

# Efficacy of Diclofenac and Ketoprofen Transdermal Patches for Postoperative Analgesia and their Effect on Renal Functions in Patients undergoing Percutaneous Nephrolithotomy: A Randomised Clinical Study

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## ABSTRACT

**Introduction:** Postoperative pain management following Percutaneous Nephrolithotomy (PCNL) is critical for patient comfort and recovery. Ketoprofen transdermal patches, a recent addition to Non Steroidal Anti-Inflammatory Drug (NSAID) analgesia, may offer better tolerability and analgesic efficacy compared to diclofenac patches.

**Aim:** To compare the efficacy of diclofenac versus ketoprofen patches for postoperative analgesia and their effects on serum creatinine in patients undergoing PCNL.

**Materials and Methods:** This double-blind, randomised clinical study included 52 patients (aged 18–60 years, American Society of Anaesthesiologists (ASA) I-II) undergoing elective PCNL at a tertiary care centre. Patients were randomly assigned to Group K (n=26, 30 mg ketoprofen patch) or Group D (n=26, 100 mg diclofenac patch). Patches were applied 30 minutes before the end of surgery. Pain was assessed using the Visual Analog Scale (VAS) at 0, 4, 8, 12, 16, 24 and 48 hours. Rescue analgesia (tramadol 50 mg) was administered for VAS  $\geq 5$ . Serum creatinine was measured preoperatively and at 24 hours postoperatively.

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 21.0, with p-value  $<0.05$  considered significant.

**Results:** Baseline demographics, including age, gender and ASA grading, were comparable between the groups. Group K had significantly lower VAS scores at eight hours ( $3.1 \pm 1.1$  vs.  $4.19 \pm 0.56$ ; p-value  $<0.001$ ), 24 hours ( $2.65 \pm 0.68$  vs.  $3.35 \pm 0.48$ ; p-value  $<0.001$ ) and 48 hours ( $2.4 \pm 0.5$  vs.  $3 \pm 0.74$ ; p-value=0.002). More patients in Group D required rescue analgesia at four hours (p-value=0.009). Group D showed a statistically significant rise in serum creatinine postoperatively (p-value=0.02), while Group K did not (p-value=0.057). The incidence of headaches was higher in Group D (19.2%), with fewer overall side-effects reported in Group K (p-value=0.05).

**Conclusion:** Ketoprofen patches provided superior analgesia and fewer adverse effects compared to diclofenac in post-PCNL patients. Both drugs demonstrated comparable renal safety over 24 hours. Ketoprofen may be a better alternative for transdermal analgesia in this setting.

**Keywords:** Anti-inflammatory agents, Non steroidal, Nephrolithiasis, Pain measurement, Postoperative care

## INTRODUCTION

Postoperative pain management remains a critical concern in modern surgical practice, particularly in urological procedures such as PCNL. PCNL has become the gold standard for treating large renal calculi, offering a minimally invasive alternative to traditional open surgery [1]. However, despite its benefits, postoperative pain control remains a significant challenge. Effective analgesia is essential not only for ensuring patient comfort but also for facilitating early mobilisation, reducing hospital stays and preventing complications. Traditional pain management approaches rely on oral, parenteral and topical analgesics, each with inherent advantages and limitations [2]. Opioids, while effective, are associated with risks such as nausea, sedation, dependence and respiratory depression, while systemic NSAIDs raise concerns regarding gastrointestinal and renal toxicity [3].

In recent years, transdermal drug delivery systems have gained attention as a promising alternative, offering sustained drug release, enhanced compliance and a reduced incidence of systemic side-effects. Among transdermal analgesics, ketoprofen has been introduced recently, while other NSAIDs, such as ketorolac and diclofenac patches, have shown significant efficacy in postoperative

pain management [4]. Diclofenac transdermal patches ensure consistent drug absorption, maintaining therapeutic plasma concentrations while minimising gastrointestinal adverse effects commonly observed with oral NSAID formulations. Studies suggest that diclofenac patches provide effective pain relief comparable to oral NSAIDs, with the added benefit of improved tolerability and fewer systemic complications [5-7].

Similarly, ketoprofen transdermal patches, which are a recent introduction, exhibit superior skin penetration and local tissue distribution, contributing to their efficacy in postsurgical analgesia. Ketoprofen, a non-selective Cyclooxygenase (COX) inhibitor, exerts both peripheral and central analgesic effects, making it a viable alternative for postoperative pain relief. Research has indicated that ketoprofen patches offer effective pain control with a potentially better side-effect profile, particularly in terms of gastrointestinal tolerance, when compared to systemic administration [8-10].

A significant concern with NSAID use, regardless of the route of administration, is its potential impact on renal function. This issue is particularly relevant in PCNL patients, who may already have compromised renal function due to underlying stone disease, surgical

trauma, or perioperative factors affecting kidney perfusion. NSAIDs, through their inhibition of COX enzymes, reduce prostaglandin synthesis, which plays a vital role in renal blood flow autoregulation. Consequently, NSAID-induced prostaglandin suppression may contribute to renal hypoperfusion, fluid imbalance and transient elevations in serum creatinine levels, particularly in patients with pre-existing renal impairment [11]. Therefore, monitoring serum creatinine levels in the post-PCNL setting is imperative to assess the renal safety profile of these analgesic options.

Despite the widespread use of diclofenac and ketoprofen patches for postoperative pain management and a thorough literature review, no studies have been found that directly compare the efficacy and renal safety of diclofenac and ketoprofen patches in PCNL patients. The increasing adoption of Enhanced Recovery After Surgery (ERAS) protocols further highlights the necessity of optimising postoperative analgesia. The ideal regimen should ensure effective pain relief, minimise the need for rescue medications, facilitate early mobilisation and mitigate systemic complications [12]. Therefore, the aim of the study was to compare the efficacy and safety of diclofenac and ketoprofen transdermal patches for postoperative pain control in patients undergoing PCNL. It also aimed to evaluate their impact on serum creatinine levels, haemodynamic stability and associated side-effects.

## MATERIALS AND METHODS

The present study was a double-blind, randomised clinical study conducted in the Department of Anaesthesiology at Dr. DY Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India from July 2024 to February 2025. The study was approved by the Institutional Ethical and Scientific Committee (Approval No. IESC/341/2023) and was registered with the Clinical Trials Registry of India. (CTRI/2024/06/069037). Written informed consent was obtained from all participants before enrolment.

**Inclusion criteria:** Patients aged between 18 and 60 years, with ASA physical status of I or II, scheduled for elective PCNL under spinal anaesthesia, were included in the study.

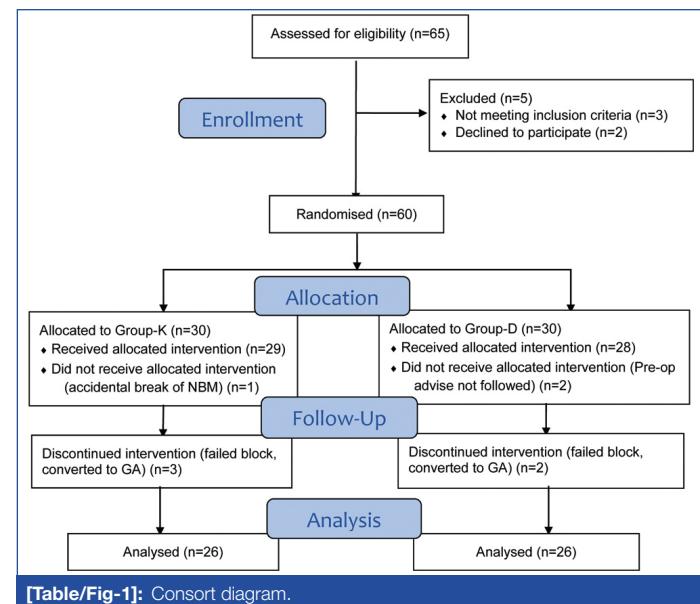
**Exclusion criteria:** Patients with ASA grade of III or higher, required emergency surgery, had known allergies to ketoprofen or diclofenac, or had spinal deformities or neurological disorders. Patients with cognitive or communication impairments, contraindications to neuraxial blockade such as local infection or coagulopathy and the presence of significant systemic illnesses, including psychiatric, cardiovascular, hepatic, renal, or neuromuscular conditions were excluded from the study.

**Sample size calculation:** The sample size was calculated based on a previous study by Rani S et al., using the statistical test of ANOVA (one-way, fixed effect, omnibus) [13]. Taking an effect size of 0.40, an alpha error of 5%, and a power of 80%, the final sample size was estimated to be 52 using G\*Power software version 3.1.9.4. After applying criteria, 52 patients were found eligible and included in the final analysis.

### Randomisation and Blinding

Patients were randomly allocated into two groups using a computer-generated random number table [Table/Fig-1]. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes. Double-blinding was maintained—neither the patients nor the investigator was aware of group assignments.

**Methodology:** Group K (n=26) received a 30 mg ketoprofen transdermal patch and Group D (n=26) received a 100 mg diclofenac patch. Both patches were applied to the anterolateral aspect of the lower thorax in the midaxillary line 30 minutes before the end of surgery. All patients were kept nil per os from midnight prior to surgery. In the preoperative area, baseline vitals, including pulse rate, non-invasive blood pressure, Electrocardiogram (ECG) and oxygen saturation, were recorded. An intravenous line was secured using



[Table/Fig-1]: Consort diagram.

a 20G cannula. Under strict aseptic precautions, a subarachnoid block was performed at the L3-L4 intervertebral space using a 26G Quincke's Babcock spinal needle, after confirming the clear and free flow of cerebrospinal fluid, with 3.5 cc of 0.5% hyperbaric bupivacaine and 25 mcg (0.5 cc) of fentanyl.

**Outcome measures:** Pain was assessed using the VAS at 0 (upon arrival in the recovery room) and at 4, 8, 12, 16, 24 and 48 hours postoperatively. Serum creatinine levels were measured preoperatively and at 24 hours postoperatively. Rescue analgesia (tramadol 50 mg IV+ondansetron 0.1 mg/kg IV) was given if VAS  $\geq 5$ . Vital parameters and adverse events were monitored throughout the study. The patch site was inspected at 48 hours for any local reactions.

## STATISTICAL ANALYSIS

Data were entered and analysed using SPSS version 21.0. Quantitative variables were expressed as mean $\pm$ SD and compared using the Student's t-test (two-tailed). Categorical variables were expressed as frequencies and percentages and analysed using the Chi-square test. A p-value  $<0.05$  was considered statistically significant.

## RESULTS

Sixty-five patients were assessed for enrollment, 60 were randomly assigned into two groups and 52 were analysed. The demographic characteristics of the subjects in both groups were comparable [Table/Fig-2].

| Age                         | Group D (n=26)   | Group K (n=26)  |
|-----------------------------|------------------|-----------------|
| Mean $\pm$ SD               | 41.5 $\pm$ 8.6   | 41.8 $\pm$ 11.2 |
| Age categories (years)      | n (%)            | n (%)           |
| 20-40                       | 15 (57.7)        | 13 (50)         |
| 41-60                       | 11 (42.3)        | 13 (50)         |
| Gender                      |                  |                 |
| Female                      | 6 (23.1)         | 5 (19.2)        |
| Male                        | 20 (76.9)        | 21 (80.8)       |
| ASA                         |                  |                 |
| I                           | 17 (65.4)        | 11 (42.3)       |
| II                          | 9 (34.6)         | 15 (57.7)       |
| Weight (kg) (Mean $\pm$ SD) | 72.08 $\pm$ 10.2 | 70.7 $\pm$ 7.6  |

[Table/Fig-2]: Demographic and clinical characteristics of patients.

Postoperatively, pulse rate was significantly lower in group K at four hours (p-value=0.004), eight hours (p-value=0.002), 16 hours (p-value <0.001) and 48 hours (p-value <0.001) [Table/Fig-3].

Similarly, Systolic Blood Pressure (SBP) was significantly lower in group K at 16 hours ( $p$ -value=0.01) and 24 hours ( $p$ -value=0.004) [Table/Fig-4], while no differences were observed at other time points. Diastolic Blood Pressure (DBP) was comparable, except for a borderline significant difference at 16 hours ( $p$ -value=0.05), although this was clinically insignificant [Table/Fig-5].

| Pulse rate (mean $\pm$ SD) (beats per minute) | Group D        | Group K         | p-value |
|---|----------------|-----------------|---------|
| Baseline                                      | 84.8 $\pm$ 4.4 | 82.7 $\pm$ 11.5 | 0.38    |
| At 4 hours                                    | 90.8 $\pm$ 9.7 | 82.4 $\pm$ 10.4 | 0.004   |
| At 8 hours                                    | 87.2 $\pm$ 9.6 | 78.7 $\pm$ 8.9  | 0.002   |
| At 12 hours                                   | 85.3 $\pm$ 7.4 | 82.1 $\pm$ 7.1  | 0.12    |
| At 16 hours                                   | 82.6 $\pm$ 5.9 | 72.6 $\pm$ 7.6  | <0.001  |
| At 24 hours                                   | 78.8 $\pm$ 9.2 | 77.3 $\pm$ 9.3  | 0.54    |
| At 48 hours                                   | 86.2 $\pm$ 7.7 | 76.8 $\pm$ 9.3  | <0.001  |

**[Table/Fig-3]:** Comparison of pulse rate among groups.

Independent t-test

| SBP (mean $\pm$ SD) (mmHg) | Group D          | Group K          | p-value |
|----------------------------|------------------|------------------|---------|
| Baseline                   | 133.3 $\pm$ 10.3 | 134.3 $\pm$ 9.3  | 0.71    |
| At 4 hours                 | 137.1 $\pm$ 9.5  | 133.3 $\pm$ 10.8 | 0.19    |
| At 8 hours                 | 130.2 $\pm$ 8.5  | 127.6 $\pm$ 9.5  | 0.302   |
| At 12 hours                | 134.6 $\pm$ 9.5  | 136.4 $\pm$ 10.7 | 0.53    |
| At 16 hours                | 134.3 $\pm$ 5.9  | 129.1 $\pm$ 8.2  | 0.01    |
| At 24 hours                | 133.4 $\pm$ 6.4  | 126.9 $\pm$ 8.9  | 0.004   |
| At 48 hours                | 132.9 $\pm$ 6.4  | 131 $\pm$ 5.1    | 0.24    |

**[Table/Fig-4]:** Comparison of Systolic Blood Pressure (SBP) among groups.

Independent t-test

| DBP (mean $\pm$ SD) (mmHg) | Group D        | Group K        | p-value |
|----------------------------|----------------|----------------|---------|
| Baseline                   | 82 $\pm$ 5.1   | 83.1 $\pm$ 3.5 | 0.35    |
| At 4 hours                 | 79 $\pm$ 5.1   | 79.3 $\pm$ 7.2 | 0.86    |
| At 8 hours                 | 77.3 $\pm$ 4.7 | 79.3 $\pm$ 6.1 | 0.19    |
| At 12 hours                | 82.6 $\pm$ 4.3 | 83.6 $\pm$ 4.3 | 0.37    |
| At 16 hours                | 78.1 $\pm$ 3.9 | 80.1 $\pm$ 3.2 | 0.05    |
| At 24 hours                | 76.6 $\pm$ 4.4 | 78.3 $\pm$ 3.1 | 0.12    |
| At 48 hours                | 78.1 $\pm$ 3.6 | 78.3 $\pm$ 4.7 | 0.84    |

**[Table/Fig-5]:** Comparison of DBP among groups.

Independent t-test

The assessment of respiratory parameters included respiratory rate and Oxygen Saturation ( $SpO_2$ ). While there was no statistically significant difference between the two groups at most time points, the respiratory rate at 12 hours postsurgery was significantly lower in group D ( $15.6\pm1.3$  breaths per minute) compared to group K ( $16.6\pm1.3$  breaths per minute,  $p$ -value=0.009), although this difference was clinically insignificant [Table/Fig-6,7].

| SpO <sub>2</sub> (mean $\pm$ SD) (%) | Group D         | Group K         | p-value |
|--------------------------------------|-----------------|-----------------|---------|
| Baseline                             | 98.8 $\pm$ 1.1  | 98.6 $\pm$ 1.1  | 0.52    |
| At 4 hours                           | 98.6 $\pm$ 0.94 | 98.3 $\pm$ 0.85 | 0.35    |
| At 8 hours                           | 98.7 $\pm$ 0.99 | 98.6 $\pm$ 0.98 | 0.57    |
| At 12 hours                          | 98.4 $\pm$ 0.81 | 98.4 $\pm$ 0.9  | 1.0     |
| At 16 hours                          | 98.9 $\pm$ 0.89 | 98.7 $\pm$ 0.95 | 0.55    |
| At 24 hours                          | 98.8 $\pm$ 0.98 | 98.5 $\pm$ 1.1  | 0.29    |
| At 48 hours                          | 98.1 $\pm$ 1.7  | 98.08 $\pm$ 1.6 | 0.87    |

**[Table/Fig-6]:** Comparison of  $SpO_2$  among groups.

Independent t-test

| RR (mean $\pm$ SD) (breaths per minute) | Group D        | Group K        | p-value |
|---|----------------|----------------|---------|
| Baseline                                | 19 $\pm$ 1.8   | 19.8 $\pm$ 2.4 | 0.14    |
| At 4 hours                              | 17.7 $\pm$ 1.7 | 17.2 $\pm$ 1.7 | 0.306   |

|             |                 |                |       |
|-------------|-----------------|----------------|-------|
| At 8 hours  | 17.5 $\pm$ 1.4  | 16.8 $\pm$ 1.4 | 0.06  |
| At 12 hours | 15.6 $\pm$ 1.3  | 16.6 $\pm$ 1.3 | 0.009 |
| At 16 hours | 15.5 $\pm$ 1.5  | 15.7 $\pm$ 1.7 | 0.62  |
| At 24 hours | 17.04 $\pm$ 1.8 | 17.3 $\pm$ 1.1 | 0.43  |
| At 48 hours | 16.3 $\pm$ 1.5  | 15.8 $\pm$ 1.7 | 0.24  |

**[Table/Fig-7]:** Comparison of respiratory rate among group.  
Independent t-test

The VAS scores were significantly higher in group D at four hours ( $p$ -value=0.04), eight hours ( $p$ -value <0.001), 24 hours ( $p$ -value <0.001) and 48 hours ( $p$ -value=0.002), indicating better pain control in group K [Table/Fig-8]. Postoperative creatinine levels significantly increased in group D ( $p$ -value=0.02) but not in group K ( $p$ -value=0.057) [Table/Fig-9]. Additionally, patients in group D reported more side-effects, particularly headache (19.2% vs. 0%,  $p$ -value=0.05), whereas nausea was comparable between groups (26.9% in group D vs. 23.1% in group K). Overall, a higher proportion of patients in group K reported no side-effects (76.9% vs. 53.8% in group D,  $p$ -value=0.05). Similarly, more patients in group D required rescue analgesia at 4 hours postoperatively (23.1% vs. 0%,  $p$ -value=0.009), while differences at other time points were not statistically significant [Table/Fig-10].

| VAS (mean $\pm$ SD) | Group D         | Group K         | p-value |
|---------------------|-----------------|-----------------|---------|
| Baseline            | 1.35 $\pm$ 0.48 | 1.4 $\pm$ 0.5   | 0.57    |
| At 4 hours          | 3.8 $\pm$ 0.76  | 3.5 $\pm$ 0.51  | 0.04    |
| At 8 hours          | 4.19 $\pm$ 0.56 | 3.1 $\pm$ 1.1   | <0.001  |
| At 12 hours         | 3.8 $\pm$ 0.46  | 3.5 $\pm$ 0.7   | 0.109   |
| At 16 hours         | 3.69 $\pm$ 0.73 | 3.3 $\pm$ 0.67  | 0.06    |
| At 24 hours         | 3.35 $\pm$ 0.48 | 2.65 $\pm$ 0.68 | <0.001  |
| At 48 hours         | 3 $\pm$ 0.74    | 2.4 $\pm$ 0.5   | 0.002   |

**[Table/Fig-8]:** Comparison of VAS among groups.

Independent t-test

| Variables (mean $\pm$ SD) | Group D         | Group K         | p-value |
|---------------------------|-----------------|-----------------|---------|
| Preoperative creatinine   | 0.95 $\pm$ 0.20 | 1.04 $\pm$ 0.22 | 0.079   |
| Postoperative creatinine  | 1.07 $\pm$ 0.16 | 1.15 $\pm$ 0.20 | 0.21    |
| p-value                   | 0.02            | 0.057           |         |

**[Table/Fig-9]:** Comparison of preoperative and postoperative creatinine within and between groups.

Independent t-test, ANOVA

| Rescue analgesia given | Group D    | Group K   | p-value |
|------------------------|------------|-----------|---------|
| Baseline               | -          | -         |         |
| At 4 hours             | 6 (23.1%)  | 0         | 0.009   |
| At 8 hours             | 7 (26.9%)  | 4 (15.4%) | 0.308   |
| At 12 hours            | 1 (3.8%)   | 3 (11.5%) | 0.29    |
| At 16 hours            | 4 (15.4%)  | 2 (7.7%)  | 0.38    |
| At 24 hours            | -          | -         | -       |
| At 48 hours            | -          | -         | -       |
| Total                  | 18 (69.2%) | 8 (30.7)  |         |

**[Table/Fig-10]:** Comparison of rescue analgesia and side-effects among groups.  
Independent t-test

## DISCUSSION

PCNL is a widely performed procedure for managing renal calculi, offering a minimally invasive alternative to open surgery. It is associated with significant postoperative pain, necessitating effective analgesic strategies to ensure patient comfort, facilitate early mobilisation and reduce hospital stays. Transdermal NSAID patches like diclofenac and ketoprofen provide sustained drug release, improved compliance and fewer gastrointestinal side-effects [5,8]. However, despite the widespread use of diclofenac and ketoprofen patches for postoperative pain management and a

thorough literature review, no studies were found directly comparing the efficacy and renal safety of diclofenac and ketoprofen patches in PCNL patients. This study aimed to address this gap by evaluating the analgesic effectiveness of diclofenac versus ketoprofen patches in post-PCNL pain management and their effect on serum creatinine.

In the present study, postoperative VAS scores showed a consistent trend of better pain control with the ketoprofen patch compared to diclofenac, particularly at later time points. While both groups started with low baseline scores—likely due to residual spinal anaesthesia—group K demonstrated a more sustained reduction in pain intensity over the 48-hour postoperative period. This suggests a stronger and longer-lasting analgesic effect with ketoprofen. These findings were consistent with those reported by Kabir KK et al., who observed significantly lower VAS scores in patients using ketoprofen patches following inguinal hernia surgeries [14]. Similarly, Rani S et al., found ketoprofen to be more effective than diclofenac in patients undergoing hysterectomy [13]. The superior efficacy of ketoprofen may be attributed to its pharmacokinetic profile, particularly its biexponential decline and longer duration of tissue-level action, which contribute to prolonged analgesia. These results reinforce the potential advantage of ketoprofen patches in postoperative pain protocols.

In present study, patients in the diclofenac group demonstrated significantly higher pulse rates during the postoperative period compared to the ketoprofen group, particularly between four and 48 hours. This trend may reflect better analgesic efficacy with ketoprofen, as an elevated heart rate is often a physiological response to inadequate pain relief. However, the literature presents variable findings. Vasava NG and Patel RV, who studied intravenous administration and Desjardins PJ et al., examining oral NSAIDs, reported no meaningful differences in heart rate [15,16]. Similarly, Jadhav R et al., observed no significant haemodynamic changes following transdermal NSAID patch application, suggesting individual variability or formulation-specific effects [17]. These discrepancies could be attributed to differences in drug delivery methods, systemic absorption and pharmacokinetics. The transdermal route in our study, offering sustained plasma levels with minimal peaks and troughs, may explain the observed variations in cardiovascular response.

Blood pressure analysis showed significant differences between the groups at specific time points. SBP was lower in group K than in group D at 16 hours ( $129.1 \pm 8.2$  vs.  $134.3 \pm 5.9$  mmHg,  $p\text{-value}=0.01$ ) and 24 hours ( $126.9 \pm 8.9$  vs.  $133.4 \pm 6.4$  mmHg,  $p\text{-value}=0.004$ ). DBP was also lower in group D at 16 hours ( $78.1 \pm 3.9$  vs.  $80.1 \pm 3.2$  mmHg,  $p\text{-value}=0.05$ ), although this was clinically insignificant, suggesting a potentially antihypertensive effect of diclofenac when administered transdermally. These findings align with a study by Aljadhey H et al., who conducted a retrospective cohort study involving 2,739 patients and reported a higher risk of hypertension with diclofenac compared to other NSAIDs, including ketoprofen, highlighting the ongoing debate regarding NSAIDs' effects on blood pressure [18]. Despite statistically significant differences in blood pressure at certain time points in present study, the variations were minor and clinically insignificant, confirming the haemodynamic safety of both diclofenac and ketoprofen patches in post-PCNL pain management.

The assessment of respiratory parameters included respiratory rate and Oxygen Saturation ( $\text{SpO}_2$ ). While there was no statistically significant difference between the two groups at most time points, the respiratory rate at 12 hours postsurgery was significantly lower in group D ( $15.6 \pm 1.3$  breaths per minute) compared to group K ( $16.6 \pm 1.3$  breaths per minute,  $p\text{-value}=0.009$ ), although this difference was clinically insignificant. Both patches preserved respiratory function, offering a key advantage over opioid-based analgesia, which carries a risk of respiratory depression. Buvanendran A and

Kroin JS, highlighted the benefits of multimodal analgesia, including fewer side-effects, faster recovery and reduced hospital stays [19]. Present study findings reinforce the respiratory safety of diclofenac and ketoprofen patches, minimising pulmonary complications in post-PCNL pain management.

Postoperatively, serum creatinine levels increased slightly in both groups. In group D, levels rose from  $0.95 \pm 0.2$  to  $1.07 \pm 0.16$  mg/dL ( $p\text{-value}=0.02$ ), indicating a significant increase. Whelton A and Hamilton CW linked diclofenac to a higher risk of acute kidney injury with long-term oral use, while Nouralizadeh A et al., found minimal renal impact from short-term NSAID use post-PCNL with proper hydration [11,20]. The transdermal route in present study may have reduced renal effects by lowering peak plasma concentrations, ensuring gradual drug release and minimising direct renal exposure. In present study, group D showed a statistically significant difference in pre- and postoperative creatinine levels compared to group K ( $p\text{-value}=0.02$ ); however, the values remained within the normal clinical range.

Rescue analgesia was required in 18 patients in group D versus 8 in group K. At four hours postsurgery, significantly more patients in group D needed rescue analgesia, while none in group K did ( $p\text{-value}=0.009$ ), suggesting a slower onset of analgesia with diclofenac. Differences at later time points were not statistically significant and by 24 to 48 hours, neither group required rescue analgesia. This correlates with lower VAS scores at 24 and 48 hours, indicating a prolonged analgesic effect. Rani S et al., reported similar findings, with six patients in the diclofenac group and three in the ketoprofen group needing rescue analgesia at eight hours, which was comparable to our results (7 in group D, 4 in group K,  $p>0.05$ ) [13]. Ketoprofen provides more balanced COX-1 and COX-2 inhibition than diclofenac, which is COX-2 selective. This may offer broader modulation of inflammation and pain in the acute postoperative setting.

Additionally, adverse effects differed, with headaches occurring only in group D (19.2%,  $p=0.05$ ). Fewer patients in group K (76.9%) compared to group D (53.8%) experienced side-effects, indicating better tolerability. These findings align with Hyllested M et al., who reported a higher incidence of headaches associated with diclofenac than with ketoprofen [21].

This study was conducted as a randomised, double-blind trial, which minimised bias and strengthened the reliability of the results. Standardised anesthetic and monitoring protocols were followed, ensuring consistency across both groups. The evaluation included not only analgesic efficacy but also renal safety, offering a broader clinical perspective. Pain scores were assessed at multiple time points postoperatively and side-effects were thoroughly monitored. Importantly, despite the widespread use of diclofenac and ketoprofen patches for postoperative pain management and a thorough literature review, no studies were found directly comparing the efficacy and renal safety of diclofenac and ketoprofen patches in the context of a major surgical procedure like PCNL, addressing a significant gap in the existing literature.

### Limitation(s)

Although VAS scores were low at 24 and 48 hours, longer-term assessments would provide a more comprehensive understanding of the sustained analgesic effects. Since the patches were applied only for 48 hours, future studies with extended follow-up are essential to evaluate prolonged efficacy, delayed toxicity and the potential development of drug tolerance. The study did not include measurement of plasma drug levels, which would have offered valuable pharmacokinetic insights. Additionally, reliance on serum creatinine alone for renal function assessment may have overlooked subtle or early changes in glomerular filtration. Incorporating sensitive biomarkers such as cystatin C, NGAL and KIM-1 in future studies could improve the detection of subclinical renal effects.

Variations in postoperative hydration status among patients also present a possible confounding factor that may have influenced both analgesic response and renal outcomes.

## CONCLUSION(S)

Present study compared diclofenac and ketoprofen patches for post-PCNL analgesia and their impact on serum creatinine levels found that ketoprofen patches provided superior pain control, particularly in the later postoperative period (24-48 hours), while also reducing the need for rescue analgesia in the first four hours. Both patches had a comparable effect on renal function, with group D showing a statistically significant but clinically insignificant change in creatinine levels. Additionally, ketoprofen patches were associated with a lower incidence of headaches, enhancing patient comfort. These findings suggest that ketoprofen may be a preferable choice for post-PCNL pain management.

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