# "EVALUATION OF EFFICACY OF TRANSDERMAL KETOPROFEN PATCH IN COMPARISON TO TRANSDERMAL DICLOFENAC PATCH AS AN ANALGESIC IN PATIENTS UNDERGOING ORTHODONTIC EXTRACTIONS – A RANDOMISED SPLIT MOUTH STUDY"


**By**

**REG.NO. – IF0220004**


*Dissertation*

*Submitted to the*
*KLE Academy of Higher Education & Research Belagavi, Karnataka*
*In partial fulfillment of the requirements for the degree of*

**MASTER OF DENTAL SURGERY**

**In**

**ORAL AND MAXILLOFACIAL SURGERY**

**(BRANCH III)**


**DEPARTMENT OF ORAL AND MAXILLOFACIAL SURGERY**
**KAHER's V K INSTITUTE OF DENTAL SCIENCES**
**BELAGAVI, KARNATAKA**


**2020 – 2023**

# KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH

## BELAGAVI, KARNATAKA

## ENDORSEMENT BY THE HEAD OF THE DEPARTMENT AND PRINCIPAL/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"EVALUATION OF EFFICACY OF TRANSDERMAL KETOPROFEN PATCH IN COMPARISON TO TRANSDERMAL DICLOFENAC PATCH AS AN ANALGESIC IN PATIENTS UNDERGOING ORTHODONTIC EXTRACTIONS – A RANDOMISED SPLIT MOUTH STUDY"** is a bonafide research work done by **REG.NO. – IF0220004.**

**Head of Department**

Professor and Head
Dept. of Oral & Maxillofacial Surgery
KLE V. K. Institute of Dental Sciences,
Belagavi

**Dr. SHRIDHAR D. BALIGA** M.D.S

Professor and Head,
Department of Oral and Maxillofacial Surgery,
KAHER's V K Institute of Dental Sciences,
Belagavi - 590010

**Date:** 26/12/22

**Place:** Belagavi

**Principal**

PRINCIPAL
KLE V.K. Institute of Dental Sciences
Nehru Nagar, BELAGAVI-590010.

**Dr. ALKA KALE** M.D.S.

Principal,
KAHER's V K Institute of Dental Sciences, Nehru Nagar,
Belagavi-590010.

**Date:** 30/12/22

**Place:** Belagavi

## UNDERTAKING

I, **REG.NO. – IF0220004** hereby declare that the information and the data nentioned in my dissertation entitled **"EVALUATION OF EFFICACY OF TRANSDERMAL KETOPROFEN PATCH IN COMPARISON TO TRANSDERMAL DICLOFENAC PATCH AS AN ANALGESIC IN PATIENTS UNDERGOING ORTHODONTIC EXTRACTIONS – A RANDOMISED SPLIT MOUTH STUDY"** belongs to me and is original.

I am aware of the definition of plagiarism as detailed below:

- An act or instance of using or closely imitating the language and thoughts of another author without authorization and the representation of that author's work as one's own, as by not crediting the original author.
- A piece of writing or other work reflecting such unauthorized use or imitation.
- The deliberate or reckless representation of another's words, thoughts or ideas as one's own without attribution in connection with submission of academic work, whether graded or otherwise.

I hereby declare that the dissertation prepared by me is original one and does not involve plagiarism anywhere. In case at a later stage it is found that I have indulged in plagiarism, then I am solely responsible for the same and the institution is at liberty to take any disciplinary action against me including cancellation of dissertation or any other penalties imposed by the university.

Date:

Place: Belagavi **REG.NO. – IF0220004**

# PLAGIARISM CHECK REPORT

## Scientific Correspondence and Review Committee


**KLE VK Institute of Dental Sciences**

**A Constituent Unit of KLE Academy of Higher Education and Research**
**(Deemed-to-be-University u/s 3 of the UGC Act, 1956)**
Nehru Nagar, Belagavi - 590 010, Karnataka State

Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)

☎: 0831-2470362
FAX: 0831-2470640
Web: http://www.kledental-bgm.edu.in
E-mail:principal@kledental-bgm.edu.in


Date : 30/12/2022 Serial No. : 148

## PLAGIARISM CHECK REPORT

Name of the Applicant : **REG.NO. – IF0220004**
UG / PG / Ph.D / Staff : Post Graduate Student
Batch & Year : 2020 – 2023
Department : Oral & Maxillofacial Surgery

The soft copy of Research Work / Manuscript by . **REG.NO. – IF0220004** entitled "Evaluation of Efficacy of Transdermal Ketoprofen patch in comparison to transdermal diclofenac patch as an analgesic in patients undergoing orthodontic extraction - A randomized Split mouth Study" under the guidance of . ...has been submitted for Anti-Plagiarism check to the Scientific Correspondence & Review Committee of KLE VK Institute of Dental Sciences using "Turn-it-in" software.

The scan has been carried out and the scanned output reveals a Similarity Index of .....6.....%, which is **within** / **not within** the acceptable limits of 10% as per the UGC guidelines.

**Member Secretary**
Scientific Correspondence and Review Committee
KLEVK Institute of Dental Sciences
KAHER-Belagavi

**Chairman**
Scientific Correspondence and Review Committee
KLEVK Institute of Dental Sciences
KAHER - Belagavi

# LIST OF ABBREVATIONS USED

| | | |
|---|---|---|
| NSAIDs | - | Non-Steroidal Anti-inflammatory drugs |
| VAS | - | Visual Analog scale |
| IV | - | Intravenous |
| IM | - | Intramuscular |

# ABSTRACT

**Introduction:** NSAIDs till day are the most prescribed analgesics for the control of post-exodontia pain and can be administered by oral, parenteral, transdermal routes etc. Transdermal patches possess the advantages of providing sustained release of the drug, are non-invasive, bypass first pass metabolism and eliminate gastrointestinal adverse effects. In this study, the efficacy of single application of Diclofenac 200 mg transdermal patch and Ketoprofen 30 mg transdermal patch for post orthodontic exodontia pain relief over 24 hours post operatively was compared.

**Materials and methods:** In the present split mouth study, 30 patients who underwent orthodontic bilateral maxillary and/or mandibular premolars extractions under local anaesthesia were included. Each patient received single transdermal Diclofenac 200 mg patch and transdermal Ketoprofen 30mg patch on outer, ipsilateral upper arm immediately post extraction in the 2 appointments in random order. The pain score was recorded every second hourly for first 24 hours post operatively using Visual Analog Scale (VAS) , requirement of rescue analgesic at various time points in first 24 hours post operatively and total number of rescue analgesic taken in first 24 hours post operatively was noted.

**Results:** No statistically significant ($p<0.05$) difference was found between the analgesic efficacy of two transdermal patches at any given time point in 24 hours by Mann-Whitney U test. Overall within each group statistical significant ($p<0.05$) difference was found by intragroup comparison of VAS pain scores at different time points in relation to VAS pain score at 0 – 2 hours after application of Transdermal Ketoprofen and Diclofenac patches respectively with Wilcoxon matched pairs test. The study patients had mean maximum pain intensity of 2.33 for Ketoprofen

transdermal patch and 2.60 for Diclofenac transdermal patch. All study patients consumed the rescue analgesic within first 12 hours post operatively with the mean value of total number of rescue analgesic taken with Ketoprofen transdermal patch (0.23) being slightly lower than Diclofenac transdermal patch (0.27) application.

**Conclusion:** In the present study, Ketoprofen transdermal patch and Diclofenac transdermal patch provide similar analgesia post orthodontic extraction. However, the patients required rescue analgesic during initial hours of post-operative follow-up period.

## TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF GRAPHS

# LIST OF PHOTOGRAPHS

# INTRODUCTION

Pain after minor or major oral surgical procedures is one of the actively studied subjects in pharmacology and pain research.[1] Monheim's has defined pain as "an unpleasant emotional experience usually initiated by a noxious stimulus and transmitted over a specialized neural network to the central nervous system where it is interpreted as such."[2] Studies have shown that sensory nociception in the oral cavity is significantly more than in many other areas of the body.[1]

In a normal atraumatic tooth extraction once the effect of the local anesthetic wears off, may cause mild to severe pain, depending on the condition of the tooth and patient perception. Production of prostaglandins at the extraction site causes post exodontia pain[3] which is an uncomfortable experience for the patients that may lead to disruption of daily routine activities and may distract the individual from essential obligations. Hence, measures should be taken to provide appropriate analgesia for an uneventful post exodontia healing phase for the patient.[4]

Administration of either peripherally acting [Non-Steroidal Anti-inflammatory Drugs (NSAIDs)] or centrally acting (opiods) drugs are used for achieving post operative analgesia. However, the majority of the post exodontia pain is managed by NSAIDs (Nonsteroidal anti-inflammatory drugs) worldwide.[5]

One of the commonly prescribed NSAIDs for post exodontia pain relief is Diclofenac. Diclofenac is a non-selective cyclooxygenase enzyme inhibitor of the aryl acetic acid group, that shows analgesic, anti-inflammatory as well as antipyretic activity.[6] Diclofenac sodium acts by potent cycle-oxygenase inhibition, reduction of arachidonic acid release, and enhancement of arachidonic acid uptake. It thereby

results in a dual inhibitory effect on both the cycle-oxygenase and lipoxygenase pathways.[7]

Ketoprofen, (RS) 2-(3-benzoylphenyl)-propionic acid, is one of the propionic acid class of NSAIDs and has analgesic and antipyretic effects. Ketopofen combines with the cyclooxygenase and thereby prevent its substrate-enzyme combination with arachidonic acid and the formation of eicosanoids, prostaglandins, and thromboxanes.[8] Ketoprofen has been well documented in various studies as an effective agent in providing post operative analgesia.[9]

These drugs can be administered using various routes of drug administration such as oral, parenteral such as intravenous (IV), intramuscular (IM), sublingual and transdermal.[5] Oral route of administration of drugs has been the route of choice in daily practice for a long time, but this route poses the disadvantages of low bioavailability due to its first pass metabolism, gastrointestinal adverse effects and patient non-compliance.[10] Other routes of administration of drugs commonly used in cases of extreme post exodontia pain are intramuscular or intravenous. Intramuscular injections of NSAIDs can lead to erythema, pruritis, oedema, abscess and necrosis. The intravenous route though provides the fastest analgesia, but its action is of short duration as it injects the entire dose within a short span which could eventually lead to systemic toxicity.[10]

To overcome the drawbacks of the most commonly used routes of drug administration newer drug delivery agent, **transdermal patch**, may be used by which the drug enters into systemic circulation through the skin or mucosa. Transdermal drug delivery systems are simple and compliant methods of delivery.[11] Transdermal patches possess the advantages of providing sustained release of the drug, non-

invasive method of drug administration, they bypass first pass metabolism and eliminate gastrointestinal adverse effects.[4]

In the present study, the efficacy of transdermal Ketoprofen patch versus transdermal Diclofenac patch in patients undergoing orthodontic extractions was compared for pain and the need for rescue analgesic after single application over 24 hours post operatively.

# AIM AND OBJECTIVES

## AIM OF THE STUDY

To compare the efficacy of transdermal Ketoprofen patch versus transdermal Diclofenac patch in patients undergoing orthodontic extractions.

## OBJECTIVES

1. To assess the pain intensity for the first 24 hours after extraction using $VAS^{24}$ pain scale;

2. To assess the requirement for rescue analgesic intake within 24 hours post-extraction; and

3. To record the number of rescue analgesic tablets taken within 24 hours post-extraction.

# REVIEW OF LITERATURE

**Darpan Bhargawa et al[4] in 2019** compared the efficacy of transdermal Ketoprofen (20 mg) and Diclofenac (200 mg) patch in patients undergoing therapeutic atraumatic first premolar extractions. Forty patients requiring therapeutic extraction of both maxillary and mandibular first premolar teeth bilaterally were included. Single transdermal Ketoprofen patch was applied for first and fourth quadrant extractions, and transdermal Diclofenac patch was applied for second and third quadrant extractions all under local anaesthesia. They concluded that Ketoprofen is superior to Diclofenac as a transdermal medicament in providing post extraction analgesia.

**Selvi et al[12] in 2016** compared Transdermal Diclofenac Patch with Intramuscular Diclofenac Injection as an Analgesic Modality Following Surgical Extraction of Impacted Mandibular Third Molars in a cross over efficacy trail. Twenty patients requiring bilateral mesioangular impacted mandibular third molars were selected for the study. After performing impaction surgery on right side, patients received 50-$cm^2$ patch, 100 mg of Diclofenac diethylamine, and after 3 weeks surgical extraction on the left side was performed and post operatively patients received injection Diclofenac. Patients were evaluated for pain for three post operative days. They concluded that Diclofenac administered by either mode of delivery as transdermal patches or IM injections has similar effectiveness but the patients showed better compliance with transdermal drug delivery.

**Hemant Bhaskar et al[13]** in 2010 compared transdermal Diclofenac patch with oral Diclofenac as an analgesic modality following multiple premolar extractions in orthodontic patients. Twenty pre-orthodontic patients requiring bilateral maxillary and

mandibular first premolar extractions were selected for the study. The right maxillary and mandibular first premolars were extracted first and 50 mg oral Diclofenac sodium tablets were prescribed to be taken thrice a day for three days. In the next appointment, the contralateral first premolars were extracted and a 100 mg transdermal Diclofenac patch was applied once a day for three days. They concluded that both Diclofenac formulations provided potent analgesia with advantage of better patient compliance for transdermal route.

**Vandana Chhabra et al[10] in 2019** evaluated the efficacy of transdermal Diclofenac patch (100 mg) in the management of post surgical pain with transalveolar extraction of impacted mandibular third. In this study transdermal Diclofenac 100 mg patch was used once daily for 3 post operative days for 100 patients and 65% of patients did not require any rescue analgesic for pain relief. They emphasized upon the usage of transdermal patch due to its low side effects as it bypasses the hepatic first pass metabolism and have several benefits such as constant and controlled drug release, ease of usage and good effectiveness.

**Anisha Perepa et al[14] in 2015** evaluated the analgesic efficacy of a Diclofenac transdermal patch with Diclofenac intra muscular injection in the immediate post operative period in patients undergoing bijaw surgeries for surgical correction of various dentofacial deformities. Sixty patients were divided into two groups: Group A (study group) received a single dose of 100 mg transdermal Diclofenac patch, Group B (control group) received 75 mg intramuscular Diclofenac. They concluded that A noninvasive application of a single dose of transdermal Diclofenac patch is more effective than intramuscular Diclofenac in the immediate post operative phase.

**Pranavi Jadhav et al[15] in 2018** compared the analgesic efficacy of Diclofenac and Ketoprofen transdermal patch, in the management of immediate post operative pain following orthognathic procedures. A randomised controlled study was conducted among 50 subjects divided into 2 groups diagnosed clinically and cephalometrically as skeletal and dental class II malocclusion, and underwent bi-jaw surgical procedure. The transdermal patches used, contained 100 mg of either Diclofenac or Ketoprofen and administered by a nurse prior to induction. They concluded that subjects in both groups were comfortable and returned to early function. However, Ketoprofen transdermal patch had an edge over the Diclofenac transdermal patch with respect to analgesic efficacy.

**Bachalli et al[16] in 2016** conducted a comparative study of Diclofenac transdermal patch (100 mg) against oral Diclofenac (100 mg) for pain control following removal of mandibular impacted third molars. Twenty healthy subjects divided into two groups with bilateral mesioangular impactions of mandibular third molar teeth underwent surgical removal under local anaesthesia. They concluded that transdermal Diclofenac sodium can be used as an alternative form of pain control following removal of impacted mandibular third molars, however considering that the analgesic potency might be lesser in the immediate post operative period, it might be prudent to use oral Diclofenac sodium for immediate post operative pain relief, following which transdermal route can be used for pain control.

**Vinod Kumar et al[17] in 2017** evaluated the role of transdermal Diclofenac (Nupatch) in post operative pain management who underwent major surgery. The study included hundred adult patients on whom Diclofenac transdermal patch (Nupatch) 50 sq.cm was applied 2-3 cm away from operative site at the zero hour

postoperatively and was changed every 24 hourly postoperatively for four days. They concluded that transdermal Diclofenac patch (Nupatch) is easy to use and is a painless application that is effective in reducing post operative pain and also lowers the need of rescue analgesia.

**Ritu Verma et al[9] in 2016** compared single dose transdermal patches of Diclofenac (100 mg) and Ketoprofen (20 mg) for post operative analgesia in lower limb orthopedic surgery. In this study 60 patients were included and 30 each were randomly allocated in the two groups who received one of the transdermal patches, and evaluated for pain in the first 24 hours post operatively. They concluded that transdermal patch of Ketoprofen and Diclofenac both are effective for post operative analgesia in lower limb orthopedic surgery under spinal anaesthesia but in Diclofenac group more patients required rescue analgesic as compared to Ketoprofen group.

**YMA Tai et al[18] in 1992** compared controlled-release Ketoprofen and Diclofenac in the control of post-surgical pain. He compared post operative dental pain following unilateral or bilateral surgical removal of lower third molars by providing preoperative treatment with controlled release Ketoprofen or Diclofenac. Fifty patients were assessed on the day of surgery and one week later for graded dental pain, consumption of paracetamol, incidence of dental bleeding, dysphagia, sleep disturbance and trismus which were similar in both groups. However, median pain scores were elevated in the Diclofenac group over Ketoprofen group.

**Deepthi Mony et al[6] in 2016** compared and evaluated the pre-emptive analgesic efficacy of preoperatively administered Ketorolac and Diclofenac for controlling post operative pain after third molar surgery. Fifty patients with similarly impacted third molars were divided in 2 groups, intramuscular injection of Ketorolac

30 mg and Diclofenac 75 mg were used in respective groups. Pain was assessed using visual analogue scale (VAS) for 3 days and rescue analgesic intake during the same period. They concluded that pre-emptive analgesic effect shown by Ketorolac was better than Diclofenac for post operative pain management after third molar surgery.

**Archana Raichurkar et al[19] in 2015** compared the efficacy of Diclofenac and Ketoprofen transdermal patch with placebo in attenuating intravenous cannulation pain in patients posted for elective surgeries. One hundred and fifty patients with ASA I and II were selected and divided into groups of 50 each with group I being Placebo control patch. Group II being Ketoprofen transdermal patch and III being Diclofenac transdermal patch that were applied 4 hours before venous cannulation and VAS score was observed. They concluded that both Diclofenac and Ketoprofen transdermal patches both provide better pain relief than placebo however Ketoprofen patch fared better in reducing the severity of pain.

**Andreas Osterwalder et al[20] in 2002** evaluated tissue absorption and distribution of Ketoprofen after patch application in subjects undergoing knee arthroscopy or endoscopic carpal ligament release. One patch with 100 mg Ketoprofen on the affected body site was applied once a day during the 6 days before the scheduled surgery on ten patients with a mean age of 45.0 ± 12.3 years, planned for arthroscopic meniscectomy (5 subjects) or endoscopic carpal tunnel decompression (5 subjects), were asked to apply. They concluded that Ketoprofen applied on the skin is able to enter the subcutaneous and intra-articular tissues, reaching concentrations significantly higher than in plasma to produce the desired pharmacological activity in situ and plasma concentrations are low enough to avoid any systemic activity or side effect.

**Ng et al[3] in 2001** compared the efficacy and adverse effects of Ketoprofen and Diclofenac in treatment of acute musculoskeletal pain. Target study patients were Chinese adults who suffered from any musculoskeletal injuries of less than 12 hours. They received either 100mg of Ketoprofen or 75 mg of Diclofenac; pain was assessed by a visual analog score and evaluations were performed at 30 minutes from treatment. They concluded that Ketoprofen and Diclofenac are equally effective and safe in the treatment of acute musculoskeletal pain in Hong Kong Chinese population.

**Mazieres et al[21] in 2005** tested the efficacy and tolerability of a 100 mg patch of Ketoprofen applied once a day for treatment of ankle sprain. One hundred sixty-three patients were randomized that included 81 Ketoprofen group and 82 placebo group. They concluded that a 7-day course of treatment with a Ketoprofen patch is useful in benign ankle sprain without revealing unexpected adverse events.

**Kostamovaara et al[22] in 1998** compared the efficacy of Ketorolac 30 mg i.v. followed by infusion at a rate of 90 mg/15.5 hour with that of Diclofenac 75 mg followed by infusion of 75 mg/15.5 hour or Ketoprofen 100 mg followed by infusion of 100 mg/ 15.5 hour on post operative pain in 85 patients after hip replacement surgery under spinal anaesthesia. He concluded that Ketorolac, Diclofenac and Ketoprofen are equally effective for pain relief after total hip replacement surgery.

**Santosh Kumar et al[11] in 2016** evaluated the efficacy of transdermal buprenorphine patch in post operative pain management in abdominal surgery. Ninety patients divided into 3 equal groups comprising Group A: Placebo patch, Group B: Buprenorphine 10 mg patch and Group C: 20 mg patch. Pain was assessed using VAS scale at 2 hours, 6 hours, 12 hours, 2$^{nd}$ day-7$^{th}$ day post operatively. It was concluded

that transdermal Buprenorphine transdermal patch was effective in attenuating post operative pain better than placebo while maintaining hemodynamic stability.

**Zia Arshad et al**[23] in 2015 compared post operative analgesia between transdermal Buprenorphine and Transdermal fentanyl between transdermal Buprenorphine and Transdermal fentanyl. Sixty patients undergoing major abdominal surgery under G.A. were divided into 2 equal groups with Group A receiving Buprenorphine 10mcg/hour TDS and Group B receiving 25 mcg/hour fentanyl TDS, 6 hours prior to surgery; and followed for three days for post operative pain relief. They concluded that both the transdermal patches were effective in post operative analgesia, however, Fentanyl is better than buprenorphine.

# MATERIALS AND METHODS

## STUDY DESIGN

An In-Vivo Single Blinded Randomised Controlled Clinical Trial – A Split Mouth Study

## STUDY POPULATION:

The study was conducted in Department Of Oral And Maxillofacial Surgery, KLE V. K. Institute of Dental Sciences, Belagavi with due permission of the institutional ethical committee. A total of 30 patients, referred from Department of Orthodontics and Dentofacial Orthopaedics with requirement of bilateral maxillary and/or mandibular premolar extraction for orthodontic intervention, were included in the study that met the inclusion and exclusion criteria. A written informed consent was obtained from them.

## INCLUSION CRITERIA

- Patients aged 15 to 30 years requiring bilateral maxillary and/or mandibular premolar extraction for orthodontic intervention.
- No known history of allergy to NSAIDs.
- Patients willing to give written informed consent for the study.

## EXCLUSION CRITERIA

- Presence of systemic disease.
- Premolars associated with periodontal and periapical pathologic features.

## MATERIALS AND ARMAMENTARIUM

### Materials:

- 200 mg Diclofenac transdermal patch
- 30 mg Ketoprofen transdermal patch

### Armamentarium:

- Face shield
- Mouth mask
- Head cap
- Surgical gloves
- Syringe 2 ml
- Local Anaesthesia with adrenaline
- Gauze pieces
- Periosteal elevator
- Premolar Extraction Forceps

## METHODOLOGY

- Assigned patients underwent extractions in the Department of Oral and Maxillofacial Surgery.

- In the first appointment or session, patients underwent atraumatic extraction of the ipsilateral maxillary and /or mandibular premolars under local anaesthesia at a single session.

- In the second appointment or session, patients underwent extraction of premolars on the contralateral side 5-7 days later.
- Extraction of teeth was carried out by conventional forceps method after administering regional anaesthesia by infiltrating or blocking the nerve with 2% lignocaine plus adrenaline 1:80,000.
- A pressure pack was placed on the extraction site.
- All patients received post-extraction instructions.
- The patch was decided in random order based on chit system.
- Each patient received single transdermal Diclofenac 200 mg patch or transdermal Ketoprofen 30mg patch on outer, ipsilateral upper arm immediately post extraction. Patients who had received Diclofenac patch in the first appointment were given Ketoprofen patch in the second appointment while the patients who had received Ketoprofen patch in the first appointment were given Diclofenac patch in the second appointment.
- All the study patients received rescue analgesic (Tablet Ketorolac 10 mg).
- The patient's post-operative pain was assessed using a 10-point visual analog scale[24] (VAS) recorded every 2 hourly (Patient Assessment sheet).
- Follow up was done 24 hours after the extraction to evaluate pain; adverse reactions, if any, associated with the patch and the need for rescue analgesic within 24 hours after the atraumatic extraction.

## METHODOLOGY WITH FLOWCHART

Patients reported to Department of Oral and Maxillofacial Surgery for Bilateral therapeutic premolar extractions.

↓

Patients underwent atraumatic extraction of the ipsilateral maxillary and /or mandibular premolars under local anaesthesia at a single session for first intervention, followed by the extraction of premolars on the contralateral side for second intervention 5-7 days later.

↓

Each patient received single transdermal Diclofenac 200 mg patch or transdermal Ketoprofen 30mg patch on outer, ipsilateral upper arm immediately post extraction.

Patients who had received Diclofenac patch in the first appointment were given Ketoprofen patch in the second appointment while the patients who had received Ketoprofen patch in the first appointment were given Diclofenac patch in the second appointment.

↓

Follow up done 24 hours after the extraction to evaluate pain; adverse reactions, if any, associated with the patch and the need for rescue analgesic every second hourly within 24 hours after the atraumatic extraction.

**Fig. 1: Personal protective Equipment**

**Fig. 2: Armamentarium used for orthodontic premolar extractions**


**Fig. 3: Transdermal Diclofenac 200 mg patch and Transdermal Ketoprofen 30 mg patch**

**Fig. 4: Immediate post extraction right upper and lower premolar extraction**

**Fig. 5: Transdermal patch applied in appointment 1**

**Fig. 6: Immediate post extraction left upper and lower premolar extraction**

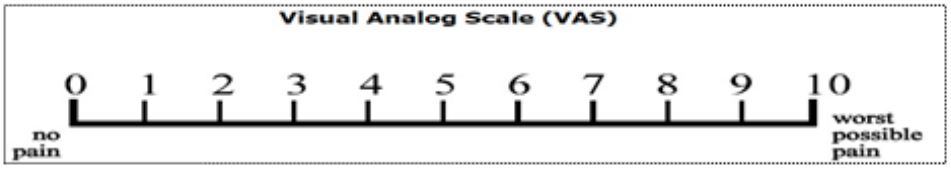
**Fig. 7: Transdermal patch applied in appointment 2**

**PATIENT ASSESSMENT SHEET**

NAME:

AGE:

OPD No.:




APPOINTMENT 1/PATCH 1:

DATE-

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TIME | | | | | | | | | | | | |
| PAIN INTENSITY | | | | | | | | | | | | |
| RESCUE ANALGESIC INTAKE | | | | | | | | | | | | |

ALLERGIC REACTION: YES / NO

APPOINTMENT 2/PATCH 2:

DATE-

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TIME | | | | | | | | | | | | |
| PAIN INTENSITY | | | | | | | | | | | | |
| RESCUE ANALGESIC INTAKE | | | | | | | | | | | | |

ALLERGIC REACTION: YES / NO

**Fig. 8: Patients were given the assessment sheets in following format to be filled every second hourly post extraction for 24 hours.**

# RESULTS

In the present study 30 patients were included who required post extraction analgesia after orthodontic bilateral maxillary and/or mandibular premolars extractions under local anaesthesia. The patients were randomly divided into two groups: **Group 1** (Transdermal Ketoprofen 30 mg patch given in first appointment and Transdermal Diclofenac 200 mg patch given in the second appointment) included **16 patients** and **Group 2** (Transdermal Diclofenac 200 mg patch given in the first appointment and Transdermal Ketoprofen 30 mg patch given in second appointment) included **14 patients**.

**Table 1: Gender wise distribution of patients**

| Gender | Number of patients | Percentage of patients |
|---|---|---|
| Male | 15 | 50.00 |
| Female | 15 | 50.00 |
| Total | 30 | 100.00 |

**Graph 1: Mean age and SD age of males and females in the study**

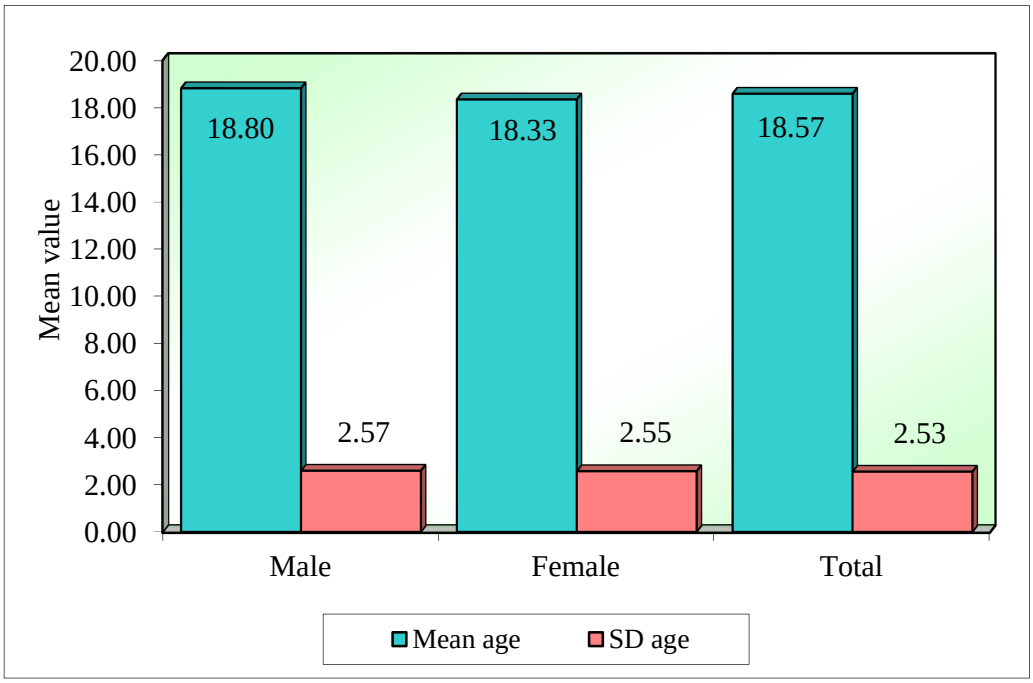
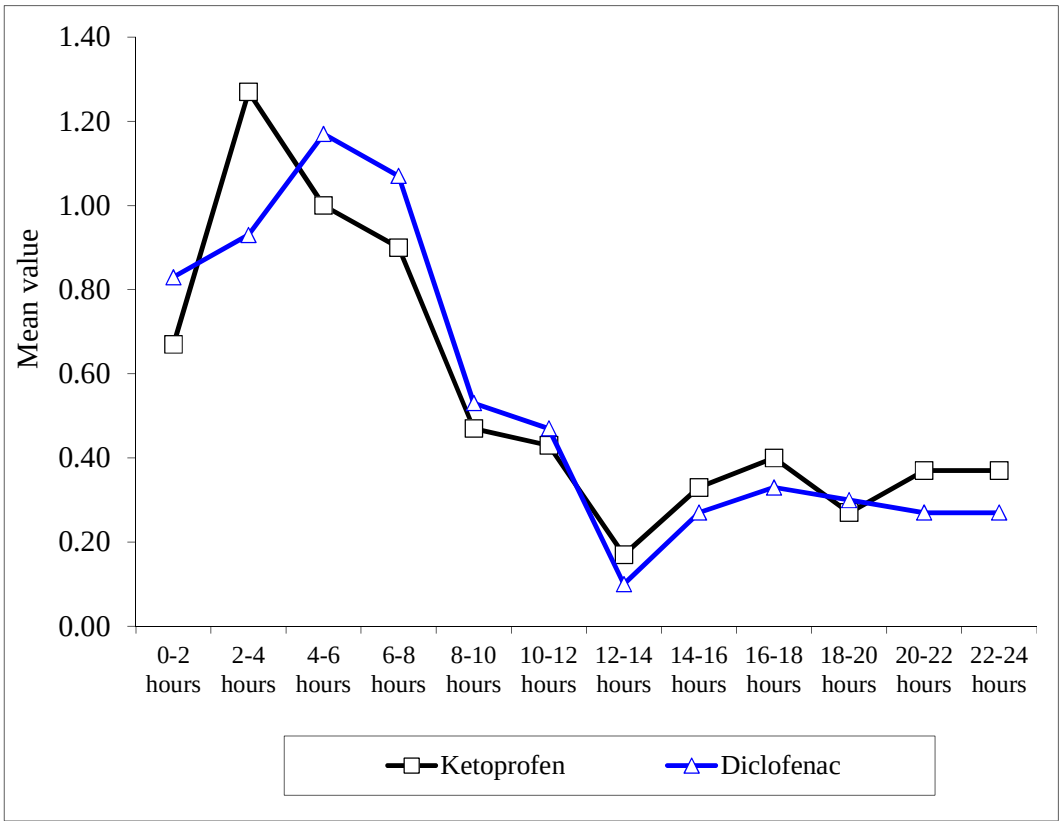


**Table 2: Comparison of VAS pain scores of Ketoprofen and Diclofenac patches by Mann-Whitney U test**

| Time points | Ketoprofen | | | Diclofenac | | | U-value | Z-value | P-value |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean rank | Mean | SD | Mean rank | | | |
| 0-2 hours | 0.67 | 1.21 | 29.87 | 0.83 | 1.32 | 31.13 | 431.00 | -0.2735 | 0.7845 |
| 2-4 hours | 1.27 | 1.87 | 28.17 | 0.93 | 0.25 | 32.83 | 380.00 | -1.0275 | 0.3042 |
| 4-6 hours | 1.00 | 1.51 | 30.42 | 1.17 | 2.02 | 30.58 | 447.50 | -0.0296 | 0.9764 |
| 6-8 hours | 0.90 | 1.77 | 29.75 | 1.07 | 2.07 | 31.25 | 427.50 | -0.3253 | 0.7450 |
| 8-10 hours | 0.47 | 1.17 | 30.87 | 0.53 | 1.46 | 30.13 | 439.00 | 0.1552 | 0.8766 |
| 10-12 hours | 0.43 | 1.61 | 30.48 | 0.47 | 1.46 | 30.52 | 449.50 | 0.0000 | 1.0000 |
| 12-14 hours | 0.17 | 0.91 | 30.03 | 0.10 | 0.40 | 30.97 | 436.00 | -0.1996 | 0.8418 |
| 14-16 hours | 0.33 | 1.15 | 30.52 | 0.27 | 1.11 | 30.48 | 449.50 | 0.0000 | 1.0000 |
| 16-18 hours | 0.40 | 1.07 | 31.00 | 0.33 | 1.21 | 30.00 | 435.00 | 0.2144 | 0.8303 |
| 18-20 hours | 0.27 | 0.98 | 30.05 | 0.30 | 1.12 | 30.95 | 436.50 | -0.1922 | 0.8476 |
| 20-22 hours | 0.37 | 1.03 | 31.08 | 0.27 | 0.94 | 29.92 | 432.50 | 0.2513 | 0.8016 |
| 22-24 hours | 0.37 | 1.00 | 31.45 | 0.27 | 0.83 | 29.55 | 421.50 | 0.4140 | 0.6789 |

Table 2 and graph 2 shows comparison of VAS pain scores at different treatment time points after application of Transdermal Ketoprofen patches and Transdermal Diclofenac patches. No statistically significant ($p<0.05$) difference was found between the analgesic efficacy of two transdermal patches at any given time point in 24 hours.

**Graph 2: Comparison of Ketoprofen and Diclofenac patches with mean values of VAS pain scores at different treatment time points**




Graph 2 shows a line diagram representing comparison of mean values of VAS pain scores at different time points after application of Ketoprofen and Diclofenac Transdermal patches.

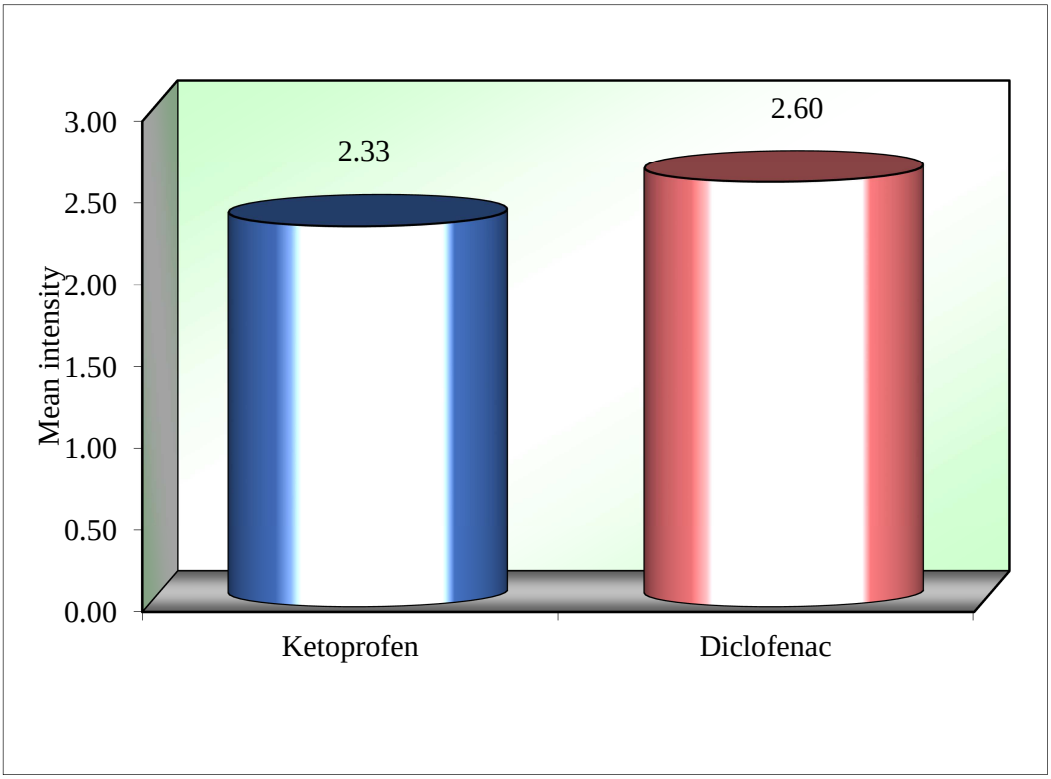
**Table 3: Comparison of VAS scores at different treatment time points with initial (0-2 hours) VAS score after application of Ketoprofen and Diclofenac Transdermal patches by Wilcoxon matched pairs test**

| Groups | Changes from 0-2 hours to | Mean Diff. | SD Diff. | % of changes | Z-value | P-value | Friedman's test | P-value |
|---|---|---|---|---|---|---|---|---|
| Ketoprofen | 2-4 hours | -0.60 | 1.38 | -90.00 | 2.2737 | 0.0230* | 54.1856 | 0.0001* |
| | 4-6 hours | -0.33 | 1.71 | -50.00 | 0.8790 | 0.3794 | | |
| | 6-8 hours | -0.23 | 1.76 | -35.00 | 0.5491 | 0.5829 | | |
| | 8-10 hours | 0.20 | 1.40 | 30.00 | 0.8736 | 0.3824 | | |
| | 10-12 hours | 0.23 | 1.04 | 35.00 | 1.2230 | 0.2213 | | |
| | 12-14 hours | 0.50 | 0.68 | 75.00 | 3.0594 | 0.0022* | | |
| | 14-16 hours | 0.33 | 1.03 | 50.00 | 2.2713 | 0.0231* | | |
| | 16-18 hours | 0.27 | 1.26 | 40.00 | 1.3278 | 0.1842 | | |
| | 18-20 hours | 0.40 | 1.38 | 60.00 | 2.1181 | 0.0342* | | |
| | 20-22 hours | 0.30 | 1.39 | 45.00 | 1.6449 | 0.1000 | | |
| | 22-24 hours | 0.30 | 1.47 | 45.00 | 1.6449 | 0.1000 | | |
| Diclofenac | 2-4 hours | -0.10 | 1.30 | -12.00 | 0.9124 | 0.3615 | 103.4617 | 0.0001* |
| | 4-6 hours | -0.33 | 2.09 | -40.00 | 0.8235 | 0.4102 | | |
| | 6-8 hours | -0.23 | 2.42 | -28.00 | 0.3314 | 0.7404 | | |
| | 8-10 hours | 0.30 | 1.73 | 36.00 | 0.7533 | 0.4513 | | |
| | 10-12 hours | 0.37 | 1.69 | 44.00 | 1.1531 | 0.2489 | | |
| | 12-14 hours | 0.73 | 1.39 | 88.00 | 2.5858 | 0.0097* | | |
| | 14-16 hours | 0.57 | 1.81 | 68.00 | 2.1658 | 0.0303* | | |
| | 16-18 hours | 0.50 | 1.91 | 60.00 | 1.7577 | 0.0788 | | |
| | 18-20 hours | 0.53 | 1.80 | 64.00 | 2.1344 | 0.0328* | | |
| | 20-22 hours | 0.57 | 1.63 | 68.00 | 2.1573 | 0.0310* | | |
| | 22-24 hours | 0.57 | 1.55 | 68.00 | 2.1315 | 0.0330* | | |

*$p<0.05$

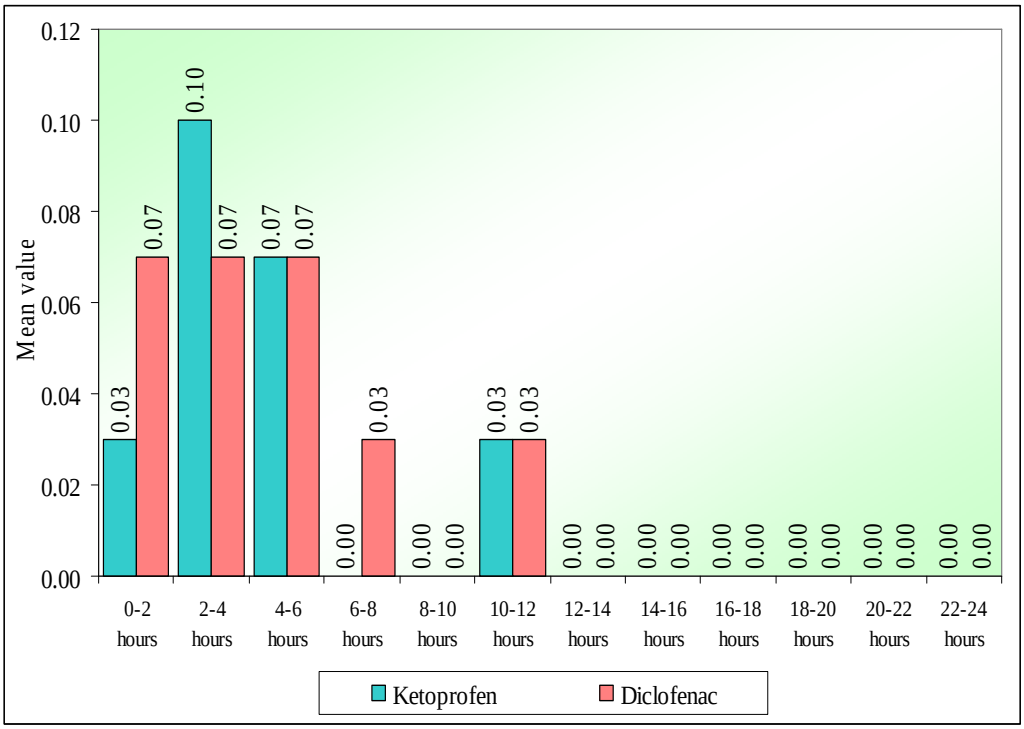
Table 3 demonstrates intragroup comparison of VAS pain scores at different time points in relation to VAS pain score at 0 – 2 hours after application of Transdermal Ketoprofen and Diclofenac patches respectively to the study patients. Statistically significant difference ($p<0.05$) in VAS pain score was found with Ketoprofen patch at time points 2-4 hours, 12-14 hours, 14-16 hours, 18-20 hours as compared to VAS pain score at 0-2 hours; and with Diclofenac group at time points 12-14 hours, 14-16 hours, 18-20 hours, 20-22 hours, 22-24 hours as compared to VAS pain score at 0-2 hours. Overall within each group statistical significant ($p<0.05$) difference was found between the VAS pain scores at different time points as compared to VAS pain score at 0-2 hours.

**Graph 3: Comparison of maximum pain intensity experienced after application of Transdermal Ketoprofen and Transdermal Diclofenac patches**



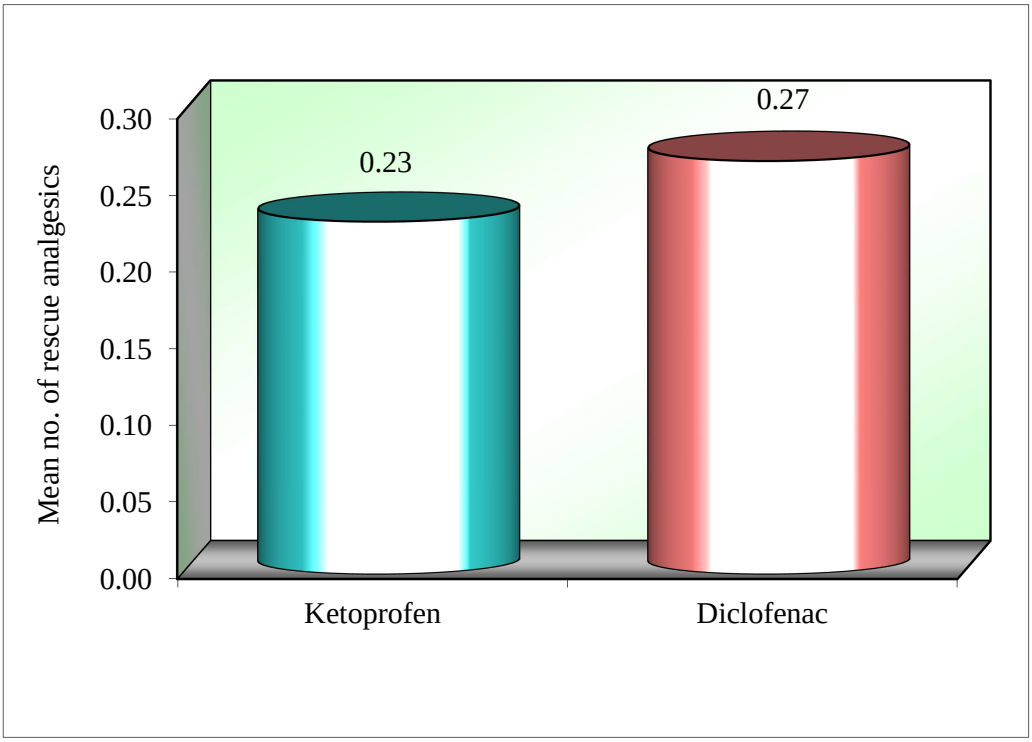

Graph 3 demonstrates the comparison of mean of maximum VAS pain score or maximum pain intensity experienced by the study patients within first 24 hours postoperatively after the application of Ketoprofen and Diclofenac transdermal patch respectively. The study patients had mean maximum pain intensity of 2.33 after Ketoprofen transdermal patch application which was slightly lower than the mean maximum pain intensity of 2.60 after Diclofenac transdermal patch.

**Graph 4: Comparison of Rescue analgesic intake at different treatment time points after application of Transdermal Ketoprofen and Transdermal Diclofenac patches**




Graph 4 is bar graph that demonstrates comparison of mean of rescue analgesics taken by the study patients at different time points with Ketoprofen and Diclofenac transdermal analgesic patches respectively. All study patients consumed the rescue analgesic within first 12 hours post operatively with maximum intake in Ketoprofen group between 2-4 hours post operatively.

**Graph 5: Comparison of Ketoprofen and Diclofenac patches with Number of Rescue analgesics**




Graph 5 compares the mean value of total number of rescue analgesic intake by the study patients in first 24 hours post extraction after application of Transdermal Ketoprofen and Transdermal Diclofenac patches respectively. The mean value of total number of rescue analgesic taken with Ketoprofen transdermal patch is 0.23 which is slightly lower than Diclofenac transdermal patch (0.27) application

# DISCUSSION

Patients relate dental treatment especially minor oral surgical procedures performed under local anaesthesia with pain. An eventful experience of badly managed pain related to dental treatment can lead patients to avoid or delay treatment and makes them apprehensive to future minor oral surgical procedures.[16] Therapeutic or orthodontic teeth extractions are many times first exodontia procedure for the patients and hence, pain management is of utmost importance in such cases for removal of fear instilled in patients related to minor oral surgical procedures.

Post extraction the medications are usually administered by oral route, but the oral route has certain disadvantages such as low bioavailability due to its first pass metabolism, gastrointestinal adverse effects and patient non-compliance.[9] This lead to use of transdermal drug delivery system.

Transdermal drug delivery has been considered a safer method for pain management postoperatively since a long time as it avoids the gastrointestinal complications. The drug contained in the transdermal patch enters the body through the dermis of the skin, after which, it diffuses into the capillaries for systemic delivery. A steady penetration of the drug across the dermis occurs, that allows for a consistent, uniform serum drug level and regulated drug absorption. Pharmacokinetic data have suggested that transdermal NSAID patches have an increased tissue concentration to excrete a therapeutic effect but with plasma concentrations low enough thus avoiding systemic complications.[9] This drug delivery system also has enhanced bioavailability, because it evades the firstpass hepatic metabolism and enzymatic or pH associated deactivation associated with oral administration.

Transdermal drug delivery is non – invasive and hence it eliminates the fear of prick or injection associated with the invasive IM or IV route of injection.[9]

Transdermal patch application has increased flexibility in terminating drug administration by patch removal. Patient compliance is henceforth improved.[25] Various analgesic drugs are available in the form of a patch, for example, fentanyl and buprenorphine, apart from diclofenac and ketoprofen. Reported data, supported by the results from clinical trials, recommend that transdermal medications are equally efficacious compared with oral administration of the same drug. Transdermal patches provide effective postoperative analgesia, not only for dentoalveolar surgical practice, but also for major procedures, such as orthognathic, abdominal, and orthopedic surgery.[26]

Diclofenac and Ketoprofen are preferred NSAID used in clinical practice for postoperative pain management. Selvi et al[12] in 2016 compared transdermal Diclofenac patch with intramuscular diclofenac injection as an analgesic modality following surgical extraction of impacted mandibular third molars in a cross over efficacy trail. They concluded that Diclofenac administered by either mode of delivery as transdermal patches or IM injections has similar effectiveness but the patients showed better compliance with transdermal drug delivery. Hemant Bhaskar et al[13] in 2010 compared transdermal diclofenac patch with oral diclofenac as an analgesic modality following multiple premolar extractions in orthodontic patients. They concluded that both diclofenac formulations provided potent analgesia with the advantage of better patient compliance for transdermal route. The above mentioned studies concluded that patient compliance with the patch was greater than that with other routes of drug administration.

Mazieres et al[21] in 2005 tested the efficacy and tolerability of a 100 mg patch of Ketoprofen applied once a day for the treatment of ankle sprain. One hundred sixty-three patients were randomized that included 81 Ketoprofen group and 82 placebo group. They concluded that a 7-day course of treatment with Ketoprofen patch is useful in benign ankle sprain without revealing unexpected adverse events. Andreas Osterwalder et al[20] in 2002 evaluated tissue absorption and distribution of Ketoprofen after patch application in subjects undergoing knee arthroscopy or endoscopic carpal ligament release. They concluded that Ketoprofen applied on the skin is able to enter the subcutaneous and intra-articular tissues, reaching concentrations significantly higher than in plasma to produce the desired pharmacological activity in situ and plasma concentrations are low enough to avoid any systemic adverse or side effect.

In the present study, 30 patients with a mean age of 18.57 ± 2.53 years who underwent orthodontic bilateral maxillary and/or mandibular premolars extractions under local anaesthesia were included and required post extraction analgesia. The extractions were done in two separate appointments with a latency period of atleast 5 days between the interventions. The study population comprised of 15 males (50%) and 15 females (50%). The purpose of the present study was to compare the analgesic efficacy of transdermal ketoprofen and diclofenac patches for patients who had undergone atraumatic extraction of first premolars for orthodontic purposes. The evaluation was done on the basis of Visual Analog Scale (VAS) pain score recorded every second hourly for first 24 hours post operatively, requirement of rescue analgesic at various time points in the first 24 hours post operatively and total number of rescue analgesic taken in the first 24 hours post operatively. Any allergic reaction or complications to the use of analgesic patches was also recorded.

The results of the present study have shown that the ketoprofen transdermal patch and diclofenac transdermal patch provide similar analgesia post orthodontic extraction. Ritu Verma et al[9] in 2016 compared single dose transdermal patches of Diclofenac (100 mg) and Ketoprofen (20 mg) for postoperative analgesia in lower limb orthopedic surgery. They concluded that transdermal patch of Ketoprofen and Diclofenac both are effective for postoperative analgesia in lower limb orthopedic surgery under spinal anaesthesia but in Diclofenac group more patients required rescue analgesic as compared to Ketoprofen group. Whereas the available literature that compared the analgesic efficiency of ketoprofen to that of diclofenac suggests that ketoprofen is a better alternative for achieving analgesia for postoperative pain management. Darpan Bhargawa et al[4] in 2019 compared the efficacy of transdermal Ketoprofen (20 mg) and Diclofenac (200 mg) patch in patients undergoing therapeutic atraumatic first premolar extractions. They concluded that Ketoprofen is superior to Diclofenac as a transdermal medicament in providing post extraction analgesia.

The results from the present study are consistent with the above studies showing a decreased mean VAS score for maximum pain intensity with ketoprofen patch application as compared to diclofenac patch application. Patients reported of lower maximal pain intensity with Ketoprofen transdermal patch application. No statistically significant ($p<0.05$) difference was found between the analgesic efficacy of two transdermal patches at any given time point in 24 hours. The mean VAS score for maximum pain intensity was 2.33 for Ketoprofen patch compared with a mean VAS score for maximum pain intensity of 2.60 for the diclofenac patch.

However, Bachalli et al[16] in 2016 conducted a comparative study of Diclofenac transdermal patch (100 mg) against oral diclofenac (100 mg) for pain

control following removal of mandibular impacted third molars. They concluded that transdermal diclofenac sodium can be used as an alternative form of pain control following removal of impacted mandibular third molars, however considering that the analgesic potency might be lesser in the immediate postoperative period, it might be prudent to use oral diclofenac sodium for immediate postoperative pain relief, following which transdermal route can be used for pain control. This finding is consistent with our study where patients had higher VAS pain score and required rescue analgesic up to 10-12 hours postoperatively after which they were comfortable. In the present study, the total number of patients who took rescue analgesic with Ketoprofen patch application was six while seven patients took rescue analgesic with Diclofenac patch application. All the patients who took rescue medication consumed them between 0 hours to 10-12 hours postoperatively. No allergic or adverse reactions were reported to either of the patches among the study participants which is similar to the available literature.

In general, according to the literature Ketoprofen has been found to be more potent than Diclofenac, although the use of Ketoprofen has not been popular in clinical practice, despite its documented potent action which might be attributed to its lack of over the counter availability. However, in our study Ketoprofen faired better in providing post exodontia analgesia than Diclofenac in terms of maximum VAS score recorded by the study patients after each of the transdermal patch application but the difference between the VAS scores was not statistically significant at any of the different time points in 24 hours follow-up period.

# CONCLUSION

Transdermal drug delivery systems are simple and compliant methods of delivery. They possess the advantages of providing sustained release of the drug, non-invasive method of drug administration, they bypass first pass metabolism and eliminate gastrointestinal adverse effects.

In conclusion, both Ketoprofen and Diclofenac transdermal patches were effective for postoperative analgesia after orthodontic extraction under local anaesthesia but the maximum pain intensity was lower with Ketoprofen transdermal patch. The patients in the current study required rescue analgesic during initial hours of post-operative follow-up period after which they were comfortable. This may indicate that analgesic potency of transdermal patches might be less immediately after application, till they achieve steady plasma concentrations requiring oral drug administration for immediate postoperative pain relief.

# BIBLIOGRAPHY


1. Fletcher MC, Spera JF. Pre-emptive and postoperative analgesia for dentoalveolar surgery. Oral Maxillofacial Surg Clin North Am. 2002; 14: 137-51.
2. Monheim LM, Bennett CR. Pain. In: Monheim, editor. Monheim's Local anesthesia and pain control in dental practice, 7th edn. Saint Louis:C.V. Mosby;1978.p.1-25.
3. P Ng et al: A comparison of ketoprofen and diclofenac for acute musculoskeletal pain relief: a prospective randomised clinical trial; Hong kong j.emerg.med.2001;8:73-77
4. Darpan Bhargava, Shaji Thomas: Comparison Between Efficacy Of Transdermal Ketoprofen And Diclofenac Patch In Patients Undergoing Therapeutic Extraction – A Randomized Prospective Split Mouth Study, j oral maxillofac surg 2019,77:1998-2003.
5. Tripathi KD: Routes of drug administration, in Tripathi KD (ed): Essentials of Medical Pharmacology (ed 6). India, Jaypee Brothers Medical Publishers Ltd, 2009, pp 8–9.
6. Deepthi Mony et al., Comparative Evaluation of Intramuscular Diclofenac and Ketorolac in Third Molar Surgery, Journal of Clinical and Diagnostic Research. 2016 Jun, Vol-10(6): ZC102-ZC106.
7. Scholer et al: Pharmacology of Diclofenac Sodium, The American Journal of Medicine, April 28 1986, Volume 80.
8. Ketoprofen | C16H14O3 – PubChem, December 2022.

9. Verma R, Kumar S, Goyal A, Chaudhary A: Comparison of single dose transdermal patches of diclofenac and ketoprofen for postoperative analgesia in lower limb orthopaedic surgery. Int J Res Med Sci 2016, 4:718.
10. Vandana Chhabra , Hemant Batra, Vandana Gupta, Ajay Chhabra, Poonam Sood: To evaluate the efficacy of transdermal diclofenac patch in the management of post surgical pain, International Journal of Scientific Research, Volume-8 | Issue-12 | December – 2019, Int J Res Med Sci. 2016 Mar;4(3):718-721.
11. Kumar S, Chaudhary AK, Singh PK, et al: Transdermal buprenorphine patches for postoperative pain control in abdominal surgery, J Clin Diagn Res, 2016, 10:UC05.
12. Selvi UPG, Kamatchi D, Babu C, et al: Comparison of transdermal diclofenac patch with intramuscular diclofenac injection as an analgesic modality following surgical extraction of impacted mandibular third molars: A cross over efficacy trail. Int J Sci Stud 2016, 4:117.
13. Bhaskar H, Kapoor P, Ragini: Comparison of transdermal diclofenac patch with oral diclofenac as an analgesic modality following multiple premolar extractions in orthodontic patients: A cross over efficacy trial. Contemp Clin Dent 2010,1:158.
14. Perepa A, Sinha BR, Uppada UK, Kumar AS: Diclofenac transdermal patch: A potential ingress to maxillofacial surgery. J Maxillofac Oral Surg 2016,16:170.
15. Jadhav P, Ramen S, Uppada UK, et al: Pre-emptive diclofenac versus ketoprofen as a transdermal drug delivery system: How they face. J Maxillofac Oral Surg, 2018,17:488.

16. Bachalli PS, Nandakumar H, Srinath N: A comparative study of diclofenac transdermal patch against oral diclofenac for pain control following removal of mandibular impacted third molars, J Maxillofac Oral Surg, 2009, 8:167.
17. Kumar V, Gupta S, Verma R: Evaluation of the role of transdermal diclofenac patch (Nupatch) in management of pain in postoperative patients. Int J Contem Med Res 2017,4:493.
18. Y M A Tai et al: Comparison of controlled-release ketoprofen and diclofenac in the control of post-surgical dental pain Journal of the Royal Society of Medicine January, 1992, Volume 85.
19. Raichurkar A, Ramachandra KKB: Placebo controlled comparative study of efficacy of diclofenac and ketoprofen transdermal patches in attenuating intravenous cannulation pain. J DentMed Sci, 2015, 14:111.
20. Osterwalder A, Reiner V, Reiner G, et al: Tissue Absorption and Distribution of Ketoprofen after Patch Application in Subjects Undergoing Knee Arthroscopy or Endoscopic Carpal Ligament Release, Arzneimittelforschung, 2002; 52(11): 822-827.
21. Mazières et al: Topical Ketoprofen Patch (100 mg) for the Treatment of Ankle Sprain- A Randomized, Double-Blind, Placebo-Controlled Study, The American Journal of Sports Medicine, 2005, Vol. 33, No. 4.
22. Kostamovaara et al: ketorolac, diclofenac and ketoprofen are equally efficacious for pain relief after total hip replacement surgery, British Journal of Anaesthesia 1998, 81:369-372.
23. Arshad Z, Prakash R, Gautam S, Kumar S: Comparison between transdermal buprenorphine and transdermal fentanyl for postoperative pain relief after major abdominal surgeries. J Clin Diagn Res, 2015, 9:UC01.

24. Mathias Haefeli et al: Pain assessment, Eur Spine J. 2006 Jan; 15(Suppl 1): S17–S24.
25. Bajaj S, Whiteman A, Brandner B: Transdermal drug delivery in pain management. Br J Anaesth Educ, 2011, 11:39.
26. McCleane G: Topical analgesics. Anesthesiol Clin, 2007, 25:825.

# ANNEXURE I – CONSENT FORM

**KLE Vishwanath Katti Institute of Dental Sciences, Belagavi**
**Department of Oral and Maxillofacaial Surgery**
**Patient Information Sheet**

**"Evaluation Of Efficacy Of Transdermal Ketoprofen Patch In Comparison To Transdermal Diclofenac Patch as an Analagesic In Patients Undergoing Orthodontic Extractions – A Randomised Prospective Split Mouth Study"**

Dear Patient,
You are invited to take part in a research study to evaluate and compare pain control after orthodontic extraction using two different analgesic patches. This research is a part of a MDS, main dissertation at KLE Academy of Higher Education and Research.

Before you decide whether to take part in the study it is important that you understand what the research is for and what you will be asked to do. Please take time to read the following information and discuss it with others if you wish to. It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep. You will be also asked to sign a consent form. You can change your mind at any time and withdraw from the study without giving any reason. The standard of care you receive will not change whether or not you decide to participate in this study. You are welcome to call me (@8054189425) if you would like any further information.

The purpose of this research study is to compare the efficacy of transdermal Ketoprofen Patch versus transdermal Diclofenac Patch in orthodontic extractions.

You have been chosen because you require extraction of your premolars for orthodontic intervention. This study will involve 30 participants who require bilateral premolars extractions for orthodontic intervention, and will be given transdermal Ketoprofen 30mg patch and transdermal Diclofenac 200mg patch, in random order, immediately post-extraction after getting informed consent. You will be asked to report for a review and follow-up visit after 24 hours.

The information gained from this research will be used to publish in scientific platforms/ journals without revealing your identity to make recommendations for the best practice and the results of the study may also lead onto further studies into the management of pain using alternative mode of drug delivery methods after orthodontic extractions.

PG Student (MDS)
Dept. of Oral and Maxillofacial Surgery
KLEVKIDS, Belagavi

**K.L.E.'s V.K. Institute of Dental Sciences**
**Department of Oral and Maxillofacial Surgery, Belagavi**
**CONSENT FOR THE STUDY**

**"EVALUATION OF EFFICACY OF TRANSDERMAL KETOPROFEN PATCH IN COMPARISON TO TRANSDERMAL DICLOFENAC PATCH AS AN ANALGESIC IN PATIENTS UNDERGOING ORTHODONTIC EXTRACTIONS – A RANDOMISED PROSPECTIVE SPLIT MOUTH STUDY."**

Date: Time: am/pm

1. I, _____ aged_____ years have been informed about my involvement in the study.
2. I agree to give my personal details like Name, Age, Sex, Address, Medical history, Past dental history and any other details required for the study to the best of my knowledge.
3. I will cooperate with the surgeon for examination and also for various investigations.
4. I permit the operator to utilize the information given by me and the results obtained from this study for presentation and publication.
5. I permit the surgeon to take my photographs to utilize it for the study and presentation purpose.
6. I am participating in this study with my own wish and the dental surgeon has explained the nature and the effect of procedure including extraction of tooth followed by application of transdermal patch for management of pain in my vernacular language.
7. The nature and purpose of the operation and the materials being used, possible alternative methods of treatment, the risk involved and the possibility of complications have been fully explained to me in my mother tongue. No guarantee or assurance has been given by anyone as to the results that may be obtained.
8. I have read and understood the above information given by surgeon about the study and willingly agree to participate in the study.

Patients / Witness Signature:
Date:
Surgeon's name: Dr.
Surgeon's signature:

## ANNEXURE II – BIOSTATISTICS CLEARANCE CERTIFICATE

**KLE V.K. Institute of Dental Sciences**
(A Constituent unit of KLE Academy of Higher Education & Research
Deemed-to-be-University u/s 3 of the UGC Act, 1956)
Nehru Nagar, Belagavi-590 010 INDIA
Re-Accredited 'A' grade by NAAC (2nd Cycle) & Placed in Category 'A' by MHRD (GoI)
: 0831-2470362
FAX:0831-2470640
Web: http://www.kledental-bgm.edu.in
E-mail:principal@kledental-bgm.edu.in

### *BiostatisticsClearanceCertificate*

This is to certify that the Biostatistics aspect of the Dissertation / Research work of **REG.NO. – IF0220004** : **Graduate Student**, under the guidance of **Department of Oral and Maxillofacial Surgery**, entitled **"Evaluation of efficacy of Transdermal patch in comparison to Transdermal Diclofenac patch as an analgesic in patients undergoing orthodontic extractions – A randomised prospective split mouth study"** has been done under my guidance and considered satisfactory.

**Place:** Belagavi
**Date:** 18.11.2022

Name and Signature of Biostatistician
(Dr. S. B. Javali)
Sr. Asso. prof. in statistics
OSM KLE IMP, Belagavi.

## ANNEXURE III – ETHICAL CLEARANCE CERTIFICATE

**Research and Ethics Committee**
**KLE V K INSTITUTE OF DENTAL SCIENCES**
**KLE University**
Accredited 'A' Grade by NAAC  Placed in Category 'A' by MHRD (GoI)
Nehru Nagar, Belagavi - 590 010, Karnataka State
☎: 0831-2470362
FAX: 0831-2470640
Web: http://www.kledental-bgm.edu.in
E-mail:principal@kledental-bgm.edu.in

Sl. No. : 1467

**CERTIFICATE**

*This is to Certify that the synopsis titled*

Evaluation of efficacy of transdermal Ketoprofen patch in comparison to transdermal diclofenac patch as an analgesic in patients undergoing Orthodontic extraction - a randomised prospective split mouth study

*Submitted by Dr.* _____ **REG.NO. – IF0220004** _____ *P. G. Student / Staff, Guided by* _____ *from Department of* Oral and Maxillofacial Surgery *has been critically evaluated by committee members and granted ethical clearance to conduct the above mentioned study*

**Date :** 5/5/21

**Member Secretary**
Research and Ethical Committee
KLEVK Institute of Dental Sciences
Belagavi

**Chairman**
Research and Ethical Committee
KLEVK Institute of Dental Sciences
Belagavi

## ANNEXURE VI – MAIN SHEET

| PATIENT NO. | NAME | AGE/GENDER | OPD NO. | TEETH EXTRACTED IN APPOINTMENT 1 | TRANSDERMAL ANALGESIC PATCH APPLIED IN APPOINTMENT 1 | TEETH EXTRACTED IN APPOINTMENT 2 | TRANSDERMAL ANALGESIC PATCH APPLIED IN APPOINTMENT 2 |
|---|---|---|---|---|---|---|---|
| 1 | SHAKEEB | 24/M | 46/13/01/21 | 14, 45 | K | 24, 35 | D |
| 2 | DEEPAK S. GAVASKAR | 18/M | 21/21/12/20 | 24, 34 | D | 14, 45 | K |
| 3 | ASHWINI A. SUTAR | 20/F | 38/6/1/21 | 14, 44 | K | 24, 34 | D |
| 4 | ARUNDHATI S. | 15/F | 6/6/3/21 | 14, 44 | K | 24, 34 | D |
| 5 | SHILPA B. SHETAGE | 18/F | 58/08/03/21 | 14, 44 | D | 24, 34 | K |
| 6 | ZAHEER S. KUMOL | 16/M | 03/1/12/20 | 14, 44 | K | 24, 34 | D |
| 7 | SAHANA PUJARI | 17/F | 58/2/11/20 | 14, 44 | K | 24, 34 | D |
| 8 | DISHA RAUTH | 15/F | 27/12/1/21 | 14, 45 | K | 24, 35 | D |
| 9 | VIDHATA R. KARKINAIK | 16/M | 31/20/3/21 | 14, 45 | K | 24, 35 | D |
| 10 | MALLIKARJUN B. NESARGI | 19/M | 63/27/09/21 | 14, 44 | D | 24, 34 | K |
| 11 | SAVITA L. KONGAGAL | 17/F | 07/03/09/21 | 14, 44 | K | 24, 34 | D |
| 12 | SACHIN R. METRI | 22/M | 17/29/11/21 | 14, 44 | D | 24, 34 | K |
| 13 | GAUTAMI G. SONADAKKE | 20/F | 25/26/10/21 | 14, 45 | D | 24, 35 | K |
| 14 | UZMA S. | 21/F | 07/21/6/21 | 15, 45 | D | 25, 35 | K |
| 15 | PRAFUL S. KAMBLE | 20/M | 31/15/11/21 | 14, 44 | D | 24, 34 | K |
| 16 | AJAY B. GADIWADDAR | 18/M | 63/25/10/21 | 14, 44 | K | 24, 34 | D |
| 17 | MUSKAN Z. DESAI | 19/F | 13/20/09/21 | 25 | D | 15 | K |
| 18 | VAISHNAVI PATIL | 19/F | 04/16/2/22 | 14, 44 | K | 24, 34 | D |
| 19 | ABHISHEK KOTALGI | 18/M | 18/13/12/21 | 14, 44 | K | 24, 34 | D |
| 20 | ASHMITA THAKUR | 18/F | 10/21/3/22 | 14, 44 | D | 24, 34 | K |
| 21 | SUPRIYA MAKAR | 18/F | 21/9/3/22 | 14 | D | 24 | K |
| 22 | SUHAS S. NAVAJEKAR | 22/M | 36/17/3/21 | 14, 44 | K | 24, 34 | D |
| 23 | PRIYANKA KOUJALAGI | 25/F | 35/21/12/21 | 24, 34 | D | 14, 44 | K |
| 24 | TEJASHWINI TANOJI | 17/F | 11/6/11/21 | 14, 44 | D | 24, 34 | K |
| 25 | SACHIN METRI | 19/ M | 30/14/3/22 | 24, 34 | K | 14, 44 | D |
| 26 | SANGMESH PUJERI | 15/M | 36/30/8/19 | 14, 44 | D | 24, 34 | K |
| 27 | ANUSHA NARENDRA | 16/F | 22/05/16/32 | 14, 44 | K | 24, 34 | D |
| 28 | PRASANN GUMALI | 21/M | 61/25/10/21 | 14, 44 | K | 24, 34 | D |
| 29 | YUVARAJ RAYOPPAGOL | 17/M | 22/9/17/59 | 24, 34 | D | 14, 44 | K |
| 30 | NAGARAJ TARIHALKAR | 17/M | 22/4/6/23 | 24, 34 | K | 14, 44 | D |
| | | | | | | | |
| | | | | | **GROUP 1 : 16** | | **GROUP 2 : 14** |

| | Ketoprofen | | | | | | | | | | | | Diclofenac | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| S.No. | 0-2 hours | 2-4 hours | 4-6 hours | 6-8 hours | 8-10 hours | 10-12 hours | 12-14 hours | 14-16 hours | 16-18 hours | 18-20 hours | 20-22 hours | 22-24 hours | 0-2 hours | 2-4 hours | 4-6 hours | 6-8 hours | 8-10 hours | 10-12 hours | 12-14 hours | 14-16 hours | 16-18 hours | 18-20 hours | 20-22 hours | 22-24 hours |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | 1 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 10 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 11 | 0 | 0 | 3 | 3 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 4 | 3 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 |
| 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 13 | 1 | 4 | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 1 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| 14 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 17 | 1 | 0 | 0 | 8 | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 1 | 0 | 1 | 0 | 9 | 0 | 0 | 0 | 1 | 3 | 1 | 0 | 0 |
| 18 | 6 | 8 | 3 | 3 | 2 | 8 | 5 | 5 | 3 | 2 | 2 | 1 | 2 | 1 | 7 | 6 | 4 | 4 | 1 | 1 | 1 | 1 | 1 | 1 |
| 19 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 21 | 2 | 4 | 2 | 3 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 22 | 0 | 4 | 4 | 0 | 0 | 0 | 0 | 4 | 4 | 5 | 5 | 5 | 3 | 1 | 6 | 4 | 6 | 6 | 0 | 0 | 0 | 0 | 1 | 1 |
| 23 | 1 | 3 | 4 | 1 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 1 | 5 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 24 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 25 | 1 | 2 | 2 | 3 | 4 | 4 | 0 | 0 | 0 | 1 | 2 | 2 | 0 | 1 | 1 | 2 | 3 | 4 | 0 | 6 | 6 | 6 | 5 | 4 |
| 26 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 27 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 28 | 1 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| 29 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| Patient No. | In First 24 hours for Ketoprofen patch | In First 24 hours for Diclofenac patch |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 1 | 1 |
| 3 | 1 | 1 |
| 4 | 3 | 4 |
| 5 | 2 | 3 |
| 6 | 0 | 0 |
| 7 | 2 | 2 |
| 8 | 2 | 2 |
| 9 | 0 | 0 |
| 10 | 1 | 1 |
| 11 | 3 | 4 |
| 12 | 0 | 0 |
| 13 | 4 | 4 |
| 14 | 1 | 1 |
| 15 | 0 | 0 |
| 16 | 0 | 0 |
| 17 | 8 | 9 |
| 18 | 8 | 9 |
| 19 | 2 | 1 |
| 20 | 2 | 2 |
| 21 | 4 | 5 |
| 22 | 5 | 6 |
| 23 | 4 | 5 |
| 24 | 5 | 5 |
| 25 | 4 | 6 |
| 26 | 0 | 0 |
| 27 | 3 | 3 |
| 28 | 2 | 2 |
| 29 | 2 | 2 |
| 30 | 1 | 0 |

| | Ketoprofen | | | | | | | | | | | | Diclofenac | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| S. No. | 0-2 hours | 2-4 hours | 4-6 hours | 6-8 hours | 8-10 hours | 10-12 hours | 12-14 hours | 14-16 hours | 16-18 hours | 18-20 hours | 20-22 hours | 22-24 hours | 0-2 hours | 2-4 hours | 4-6 hours | 6-8 hours | 8-10 hours | 10-12 hours | 12-14 hours | 14-16 hours | 16-18 hours | 18-20 hours | 20-22 hours | 22-24 hours |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 11 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 13 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 17 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 18 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 19 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 21 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 22 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 23 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 24 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 26 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 27 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 28 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 29 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| Patient No. | In First 24 hours with Ketoprofen patch | In First 24 hours with Diclofenac patch |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 0 | 0 |
| 3 | 0 | 0 |
| 4 | 1 | 1 |
| 5 | 0 | 0 |
| 6 | 0 | 0 |
| 7 | 0 | 0 |
| 8 | 0 | 0 |
| 9 | 0 | 0 |
| 10 | 0 | 0 |
| 11 | 1 | 1 |
| 12 | 0 | 0 |
| 13 | 1 | 1 |
| 14 | 0 | 0 |
| 15 | 0 | 0 |
| 16 | 0 | 0 |
| 17 | 0 | 1 |
| 18 | 2 | 2 |
| 19 | 0 | 0 |
| 20 | 0 | 0 |
| 21 | 1 | 1 |
| 22 | 0 | 0 |
| 23 | 0 | 0 |
| 24 | 1 | 1 |
| 25 | 0 | 0 |
| 26 | 0 | 0 |
| 27 | 0 | 0 |
| 28 | 0 | 0 |
| 29 | 0 | 0 |
| 30 | 0 | 0 |