

Comparison of Epidural Tramadol and Fentanyl for Postoperative Analgesia in Patients Undergoing Total Knee Replacement: A Prospective Comparative Study

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Abstract:

Background: Total knee replacement is associated with considerable postoperative pain that can interfere with early mobilization and rehabilitation. Epidural opioids provide effective analgesia, but their comparative analgesic profiles may differ.

Methods: This prospective comparative study was conducted at Vencer Hospital, Pune, from 1 August 2025 to 31 July 2026 among 60 patients undergoing elective total knee replacement. Patients were divided into Group T receiving epidural tramadol (n=30) and Group F receiving epidural fentanyl (n=30). Postoperative VAS scores, onset and duration of analgesia, time to first rescue analgesia, rescue analgesic requirement and adverse effects were compared.

Results: Baseline characteristics were comparable between the groups. The onset of analgesia was significantly faster with fentanyl (7.2 ± 2.1 vs 12.8 ± 3.4 min; $p < 0.001$), with significantly lower VAS scores at 2 and 4 hours. Tramadol provided a significantly longer duration of analgesia (10.6 ± 2.3 vs 7.8 ± 1.9 h; $p < 0.001$) and longer time to first rescue analgesia (11.2 ± 2.5 vs 8.3 ± 2.0 h; $p < 0.001$). Rescue analgesia was required in 40.0% of the tramadol group compared with 66.7% of the fentanyl group ($p = 0.038$). Adverse effects were comparable between groups.

Conclusion: Epidural fentanyl provided faster and superior early postoperative analgesia, whereas epidural tramadol produced longer-lasting analgesia and reduced rescue analgesic requirements after total knee replacement. Both agents demonstrated acceptable safety profiles.

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Introduction

Total knee replacement (TKR) is commonly associated with moderate to severe postoperative pain, particularly during the first 24–48 hours. Inadequately controlled pain can delay mobilization, interfere with physiotherapy, prolong hospitalization, and adversely affect early functional recovery.

Effective postoperative analgesia is therefore an essential component of perioperative management following TKR [1]. A multimodal approach incorporating systemic analgesics and regional

techniques is currently recommended to improve pain relief while minimizing opioid-related adverse effects [2]. Although peripheral nerve blocks and local infiltration techniques are increasingly used, epidural analgesia remains an effective option for providing sustained analgesia after major lower-limb surgery [3].

Opioids administered through the epidural route provide effective analgesia by acting on spinal opioid receptors. Tramadol is a centrally acting analgesic with weak μ -opioid receptor agonism and

inhibition of serotonin and noradrenaline reuptake. Epidural tramadol has demonstrated satisfactory postoperative analgesia following lower-limb orthopaedic procedures, with a relatively low incidence of respiratory depression [4]. Comparative studies have also evaluated tramadol and fentanyl as epidural adjuvants and demonstrated differences in analgesic characteristics and adverse-effect profiles [5].

Fentanyl is a potent, highly lipophilic μ -opioid receptor agonist characterized by rapid onset of analgesia. Epidural fentanyl has been successfully used following TKR and can provide effective postoperative pain control when combined with local anaesthetic agents [6]. Further studies of epidural fentanyl-based regimens in TKR have demonstrated satisfactory analgesia and reduced postoperative pain scores [7].

Although both epidural tramadol and fentanyl have been used for postoperative analgesia, direct comparative evidence evaluating their analgesic onset, duration, rescue analgesic requirements and adverse-effect profiles specifically in patients undergoing total knee replacement remains limited. Therefore, the present study was undertaken to compare the postoperative analgesic efficacy and safety profiles of epidural tramadol and fentanyl following total knee replacement.

Materials and Methods

Study Design and Setting: This prospective comparative study was conducted at Vencer Hospital, Pune, from 1 August 2025 to 31 July 2026. A total of 60 patients undergoing elective total knee replacement were enrolled and divided into two groups of 30 patients each.

Ethical Considerations: The study was conducted after obtaining approval from the Institutional Ethics Committee of Vencer Hospital, Pune. Written informed consent was obtained from all participants before enrolment.

Study Population: Adult patients undergoing elective primary TKR under neuraxial anaesthesia with postoperative epidural analgesia were considered for inclusion. Patients with contraindications to epidural analgesia, known hypersensitivity to tramadol or fentanyl, chronic opioid use, significant neurological or psychiatric illness affecting pain assessment, severe hepatic or renal dysfunction, coagulation abnormalities, infection at the epidural insertion site, or inability to understand the pain scoring system were excluded.

Study Groups: The 60 eligible patients were allocated into two equal groups:

- **Group T (n=30):** received epidural tramadol for postoperative analgesia.

- **Group F (n=30):** received epidural fentanyl for postoperative analgesia.

Group T received tramadol 1 mg/kg epidurally, while Group F received fentanyl 1 μ g/kg epidurally. In both groups, the study drug was diluted with 0.9% normal saline to a total volume of 10 mL and administered as a single epidural bolus. Other perioperative analgesic medications were kept uniform in both groups as far as possible to minimize confounding.

Procedure: Pre-anaesthetic evaluation included demographic characteristics, medical history, physical examination, relevant laboratory investigations, and assessment of ASA physical status. Patients were familiarized with the Visual Analogue Scale (VAS) for postoperative pain assessment, where 0 represented no pain and 10 represented the worst imaginable pain.

Standard monitoring, including electrocardiography, non-invasive blood pressure and peripheral oxygen saturation, was instituted in the operating room. An epidural catheter was placed using standard aseptic precautions. Total knee replacement was performed according to a standardized institutional surgical and anaesthetic protocol. After completion of surgery and once the patient had been transferred to the postoperative recovery area, the assigned study drug was administered through the epidural catheter as a single 10-mL bolus. Onset of analgesia was defined as the time from epidural study-drug administration until the VAS score decreased to <4 . Duration of effective analgesia was defined as the interval from onset of effective analgesia (VAS <4) until the VAS reached ≥ 4 or rescue analgesia was requested, whichever occurred first. Pain intensity was assessed using the 0–10 Visual Analogue Scale (VAS) immediately before epidural study-drug administration (0 hour) and at 2, 4, 6, 12 and 24 hours thereafter. A VAS score <4 was considered acceptable pain control. The onset of analgesia, duration of effective analgesia, time to first rescue analgesic and total rescue analgesic requirement during the first 24 hours were recorded. Haemodynamic variables, including heart rate and blood pressure, were monitored at corresponding intervals.

Patients were observed for adverse effects including nausea, vomiting, pruritus, sedation, dizziness, urinary retention, hypotension and respiratory depression. Rescue analgesia was administered when the VAS score was ≥ 4 or earlier if requested by the patient because of inadequate pain relief. The time from epidural study-drug administration to the first rescue analgesic was documented, and all rescue doses administered during the first 24 postoperative hours were recorded.

Outcome Measures: The primary outcomes were duration of effective analgesia and postoperative pain intensity assessed using VAS. Secondary outcomes included time to first rescue analgesia, total rescue analgesic consumption during 24 hours, haemodynamic changes and incidence of drug-related adverse effects.

Statistical Analysis: Data were entered into Microsoft Excel and analysed using appropriate statistical software. Continuous variables were expressed as mean $\pm$ standard deviation and categorical variables as frequency and percentage.

Continuous variables between the two groups were compared using the independent-samples t-test or Mann-Whitney U test according to data distribution. Repeated postoperative pain measurements were analysed using repeated-

measures analysis where appropriate. Categorical variables were compared using the Chi-square test or Fisher's exact test. A p-value <0.05 was considered statistically significant.

Results

A total of 60 patients undergoing total knee replacement were included, with 30 patients each in the epidural tramadol group (Group T) and epidural fentanyl group (Group F).

Both groups were comparable with respect to age, sex, BMI and ASA physical status ($p>0.05$).

Epidural fentanyl produced a faster onset of analgesia and lower early postoperative VAS scores, whereas epidural tramadol provided a significantly longer duration of analgesia and delayed the requirement for rescue analgesics.

Table 1: Baseline characteristics of the study groups

Parameter		Group T: Tramadol (n=30)	Group F: Fentanyl (n=30)	p-value
Age (years), mean $\pm$ SD		64.3 $\pm$ 6.8	63.7 $\pm$ 7.1	0.740
Gender	Male, n (%)	13 (43.3)	14 (46.7)	0.795
	Female, n (%)	17 (56.7)	16 (53.3)	
BMI (kg/m ²), mean $\pm$ SD		27.2 $\pm$ 3.1	27.6 $\pm$ 3.3	0.630
ASA Grade	ASA I, n (%)	8 (26.7)	7 (23.3)	0.766
	ASA II, n (%)	22 (73.3)	23 (76.7)	
Duration of surgery (min), mean $\pm$ SD		104.8 $\pm$ 15.7	102.6 $\pm$ 14.9	0.580

No statistically significant differences were observed in the measured baseline demographic and perioperative characteristics between the two groups.

Table 2: Comparison of postoperative pain scores and analgesic outcomes

Outcome	Group T: Tramadol (n=30)	Group F: Fentanyl (n=30)	p-value
Onset of analgesia (min)	12.8 $\pm$ 3.4	7.2 $\pm$ 2.1	<0.001
VAS at 2 h	2.1 $\pm$ 0.8	1.6 $\pm$ 0.7	0.012
VAS at 4 h	2.3 $\pm$ 0.9	1.8 $\pm$ 0.8	0.027
VAS at 6 h	2.5 $\pm$ 0.9	2.3 $\pm$ 0.8	0.366
VAS at 12 h	3.0 $\pm$ 1.0	3.4 $\pm$ 1.1	0.147
VAS at 24 h	3.1 $\pm$ 1.0	3.3 $\pm$ 1.1	0.463
Duration of effective analgesia (h)	10.6 $\pm$ 2.3	7.8 $\pm$ 1.9	<0.001
Time to first rescue analgesia (h)	11.2 $\pm$ 2.5	8.3 $\pm$ 2.0	<0.001
Rescue analgesia required, n (%)	12 (40.0)	20 (66.7)	0.038
Total rescue analgesic doses/24 h	0.7 $\pm$ 0.6	1.2 $\pm$ 0.8	0.008

Fentanyl demonstrated a significantly faster onset and lower VAS scores during the early postoperative period at 2 and 4 hours. However, tramadol produced a significantly longer duration of effective analgesia (10.6 $\pm$ 2.3 vs 7.8 $\pm$ 1.9 hours; $p<0.001$) and prolonged the time to first rescue analgesic. Rescue analgesia was required in 40.0% of patients receiving tramadol compared with 66.7% receiving fentanyl ($p=0.038$).

Table 3: Comparison of adverse effects between the study groups

Adverse effect	Group T: Tramadol (n=30), n (%)	Group F: Fentanyl (n=30), n (%)	p-value
Nausea	5 (16.7)	2 (6.7)	0.424
Vomiting	3 (10.0)	1 (3.3)	0.612
Pruritus	1 (3.3)	5 (16.7)	0.195
Sedation	2 (6.7)	4 (13.3)	0.671
Hypotension	1 (3.3)	2 (6.7)	1.000
Respiratory depression	0 (0.0)	1 (3.3)	1.000
Urinary retention	2 (6.7)	3 (10.0)	1.000
Any adverse effect	9 (30.0)	12 (40.0)	0.417

Nausea and vomiting were numerically more frequent with tramadol, whereas pruritus and sedation occurred more often with fentanyl; however, these differences were not statistically significant. No serious adverse event requiring prolonged intervention was observed. One patient in the fentanyl group developed transient respiratory depression and responded to appropriate monitoring and management.

Discussion

Effective pain control following total knee replacement is important for early mobilization, physiotherapy and functional recovery. In the present study, both epidural tramadol and fentanyl provided satisfactory postoperative analgesia, although their analgesic profiles differed. Fentanyl produced a significantly faster onset and lower VAS scores during the early postoperative period, whereas tramadol provided a longer duration of effective analgesia and reduced the subsequent requirement for rescue analgesics. The role of epidural analgesia after TKR has been extensively evaluated. Gerrard et al. [8] reported that epidural analgesia provides effective pain control after total knee replacement, although peripheral nerve blocks may offer advantages in terms of certain adverse effects. These findings support the effectiveness of neuraxial analgesia while emphasizing the need to balance analgesic efficacy with tolerability.

The prolonged analgesic effect observed with tramadol in the present study is consistent with its pharmacological characteristics. Earlier clinical evaluation of epidural tramadol demonstrated effective and sustained postoperative pain relief [9]. Tramadol differs from conventional pure opioid agonists through its combined weak μ -opioid activity and inhibition of monoamine reuptake, which may contribute to its prolonged analgesic action. Evidence from TKA patients receiving systemic tramadol-containing regimens has also demonstrated its usefulness as a component of postoperative multimodal analgesia [10].

Modern postoperative pain management following TKR increasingly incorporates regional and multimodal techniques. Continuous regional analgesic techniques can provide prolonged pain control and reduce systemic opioid requirements [11]. Similarly, periarticular multimodal drug infiltration and peripheral nerve blocks have demonstrated effective postoperative analgesia following TKA [12]. These developments are important because analgesic strategies should facilitate early rehabilitation while minimizing opioid-related adverse effects. Recent evidence continues to support individualized multimodal analgesia following knee arthroplasty. Comparative evaluation of different postoperative analgesic

techniques has demonstrated that effective regional approaches can reduce pain and support postoperative recovery [13]. Furthermore, newer peripheral nerve-targeted techniques aim to provide analgesia while preserving motor function and facilitating early rehabilitation [14]. In the present study, nausea and vomiting occurred somewhat more frequently with tramadol, whereas pruritus and sedation were numerically more frequent with fentanyl; however, the differences were not statistically significant. Overall, both epidural drugs had acceptable safety profiles.

Limitations of study: This study has few limitations. The sample size was relatively small and the study was conducted at a single centre, which may limit the generalizability of the findings. The study evaluated analgesic outcomes only during the immediate postoperative period and did not assess longer-term functional recovery or patient satisfaction. In addition, details of the standardized multimodal analgesic regimen and the allocation method should be clearly defined to minimize potential confounding.

Future Recommendations: Future studies should include larger, multicentre, adequately powered randomized trials comparing standardized epidural tramadol and fentanyl regimens. Further research should also evaluate functional recovery, time to mobilization, physiotherapy outcomes, patient satisfaction, opioid-related adverse effects and length of hospital stay in addition to postoperative pain scores and rescue analgesic requirements.

Conclusion

Both epidural tramadol and fentanyl provided effective postoperative analgesia following total knee replacement. Fentanyl produced a faster onset and better early pain control, whereas tramadol provided a longer duration of analgesia with delayed and reduced rescue analgesic requirement. Adverse effects were comparable between the groups. Thus, the two agents demonstrated different analgesic profiles that may guide selection according to postoperative analgesic requirements.

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