

Research Article

Comparison of single dose transdermal patches of diclofenac and ketoprofen for postoperative analgesia in lower limb orthopaedic surgery

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ABSTRACT

Background: Transdermal patch is a very simple and painless method for providing postoperative analgesia. The aim of the study was to compare the efficacy and safety of transdermal patch of ketoprofen in comparison to diclofenac patch for postoperative analgesia. It is a randomized single blind study.

Methods: Sixty patients were randomly allocated to receive either ketoprofen or diclofenac patch at the end of surgery under spinal anaesthesia. Statistical analyses used, data were analyzed using statistical package for social sciences version 15.0.

Results: In diclofenac group the post-operative VAS was 2.4 ± 0.72 and in ketoprofen group, post-operative VAS was 1.4 ± 0.3 which was significantly low when compared to group D ($p < 0.05$ value). 11 patients in group D and 3 patients in group K required rescue analgesia (Inj. tramadol) in the first 24 hours which was statically significant ($p < 0.05$).

Conclusions: Both ketoprofen and diclofenac transdermal patch are effective for postoperative analgesia but less number of patients required rescue analgesic in ketoprofen group.

Keywords: Pain, Transdermal patch, Ketoprofen, Diclofenac

INTRODUCTION

Post-operative pain after any type of surgery can have very detrimental effects and if appropriate analgesia is not provided, it can affect respiratory, cardiovascular, gastrointestinal, urinary, and endo-crinological systems as well as have chronic effects like delayed recovery and chronic pain.¹ Most commonly used drugs for postoperative analgesia are NSAIDs worldwide. They can be used orally, intravenously (i.v.), intramuscularly (i.m.) and as transdermal patches. Transdermal delivery drug system avoids the pain associated with i.v. and i.m. routes and is an option for patients who don't tolerate the oral drug especially in postoperative period. Also topical NSAIDs have a reduced risk of upper gastrointestinal

complications such as gastric and peptic ulcers, and dyspepsia because of low systemic concentrations.² In this study we had compared transdermal diclofenac patch with ketoprofen patch for postoperative analgesia. The primary end point is VAS score and total requirement of rescue analgesic first 24 hours of surgery. The secondary end points are time to rescue analgesic and adverse effects like nausea and vomiting.

METHODS

The study was conducted in a tertiary care centre with the approval of ethical committee of the institution. A written and informed consent was obtained from all patients. Patients included for the study were all ASA physical

status I or II, of either sex (18-50 years) presenting for lower limb surgery. Patients who had contraindications to spinal anaesthesia, allergy to drug, patients of heart block and patients with clinical features or a history of renal pathology, bronchial asthma, active peptic ulceration, or any other allergic reactions induced by aspirin or other NSAIDs, were excluded. All patients received a tablet of diazepam 0.2mg/kg orally the night before surgery. On the day of the surgery, an 18-gauge intravenous line was secured and routine monitors were attached to the patients in operation theatre. Both groups did not receive any intravenous analgesics or sedatives during the surgery. On arrival in the operating room, patients were preloaded with Lactated Ringer's solution @15ml/kg. All patients were monitored with automated non invasive blood pressure (NIBP), pulse oximetry, an electrocardiogram. All participants were administered subarachnoid block in the sitting, using 0.5% hyperbaric bupivacaine (2.5 ml) and fentanyl 50µg using a 23- or 25-gauge Quincke's needle to obtain a sensory level block of T6-T8. The 60 participants in the study were randomly allocated into two groups of 30, using a computer-generated randomisation table. The diclofenac (D) group received a single dose of a transdermal diclofenac patch 100 mg (Nupatch from Zydus Cadilla 100 mg per 50 cm²), and the ketoprofen (K) group received a single dose of transdermal ketoprofen patch 20 mg (ketoplast patch from zuventus 20 mg per 70 cm²). All the patients were blind about the study drug used but the patches come in different size so it was difficult to keep the observer blind in this study. Pain was assessed postoperatively at the end of surgery (0 hr), 1, 2, 4, 8, 12, 16, 20 and 24 hours using a VAS. At any time during the study, if the VAS was more than, or equal to, four, then an injection of tramadol 100 mg was administered intravenously as rescue analgesia and the time at which rescue analgesia was given was noted. The total consumption of rescue analgesic in first 24 hours was reported.

Statistics

The sample size was calculated using the principal variable, the visual analogue scale (VAS) scores for postoperative pain, and considering a difference of 2 cm as clinically significant (estimated mean standard deviation 1.5-2.5 cm). The total sample size was calculated as 60 with a type I error of 0.05, and a statistical power of 90%. Statistical analysis was done by SPSS15.0. Parametric data were reported as arithmetic mean±standard deviation and analysed by using student unpaired t test. Continuous covariates were compared using analysis of variance ANOVA. The comparison was studied using chi-squared test or the Fisher's exact test as appropriate, with the p value reported at the 95% confidence interval. p<0.05 was considered statistical significant.

RESULTS

We have included total 60 patients in this study (30 in each group). The demographic profile of both groups was

comparable (Table 1). The average age of patients in group D was 41.27±5.64 years and 40.4±4.74 years in group K. The duration of surgery in group D was 129.8±19.9 min and 133.5±20.4 min (p>0.05). In group D the post operative VAS was 2.4±0.72 and in group K, post operative VAS was 1.4±0.3 which was significantly low when compared to group D (p<0.05 value). We observed that 11 patients in group D and 3 patients in group K required rescue analgesia (Inj. Tramadol) in the first 24 hours which was statically significant (p<0.05). The dose required for rescue analgesia in group D was 36.7±49 mg and group K was 10±30.5 mg which was also statically significant. The time to rescue analgesia was comparable in both groups (Table 2). We did not observed any significant allergic reaction to any of the drug patches but 8 (26.7%) patients in group D and 6 (20%) patients in group K (p>0.05) experienced nausea/vomiting which was managed symptomatically.

Table 1: Demographic profile.

	Group D (n=30)	Group K (n=30)	P value
Age (years)	44.4±8.3	42.6±8.0	0.4
Sex (M:F)	18:12	22:8	0.4
Height (cms)	151.5±5.1	149.5±6.0	0.15
ASA I:II	22:8	26:4	0.33
Duration of surgery (in min)	129.8±19.9	133.5±20.4	0.5

Table 2: Showing clinical particulars.

	Group D (n=30)	Group K (n=30)	p value
Postoperative VAS score	2.4±0.72	1.4±0.3	0.002
No. of patient who required rescue analgesic in first 24 hours	11	3	0.03
Total requirement of rescue analgesic in first 24 hours (mg)	100	100	-
Time to rescue analgesic (min.)	114±24	103±21	>0.5

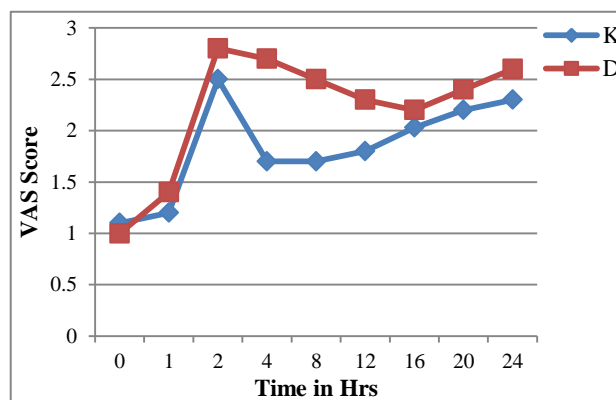


Figure 1: Showing VAS score.

DISCUSSION

Transdermal drug delivery system is a very good method of pain management in postoperative period as it avoids the first pass metabolism and gastrointestinal complications associated with oral route and pain associated with i.m. or i.v. route. The drug contained in the transdermal patch enters the body through skin and then diffuses into capillaries for systemic delivery. The steady permeation of drug across the skin allows for consistent and uniform serum drug levels.^{3,4} NSAIDs are the commonly used drug for postoperative analgesia. Diclofenac patch is being used for postoperative analgesia very commonly and it has been observed that diclofenac patch in comparison with standard analgesic regimen reduces analgesic requirement as well as result in early hospital discharge.⁵ The efficacy and tolerability of diclofenac patch in comparison to its other various formulations for postoperative analgesia has been observed. Funk L et al observed that transdermal diclofenac patches provides significantly better pain relief as compared to diclofenac tablets in the early postoperative period following arthroscopic shoulder surgery.⁶ Krishnan R et al also observed that intra-operative application of a single dose of 100 mg transdermal diclofenac patch is as effective as a single dose of intramuscular diclofenac (75 mg).⁷ In their study they observed that three patients had gastritis and two patients had pain at injection site out of 30 patients in patients receiving intramuscular diclofenac group while with patch two patients developed erythema at the site where the patch was applied.

Ketoprofen, (RS) 2-(3-benzoylphenyl)-propionic acid, is one of the propionic acid class of NSAIDs and has analgesic and antipyretic effects. Ketoprofen in oral, i.v., i.m. preparations has been used by various authors for postoperative analgesia and they observed that ketoprofen is an effective analgesic for moderate to severe acute postoperative pain.⁸⁻¹⁰ In a study done by Velásquez GC et al where they evaluate the pre-emptive analgesic of intramuscular ketoprofen (100 mg) with i.m. diclofenac (75 mg) after mandibular third molar surgery observed that patients with ketoprofen had lower pain intensity scores as compared to diclofenac group.¹¹ Sarzi-Puttini P et al also observed in their meta analyses that orally administered ketoprofen (50-200 mg/day) relieves moderate to severe pain and improves functional status and general condition more better than of diclofenac (75-150 mg/day).¹²

Ketoprofen transdermal patches in various doses have been found to be more effective than placebo in both traumatic and non traumatic pain without any additional side effects.^{13,14} As till date there is no study which has evaluated the role of ketoprofen patch for postoperative analgesia. So in this study we have assessed the efficacy of ketoprofen patch for postoperative analgesia and compared it with diclofenac patch. Although the usual dose of ketoprofen used in various studies through

various routes varied from 20 to 150 mg for post operative analgesia and we could not find any study suggesting transdermal dose for ketoprofen, we used commercially available 20 mg ketoprofen patch. When we compared this dose of ketoprofen with 100 mg diclofenac patch, we found this to be better.

In our study we have observed that VAS score remained significantly low in ketoprofen group and only 3 patients in ketoprofen group required rescue analgesia in the first 24 hours but in diclofenac 11 patients required rescue analgesia but none of the patient in any group required another dose of rescue analgesic in first 24 hours.

CONCLUSION

To conclude, transdermal patch of ketoprofen and diclofenac both are effective for postoperative analgesia in lower limb orthopaedic surgery under spinal anaesthesia but in diclofenac group more patients required rescue analgesic as compared to ketoprofen group. Furthermore studies are required to prove its efficacy and safety in various other types of surgeries.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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