

# Comparative Evaluation of Transdermal Ketoprofen and Diclofenac Patches for Postoperative Pain Management Following Bilateral Minor Oral Surgical Procedures: A Prospective Randomized Split-Mouth Clinical Study

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## Abstract

### Background

Postoperative pain following minor oral surgical procedures remains a significant clinical challenge, often affecting patient comfort, recovery, and treatment compliance. Nonsteroidal anti-inflammatory drugs (NSAIDs) are routinely used for pain control; however, systemic administration is frequently associated with gastrointestinal adverse effects and reduced patient compliance. Transdermal drug delivery systems provide sustained analgesia, improved bioavailability, and reduced systemic complications. Ketoprofen and Diclofenac are commonly employed NSAIDs available in transdermal formulations, although comparative evidence regarding their postoperative analgesic efficacy in oral surgery remains limited.

### Aim

To compare the analgesic efficacy and safety of transdermal Ketoprofen and Diclofenac patches in postoperative pain control following bilateral minor oral surgical procedures.

### Materials and Methods

A prospective randomized split-mouth clinical study was conducted among 30 patients undergoing bilateral minor oral surgical procedures at the Department of Oral and Maxillofacial Surgery, People's Dental Academy, Bhopal, India, between March 2024 and February 2025. Patients received either transdermal diclofenac patch (200 mg) or ketoprofen patch (30 mg) during the first appointment, followed by crossover administration during the second procedure. Randomization was performed using a lottery method, and patients were blinded to the administered intervention. Pain intensity was assessed using a 10-point Visual Analogue Scale (VAS) at 2, 6, 12, and 24 hours postoperatively. Rescue analgesic requirement and adverse effects were also evaluated. Statistical analysis was performed using paired t-test and McNemar test, with  $p < 0.05$  considered statistically significant.

### Results

Both transdermal patches demonstrated comparable analgesic efficacy during the immediate postoperative period at 2 hours ( $p = 0.8012$ ). However, ketoprofen showed significantly lower VAS pain scores at 6 hours ( $0.767 \pm 0.568$  vs  $0.200 \pm 0.407$ ,  $p = 0.0001$ ), 12 hours ( $1.067 \pm 0.640$  vs  $1.700 \pm 0.837$ ,  $p = 0.0046$ ), and 24 hours ( $1.767 \pm 0.728$  vs  $3.333 \pm 0.711$ ,  $p < 0.0001$ ) compared to diclofenac. Rescue analgesic requirement during 12–24 hours was

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significantly lower in the ketoprofen group (26.7%) compared to the diclofenac group (73.3%) ( $p = 0.0003$ ). Both interventions demonstrated favorable safety profiles, with only minimal adverse effects reported.

## Conclusion

Although both transdermal diclofenac and ketoprofen patches provided effective early postoperative pain relief, ketoprofen demonstrated superior sustained analgesic efficacy with reduced rescue analgesic requirement and comparable safety. Transdermal ketoprofen may therefore represent a more effective modality for postoperative pain management in minor oral surgical procedures.

**Keywords:** Transdermal drug delivery system, Ketoprofen patch, Diclofenac patch, Postoperative pain, Minor oral surgery, NSAIDs, Visual analogue scale

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## Introduction

Postoperative pain is one of the most common complications following oral and maxillofacial surgery and significantly affects patient comfort, recovery, and treatment outcomes. Effective pain management is therefore an essential component of perioperative care. Minor oral surgical procedures such as impacted third molar removal commonly result in postoperative inflammatory pain.

NSAIDs are widely used for postoperative pain control by inhibiting cyclooxygenase-mediated prostaglandin synthesis. However, oral NSAIDs may be associated with gastrointestinal adverse effects and reduced patient compliance.<sup>4</sup> Transdermal drug delivery systems (TDDS) have emerged<sup>8,9,10</sup> as alternative to conventional oral and parenteral routes of drug administration. Transdermal patches provide controlled and sustained release of medications through the skin, bypassing hepatic first-pass metabolism while maintaining relatively stable plasma drug concentrations and minimizes gastrointestinal adverse effects.

Diclofenac and ketoprofen have gained considerable popularity in transdermal formulations. Diclofenac is a widely prescribed non-selective COX inhibitor with proven analgesic efficacy in musculoskeletal and postoperative pain conditions. In addition to COX inhibition, ketoprofen also inhibits lipooxygenase pathways and bradykinin-mediated inflammatory mechanisms, potentially contributing to prolonged analgesic effects.

Previous investigations have demonstrated<sup>11,12,14</sup> the effectiveness of both transdermal diclofenac and ketoprofen patches in managing postoperative pain. However, direct comparative evidence between these two modalities in minor oral surgical procedures remains sparse and inconclusive. Furthermore, most available studies employ parallel-group designs that may be influenced by interindividual variability in pain threshold, healing capacity, and inflammatory response.

Therefore, the present study was undertaken to comparatively evaluate the analgesic efficacy, requirement of rescue analgesics, and safety profile of transdermal ketoprofen and diclofenac patches in patients undergoing bilateral minor oral surgical procedures using a prospective randomized split-mouth clinical design.

Aim of the Study, is to compare the efficacy of transdermal ketoprofen and diclofenac patches in postoperative pain control following bilateral minor oral surgical procedures.

## Objectives

1. To evaluate postoperative pain intensity using Visual Analogue Scale (VAS) scores at 2, 6, 12, and 24 hours.
2. To assess the requirement of rescue analgesics during postoperative recovery.
3. To compare the incidence of adverse effects associated with both transdermal patches.

## Materials and Methods

A prospective, randomized, split-mouth clinical study was conducted in the Department of Oral and Maxillofacial Surgery, People's Dental Academy, Bhopal, Madhya Pradesh, India, between March 2024 and February 2025. The study protocol was reviewed and approved by the Institutional Ethical Committee of People's Dental Academy (Approval No: PDA/IEC/2024/008/02). Written informed consent was obtained from all participants before enrolment. A total of 30 patients requiring bilateral minor oral surgical procedures were included in the study.

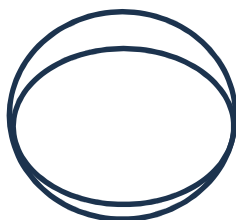
Inclusion criteria was, patients willing to participate in the study, bilateral minor oral surgical procedures, Bilateral impacted mandibular or maxillary third molars, Bilateral impacted maxillary or mandibular canines. Patients with unilateral minor oral surgical procedures, known allergy or hypersensitivity to NSAIDs, Pregnant or lactating women, Severe uncontrolled metabolic or cardiovascular disorders, History of chemotherapy or radiotherapy and Patients

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unwilling to comply with study protocol were excluded from the study.



**Fig 1- OPG Impacted mandibular 3<sup>rd</sup> molar**



**Fig. 2: (A) Transdermal ketoprofen patch on the skin of deltoid muscle region**

**(B) Transdermal diclofenac patch on**

**the skin of deltoid muscle region**

Randomization was performed using a lottery method. During the first surgical appointment, patients received either a transdermal diclofenac patch (200 mg) or a transdermal ketoprofen patch (30 mg) immediately after surgery. During the second appointment, the alternative patch was administered, thereby ensuring crossover allocation. Patients were

blinded to the type of transdermal patch used during each procedure.

**Surgical Procedure**

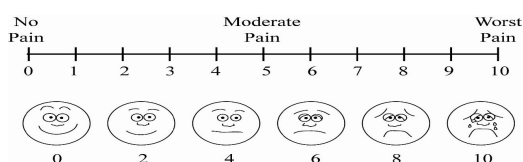
All surgeries were performed under standardized aseptic conditions. A comprehensive case history and clinical examination were conducted preoperatively. All procedures were performed under standardized surgical protocols by the same surgeon under local

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anesthesia. Following completion of the procedure, the allocated transdermal patch was applied over the ipsilateral deltoid region of the upper arm immediately after surgery.

## Postoperative Evaluation

Postoperative pain intensity was assessed using a 10-point Visual Analogue Scale (VAS), pain scores were recorded following surgery at 2 hours, 6 hours, 12 hours and 24 hours.



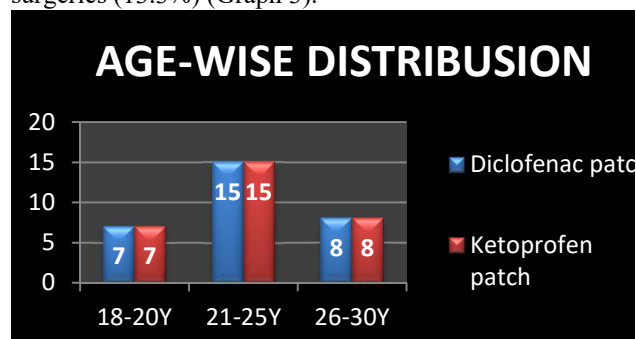
**Fig 4- 10 point VAS scale**

Participants were instructed to consume Ketorolac 10 mg as rescue analgesia if pain became intolerable during the first 24 postoperative hours. Rescue analgesic requirement was documented in two intervals 0–12 hours and 12–24 hours.

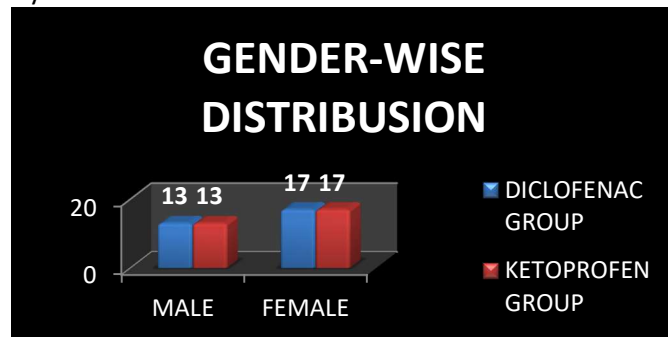
## Results

Data were entered into Microsoft Excel and analyzed using SPSS version 21.0. The Shapiro–Wilk test was used to assess data normality. Paired t-test was used to compare postoperative VAS pain scores between interventions and McNemar test was used for categorical variables including rescue analgesic requirement and adverse effects, a p-value <0.05 was considered statistically significant.

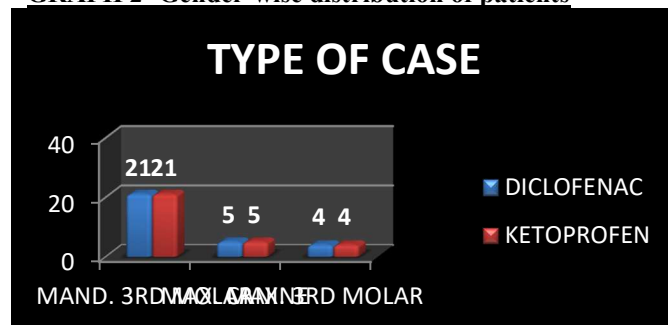
The majority of participants belonged to the 21–25 years age group (50%), followed by 26–30 years (26.7%) and 18–20 years (23.3%) (Graph 1). Among the participants, 17 patients (56.7%) were females, while 13 patients (43.3%) were males (Graph 2). Most participants underwent mandibular third molar surgeries (70%), followed by maxillary canine procedures (16.7%) and maxillary third molar surgeries (13.3%) (Graph 3).



**GRAPH 1- Age wise distribution of patients**

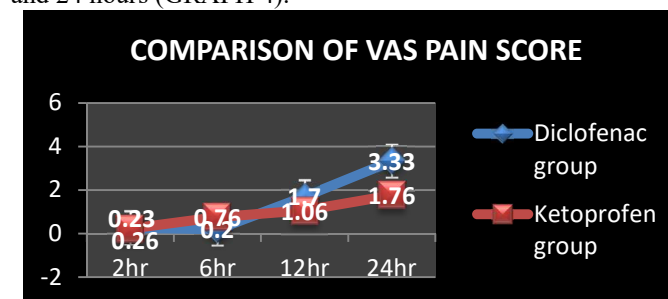


**GRAPH 2- Gender-wise distribution of patients**



**GRAPH 3- Distribution by Type of Case**

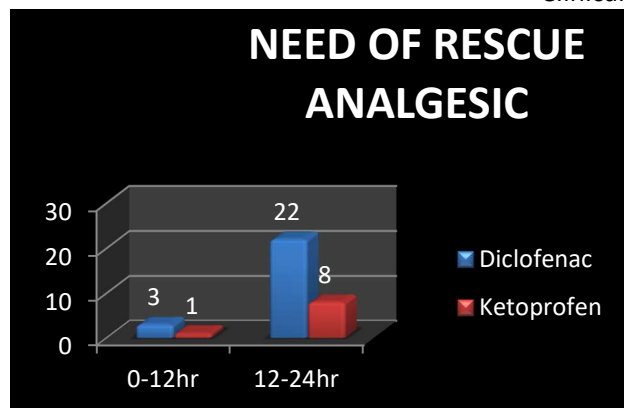
Pain scores were comparable at 2 hours but were significantly lower in the ketoprofen group at 6, 12, and 24 hours (GRAPH 4).



**GRAPH 4- Comparison of VAS Pain Scores at 2, 6, 12, and 24 Hours**

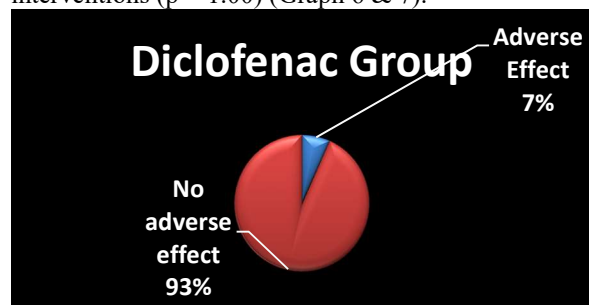
In early Phase (0–12 Hours), the requirement was low for both groups (10% for Diclofenac vs. 3.3% for Ketoprofen), with no statistically significant difference ( $p = 0.3256$ ), and late Phase (12–24 Hours) a sharp increase in rescue medication was noted in the Diclofenac group, where 73.3% of patients required additional analgesia. In contrast, only 26.7% of the Ketoprofen group required extra medication. This difference was highly significant ( $p = 0.0003$ ) (Graph 5).

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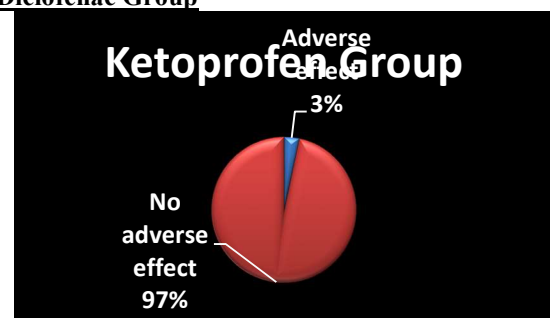


**Graph 5: Rescue Analgesic Requirement — 0–12 Hours & 12–24 Hours**

Only minimal adverse events were reported during the study period. Nausea and vomiting occurred in two patients (6.66%) receiving diclofenac and one patient (3.33%) receiving ketoprofen. No cases of dizziness, allergic reaction, or severe local adverse effects were observed. No statistically significant difference in adverse events was found between the two interventions ( $p = 1.00$ ) (Graph 6 & 7).



**Graph 6: Incidence of Adverse Effects in Diclofenac Group**



**Graph 7: Incidence of Adverse Effects in Ketoprofen Group**

## Discussion

Effective postoperative pain management remains a critical determinant of patient comfort, recovery, and treatment acceptance following oral surgical

procedures. Surgical trauma induces<sup>1,4</sup> local inflammatory reactions characterized by the release of prostaglandins, bradykinin, cytokines, and other inflammatory mediators that sensitize peripheral nociceptors and contribute to postoperative pain. NSAIDs remain the most frequently prescribed analgesics in oral and maxillofacial surgery because of their ability to inhibit cyclooxygenase-mediated prostaglandin synthesis.

Transdermal drug delivery systems have gained<sup>8,9,10</sup> increasing clinical relevance due to their ability to provide sustained drug release, improved patient compliance, reduced gastrointestinal adverse effects, and avoidance of hepatic first-pass metabolism.

The split-mouth design minimized interindividual variability. In the immediate postoperative period at 2 hours, both ketoprofen and diclofenac patches demonstrated comparable analgesic efficacy with no statistically significant difference in VAS scores. This finding indicates that both NSAIDs are effective in controlling early inflammatory pain following minor oral surgery.

However, significant differences became evident during later postoperative intervals. At 6, 12, and 24 hours, ketoprofen demonstrated significantly lower VAS pain scores compared with diclofenac. The most pronounced difference was observed at 24 hours, where the diclofenac group demonstrated substantially higher pain scores than the ketoprofen group. These findings suggest that ketoprofen provides more sustained postoperative analgesia during the peak inflammatory phase.

The findings of the present study are consistent<sup>11,12,14</sup> with those reported by Bhargava et al., who demonstrated that ketoprofen transdermal patches produced superior postoperative analgesia compared

with diclofenac following orthodontic premolar extractions. Similarly, Pandey et al. reported lower maximal pain intensity and better overall pain control with ketoprofen compared with diclofenac transdermal patches following orthodontic extractions.

Comparable findings were also observed in orthognathic surgical procedures. Bachalli et al. demonstrated significantly prolonged duration of analgesia with ketoprofen transdermal patches compared to diclofenac. The authors reported a mean analgesic duration of approximately 20 hours for ketoprofen compared to 13 hours for diclofenac, further supporting the prolonged pharmacological action of ketoprofen.

An important clinical finding in the present study was the significantly lower requirement for rescue analgesics in the ketoprofen group during the 12–24

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hour postoperative interval. While rescue analgesic consumption was minimal and comparable during the first 12 hours, substantially more patients receiving diclofenac required supplementary analgesics during the later postoperative period.

The reduced need for rescue analgesia observed in the ketoprofen group aligns with previous investigations. Daya Shankar et al.<sup>2</sup> reported that patients receiving diclofenac patches required significantly more supplementary analgesics within the first 24 hours compared with ketoprofen-treated patients.

Only mild nausea and vomiting were observed in a small number of patients, and no severe adverse effects such as allergic reactions, dizziness, or significant local skin irritation were reported. The absence of major adverse effects supports the safety and clinical acceptability of transdermal NSAID delivery systems.

The reduced incidence of systemic complications associated with transdermal administration may be attributed to bypassing the gastrointestinal tract and hepatic first-pass metabolism. Lower systemic plasma concentrations reduce gastrointestinal mucosal irritation while still maintaining adequate local tissue drug levels for analgesia. Previous literature has similarly demonstrated the favorable safety profile of transdermal NSAIDs. Talnia et al.<sup>13</sup> reported minimal systemic adverse effects with diclofenac transdermal patches compared with oral diclofenac formulations. Furthermore, multiple studies have emphasized improved patient tolerability and compliance associated with transdermal analgesic systems.

Another important advantage of transdermal delivery systems is improved patient convenience and compliance. Oral analgesics require repeated dosing and may be poorly tolerated in patients experiencing nausea, dysphagia, or postoperative discomfort. In contrast, transdermal patches provide painless, sustained, and non-invasive drug delivery over extended periods, making them particularly suitable for ambulatory oral surgical procedures.

The findings of the present study therefore suggest that although both diclofenac and ketoprofen transdermal patches are effective modalities for postoperative pain management, ketoprofen demonstrates superior sustained analgesic efficacy, reduced rescue analgesic requirement, and comparable safety profile. These properties make ketoprofen a preferable transdermal NSAID option in minor oral surgical procedures.

## Limitations

The present study has certain limitations. The sample size was relatively small, which may limit generalizability of the findings. Pain assessment was restricted to the first 24 postoperative hours, and longer follow-up periods may provide additional

insight into prolonged analgesic efficacy. The onset of analgesic action was not assessed, limiting comparison of the time to onset of pain relief between the two transdermal patches. Pain perception is inherently subjective, and although the Visual Analogue Scale is widely accepted, interindividual variation cannot be completely eliminated. Additionally, plasma drug concentrations were not measured, preventing pharmacokinetic correlation with analgesic response. Future multicenter studies with larger sample sizes and extended follow-up durations are recommended.

## Conclusion

Within the limitations of this study, transdermal ketoprofen appears to be a more effective option than diclofenac for postoperative pain management following bilateral minor oral surgical procedures.

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