Original Article - Comparative Study

Efficacy of Transdermal Diclofenac Patch as an Analgesic Following Premolar Extractions in Orthodontic Patients

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Abstract

Aim: The aim of the study was to evaluate the efficacy of transdermal diclofenac patch versus oral diclofenac tablet as analgesic following premolar extractions in orthodontic patients. **Materials and Methods:** Thirty-three symmetrical pairs of indicated premolars (either first or second) were included for the present study. Each patient was given either transdermal diclofenac sodium patch 100 mg once a day or oral diclofenac tablet 50 mg twice a day for 3 days after the extraction. Pain was assessed by a 10-point visual analog scale and 4-point verbal rating scale given to the patient for each day for 3 days after the extraction. All observational findings were recorded, tabulated, and analyzed statistically. **Results:** This study consisted of 33 patients with a mean age of 18.73 ± 3.677 years. Out of 33 patients included in this study, 5 were male and 28 were female. The result of the study showed that consecutive postoperative days transdermal diclofenac patch was slightly more efficient in controlling the postoperative pain in the extraction done for the orthodontic purpose than diclofenac oral tablet, however statistically no significant difference was observed using Chi-square test ($P > 0.05$). **Conclusion:** Transdermal diclofenac patch showed potential analgesic modality for the management of mild-to-moderate intensity pain in premolar orthodontic extraction, with lower incidence of systemic adverse effects. However, cost and availability may limit the use of transdermal patch.

Keywords: Dental extraction, diclofenac sodium oral tablet, transdermal diclofenac patch

Introduction

The premise of successful treatment is based not only on the correct operative technique but also on the prevention and management of postoperative complications such as pain and swelling.[1] The international association for the study of pain has defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage."[2]

Over the years, opioids have been administered to allay anxiety and to reduce pain associated with surgery.[2] Nonsteroidal anti-inflammatory drugs (NSAIDs), commonly prescribed in dental practice for the management of pain,[3] are among the most frequently prescribed drugs worldwide.[4] There are various routes of analgesic administration, among which oral analgesics is commonly prescribed for the management of pain. These users may develop gastrointestinal adverse effects of a sufficient degree requiring physician's intervention.[4]

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The mechanism of action of NSAIDs is based on the inhibition of cyclooxygenase 1 and 2 (COX-1 and COX-2) key enzymes in prostaglandin synthesis.[4,5] Diclofenac, an NSAID is an anti-inflammatory, analgesic, and antipyretic drug, is being used widely for postoperative analgesics. When used through the oral route, however, only about 50% of the absorbed dose of diclofenac becomes systemically available, due to the first-pass metabolism and due to the high plasma concentrations attained; oral diclofenac has the potential for

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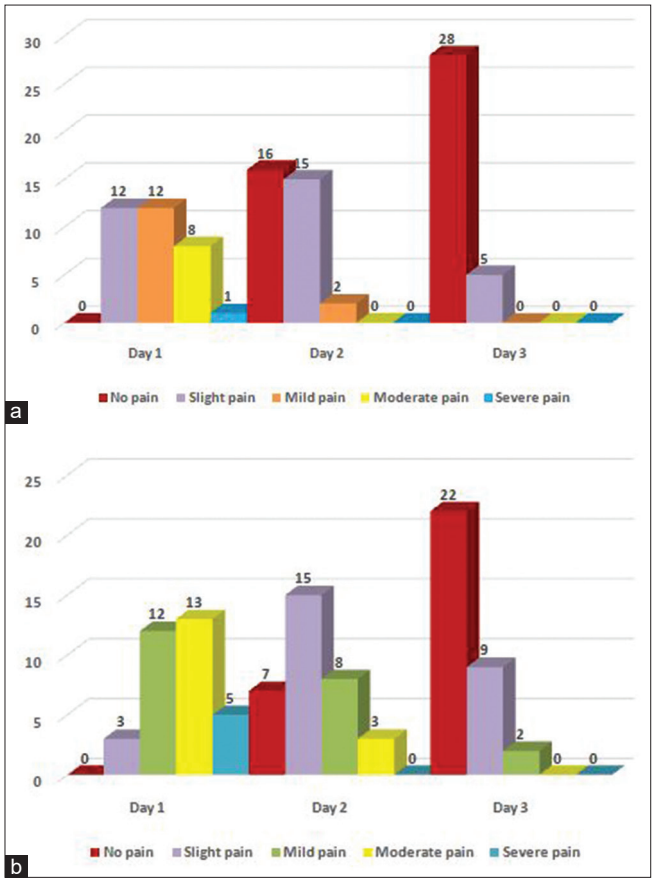
significant adverse reactions, particularly those involving the gastrointestinal tract.[6,7]

In recent years, an increasing number of topical NSAIDs have become available, among which transdermal drug delivery system (TDDS) is the most efficient in pain relief, with fewer side effects and good patient compliance.[8] Transdermal patches have been developed as innovative topical delivery systems for diclofenac.[6] The advantages of this route include painless, nonirritant, increased bioavailability, and it can be applied for 24 h.[2]

The present study was carried out to compare transdermal diclofenac patch and oral diclofenac sodium tablets in terms of the postoperative analgesia, patient tolerability, adverse events, and compliance.

Materials and Methods

A prospective study was conducted in 33 patients requiring the extraction of bilateral premolars for the orthodontic purpose (therapeutic extraction) in the outpatient department of oral and maxillofacial surgery. All patients were informed about the study, and an informed consent was obtained. The study was carried out after due approval from the institutional research and ethics committee.



Graph 1: (a) Visual analog scale scores in diclofenac patch group. (b) Visual analog scale scores in the diclofenac tablet group

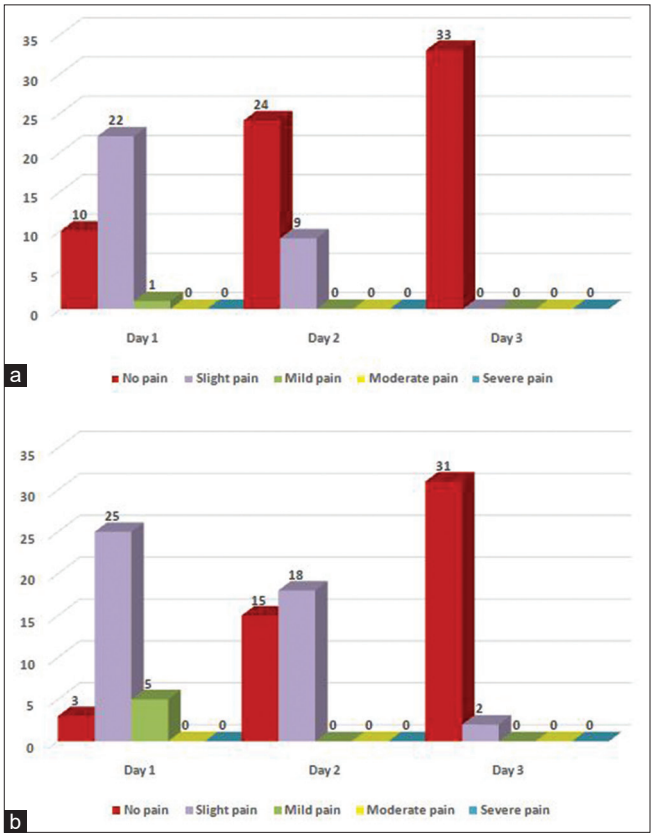
Extraction and postoperative medication

The present study included 33 patients in which the extraction of bilateral premolars (either first or second) was indicated for the orthodontic purpose. For the extraction, 2% lignocaine hydrochloride with adrenaline 1:2,00,000 was used as anesthetic solution according to the site selected. The extraction procedure was done under strict aseptic protocols. All extractions were done by the same surgeon to eliminate operator-induced bias in the study. Each patient was given either transdermal diclofenac sodium patch 100 mg once a day or oral diclofenac sodium tablet 50 mg twice a day for 3 days after the extraction. The patient was advised to apply the diclofenac patch after every 24 h for the next 3 days.

Determining the site of tooth extraction was done with a coin toss method in which the head side represented the right side and the tail side represented the left side. Objective and subjective signs and symptoms were evaluated to establish the onset of local anesthesia. After achieving local anesthesia, premolars of the selected side were extracted.

Determining the choice of analgesic was also done using the coin toss method for each time. The head side represented the use of transdermal diclofenac patch and the other side represented the use of oral diclofenac tablet.

Pain was assessed by a 10-point visual analog scale (VAS) and 4-point verbal rating scale (VRS) given to the patient



Graph 2: (a) Verbal rating scale scores in diclofenac patch group. (b) Verbal rating scale scores in the diclofenac tablet group

for each day for 3 days after the extraction. Tolerability was assessed by the patient using 4-point tolerability scale (excellent, good, fair, and poor). Safety was evaluated on the basis of the occurrence of adverse effects. The data were analyzed using the Chi-square test. Patients were reviewed on first, second, and third postextraction days. All observational findings were recorded, tabulated, and analyzed statistically.

Statistical analysis and results

This study consisted of 33 patients with a mean age of 18.73 ± 3.677 years. Out of 33 patients included in this study, 5 (15.2%) were male and 28 (84.4%) were female [Table 1]. On comparison of pain at VAS between two groups, in the second and second visits, a statistically significant difference was observed by Chi-square test with *P* value 0.026 and 0.018, respectively, however in the third visit, results were not statistically significant but better efficacy in pain control was observed in diclofenac patch group [Table 2 and Graph 1a and b].

Similarly, comparison of pain scale scores in VRS at first and second visits between two groups showed a statistically significant difference with the Chi-square test with *P* value 0.036 and 0.044, respectively. However, in the third visit, no statistically significant difference was observed [Table 3 and Graph 2a and b].

Discussion

NSAIDs are drugs commonly prescribed in dental practice for the management of pain though reasonably safe in most cases in prescribed dosages and for short durations.[3] Their mechanism of action is the reduction of prostaglandin production by inhibition of COX.[8] Prostaglandins are compounds collectively known as "eicosanoids," synthesized from dietary essential fatty acids primarily linoleic acid, metabolized to arachidonic acid.[5]

Prostaglandins have long been known to be mucoprotective and ulcer healing agents. They protect gastrointestinal mucosa by forming a cytoprotective layer and increasing the secretion of bicarbonate ions that neutralize the gastric acidity. NSAIDs are divided into selective (inhibiting COX-2) and nonselective (inhibiting both COX-1 and COX-2). Conventional NSAIDs cause nonselective inhibition of COX, which leads to the reduction in bicarbonate secretion and reduced mucous production.[5]

Most NSAIDs are weak organic acids and have low pKa; therefore, they remain unionized in the stomach and are absorbed appreciably from the stomach. However, once they breach the cell membranes of stomach cells and reach within, they encounter a basic PH known as "trapping" of the drugs inside the cell. This topical effect is considered as an important mechanism of gastroduodenal damage associated with NSAIDs use, e.g., ulcers, severe bleeding, perforation, and obstruction.[4] The extensive use of prescribed and over the counter NSAIDs associated with significant adverse effect

Table 1: Descriptive statistics of age of the study subjects

Gender	*n* (%) total=100		Males	Females	Total
Males	5 (15.2%)	Mean age	15.4	19.3	18.73
Females	28 (84.8%)	Age range	13-17	14-29	13-29

Table 2: Comparison of pain VAS scale between the two groups and within the group

	Diclofenac patch group	Diclofenac tablet group	Total	Chi square test (*P*)
Day 1 (Visit)				
No pain	0	0	0	0.026*
Slight pain	12	3	15	
Mild pain	12	12	24	
Moderate pain	8	13	21	
Severe pain	1	5	6	
Day 2 (Visit)				
No pain	16	7	23	0.018*
Slight pain	15	15	30	
Mild pain	2	8	10	
Moderate pain	0	3	3	
Severe pain	0	0	0	
Day 3 (Visit)				
No pain	28	22	50	0.145NS
Slight pain	5	9	14	
Mild pain	0	2	2	
Moderate pain	0	0	0	
Severe pain	0	0	0	
Total	33	33	66	
Friedman test (*P*)	<0.001*	<0.001*		

*Denotes statistically significant *P*<0.05. NS denotes not statistically significant *P*>0.05

Table 3: Comparison of pain VRS scale between the two groups and within the group

	Day 1			Day 2		Day 3		Total	Friedman test
	No pain	Slight pain	Mild pain	No pain	Slight pain	No pain	Slight pain		*P*
Patch	10	22	1	24	9	33	0	33	<0.001*
Tablets	3	25	5	15	18	31	2	33	<0.001*
Total	13	47	6	39	27	64	2	66	
P (Chi-square test)		0.036*			0.044*		0.492 NS		

*Denotes statistically significant *P*<0.05. NS denotes not statistically significant *P*>0.05

profiles has prompted the alternative method of drug delivery system.[8]

A newly TDDSs, also known as "patches," are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin at a programmed rate to reach the systemic circulation. The first transdermal system was approved by the Food and Drug Administration (FDA) in 1979 for the prevention of nausea and vomiting.[9] Advantages of transdermal diclofenac patch are compared with oral and parenteral route, e.g., avoidance of the first-pass metabolism, gastrointestinal incompatibility, and predictable and extended duration of the activity.[10,11]

It also provides the utilization of drugs with a short biological half-life, narrow therapeutic window, and improves physiological and pharmacological response. The mechanism of transportation of transdermal drugs is through the stratum corneum (being the uppermost layer of dead epidermal cells), viable epidermis (devoid of blood vessels), stratum lucidum, stratum granulosum, stratum spinosum, stratum germinativum, and the dermis (containing blood vessels).[10] There are three ways in which a drug molecule can cross the intact stratum corneum, through skin appendages (transappendageal and shunt routes), intercellular lipid domain, and transcellular route.[10]

Topical preparations of NSAIDs have been tested in various clinical trials, and they were found to have a therapeutic role in minimizing chronic and acute pain.[12] The plasma concentrations achieved by the topical or the transdermal administration of NSAIDs are considerably lower than that produced by oral NSAIDs leading to lower incidence of adverse effect.

All NSAIDs reach the targeted site of activity only after the drug enters the systemic circulation. To have an adequate local effect, oral and parenteral NSAIDs must produce relatively high systemic levels. In contrast, topically applied NSAIDs can provide direct and local relief without systemic activity. Thus, the advantage of drug delivered topically is to produce clinically meaningful results without systemic side effects or drug interactions.[13]

The present study included 33 patients whose age ranged from 13 years to 29 years, with a mean age of 18.73 years. A similar study done by Bhaskar *et al*.[6] had patients whose age ranged from 14 to 16 years, with a mean age of 17.5 years and gender distribution of 28 females (84.4%) and 5 males (15.2%). This is also in accordance with Prithvi *et al*.[1] who included twenty patients in which 13 were male (65%) and 7 (35%) were female.

Comparison of pain with VAS between two groups and also within group comparison was done using the Friedman test. In the diclofenac patch group, the difference in VAS pain scale scores at different visit was found statistically significant with a *P* value of 0.001. In the diclofenac tablet group, the difference in VAS pain scale scores at different visit was statistically significant using the Friedman test with $P = 0.001$. The results of the present study showed that the transdermal diclofenac patch was efficient in controlling pain postoperative which is in consistent with the study done by Tejaswi *et al*.[14] in which the transdermal diclofenac patch was effective in postoperative pain control following root coverage procedures with subepithelial connective tissue grafts. They used VAS for pain assessment. Pain tolerance was higher with the transdermal diclofenac patch when compared to oral administration. In their study, a significant reduction in pain intensity was observed only in the transdermal diclofenac patch. A similar study was carried out by Bhaskar *et al*.,[6] in which they assessed the pain with the use of oral diclofenac tablets and transdermal diclofenac patch following multiple premolar extractions in patients undergoing orthodontic extraction. They concluded that the transdermal patch provides as potent analgesia as the oral tablets with an added advantage of better patient compliance.

On comparison of the pain at VRS between two groups and also within group comparison using Friedman test, in the diclofenac patch group, the difference in VRS pain scale at different visit was statistically significant with $P = 0.001$. This finding is in agreement with the study done by Prithvi *et al*.,[1] who evaluated the analgesic efficacy of oral diclofenac sodium against diclofenac sodium transdermal patch in the management of postoperative pain following surgical removal of impacted mandibular third molars. They used VAS and VRS scales for the evaluation and concluded that transdermal diclofenac sodium can be used as an alternative form of pain control following the removal of impacted mandibular third molars.

Conclusion

Transdermal diclofenac patch showed potential analgesic modality for the management of mild-to-moderate intensity pain in premolar orthodontic extraction, with lower incidence of systemic adverse effects. However, cost and availability may limit the use of transdermal patch.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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