperative pain relief in terms of duration of analgesia, side effects, and patient satisfaction.

MATERIALS AND METHODS

This was a Prospective simple randomized single-blind observational Study carried out in the Anesthesia department of a 650 bedded tertiary care hospital over a period of 6 months from December 2017 to May 2018. 88 patients who were scheduled for major lower limb orthopedic surgeries were recruited during the study period out of 119 patients screened. Approval from the Institutional Ethical Committee was obtained (NCP/IEC/2017/No.083).

Inclusion criteria

- Age group: 30-70 years
- Patients posted for major lower limb orthopedic surgeries under subarachnoid

block with ASA-1 or ASA-2 grade

Exclusion criteria

- Special populations
- Pregnant and lactating women
- History of allergy to drugs
- Severe kidney and liver disease
- Patients with neuropathies or nerve injuries
- Patients with pain due to cause other than presenting disease
- Age <30 and >70 years
- ASA ≥ GRADE 3
- Patients on anticoagulants or having hematological abnormalities
- Contraindication for spinal anesthesia: Septicemia, increased ICP, infections, shock

Out of 119 patients screened, 88 completed the study. The 88 patients were divided into two groups by simple randomization. Group A (44 Patients) received buprenorphine transdermal patch before surgery (10 mcg) and Group B (44 Patients) received diclofenac transdermal patch before surgery (200 mg). All patients were pre-medicated orally with Ranitidine 150 mg and Metoclopramide 10 mg. Inj. glycopyrrolate 0.2 mg (anti-muscarinic) was used as Pre-operative medication to reduce gastric secretions, block cardiac vagal inhibitory reflexes during induction of anesthesia. The transdermal patch application was done half an hour prior to the subarachnoid block. A Lumbar puncture was performed at the L3-L4 level through the midline approach using a 25-Gauze Quincke needle with the hole pointing upwards. Sub-arachnoid block was given in a lateral position using 3 ml of 0.5% bupivacaine. Once the patient was shifted to the ICU, postoperative pain assessment following patch application was done every 4 hours for 24 hours using VAS and FPS. Patient satisfaction with the use of transdermal patch and its related side-effects were also evaluated. For breakthrough pain, Inj. Paracetamol 1 g stat was given as rescue analgesia. The source of data includes Patient interview, Patient case sheets, Anesthesia chart, Physician interaction, VAS (visual analog scale), FPS (faces pain scale) and a 4-point patient satisfaction scale.

Visual Analogue Scale (0-10 cm scale)

- 0: No pain
- 2: Mild pain
- 5: Moderate pain
- 6: Severe pain
- 10: Worst pain ever

Faces Pain Scale (Revised-FPS)

- 0- No pain
- 2- Mild, annoying pain
- 4- Nagging, uncomfortable, troublesome pain
- 6- Distressing, miserable pain
- 8- Intense, dreadful, horrible pain
- 10- Worst possible, unbearable, excruciating pain

Patient Satisfaction 4-Point Scale

- Excellent: 75% to 100% pain relief
- Good: 50% to 74% pain relief
- Fair: 25% to 49% pain relief
- Poor: 0% to 24% pain relief

Statistical analysis

The data entry and statistical analysis were done using software SPSS version 17 and results were analyzed statistically using

student's t-test (unpaired). A P-value of less than 0.05 was considered to be statistically significant.

1. Analysis of efficacy using VAS Score was done using SPSS Independent Samples T-Test. Equal variances assumed and obtained a mean difference of -0.37, std. error of 0.12 with -0.61 lower and -0.13 upper confidence interval. There was a difference in the VAS score between buprenorphine and diclofenac transdermal patches, t (86)=3.11, p=0.003.

2. Analysis of efficacy using FPS Score was done using SPSS Independent Samples T-Test. Equal variances assumed and obtained a mean difference of -0.43, std. error of 0.14 with -0.7 lower and -0.15 upper confidence interval. There was a difference in the FPS score between buprenorphine and diclofenac transdermal patches, t (86)=3.08, p=0.003.

3. Analysis of Patient satisfaction was done using SPSS Independent Samples T-Test. Equal variances were assumed and obtained a mean difference of 3.49, std. error of 1.22 with 1.06 lower and 5.92 upper confidence interval. There was a difference in Patient satisfaction between buprenorphine and diclofenac transdermal patches, t (86)=2.85, p=0.005.

RESULTS

Categorization of study population

In the total study population of 88 patients, a higher percentage of patients come under the age range of 61-70 years (62.5%). 54.5% of patients in the buprenorphine group and 70.5% of patients in the diclofenac group were 61-70 years old (Tables 1 and 2).

Age group	Groups		
	Buprenorphine	Diclofenac	Total
30-40	9	3	12
	20.45%	6.80%	13.60%
41-50	4	7	11
	9.15%	15.90%	12.50%
51-60	7	3	10
	15.90%	6.80%	11.40%
61-70	24	31	55
	54.50%	70.50%	62.50%
Total	44	44	88
	100%	100%	100%

Table 1: Categorization of study population based on age range (years).

Diagnosis	Group				Total	
	Buprenorphine	%	Diclofenac	%	Patients	%
Femur fracture	10	22.7	13	29.5	23	26.13%
IT fracture of femur	11	25	7	15.9	18	20.45%
Meniscal tear	3	6.8	7	15.9	10	11.36%
Gardens type 1 fracture	4	9.1	6	13.6	10	11.36%
Gardens type 2 fracture	0	0	2	4.5	2	2.27%
Boyd and griffin type 1 fracture	0	0	3	6.8	3	3.40%
Boyd and griffin type 2 fracture	3	6.8	5	11.4	8	9.09%
Tibial and fibular fracture	3	6.8	1	2.3	4	4.54%
Bimalleolar fracture	6	13.6	0	0	6	6.81%
Calcaneal fracture	2	4.5	0	0	2	2.27%
Patellar ligament tear	1	2.3	0	0	1	1.14%
Implant failure with IT fracture	1	2.3	0	0	1	1.14%

Table 2: Categorization of study population based on diagnosis.

Patients with Femur fractures were the majority (22.7% in buprenorphine group and 29.5% in the diclofenac group) followed by patients with intertrochanteric (IT) fracture of the

femur (25% in the buprenorphine group and 15.9% in the diclofenac group) (Tables 2 and 3).

Type of surgery	Group				Total	
	Buprenorphine	%	Diclofenac	%	Patients	%
DHS	2	4.5	9	20.5	11	13
Total knee replacement	1	2.3	2	4.5	3	3.4
CRIF with PFN	19	43.2	17	38.6	36	40.9
Bipolar hemiarthroplasty	6	13.6	8	18.2	14	15.9
ORIF with DFLP	1	2.3	4	9.1	5	5.68
IM nailing	2	4.5	2	4.5	4	4.54
ORIF with plate and screw	7	15.9	1	2.3	8	9.09
Arthroplasty	0	0	1	2.3	1	1.13
Meniseal balancing and repair	1	2.3	0	0	1	1.13
ORIF with calcaneal recone plate	2	4.5	0	0	2	2.27
Patellar ligament repair	1	2.3	0	0	1	1.13
Implant removal	2	4.5	0	0	2	2.27

Table 3: Categorization of study population based on the type of surgery.

Patients who were scheduled for CRIF with PFN were the majority (Table 4).

Asa grade	Groups		
	Buprenorphine	Diclofenac	Total
1	15	16	31
	34.10%	36.40%	35.25%
2	29	28	57
	65.90%	63.60%	64.75%
Total	44	44	88
	100%	100%	100%

Table 4: Categorization of study population based on ASA grade.

ASA I and II grades were only included and there were more patients from ASA II grade (64.7%) than ASA I grade (35.2%) (Table 5).

Rescue analgesia	Groups		
	Buprenorphine	Diclofenac	Total
Given	19	20	39
	43.20%	45.50%	44.32%
Not given	25	24	49
	56.80%	54.50%	55.68%
Total	44	44	88
	100%	100%	100%

Table 5: Categorization of study population based on rescue analgesia.

39 patients (44.31%) out of a total of 88 patients required rescue analgesia once in the first 24 hours. 19 patients (43.2%) in the buprenorphine group and 20 patients (45.5%) in the diclofenac group required rescue analgesia (Table 6 and Figure 1).

VAS and FPS score comparison

	Mean Vas Score					
	4th hour	8th hour	12th hour	16th hour	20th hour	24th hour
Diclofenac	5.13	3.86	3.63	3.52	3.36	2.72

Bupren orphine	4.81	3.79	3.52	3.04	2.54	2.34

Table 6: Mean VAS score comparison table.

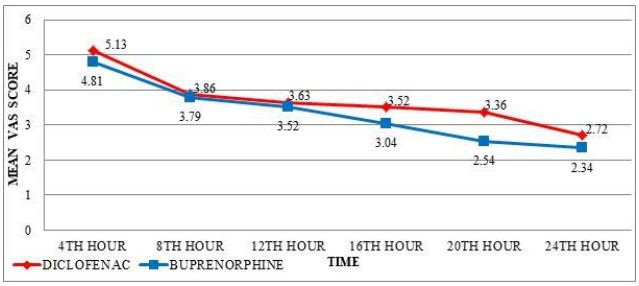

Figure 1: Mean VAS score comparison figure.

From the Mean VAS score comparison, patients in the diclofenac group experienced more pain than patients in the buprenorphine group at all time intervals (Table 7 and Figure 2).

	Mean FPS Score					
	4th hour	8th hour	12th hour	16th hour	20 th hour	24th hour
Diclofe nac	5.51	3.95	3.45	3.31	2.95	2.02
Bupren orphine	5.13	3.72	3.31	2.5	2.04	2

Table 7: Mean FPS score comparison table.

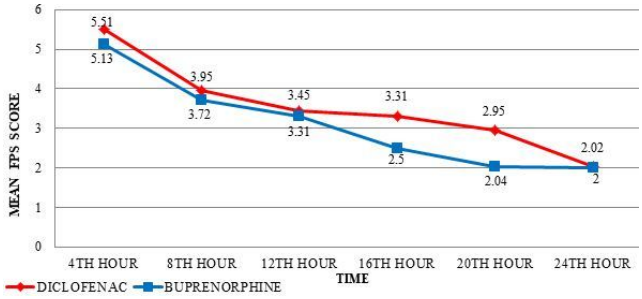

Figure 2: Mean FPS score comparison figure.

From the Mean FPS score comparison, patients in the diclofenac group experienced more pain than patients in the buprenorphine group at all time intervals (Table 8 and Figure 3).

Hour	Max Vas Score	Group			
		Buprenorphine		Diclofenac	
		%	Frequency	%	Frequency
4th	6	15.9	7	34.1	15
8th	5	11.4	5	18.2	8
12th	5	4.5	2	13.6	6
16th	5	-	0	9.1	4
20th	5	-	0	4.5	2
24th	3	34.1	15	72.7	32

Table 8: Maximum VAS score comparison table.

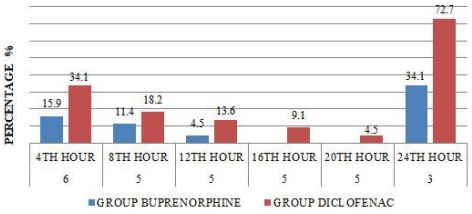

Figure 3: Maximum VAS score comparison figure.

From the maximum VAS score comparison, the maximum VAS score for diclofenac group is higher than buprenorphine group at every 4th hour (Table 9 and Figure 4).

Hour	Max FPS Score	Buprenorphine		Diclofenac	
		%	Frequency	%	Frequency
4th	6	56.8	25	75	33
8th	6	4.5	2	15.9	7
12th	6	-	-	9.1	4
16th	6	-	-	4.5	2
20th	4	2.3	1	47.7	21
24th	2	-	-	2.3	1

Table 9: Maximum FPS score comparison table.

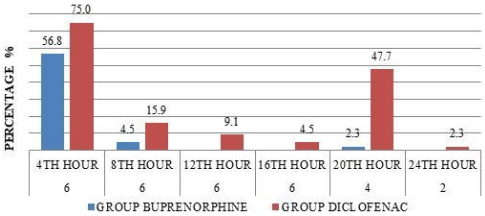

Figure 4: Maximum FPS score comparison figure.

From the maximum FPS score comparison, the maximum FPS score for the diclofenac group is higher than buprenorphine group at every 4th hour.

Analysis of efficacy

Analysis of efficacy using VAS Score: It was done using SPSS Independent Samples T-Test. Equal variances assumed and obtained a mean difference of -0.37, std. error of 0.12 with -0.61 lower and -0.13 upper confidence interval. There was a difference in the VAS score between buprenorphine and diclofenac transdermal patches, t (86)=3.11, p=0.003.

Analysis of efficacy using FPS Score: It was done using SPSS Independent Samples T-Test. Equal variances assumed and obtained a mean difference of -0.43, std. error of 0.14 with -0.7 lower and -0.15 upper confidence interval. There was a difference in the FPS score between buprenorphine and diclofenac transdermal patches, t (86)=3.08, p=0.003 (Figure 5).

Assessment of adverse effects

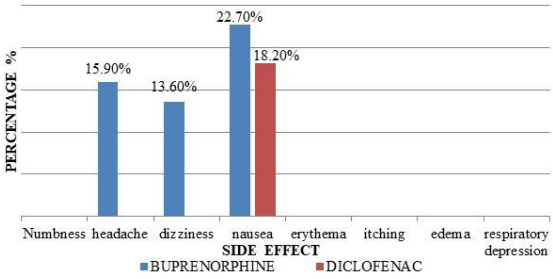

Figure 5: Assessment of adverse effects.

Major adverse effects were not seen in the study. Patients in the buprenorphine group complained of nausea (22.7%), headache (15.9%), and dizziness (13.6%) while patients in the diclofenac group complained of nausea (18.2%), which was managed symptomatically.

Assessment of patient satisfaction

Majority of patients in both groups expressed their satisfaction with transdermal patch therapy as GOOD (93.18%). Analysis of Patient satisfaction was done using SPSS Independent Samples T-Test. Equal variances were assumed and obtained a mean difference of 3.49, std. error of 1.22 with 1.06 lower and 5.92 upper confidence interval. There was a difference in Patient satisfaction between buprenorphine and diclofenac transdermal patches, t (86)=2.85, p=0.005 (Figure 6).

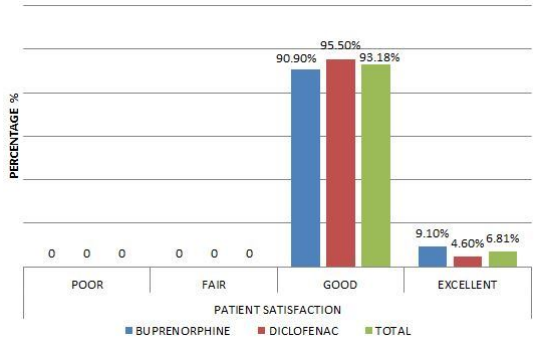

Figure 6: Assessment of patient satisfaction.

DISCUSSION

Patient undergoing elective orthopedic surgery suffers a lot of tissue trauma and intense post-operative pain [5,6]. Hence pain relief is of utmost importance in these groups of patients. Transdermal Drug Delivery System (TDS) provides a safe, convenient and sustained method of drug delivery. Due to the slow release of drug and avoiding sudden peaks in plasma drug levels, TDS also decreases the incidence of adverse effects associated with drugs [7,8].

In our study, the mean age of group buprenorphine and group diclofenac was 56 years (± 13.95) and 60 years (± 11.34) respectively and most of the patients were in 61-70 age group. Patient demographic details were comparable in both groups. Similar patient demographic details were seen in a study conducted by Desai et al. [9], where the average age in transdermal buprenorphine group was 59.9 (± 12.8) and in oral tramadol group was 63.7 (± 14.4) years and where about 6 in 10 subjects were females [10].

Studies using transdermal diclofenac patch were found to reduce the severity of postoperative pain in patients. There are very few studies using transdermal buprenorphine for postoperative analgesia. In the present study, the average pain score using VAS and FPS-R at 4^{th}, 8^{th}, 12^{th}, 16^{th}, 20^{th} and 24^{th} hours was significantly higher in the diclofenac group than buprenorphine group ($P<0.05$). Therefore, Buprenorphine transdermal patch is more effective in controlling postoperative pain than diclofenac transdermal patch.

In two separate descriptive studies, noted satisfactory analgesia 24 hours after the surgery in almost 75% of patients [11]. They concluded that transdermal buprenorphine can be used safely for providing effective postoperative analgesia with a high satisfaction rating by the patients. Desai et al. in their study concluded that TDB is a safe and feasible approach to moderate post-operative pain management [9]. Phalgune et al. conducted a study which also concluded that buprenorphine was more effective than tramadol for postoperative analgesia in laparotomy cases [12]. Safinaz et al. showed that diclofenac patch and intramuscular injection were equally effective in the prevention of postoperative pain after laparoscopic surgery under general anesthesia and that transdermal diclofenac patch was superior to intramuscular diclofenac injection for patient tolerance [13].

Major adverse effects were not seen in the study. However, Patients in the buprenorphine group complained of nausea (22.7%), headache (15.9%), and dizziness (13.6%) while patients in the diclofenac group complained of nausea (18.2%). Desai et al. noted a very low incidence of side effects, particularly PONV with transdermal buprenorphine [9].

93.18% of the total of 88 patients in both the groups reacted that the transdermal patch therapy was good and the patient satisfaction for transdermal patches of buprenorphine was 3.4% more than diclofenac. In similar results were seen where 15 patients in group Buprenorphine and 18 patients in group Diclofenac reported good satisfaction towards the transdermal patch therapy [14].

In the search for a new long-acting and strong analgesic, buprenorphine in this study proved to be superior to diclofenac in the control of postoperative pain. The present research substantiates the findings of these studies.

CONCLUSION

VAS and FPS scores for the diclofenac transdermal patch were greater and there was a 3.4% increase in patient satisfaction for the buprenorphine transdermal patch. Hence, Buprenorphine transdermal patch is more effective in controlling postoperative pain than diclofenac transdermal patch. Major adverse effects were not seen in the study. However, headache, dizziness, and nausea were seen in some patients, which were managed symptomatically.

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