

Comparative Study of Effect of Periarticular Fentanyl and Dexmedetomidine Injection for Pain Management in Total Knee Arthroplasty a Randomized Control Trial

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Learning Point of the Article:

Periarticular dexmedetomidine provides superior post-operative analgesia, reduces analgesic requirements, and supports recovery after total knee arthroplasty.

Abstract

Introduction: Post-operative pain following total knee arthroplasty (TKA) remains a major challenge and may delay rehabilitation, ambulation, and functional recovery. Periarticular infiltration analgesia has emerged as an effective component of multimodal pain management protocols. Dexmedetomidine and fentanyl are commonly used analgesic adjuvants; however, comparative evidence regarding their periarticular use in TKA remains limited.

Objectives: The aim of the study was to compare the analgesic efficacy of periarticular fentanyl and dexmedetomidine injection in patients undergoing TKA by evaluating post-operative pain relief, duration of analgesia, cumulative analgesic requirement, time to ambulation, and duration of hospital stay following surgery.

Materials and Methods: This prospective hospital-based randomized controlled trial was conducted in the Department of Orthopaedics at Teerthanker Mahaveer Medical College and Research Centre over 18 months. A total of 90 patients undergoing TKA were randomly allocated into three groups comprising 30 patients each: Group A (Bupivacaine + Fentanyl), Group B (Bupivacaine + Dexmedetomidine), and Group C (Bupivacaine + Saline). Post-operative pain was assessed using the Visual Analog Scale. Cumulative analgesic requirement, ambulation time, hospital stay, and post-operative morbidity scores were also evaluated. Appropriate statistical tests and multiple linear regression analysis were applied.

Results: Patients receiving periarticular dexmedetomidine demonstrated significantly lower post-operative pain scores at 6 h (5.63 ± 1.06) compared with fentanyl (6.50 ± 1.10) and saline groups (7.23 ± 1.22) ($P = 0.021$). The dexmedetomidine group also showed the lowest cumulative post-operative diclofenac requirement (597.50 ± 153.17 mg) compared with the fentanyl (680.00 ± 132.02 mg) and saline groups (758.33 ± 109.13 mg) ($P = 0.001$). Regression analysis identified dexmedetomidine as an independent predictor of reduced post-operative analgesic requirement ($\beta = -102.4$, $P = 0.001$).

Conclusion: Periarticular dexmedetomidine infiltration provided superior post-operative analgesia, reduced cumulative analgesic consumption, and improved post-operative recovery following TKA compared with fentanyl and saline infiltration.

Keywords: Total knee arthroplasty, dexmedetomidine, fentanyl, periarticular infiltration, post-operative analgesia, Visual Analog Scale.

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Introduction

Total knee arthroplasty (TKA) is one of the most frequently performed and successful orthopedic procedures for the management of advanced degenerative knee diseases, particularly end-stage osteoarthritis [1]. The procedure involves replacement of the damaged femoral condyles and tibial articular surfaces using metallic and polyethylene prosthetic implants to relieve pain, improve mobility, restore joint function, and enhance quality of life. Since the development of the first hinge knee prosthesis by Walldius in the 1950s and the subsequent evolution of condylar prosthetic systems in the 1970s, substantial advancements have occurred in implant design, surgical techniques, perioperative care, and rehabilitation protocols [2,3]. Despite these developments, post-operative pain following TKA continues to remain a major clinical challenge and significantly influences early mobilization, functional recovery, patient satisfaction, and duration of hospital stay [4].

Post-operative pain after TKA is often severe due to extensive soft-tissue handling, periosteal trauma, and inflammatory mediator release during surgery. Inadequate pain management may result in delayed ambulation, prolonged immobilization, increased opioid consumption, joint stiffness, thromboembolic complications, and delayed rehabilitation [5,6]. Therefore, optimization of post-operative analgesia has become an essential component of enhanced recovery protocols in TKA patients. Multimodal analgesic strategies are currently preferred because they provide effective pain relief while reducing opioid-related adverse effects [7].

Among various analgesic techniques, periarticular infiltration analgesia has gained considerable popularity as an adjunctive modality for post-operative pain control in TKA [8,9]. Periarticular injection involves administration of analgesic agents around highly nociceptive structures of the knee joint during surgery, including the infrapatellar fat pad, periosteum, collateral ligament insertions, retinacula, and pes anserine region [10]. This targeted local analgesic approach provides effective pain relief, improves post-operative range of motion, facilitates early ambulation, and reduces systemic analgesic requirements [11].

Several pharmacological agents such as local anesthetics, opioids, corticosteroids, epinephrine, ketorolac, and α_2 -adrenergic receptor agonists have been used in periarticular analgesic cocktails with encouraging results [12]. Dexmedetomidine, a highly selective α_2 -adrenergic agonist, possesses analgesic, sedative, sympatholytic, and anti-inflammatory properties and has shown promising efficacy in

prolonging post-operative analgesia and reducing analgesic consumption after TKA [13,14]. Fentanyl, a potent synthetic opioid with rapid onset and strong analgesic potency, is also widely used for perioperative pain management. Although both agents have demonstrated beneficial analgesic effects, comparative evidence regarding their periarticular administration in TKA remains limited [15,16].

Therefore, the present randomized controlled trial was undertaken to compare the effects of periarticular fentanyl and dexmedetomidine injection for post-operative pain management in patients undergoing TKA, with particular emphasis on analgesic duration; post-operative pain relief, cumulative analgesic requirement, ambulation, and duration of hospital stay [17].

Materials and Methods

The present study was a prospective, hospital-based randomized controlled trial conducted in the Department of Orthopaedics at Teerthanker Mahaveer Medical College and Research Centre after obtaining approval from the Institutional Ethics Committee (IEC Approval No. TMU/IEC/PG 2034-25/120, dated June 10, 2024). The study was carried out over a period of 18 months, and all procedures adhered to ethical guidelines for biomedical research involving human participants.

The study population comprised patients undergoing TKA during the study period. Eligible participants fulfilling predefined inclusion and exclusion criteria were enrolled after obtaining written informed consent. Patients of either gender aged between 18 and 80 years undergoing TKA for primary osteoarthritis, secondary osteoarthritis due to septic arthritis or tuberculosis, or post-traumatic arthritis were included in the study. Patients undergoing revision surgery or second-stage TKA, fresh peri-knee trauma, neurological disorders affecting

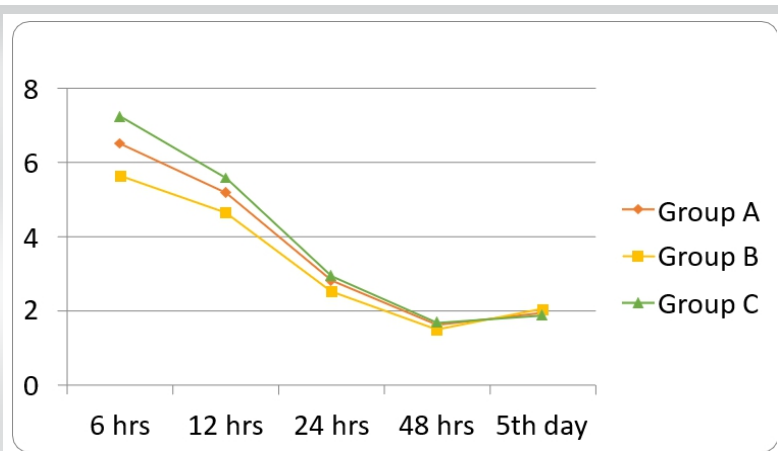


Figure 1: Trend of post-operative Visual Analog Scale scores.

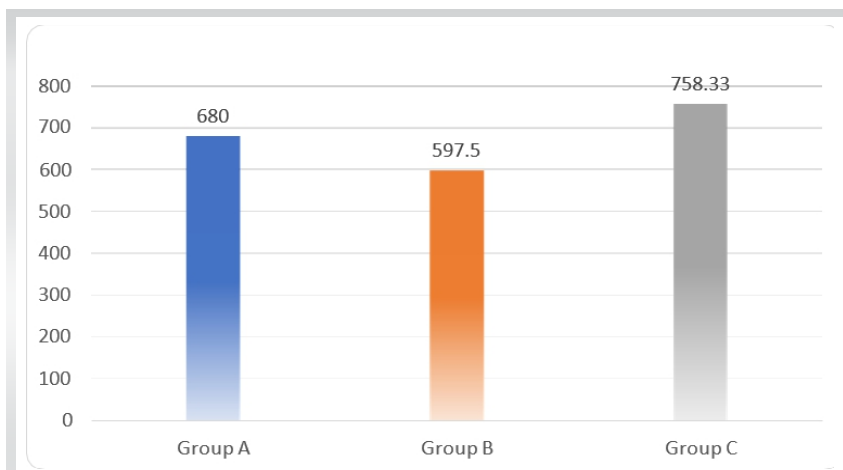


Figure 2: Post-operative analgesic requirement.

mobility, major psychiatric illness, or those unwilling to participate were excluded.

Participants were randomly allocated into study groups using a computer-generated randomization method with adequate allocation concealment to minimize selection bias. Each participant received the assigned periarticular analgesic intervention according to the study protocol.

Detailed demographic, clinical, and pre-operative functional data were recorded using a predesigned pro forma. All patients underwent TKA under standard aseptic precautions and institutional operative protocols. Intraoperative and post-operative parameters were documented systematically.

Post-operative evaluation included assessment of duration of analgesia, pain relief, cumulative analgesic requirement, duration to ambulation, and length of hospital stay. Outcome measures were assessed using standardized clinical assessment tools at predefined follow-up intervals. Collected data were analyzed using appropriate statistical methods to evaluate treatment efficacy and post-operative outcomes.

Sample size estimation

The sample size was calculated using the standard formula for comparison of means between two independent groups, considering mean values of 1.758 and 2.546 with standard deviations of 0.435 and 0.506, respectively. A confidence interval of 99% ($(Z_{1-\alpha/2}=2.58)$) and study power of 80% ($(Z_{1-\beta}=0.84)$) were considered for estimation. The calculated minimum sample size was 27 participants in each group. After accounting for an anticipated attrition rate of 15%, the final sample size was increased to 30 participants per group, resulting in a total study population of 90 patients.

Statistical analysis

Quantitative variables were expressed as mean $\pm$ standard deviation, whereas qualitative variables were presented as frequency and percentage. Appropriate inferential statistical tests were applied according to the nature and distribution of variables. Comparative analysis between study groups was performed using suitable statistical methods, and a $P < 0.05$ was considered statistically significant.

Results

A total of 90 patients undergoing TKA were enrolled and randomly allocated into three equal groups comprising 30 patients each: Group A (Bupivacaine + Fentanyl), Group B (Bupivacaine + Dexmedetomidine), and Group C (Bupivacaine + Saline). Baseline demographic characteristics were comparable among the three study groups. The majority of participants in Group A belonged to the 51–60 years age group, whereas most patients in Groups B and C were aged above 50 years. The mean age of patients in Groups A, B, and C was 57.17 ± 5.89 years, 58.97 ± 5.92 years, and 60.33 ± 6.33 years, respectively, without statistically significant intergroup variation ($P > 0.05$). Baseline demographic characteristics are summarized in Table 1.

Post-operative pain assessment using the Visual Analog Scale (VAS) demonstrated progressive reduction in pain scores from 6 h to the 5th post-operative day across all study groups. Patients receiving periarticular dexmedetomidine (Group B) consistently demonstrated the lowest VAS scores at all post-operative intervals, followed by Group A and Group C. At 6 h postoperatively, the mean VAS score was significantly lower in Group B (5.63 ± 1.06) compared with Group A (6.50 ± 1.10) and Group C (7.23 ± 1.22) ($P = 0.021$). Post hoc Tukey analysis

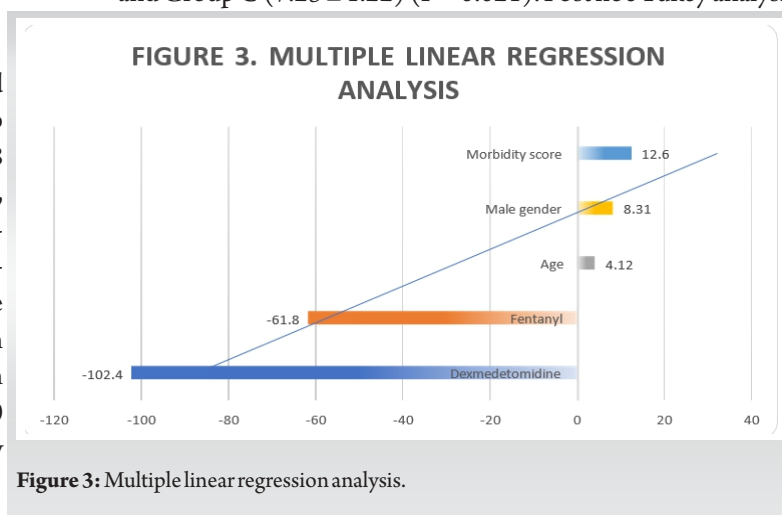


Figure 3: Multiple linear regression analysis.

Table 1: Baseline demographic characteristics of study participants

Variable	Group A (Bupivacaine+Fentanyl)	Group B (Bupivacaine+Dexmedetomidine)	Group C (Bupivacaine+Saline)	Statistical test	P-value
	n (%)	n (%)	n (%)		
Age group (Years)					
41–50	5 (16.67)	4 (13.33)	4 (13.33)	Analysis of variance=2.819	0.067
51–60	17 (56.67)	13 (43.33)	9 (30.00)		
>60	8 (26.67)	13 (43.33)	17 (56.67)		
Total	30 (100)	30 (100)	30 (100)		
Mean±standard deviation	57.17±5.89	58.97±5.92	60.33±6.33		
Gender					
Female	9 (30.0)	16 (53.3)	18 (60.0)	Chi-square=1.189	0.044*
Male	21 (70.0)	14 (46.7)	12 (40.0)		
Total	30 (100)	30 (100)	30 (100)		

demonstrated a significant difference between Group B and Group C at 6 h ($P = 0.045$), indicating superior early post-operative analgesia with dexmedetomidine infiltration. Subsequent post-operative intervals showed comparable pain scores among study groups ($P > 0.05$). Detailed comparison of post-operative VAS scores is presented in Table 2 and illustrated in Fig. 1.

Assessment of cumulative post-operative analgesic requirement demonstrated significantly lower diclofenac consumption among patients receiving periarticular dexmedetomidine. Group B required the least cumulative post-operative diclofenac dose (597.5 ± 153.17 mg), followed by Group A (680 ± 132.02 mg) and Group C (758.33 ± 109.13 mg), showing statistically significant intergroup variation ($P = 0.001$). Post hoc analysis further demonstrated significant differences between all study groups, confirming superior analgesic efficacy of dexmedetomidine compared with fentanyl and saline infiltration. These observations are summarized in Table 3 and represented in Fig. 2.

Evaluation of post-operative recovery parameters demonstrated that patients in Groups A and B achieved ambulation earlier (2.43 ± 0.50 days) compared with Group C

(2.50 ± 0.50 days), although the difference was not statistically significant ($P > 0.05$). Similarly, the shortest mean duration of hospital stay was observed in Group B (6.30 ± 1.23 days), followed by Group C (6.53 ± 1.22 days) and Group A (6.60 ± 1.32 days), without statistically significant intergroup variation ($P = 0.220$). These findings suggest relatively faster post-operative recovery among patients receiving dexmedetomidine-based periarticular infiltration. Recovery-related outcomes are summarized in Table 4. (Fig. 3).

Morbidity score analysis demonstrated a progressive increase in post-operative morbidity scores from day 1 to day 3 across all study groups. Although all patients

demonstrated excellent morbidity scores on day 1 and good scores on day 2, Group A showed the highest mean morbidity score on post-operative day 3 (25.20 ± 0.66), followed by Group B (24.93 ± 0.78) and Group C (24.57 ± 0.72). However, intergroup comparison revealed no statistically significant variation in morbidity scores at any post-operative interval ($P > 0.05$). Morbidity score analysis is summarized in Table 5.

Advanced statistical analysis using multiple linear regression demonstrated that periarticular dexmedetomidine infiltration independently reduced post-operative analgesic requirement compared with fentanyl and saline groups. Dexmedetomidine showed the strongest negative association with cumulative post-operative diclofenac consumption ($\beta = -102.4$, $P = 0.001$), whereas increasing morbidity scores were significantly associated with greater post-operative analgesic requirement ($\beta = 12.6$, $P = 0.003$). Age and gender did not demonstrate a statistically significant association with post-operative analgesic consumption. These findings indicate that periarticular dexmedetomidine provides superior analgesic

Table 2: Mean VAS score at different post-operative time intervals

Time interval	Group A Mean±SD	Group B Mean±SD	Group C Mean±SD	P-value
6 h	6.50±1.10	5.63±1.06	7.23±1.22	0.021*
12 h	5.17±0.74	4.63±0.85	5.57±0.89	0.06
24 h	2.80±0.61	2.50±0.57	2.93±0.82	0.077
48 h	1.60±0.56	1.47±0.50	1.67±0.54	0.091
5 th Post-operative day	1.93±0.73	2.03±0.71	1.87±0.77	0.082

SD: Standard deviation, VAS: Visual Analog Scale

Table 3: Mean post-operative analgesic requirement among study groups

Study group	Mean diclofenac dose (mg)±SD
Group A (Bupivacaine+Fentanyl)	680.00±132.02
Group B (Bupivacaine+Dexmedetomidine)	597.50±153.17
Group C (Bupivacaine+Saline)	758.33±109.13
ANOVA	23.665
P-value	0.001*

SD: Standard deviation, ANOVA: Analysis of variance

Table 4: Post-operative recovery parameters among study groups

Parameter	Group A	Group B	Group C	P-value
Days to ambulation	2.43±0.50	2.43±0.50	2.50±0.50	0.088
Length of hospital stay (days)	6.60±1.32	6.30±1.23	6.53±1.22	0.22

efficacy and improved post-operative pain control following TKA. Regression analysis findings are summarized in Table 6.

Discussion

Post-operative pain management following TKA remains a major concern because inadequate analgesia may delay mobilization, impair rehabilitation, prolong hospital stay, and increase post-operative analgesic consumption. The present randomized controlled trial compared periarticular fentanyl and dexmedetomidine infiltration for post-operative analgesia in TKA patients and demonstrated superior analgesic efficacy with dexmedetomidine-based periarticular infiltration. In the present study, patients receiving dexmedetomidine showed significantly lower post-operative pain scores, reduced cumulative analgesic requirement, relatively earlier ambulation, and shorter duration of hospital stay compared with fentanyl and saline groups.

Post-operative pain assessment using the VAS demonstrated significantly lower pain scores in the dexmedetomidine group during the early post-operative period. At 6 h post-operatively, the mean VAS score in Group B was 5.63 ± 1.06 compared with 6.50 ± 1.10 in the fentanyl group and 7.23 ± 1.22 in the saline group ($P = 0.021$). These findings are comparable with those of Jia D et al. [18], who demonstrated prolonged post-operative analgesia and delayed first rescue analgesic requirement following intra-articular dexmedetomidine administration after knee arthroscopy. Similarly, Chan et al. [19] reported significantly reduced post-operative morphine consumption with dexmedetomidine during TKA, with cumulative morphine requirement reduced to 29.2 mg compared with 61.2 mg in controls during the first 24 post-operative h. The opioid-sparing effect observed in their study closely correlates with the present findings, where cumulative post-operative diclofenac consumption was lowest in the dexmedetomidine group (597.50 ± 153.17 mg) compared with the fentanyl group (680.00 ± 132.02 mg) and saline group (758.33 ± 109.13 mg) ($P = 0.001$).

The superior analgesic efficacy of dexmedetomidine observed in the present study is further supported by Manuar et al. [20], who demonstrated significantly

Table 5: Mean morbidity score at different post-operative intervals

Time interval	Group A Mean±SD	Group B Mean±SD	Group C Mean±SD	P-value
Day 1	4.80±0.71	4.83±0.79	5.10±0.75	0.133
Day 2	14.76±0.72	14.96±0.80	14.76±0.89	0.066
Day 3	25.20±0.66	24.93±0.78	24.57±0.72	0.2

SD: Standard deviation

prolonged duration of analgesia and lower rescue analgesic requirement with dexmedetomidine-based analgesic protocols. Their study reported the first rescue analgesic requirement at 380.61 min in the dexmedetomidine group compared with 244.09 min in controls. Salem et al. [21] also compared dexmedetomidine and fentanyl as adjuvants to intra-articular bupivacaine and reported significantly improved post-operative analgesia with both agents. Although their study demonstrated slightly longer analgesia duration with fentanyl, the present study showed comparatively lower post-operative pain scores and reduced cumulative analgesic requirement with dexmedetomidine infiltration following TKA. This variation may be attributed to differences in surgical procedure, periarticular infiltration technique, and post-operative rehabilitation protocols.

The present study also demonstrated relatively earlier ambulation (2.43 ± 0.50 days) and shorter hospital stay (6.30 ± 1.23 days) in the dexmedetomidine group compared with saline controls, although these differences did not achieve statistical significance. Improved post-operative analgesia likely facilitated better patient mobilization and functional recovery. Similar observations were reported by Zhao et al. [22], who demonstrated reduced post-operative opioid requirement and delayed rescue analgesia with dexmedetomidine-based periarticular infiltration following TKA. Furthermore, regression analysis in the present study demonstrated that

Table 6: Multiple linear regression analysis for predictors of post-operative analgesic requirement

Variable	Beta coefficient (β)	95% Confidence interval	P-value
Dexmedetomidine group	-102.4	-158.6—46.2	0.001*
Fentanyl group	-61.8	-118.5—15.7	0.018*
Age	4.12	-1.62—9.85	0.142
Male gender	8.31	-16.2—32.8	0.491
Morbidity score	12.6	4.8—20.3	0.003*

dexmedetomidine independently reduced post-operative analgesic requirement ($\beta = -102.4$, $P = 0.001$), confirming its strong analgesic efficacy even after adjustment for confounding variables.

Lu et al. [23] reported that intra-articular fentanyl effectively reduced post-operative pain following knee arthroscopy, which is comparable to the improved analgesic outcomes observed in the fentanyl group of the present study when compared with saline controls. However, dexmedetomidine demonstrated comparatively greater analgesic efficacy, likely due to its combined anti-nociceptive, anti-inflammatory, and sympatholytic effects mediated through α_2 -adrenergic receptor agonism. No significant adverse effects were observed in the present study, indicating that periarticular dexmedetomidine infiltration appears to be a safe and effective adjunct for post-operative pain management following TKA.

Conclusion

Periarticular dexmedetomidine infiltration provided superior post-operative analgesia following TKA compared with

fentanyl and saline infiltration. It significantly reduced post-operative pain scores and cumulative analgesic requirement while facilitating earlier ambulation and shorter hospital stay. The findings of the present study support dexmedetomidine as a safe and effective adjunct in multimodal periarticular analgesic protocols for improving post-operative pain control and functional recovery after TKA.

Clinical Message

Periarticular dexmedetomidine appears to be a safe and effective adjunct for post-operative analgesia following total knee arthroplasty. It provides superior early pain relief, significantly reduces cumulative analgesic requirements, and may facilitate earlier ambulation and shorter hospital stay. These findings support its use as part of a multimodal periarticular analgesic protocol for improved post-operative pain control and functional recovery.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

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