

Comparative Evaluation of Diclofenac and Ketorolac Transdermal Patch for Pain Management Post Periodontal Surgical Procedure-A Clinical Trial

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ABSTRACT

Background: Transdermal delivery offers several benefits over oral delivery, including smooth, continuous drug delivery, increased bioavailability, and reduced drug-drug interactions. Patches can be easily applied by the caregiver, and they provide a visual cue that the medication has been administered.

Aim: To evaluate analgesic efficacy of the ketorolac vs. diclofenac dermal patch post periodontal surgical procedures.

Material and methods: Sample size (30) was calculated using G-power with the power set at 95%. All included individuals were randomly divided into 2 study groups. Group 1 received diclofenac and group 2 received a ketorolac transdermal patch. The patch was applied immediately after the periodontal flap surgery. Number of rescue medicine and VAS scores for all the individuals was recorded at 3 hours and 6 hours post operatively.

Results: Diclofenac transdermal patch was found to be more effective in pain relief than that of the ketorolac patch. Number of rescue medicines consumed by the individuals in the ketorolac patch was significantly higher than that of the diclofenac group. No sex predilection was seen in any of the results.

Conclusion: Diclofenac transdermal patch proved to be much better for pain management post periodontal surgical therapy.

Key words: Diclofenac, Ketorolac, Periodontal surgical procedure transdermal patch

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INTRODUCTION

The aims and objectives of the present study was to compare and evaluate the analgesic efficacy of diclofenac transdermal patch and ketorolac transdermal patch during postoperative period in patient undergoing quadrant periodontal flap surgery and to compare and evaluate the patient compliance, tolerance, and adverse reaction following the use of NuPatch® and oral diclofenac sodium.

Periodontal diseases are amongst the group of inflammatory diseases which result in bone loss and eventually loss of teeth and periodontium. Periodontal surgical procedures are aimed to resolve the inflammatory process by eradicating the causative agents. Successful periodontal treatment is not only based on correct surgical technique but also on the prevention and management of postoperative pain and complications.

Pain is an inevitable outcome of any periodontal surgery. Pain is one of the most commonly experienced symptoms and adverse effects after periodontal surgery. Hence, surgeons strive for an analgesic modality that would

provide profound analgesia and would be best tolerated by the patient, hence ensuring patient compliance.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most widely used therapeutic class of analgesic compounds used to relieve postoperative pain [1,2]. Diclofenac is the most extensively used for postoperative inflammatory conditions, and it affords quick relief of pain and swelling [1-3]. Oral, parenteral, nasal and transdermal are few of the ways by which analgesics can be administered. Main disadvantage of the oral route is that only 50% of the drug is available for the body post first pass metabolism. Administration of oral drugs in the patients with physical and mental challenges is a huge task.

Transdermal patches offer several advantages over the oral route such as bypassing first pass metabolism, slow controlled absorption, constant plasma concentration which is maintained for a longer duration, no patient dependence for drug doses, no gastric discomfort, and flexibility of terminating the drug administration by simply removing the patch from the skin Hence the transdermal drug delivery system got importance in recent years.

Recently, drugs can be delivered across the skin to have an effect on the tissues adjacent to the site of application or to have an effect after distribution through the circulatory system [4]. This concept has led to the development of transdermal patches. A transdermal patch or skin patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream [5]. Transdermal drug delivery system provides a means to sustain drug delivery as well as to reduce the intensity of action and thus reduce the side effects associated with its oral administration.

Diclofenac belongs to the Aryl acetic acid group of NSAIDs whereas Ketorolac belongs to the Pyrrolo-pyrrole derivatives group [3]. Both the drugs have been proven for their excellent analgesic properties when administered orally hence this study was designed to see their effectiveness when used as a transdermal patch.

MATERIALS AND METHODS

The study was carried out Saveetha dental college and hospital Chennai. It was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013. Ethical and research committee approval was granted before commencing the study (IHEC Ref No: IHEC/SDC/PERIO-1901/21/47).

Patient selection

The study was conducted in the Department of Periodontology, Saveetha Dental College and Hospital, Chennai, India. Sample size calculation was done using G-power where the confidence interval was set at 95%. A total of 30 systemically healthy patients with chronic periodontitis were selected from the outpatient department. Patients were classified as having chronic periodontitis on the basis of the 1999 consensus classification of periodontal diseases. Patients were randomly allotted in 2 groups by a third person who wasn't part of the study by choosing one of the 2 envelopes containing patches. All the patients were informed about the study and a written informed consent was acquired prior to the commencement of the study.

Patch application

Randomly selected patch was stuck on a patient's arm just before the surgical procedure. VAS score was

recorded at 3 hour and 6 hour interval post operatively. Patients were given unnamed plain Paracetamol tablets (650 mg) in an unnamed container in case of emergency. Patients were asked to keep track of the number of medications consumed at the end of 6 hours (Figure 1). Patients were also enquired about any signs of adverse effects at the patch site (burning sensation, rash etc.).



Figure 1: Transdermal patches used for the study.

Statistical analysis

SPSS version 24 was used to do the statistical analysis. ANOVA was done for intra group comparisons. Paired t-test was done for the inter group statistics.

RESULTS

As seen in the Table 1 11 individuals in the diclofenac group did not require any rescue medicine whereas 3 in the ketorolac group were comfortable without medicine.

3 individuals consumed 1 tablet in group 1 and 9 in group 2.

None of the individuals in group 1 consumed 2 tablets whereas 4 individuals in group 2 took 2 tablets in the observational period. Table 2 show a significant difference between 2 groups when the number of rescue medicines was compared.

Table 3 shows significance between VAS scores of 2 study groups for the selected study parameters. As highlighted VAS score at 3 hours shows significant difference of 0.021 (Figure 2).

Table 1: Denoting the groupwise distribution of the number of people who required rescue medicine and the number of rescue medicines consumed by the individuals.

Group		Number rescue medication			Total
		No medicine	1 Tablet	2 Tablets	
Group	Diclofenac Patch	11	3	0	14
	Ketorolac Patch	3	9	4	16
Total		14	12	4	30

Table 2: Showing the presence/absence of discomfort in each group.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	No discomfort	24	80	80	80
	Discomfort present	6	20	20	100
	Total	30	100	100	

Table 3: ANOVA table showing correlation amongst groups and the F values of each.

		Sig.
VAS after 3 hours	Between Groups	0.021
Vas after 6 hours	Between Groups	0
Number Rescue medication	Between Groups	0
Discomfort at patch site	Between Groups	0.106
Gender	Between Groups	0.448

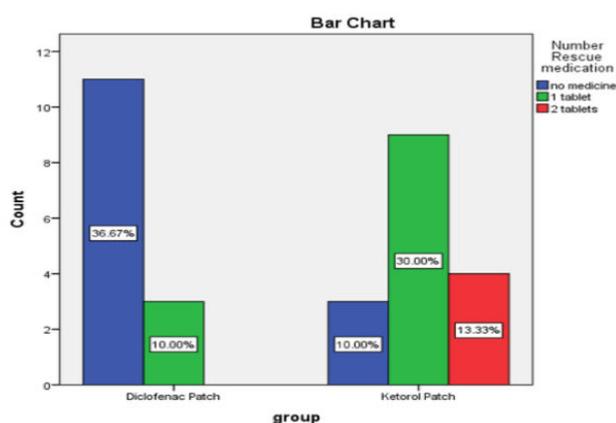


Figure 2: Bar diagram showing number of rescue medication used in each study group. Where blue represents no medicine consumed green colour represents 1 tablet and red represents 2 tablets consumed.

DISCUSSION

Diclofenac, a benzene acetic acid derivative, is one of the most frequently prescribed NSAIDs after periodontal surgical procedures. Diclofenac patches are well tolerated and could be utilized as an alternative to short-term NSAIDs [6,7]. Diclofenac comprises the ideal characteristics for transdermal application: Smaller dose, poor bioavailability, and short biological half-life. In the study done by Murthykumar et al. [8] it was proved that oral diclofenac administration was much better than that of the transdermal patch for the first 8 hours post-surgical procedure [8].

According to Trombelli et al. [9] preoperative treatment with ketorolac significantly reduced initial pain intensity and delayed the onset of postoperative pain. Walton GM et al in a study states that both analgesic preparations were more effective than that ketorolac provided a similar degree of pain relief to that of diclofenac. Hungund et al. [10] showed that 10-mg ketorolac

administered immediately before periodontal surgery was effective for alleviating the operative painful sequelae.

A study was done using ketorolac transdermal patch for evaluation of its efficacy post periodontal surgical treatment which showed that Adhesive film containing 30 mg of KT was effective in controlling post-surgical pain with no observable gastrointestinal effects [11–13].

Saturation transfer difference NMR (STD-NMR) spectroscopy has emerged as a powerful screening tool and a straightforward way to study the binding epitopes of active compounds in early stage lead discovery in pharmaceutical research [14]. Many of the articles as mentioned above have given advantages of using ketorolac and diclofenac for postoperative pain management in the periodontal field hence we decided to compare transdermal patches of both the drugs which was not done previously. Hence we decided to compare the patches post periodontal surgical treatment.

Our study results are in accordance with the results seen in the study done by Kim et al. [7] where it was proved that poor aqueous solubility of ketorolac is responsible for its slower transmission through the skin. Whereas diclofenac shows excellent transdermal activity when compared with ketorolac.

Transdermal drug delivery system is not only the future of drug delivery systems but it has equally promising advantages over oral drug administration. No statistical difference between two routes of diclofenac at any of the time intervals in postoperative pain management following dental implant placement [8,15]. Bachalli et al. stated that there is significant efficacy of oral diclofenac sodium on the 1st postoperative day when drug administered Trans dermally [16].

LIMITATIONS AND FUTURE PROSPECTS

As all the drugs are administered in different dosage concentrations none of the commercially available

patches are in similar concentration. Transdermal patches of choice are hard to procure for general public in the selected study population. If not as complete replacement the transdermal patches can definitely be used as adjunct to the oral analgesic drug regimen. It is highly suitable for unco-operative and elderly patients. Modified transdermal patches with effective concentration for oral analgesia.

CONCLUSION

Within the limits of this study it can be concluded that diclofenac patches are significantly effective. Transdermal drug delivery can be safely used to avoid common adverse effects of NSAIDs as they bypass the first pass metabolism.

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