e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2025; 16(11); 61-66

Original Research Article

# To Evaluate Efficacy of Transdermal Buprenorphine Patch Versus Intraoperative Cocktail Injection for Postoperative Pain Relief in Total Knee Arthroplasty

**Nikhil Agrawal[1], Ashish Gohiya[2], Anurag Tiwari[3], Ashutosh Singh Rajavat[1], Harsh Agrawal[4]**

[1]Resident, Department of Orthopaedics, Gandhi Medical College, Bhopal, Madhya Pradesh, India
[2]Professor, Department of Orthopaedics, Gandhi Medical College, Bhopal, Madhya Pradesh, India
[3]Assistant Professor, Department of Orthopaedics, Gandhi Medical College, Bhopal, Madhya Pradesh, India
[4]Intern, Gandhi Medical College, Bhopal, Madhya Pradesh, India

**Received: 07-09-2025 / Revised: 06-10-2025 / Accepted: 07-11-2025**
**Corresponding Author: Nikhil Agrawal**
**Conflict of interest: Nil**

**Abstract:**

**Introduction:** Postoperative pain management plays a pivotal role in the outcome of knee arthroplasty and is a major challenge affecting recovery and patient satisfaction. While opioids and NSAIDs remain standard, their side effects limit long-term use. Transdermal buprenorphine patches and intraoperative multimodal cocktail injections are emerging alternatives, each with unique pharmacologic benefits. However, no study to date has directly compared these two modalities. This study aims to compare their efficacy in managing postoperative pain following total knee arthroplasty.

**Materials and Methods:** This observational analytical study was conducted at Gandhi Medical College and Hamidia Hospital, Bhopal, from May 2023 to October 2024. Fifty adult patients undergoing total knee arthroplasty were randomized into two groups (n=25 each). Group 1 received a 10 mg transdermal buprenorphine patch applied 12 hours preoperatively. Group 2 received a 45 mL intraoperative cocktail injection consisting of ropivacaine, cefuroxime, triamcinolone, ketorolac, adrenaline, and normal saline. Pain was assessed using the Visual Analog Scale (VAS) pre operatively and at 4, 8, 12, 24, 48, 72, and 120 hours post operatively. The requirement and timing of rescue analgesia were recorded for comparing the two modalities.

**Results:** Demographic and surgical parameters were comparable between groups. VAS scores were not significantly different preoperatively or at 4 hours postoperatively ($p = 0.81$ and $p = 0.33$). However, the intraoperative cocktail group had significantly lower VAS scores at 8, 12, 24 and 48hours ($p < 0.05$). At 72 and 120 hours, buprenorphine patch group showed slightly better pain control, though not statistically significant ($p = 0.48$ and $p= 0.06$). Rescue analgesia was required in 88% of patients in the buprenorphine group versus 64% in the cocktail group. The mean number of rescue doses was higher in the patch group (3.56 vs. 1.84). The time to first rescue dose was significantly delayed in the cocktail group ($p = 0.04$). No major complications were noted in either group.

**Conclusion:** Intraoperative cocktail injections offer superior early postoperative pain control and reduce the need for rescue analgesia. Buprenorphine patches provide sustained analgesia beyond 72 hours. Both are safe and effective; their selection should be individualized based on clinical context and patient needs. This is the first study to directly compare these two modalities, addressing a significant gap in postoperative analgesia in total knee arthroplasty.

**Keywords:** Total knee arthroplasty, Transdermal buprenorphine patch, cocktail injection, post operative pain



## Introduction

Knee arthroplasty is a highly successful orthopaedic procedure used to treat end-stage joint diseases such as osteoarthritis, rheumatoid arthritis and avascular necrosis, significantly improving pain and function in affected patients [1]. Total knee arthroplasty (TKA) has seen a steady rise globally due to advances in surgical techniques, prosthetic designs, and perioperative care [2]. However, effective postoperative pain control remains a key challenge, as inadequate analgesia may delay rehabilitation, increase morbidity, and compromise overall surgical outcomes [3].

Traditional pain management approaches such as opioids, NSAIDs, and regional anaesthesia carry

limitations, including systemic side effects, dependence, and delayed mobilisation. In response, alternative methods such as transdermal drug delivery systems and periarticular multimodal injections have gained popularity. Transdermal buprenorphine, a semi-synthetic opioid with high μ-receptor affinity and a prolonged half-life, offers continuous analgesia with fewer systemic effects compared to oral opioids [4,5]. Studies have shown that buprenorphine patches provide effective pain relief in orthopaedic procedures, reduce opioid consumption, and improve patient compliance [5,6].

In parallel, intraoperative multimodal cocktail injections—comprising local anaesthetics, corticosteroids, NSAIDs, and sometimes opioids—deliver targeted pain relief at the surgical site [7]. This technique has been associated with reduced systemic opioid use, earlier mobilisation, and fewer complications [6,7]. Despite the growing use of both techniques, there is a paucity of studies directly comparing transdermal buprenorphine with intraoperative cocktail injections.

This observational study addresses this gap by comparing the efficacy and safety of transdermal buprenorphine patches versus intraoperative cocktail injections in managing postoperative pain following knee arthroplasty.

## Materials and Methods

This was a single-centre, prospective observational analytical study conducted in the Department of Orthopaedics at Gandhi Medical College and Hamidia Hospital, Bhopal, India. The study was carried out over a period of 12 months from May 2023 to April 2024, following approval from the Institutional Ethics Committee. A total of 50 adult patients undergoing total knee arthroplasty (TKA) were enrolled after obtaining informed written consent. Patients were included if they were scheduled for total knee arthroplasty and consented to receive either transdermal buprenorphine patch or intraoperative analgesic cocktail injection for postoperative pain management based using random number table.

### Inclusion Criteria

- Patients who were aged between 18 and 85 years.
- Patients who had not undergone any knee surgery in the past.

### Exclusion Criteria

Patients were excluded if they had:

- Known hypersensitivity to buprenorphine or any component of the analgesic cocktail
- Uncontrolled diabetes mellitus
- Deranged liver or renal function tests
- Contraindications to any of the medications in the analgesic cocktail

General condition of the patient was assessed and vitals, height, weight and BMI of the patient was recorded. Routine pre operative blood investigations were done. Patients were screened for comorbidities like hypertension, diabetes mellitus, rheumatoid arthritis or any other immunocompromised conditions and history of oral or systemic steroid intake and any immunosuppressant medication was taken. Patients were divided into two groups (n=25 each) based on the postoperative analgesic modality.

- **Group 1 (Buprenorphine Patch Group):** Patients received a 10 mg transdermal buprenorphine patch which was applied on chest or outer side of upper 1/3$^{rd}$ of arm after sensitivity testing. Patch was applied on clean, dry, hairless skin without scars 12 hours before the surgery so that it reaches it's analgesic threshold level at time of surgery. Patch was retained postoperatively for 7 days unless removed due to complications such as erythema or itching.
- **Group 2 (Cocktail Injection Group):** Patients received a 45 mL intraoperative periarticular analgesic cocktail injected subperiosteally and around the hip joint structures. The cocktail consisted of:
    - 20 mL of 0.2% ropivacaine
    - 1.5 g cefuroxime
    - 1 mL of 40 mg/mL triamcinolone
    - 1 mL of 30 mg/mL ketorolac
    - 0.5 mL adrenaline
    - 20 mL normal saline

Cocktail was injected either subperiosteally in anterior, posterior, medial and lateral surface of femur & anteromedial, anterolateral, posteromedial and posterolateral surface of tibia, or a periarticular injection will be given in capsule, lateral collateral ligament, medial collateral ligament, patellar tendon and quadriceps.

All patients received spinal anesthesia during surgery with no regional blocks and total knee arthroplasty was done by standard medial parapatellar approach.

**Figure 1: Application of 10 mg transdermal buprenorphine patch**

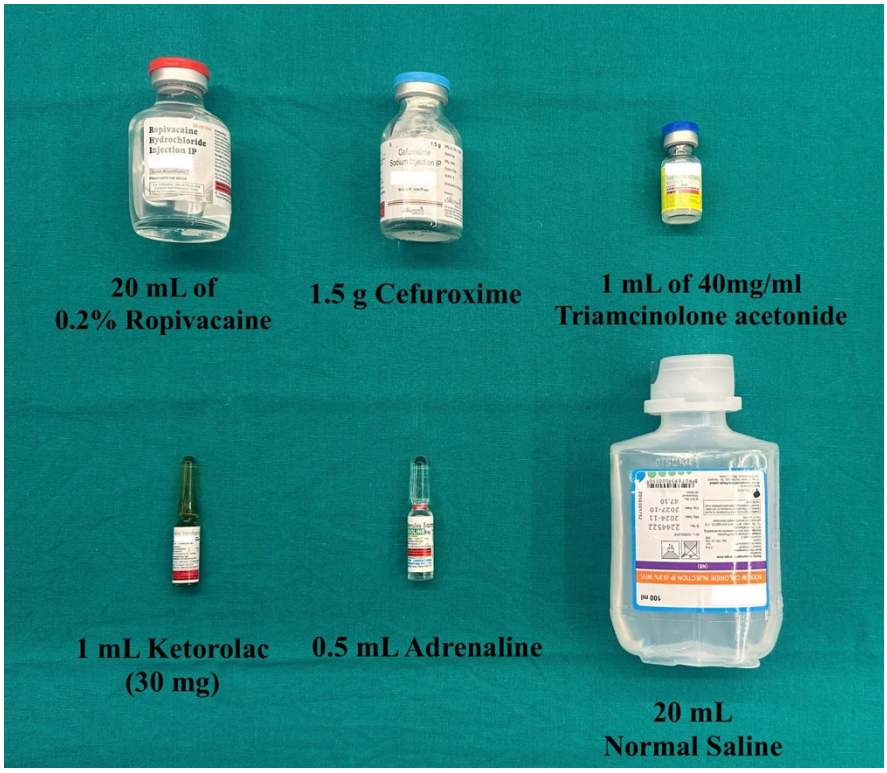


**Figure 2: Components of intraoperative cocktail injection**

**Pain assessment and rescue analgesia**

Pain scores were assessed using the Visual Analog Scale (VAS) preoperatively and at 4, 8, 12, 24, 48, 72 and 120 hours postoperatively. Patients did not receive any analgesia post operatively and rescue analgesia was given if VAS score was > 6 in the following manner intramuscular Diclofenac 75 mg injection.

In case pain was not relieved in 30 minutes it was followed by intravenous Tramadol injection (1 ampoule in 100 ml normal saline) and then followed by intravenous Paracetamol 1 g infusion. Analysis was done by comparing post operative VAS scores and requirement of rescue analgesia.

Statistical analysis was done using Epi Info 7.0 software and variables were compared using unpaired t-test and chi square test. p- value < 0.05 was considered statistically significant.

**Results**

50 patients undergoing total knee arthroplasty (25 per group) completed the study. Both groups were comparable in terms of baseline demographic and clinical characteristics.

The mean age of patients in buprenorphine group was 66.8 ± 8.26 years and in cocktail group was 68.88 ± 6.26 years (p = 0.32). Both groups demonstrated similar male to female ratios and both groups were comparable with respect to side of involvement (right vs left hip), varus/valgus deformity, surgical time and blood loss (Table 1).

**Table 1: Baseline characteristics of participants in both groups**

| Parameters | | Buprenorphine patch | Intra-operative cocktail | Total n (%) | Pearson chi-square/t value | p-value |
|---|---|---|---|---|---|---|
| Age (years) | 50–60 | 6 (24%) | 1 (4%) | 7 (14%) | 1.003 | 0.32 |
| | 61–70 | 13 (52%) | 17 (68%) | 30 (60%) | | |
| | 71–80 | 4 (16%) | 4 (16%) | 8 (16%) | | |
| | >80 | 2 (8%) | 3 (12%) | 5 (10%) | | |
| Sex | Male | 14 (56%) | 13 (52%) | 27 (54%) | 0.08 | 0.78 |
| | Female | 11 (44%) | 12 (48%) | 23 (46%) | | |
| Side Involved | Right | 12 (48%) | 14 (56%) | 26 (52%) | 0.32 | 0.57 |
| | Left | 13 (52%) | 11 (54%) | 24 (48%) | | |
| Coronal plane deformity | Varus | 24 (96%) | 23 (92%) | 47 (94%) | 0.35 | 0.55 |
| | Valgus | 1 (4%) | 2 (8%) | 3 (6%) | | |
| Surgical time | | 67 ± 5.72 | 68.16 ± 5.45 | 67.58 ± 5.56 | 0.734 | 0.467 |
| Blood loss | | 144.84 ± 23.92 | 150.76 ± 23.09 | 147.8 ± 23.46 | 0.89 | 0.378 |

Data is expressed as frequencies (percentages). Statistical significance was determined using the Chi-square test and unpaired t-test, with $p < 0.05$ regarded as significant.

**Pain Scores**

VAS scores were not significantly different preoperatively or at 4 hours postoperatively (p = 0.81 and p = 0.33). However, the intraoperative cocktail group had significantly lower VAS scores at 8, 12, 24 and 48 hours ($p < 0.05$). At 72 and 120 hours, buprenorphine patch group showed slightly better pain control, though not statistically significant (p = 0.48 and p = 0.06).

**Table 2: Analysis of mean VAS score between study groups**

| Time interval (hours) | Buprenorphine patch Mean ± SD | Intra-operative cocktail Mean ± SD | p value |
|---|---|---|---|
| Pre-op | 6.64 ± 0.99 | 6.76 ± 1.31 | 0.81 |
| Post-op 4 h | 4.24 ± 0.88 | 4.52 ± 1.12 | 0.33 |
| Post-op 8 h | 7.44 ± 1.04 | 6.08 ± 1.00 | < 0.001 |
| Post-op 12 h | 7.32 ± 1.03 | 6.04 ± 1.14 | < 0.001 |
| Post-op 24 h | 6.52 ± 1.33 | 5.56 ± 1.00 | 0.006 |
| Post-op 48 h | 5.04 ± 0.89 | 4.60 ± 0.50 | 0.037 |
| Post-op 72 h | 3.80 ± 0.76 | 4.00 ± 1.19 | 0.48 |
| Post-op 120 h | 2.80 ± 0.87 | 3.36 ± 1.19 | 0.06 |

**Rescue analgesia**

The need for rescue analgesia was greater among patients in the buprenorphine group (88%) compared to those in the cocktail group (64%). The average number of rescue injections per patient was also higher in the buprenorphine group (3.56 vs. 1.84). The cocktail group demonstrated a significantly longer time to the first rescue dose (p = 0.04), reflecting better early postoperative analgesia.

**Discussion**

Effective analgesia after total knee arthroplasty (TKA) remains crucial to enable early mobilization, improve rehabilitation outcomes and reduce opioid consumption. This study evaluates and compares the efficacy of two analgesic modalities – transdermal buprenorphine patch and intraoperative cocktail injection for postoperative pain control in patients undergoing total knee arthroplasty.

In this study, the demographic comparison revealed no statistically significant difference between the groups in terms of age (p = 0.32) and sex distribution (p = 0.78) confirming baseline equivalence. Similarly, distribution of patients in 2 groups based on side involved (p = 0.57), coronal plane deformity ie varus and valgus deformity (p = 0.55), surgical

time (p = 0.734) and blood loss (p = 0.89) showed no significant differences.

This comparability across demographic and surgical characteristics ensures that the differences observed in analgesic outcomes are likely attributable to mode of analgesia rather than confounding factors. This is supported by Londhe et al., who noted no baseline differences when comparing analgesic strategies in arthroplasty. [8]

One of the key findings of this study was the difference in VAS scores measured preoperatively and postoperatively at 4, 8, 12, 24, 48, 72 and 120 hours. There was no statistically significant difference in VAS scores preoperatively (p = 0.81) and at 4 hours postoperatively (p = 0.33). However, at 8 hours, the cocktail group reported significantly lower pain scores (6.08 ± 1.00) compared to the buprenorphine group (7.44 ± 1.04, p < 0.001). This pattern persisted at 12 hrs (p = < 0.001), 24 hrs (p = 0.006) and 48 hrs (p = 0.037) confirming superior early analgesic efficacy of intraoperative cocktail group. This observation aligns with results from Fu et al. and Hannon et al., who documented strong early-phase pain control using intraoperative cocktail injections. [9,10]

At 72 and 120 hours postoperatively, the buprenorphine patch group demonstrated lower mean VAS scores (3.80 ± 0.76 and 2.80 ± 0.87, respectively) compared to the intraoperative cocktail group (4.00 ± 1.19 and 3.36 ± 1.19, respectively). However, these differences were not statistically significant (p = 0.48 at 72 hours and p = 0.06 at 120 hours). The relatively lower pain scores in the buprenorphine group may be explained by its pharmacokinetic profile, which ensures continuous analgesic delivery through transdermal absorption that favours sustained analgesia. [4,11]

A crucial outcome measure of this study was requirement of rescue analgesia. In cocktail group, 34 % of patients did not require any rescue analgesia while only 12% of patients in buprenorphine group managed without it. A mean of 1.84 rescue analgesia injections per patient were given in cocktail group while 3.56 injections per patient were required in buprenorphine group. Moreover, most buprenorphine patients required their first rescue dose within 8 hours, highlighting insufficient early pain coverage. Deng et al.'s meta-analysis supports these findings by concluding that cocktail injections, especially when steroids are added, delay pain recurrence and reduce rescue needs. [12]

The pragmatic implication is that the two modalities are complementary rather than mutually exclusive. Periarticular infiltration addresses the nociceptive and inflammatory sources at the surgical site during the period of highest nociceptive input (first 48 hours), while transdermal buprenorphine provides a steady systemic opioid level that may smooth later recovery and reduce late-phase pain spikes. Fang et al. and other recent cohort reports suggest that combining a transdermal buprenorphine patch with perioperative multimodal analgesia (including periarticular infiltration and non-opioid systemic agents) may yield the most consistent pain control across both early and late postoperative phases. [6,13]

A few study-level differences warrant emphasis when comparing our outcomes to the published TKA literature. First, ingredients and volumes of periarticular cocktails vary widely between studies (local anaesthetic type/concentration, inclusion of steroid, NSAID, epinephrine, etc.) and these compositional differences influence both duration and magnitude of analgesia; thus, direct effect-size comparisons should consider cocktail formulation. Second, buprenorphine patch dose and timing matter: earlier TKA reports used different patch strengths and varied the preoperative application window; the time to steady-state transdermal concentration explains some heterogeneity in early pain outcomes. Third, many published TKA trials couple periarticular injection with peripheral nerve blocks (or compare intra articular vs peri articular vs combined), while in our study no additional regional blocks were used—this isolation helps highlight the independent contributions of the two modalities. [14,15]

Importantly, this study fills a significant gap in existing literature. While multiple studies have individually assessed buprenorphine patches and cocktail injections for postoperative analgesia in orthopaedic procedures, there is no direct comparative study between these two modalities. Our study provides evidence-based insights into their relative effectiveness, contributing to clinical decision-making in the selection of analgesic strategies for knee arthroplasty patients. With growing emphasis on multimodal pain control and reducing opioid burden, such comparative evaluations are highly valuable in tailoring analgesia based on patient needs and surgical context. [4,10]

## Conclusion

This comparative study between transdermal buprenorphine patch and intraoperative cocktail injection for postoperative pain management in total knee arthroplasty highlights distinct advantages of both modalities. Intraoperative cocktail injection demonstrated superior efficacy during early postoperative phase, particularly between 8 and 48 hours with a statistically significant reduction in pain score and patients requiring fewer doses of rescue analgesia.

In contrast, transdermal buprenorphine patch provided sustained analgesia particularly 72 hours after the procedure. Although not statistically significant this prolonged effect corresponds to the sustained release mechanism of transdermal buprenorphine

patch, making it a promising option for long term pain control.

Further large scale, multicentric randomised controlled trials are recommended to validate these findings and assess patient reported outcomes and side effect profiles over longer follow up durations.

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