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Comparative Efficacy Of Intravenous Fentanyl Versus Tramadol For Postoperative Pain Management Following Appendectomy: A Prospective Randomized Study

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ABSTRACT

Background: Effective postoperative pain management remains a critical component of surgical care, significantly influencing patient recovery and clinical outcomes. Appendectomy, one of the most commonly performed emergency surgical procedures worldwide, necessitates optimal analgesic strategies to minimize postoperative discomfort and facilitate early mobilization. Both fentanyl and tramadol are widely utilized for postoperative analgesia, yet comparative evidence regarding their efficacy and safety profiles in appendectomy patients remains limited.

Methods: This prospective randomized controlled trial was conducted from June 2023 to July 2024 at a tertiary care teaching hospital. A total of 100 patients undergoing emergency or elective appendectomy were randomly allocated into two equal groups: Group F received intravenous fentanyl (1 µg/kg) and Group T received intravenous tramadol (1 mg/kg) for postoperative analgesia. Pain intensity was assessed using the Visual Analogue Scale at multiple time intervals (0, 2, 4, 6, 12, and 24 hours postoperatively). Secondary outcomes included time to first rescue analgesia, total analgesic consumption, adverse effects, and patient satisfaction scores.

Results: The fentanyl group demonstrated significantly lower mean VAS scores compared to the tramadol group at 2 hours (2.34±0.82 vs 3.76±1.12, $p<0.001$), 4 hours (2.68±0.94 vs 3.92±1.24, $p<0.001$), and 6 hours (3.12±1.08 vs 4.28±1.36, $p<0.001$) postoperatively. Time to first rescue analgesia was significantly prolonged in Group F (4.82±1.26 hours vs 3.34±0.98 hours, $p<0.001$). The incidence of nausea and vomiting was higher in the tramadol group (34% vs 18%, $p=0.048$), while both groups showed comparable rates of other adverse effects. Patient satisfaction scores were significantly higher in the fentanyl group (8.24±1.12 vs 7.16±1.48, $p<0.001$).

Conclusion: Intravenous fentanyl provided superior postoperative analgesia with better pain control, prolonged duration of action, and higher patient satisfaction compared to tramadol in patients undergoing appendectomy, with an acceptable adverse effect profile. These findings support the preferential use of fentanyl for postoperative pain management in appendectomy patients.

Keywords*: Intravenous Fentanyl Versus, Appendectom, emergency surgical.*

INTRODUCTION

Acute appendicitis represents one of the most prevalent surgical emergencies encountered in clinical practice, with appendectomy being performed as the definitive treatment modality across all age groups worldwide. The lifetime risk of developing appendicitis approximates 7-8%, making it a condition of substantial public health significance.(1) Despite advances in surgical techniques, including the widespread adoption of laparoscopic approaches, postoperative pain management remains a critical determinant of patient recovery, hospital length of stay, and overall clinical outcomes.

Inadequate pain control following appendectomy can lead to numerous complications including delayed mobilization, increased risk of thromboembolic events, prolonged hospital stays, and diminished patient satisfaction.(2)

The pathophysiology of postoperative pain involves a complex interplay of peripheral and central sensitization mechanisms. Surgical trauma initiates an inflammatory cascade characterized by the release of numerous mediators including prostaglandins, bradykinin, substance P, and cytokines, which sensitize peripheral nociceptors.(3) This peripheral sensitization, combined with central nervous system changes, creates a state of heightened pain sensitivity that, if inadequately managed, can progress to chronic pain syndromes. The contemporary understanding of pain mechanisms has led to the development of multimodal analgesia strategies that target different components of the pain pathway, thereby optimizing pain relief while minimizing adverse effects associated with high-dose single-agent therapy. Opioid analgesics remain cornerstone agents in the management of moderate to severe postoperative pain, functioning primarily through activation of μ-opioid receptors distributed throughout the central and peripheral nervous systems. Among the various opioid options available, fentanyl and tramadol represent two commonly utilized agents with distinct pharmacological profiles that warrant comparative evaluation. Fentanyl, a synthetic opioid, possesses potency approximately 80-100 times greater than morphine and exhibits rapid onset of action, high lipid solubility, and relatively short duration of effect.(4) Its pharmacokinetic properties make it particularly suitable for acute pain management scenarios where rapid analgesia is desired. The drug undergoes extensive hepatic metabolism primarily through the cytochrome P450 3A4 enzyme system, producing inactive metabolites that are subsequently eliminated renally.

Tramadol, conversely, represents a centrally acting analgesic with a dual mechanism of action that differentiates it from traditional opioids. The drug functions both as a weak μ-opioid receptor agonist and as an inhibitor of norepinephrine and serotonin reuptake, contributing to its analgesic efficacy through complementary pathways.(5) This unique pharmacological profile theoretically offers advantages in terms of reduced respiratory depression and lower abuse potential compared to pure μ-opioid agonists. Tramadol undergoes hepatic metabolism via multiple cytochrome P450 isoenzymes, particularly CYP2D6, which converts it to O-desmethyltramadol (M1), an active metabolite with significantly greater opioid receptor affinity than the parent compound. The contribution of this metabolite to overall analgesic efficacy introduces pharmacogenetic considerations, as individuals with poor CYP2D6 metabolizer status may experience reduced analgesic benefit.

The comparative evaluation of these two agents in the specific context of appendectomy assumes particular importance given the high volume of these procedures performed globally and the heterogeneous nature of pain management practices across different healthcare settings. Previous investigations examining opioid analgesics in surgical populations have yielded variable results, with some studies demonstrating superior efficacy of fentanyl while others have suggested comparable effectiveness between agents.(6) However, many of these studies have been limited by small sample sizes, heterogeneous surgical populations, inconsistent outcome measures, or inadequate assessment of patient-centered outcomes. Furthermore, the literature specifically addressing postoperative analgesia following appendectomy remains relatively sparse, with few well-designed randomized controlled trials directly comparing fentanyl and tramadol in this surgical population.

Pain assessment methodologies have evolved considerably, with the Visual Analogue Scale (VAS) emerging as a widely validated and reproducible instrument for quantifying subjective pain intensity. The VAS typically consists of a 10-centimeter line with endpoints labeled as 'no pain' and 'worst imaginable pain,' allowing patients to mark their perceived pain level along this continuum.(7) This simple yet effective tool demonstrates excellent reliability and sensitivity to changes in pain intensity over time, making it particularly suitable for longitudinal postoperative pain assessment. Additionally, the VAS facilitates statistical analysis and cross-study comparisons, enhancing the generalizability of research findings. Complementary outcome measures including time to first rescue analgesia, total analgesic consumption, and patient satisfaction scores provide a comprehensive assessment of analgesic efficacy that extends beyond simple pain intensity measurements.

Safety considerations constitute an integral component of analgesic selection, as all opioid agents carry inherent risks of adverse effects that must be carefully balanced against therapeutic benefits. Common opioid-related adverse effects include nausea, vomiting, pruritus, urinary retention, constipation, and respiratory depression, with individual agents demonstrating varying propensities toward specific side effects.(8) Fentanyl, owing to its high potency and rapid onset, carries particular risk for respiratory depression when administered in excessive doses or to opioid-naive patients. However, its relatively short duration of action may offer safety advantages in terms of reversibility should adverse effects occur. Tramadol, while generally associated with lower risk of respiratory depression compared to traditional opioids, exhibits a unique adverse effect profile that includes increased risk of seizures, particularly at higher doses or in patients with predisposing factors, and potential for serotonin syndrome when combined with other serotonergic medications.(9)

The economic implications of analgesic selection merit consideration within the broader context of healthcare resource utilization. Inadequate postoperative pain control has been associated with prolonged hospital length of stay, increased nursing workload, higher rates of readmission, and progression to chronic pain states requiring ongoing medical management.(10) Conversely, optimal pain management facilitating early mobilization and discharge can reduce overall healthcare costs while improving patient outcomes. The comparative cost-effectiveness of different analgesic strategies depends not only on drug acquisition costs but also on factors including adverse effect profiles, nursing time requirements for administration and monitoring, and impact on hospital length of stay. These economic considerations assume particular relevance in resource-limited settings where cost-effectiveness analyses may inform formulary decisions and clinical practice guidelines.

Patient satisfaction represents an increasingly recognized quality metric in healthcare delivery, reflecting not merely the technical success of medical interventions but the holistic patient experience encompassing pain control, communication, and overall care quality. In the postoperative setting, patient satisfaction correlates strongly with perceived adequacy of pain management, suggesting that effective analgesia constitutes a fundamental component of patient-centered care. Understanding patient preferences and experiences with different analgesic regimens can inform clinical decision-making and facilitate shared decision-making processes that incorporate patient values alongside clinical evidence.

Despite the widespread clinical use of both fentanyl and tramadol for postoperative analgesia, significant gaps persist in the evidence base regarding their comparative effectiveness in specific surgical populations. The heterogeneity of published studies in terms of dosing regimens, timing of administration, outcome measures, and follow-up durations limits the ability to draw definitive conclusions regarding optimal analgesic selection. Additionally, many existing studies have focused primarily on pain intensity as the sole outcome measure, neglecting other clinically relevant endpoints such as functional recovery, quality of life, and long-term outcomes. This knowledge gap underscores the need for well-designed comparative effectiveness research that incorporates comprehensive outcome assessment and adequate statistical power to detect clinically meaningful differences between interventions.

The present study was therefore conceived to address these limitations through a prospective randomized controlled trial design comparing intravenous fentanyl versus tramadol for postoperative pain management in patients undergoing appendectomy. By employing rigorous methodology including random allocation, standardized dosing protocols, validated outcome measures, and comprehensive safety assessment, this investigation aimed to generate high-quality evidence to inform clinical practice regarding optimal analgesic selection in this common surgical population. The findings of this study have potential implications not only for immediate postoperative care but also for the development of evidence-based institutional protocols and clinical practice guidelines addressing postoperative pain management in surgical patients.

AIMS AND OBJECTIVES

The primary aim of this prospective randomized controlled trial was to compare the analgesic efficacy of intravenous fentanyl versus tramadol for postoperative pain management in patients undergoing appendectomy. The study sought to determine which agent provided superior pain control as assessed by Visual Analogue Scale scores at multiple time intervals during the first 24 hours following surgery. Additionally, the investigation aimed to evaluate the duration of analgesia provided by each agent as measured by time to first rescue analgesia requirement.

The secondary objectives encompassed comprehensive assessment of safety profiles including incidence and severity of adverse effects such as nausea, vomiting, respiratory depression, pruritus, and sedation in both treatment groups. The study also aimed to evaluate total postoperative analgesic consumption, patient satisfaction scores, and any differences in recovery parameters between the two groups. Furthermore, the investigation sought to identify any demographic or clinical factors that might predict differential response to either analgesic agent, thereby informing personalized analgesic selection strategies in clinical practice.

MATERIALS AND METHODS

Study Design and Setting

This prospective randomized study was conducted in the Department of Surgery in collaboration with the Department of Anaesthesiology at a tertiary care teaching hospital over a period of 13 months from June 2023 to July 2024. The study protocol received approval from the Institutional Ethics Committee prior to commencement, and the trial was registered with the Clinical Trials Registry. All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments.

Sample Size Calculation

Sample size calculation was performed using statistical software based on anticipated differences in mean Visual Analogue Scale scores between groups. Assuming a clinically significant difference of 1.0 point on the VAS scale, with a standard deviation of 1.5, alpha error of 0.05, and desired power of 80%, the minimum required sample size was

calculated as 45 patients per group. To account for potential dropouts and protocol violations, a total of 100 patients were enrolled, with 50 patients randomly allocated to each treatment group.

Patient Selection

Adult patients aged 18-65 years scheduled for emergency or elective appendectomy were screened for eligibility. Inclusion criteria comprised confirmed diagnosis of acute appendicitis based on clinical examination and radiological investigations, American Society of Anesthesiologists physical status classification I or II, and provision of written informed consent for study participation. Exclusion criteria included known hypersensitivity to fentanyl or tramadol, history of opioid abuse or dependence, chronic pain conditions requiring regular analgesic use, significant hepatic or renal dysfunction, pregnant or lactating women, patients with contraindications to general anaesthesia, history of seizure disorders, patients receiving monoamine oxidase inhibitors or selective serotonin reuptake inhibitors, and inability to comprehend or utilize the Visual Analogue Scale for pain assessment.

Randomization and Blinding

Eligible patients who provided informed consent were randomly allocated to either Group F (fentanyl) or Group T (tramadol) using computer-generated random number sequences. The randomization sequence was concealed in sequentially numbered, sealed, opaque envelopes that were opened only after patient enrollment by an independent research coordinator not involved in patient care or outcome assessment. While the anaesthesiologist administering the study medication was necessarily aware of group allocation, postoperative pain assessments were conducted by trained nursing staff blinded to treatment assignment. The statistical analyst remained blinded to group allocation until completion of data analysis.

Anaesthetic Protocol

All patients underwent standardized preoperative evaluation including detailed history, physical examination, and relevant laboratory investigations. Patients were kept nil per oral for at least 6 hours prior to surgery. In the operating room, standard monitoring including electrocardiography, non-invasive blood pressure, pulse oximetry, and capnography was established. Anaesthesia was induced with intravenous propofol (2 mg/kg) and fentanyl (2 μg/kg), with muscle relaxation achieved using atracurium (0.5 mg/kg). Following tracheal intubation, anaesthesia was maintained with isoflurane in oxygen-air mixture, with additional doses of atracurium administered as needed. All patients received intravenous ondansetron (4 mg) approximately 30 minutes before completion of surgery for prophylaxis against postoperative nausea and vomiting.

Study Intervention

At the completion of surgery, immediately before reversal of neuromuscular blockade, patients received the assigned study medication. Group F patients received intravenous fentanyl at a dose of 1 μg/kg, diluted in 10 mL normal saline and administered slowly over 2-3 minutes. Group T patients received intravenous tramadol at a dose of 1 mg/kg, similarly diluted in 10 mL normal saline and administered over 2-3 minutes. The study medications were prepared by the anaesthesiologist in identical syringes to maintain blinding of outcome assessors. After reversal of neuromuscular blockade with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg), patients were extubated and transferred to the post-anaesthesia care unit for monitoring.

Outcome Assessment

The primary outcome measure was pain intensity assessed using the Visual Analogue Scale at predefined time intervals: immediately upon arrival in the post-anaesthesia care unit (0 hours), and at 2, 4, 6, 12, and 24 hours postoperatively. The VAS consisted of a 10-cm horizontal line with endpoints labeled 'no pain' (0) and 'worst imaginable pain' (10), and patients marked their perceived pain level on this line. The distance from the 'no pain' endpoint to the patient's mark was measured in centimeters to yield a numerical pain score. Patients were familiarized with the VAS scoring system during the preoperative period to ensure accurate assessment.

Secondary outcomes included time to first rescue analgesia, defined as the interval from administration of study medication to patient request for additional pain relief. When patients reported VAS scores exceeding 4 or specifically requested additional analgesia, rescue medication consisting of intravenous diclofenac sodium (75 mg) was administered. If pain persisted despite rescue medication, additional tramadol (50 mg intravenous) was administered as needed. Total analgesic consumption during the 24-hour study period was recorded for all patients. Adverse effects including nausea, vomiting, respiratory depression (respiratory rate less than 10 breaths per minute), sedation (assessed using Ramsay Sedation Scale), pruritus, and urinary retention were systematically documented. Patient satisfaction with pain management was assessed at 24 hours postoperatively using an 11-point numerical rating scale ranging from 0 (completely dissatisfied) to 10 (completely satisfied).

Follow-up Protocol

All patients were monitored continuously in the post-anaesthesia care unit for the first 6 hours postoperatively, during which vital signs, pain scores, and adverse effects were recorded at regular intervals. Subsequently, patients were transferred to the surgical ward where monitoring continued with pain assessments at 12 and 24 hours. Nursing staff responsible for pain assessments received standardized training in VAS administration and adverse effect recognition prior to study commencement. Any serious adverse events were immediately reported to the principal investigator and institutional ethics committee. Patients were followed until hospital discharge to ensure complete data collection and to monitor for any delayed adverse effects.

Statistical Analysis

Statistical analysis was performed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). Data were assessed for normality using the Shapiro-Wilk test. Continuous variables with normal distribution were expressed as mean ± standard deviation and compared between groups using independent samples t-test. Continuous variables with non-normal distribution were expressed as median with interquartile range and compared using Mann-Whitney U test. Categorical variables were expressed as frequencies and percentages and analyzed using chi-square test or Fisher's exact test as appropriate. Pain scores at different time intervals were compared using repeated measures analysis of variance with post-hoc Bonferroni correction for multiple comparisons. Time to first rescue analgesia was analyzed using Kaplan-Meier survival analysis with log-rank test for group comparison. A p-value of less than 0.05 was considered statistically significant for all analyses. All statistical tests were two-tailed, and confidence intervals were calculated at the 95% level.

RESULTS

Patient Demographics and Baseline Characteristics

A total of 100 patients were enrolled in the study and randomly allocated into two groups of 50 patients each. All enrolled patients completed the study protocol without any dropouts or protocol violations. The demographic and baseline clinical characteristics are presented in Table 1. Both groups were comparable with respect to age, gender distribution, body mass index, American Society of Anesthesiologists physical status classification, and duration of surgery. There were no statistically significant differences between groups in any baseline parameter, confirming successful randomization and comparable study groups.

(See Table 1)

Pain Intensity Assessment

Visual Analogue Scale scores at various time intervals are presented in Table 2. Immediately postoperatively, both groups demonstrated comparable pain scores (Group F: 1.86±0.74 vs Group T: 1.92±0.68, p=0.674). However, statistically significant differences emerged at subsequent time points. At 2 hours postoperatively, the fentanyl group showed significantly lower mean VAS scores compared to the tramadol group (2.34±0.82 vs 3.76±1.12, p<0.001). This significant difference persisted at 4 hours (2.68±0.94 vs 3.92±1.24, p<0.001) and 6 hours (3.12±1.08 vs 4.28±1.36, p<0.001) postoperatively. By 12 hours, pain scores remained lower in the fentanyl group, though the difference was less pronounced (3.84±1.22 vs 4.42±1.54, p=0.038). At 24 hours postoperatively, both groups showed comparable pain intensity (4.12±1.38 vs 4.36±1.62, p=0.425), likely reflecting the influence of rescue analgesia administration in both groups.

(See Table 2)

Rescue Analgesia Requirements

Analysis of rescue analgesia requirements revealed significant differences between groups as shown in Table 3. The mean time to first rescue analgesia was significantly longer in Group F compared to Group T (4.82±1.26 hours vs 3.34±0.98 hours, p<0.001), indicating prolonged duration of effective analgesia with fentanyl. The proportion of patients requiring rescue analgesia within the first 4 hours was significantly lower in the fentanyl group (28% vs 56%, p=0.004). Total analgesic consumption during the 24-hour study period, including both study medication and rescue analgesia, was significantly lower in Group F. Kaplan-Meier survival analysis demonstrated that patients in the fentanyl group had significantly longer analgesic duration compared to those in the tramadol group (log-rank test p<0.001).

(See Table 3)

Adverse Effects Profile

The incidence of adverse effects in both groups is detailed in Table 4. Nausea and vomiting represented the most commonly observed adverse effects, with significantly higher incidence in the tramadol group compared to the fentanyl group (34% vs 18%, p=0.048). The severity of nausea was generally mild to moderate in both groups, with only two patients in the tramadol group requiring additional antiemetic medication beyond the prophylactic ondansetron. Pruritus was observed more frequently in the fentanyl group, though the difference did not reach statistical significance (14% vs 8%, p=0.303). Sedation scores, assessed using the Ramsay Sedation Scale, were comparable between groups at all time intervals, with most patients maintaining a score of 2-3 indicating appropriate sedation levels. No patients in either group experienced clinically significant respiratory depression, defined as respiratory rate below 10 breaths per minute or

oxygen saturation below 90% on room air. One patient in the fentanyl group and two patients in the tramadol group experienced urinary retention requiring catheterization, but this difference was not statistically significant (p=0.558).
(See Table 4)

Patient Satisfaction and Recovery Parameters
Patient satisfaction scores assessed at 24 hours postoperatively are presented in Table 5. The fentanyl group demonstrated significantly higher mean satisfaction scores compared to the tramadol group (8.24±1.12 vs 7.16±1.48, p<0.001). When categorized into satisfaction levels, 74% of patients in Group F reported high satisfaction (scores 8-10) compared to 52% in Group T (p=0.019). Recovery parameters including time to first ambulation and hospital length of stay showed favorable trends in the fentanyl group, though these differences did not achieve statistical significance. The mean time to first ambulation was 8.4±2.6 hours in Group F versus 9.8±3.2 hours in Group T (p=0.062), while mean hospital length of stay was 2.8±0.9 days versus 3.1±1.1 days respectively (p=0.145).
(See Table 5)

Hemodynamic Parameters
Hemodynamic parameters including heart rate, systolic blood pressure, and diastolic blood pressure were monitored at regular intervals throughout the study period as shown in Table 6. Both groups maintained stable hemodynamic profiles with no clinically significant differences in mean heart rate or blood pressure measurements at any time point. The stability of vital signs in both groups confirmed the hemodynamic safety of the analgesic regimens employed. No patients required interventions for hemodynamic instability attributable to study medications. Mean arterial pressure remained within normal physiological range in both groups throughout the observation period, with no instances of significant hypotension or hypertension requiring treatment.
(See Table 6)

TABLES

Table 1: Demographic and Baseline Clinical Characteristics

Parameter	Group F (Fentanyl) n=50	Group T (Tramadol) n=50
Age (years)	36.4 ± 12.8	38.2 ± 14.1
Gender (Male/Female)	28/22	31/19
BMI (kg/m²)	24.6 ± 3.2	25.1 ± 3.6
ASA Status (I/II)	38/12	35/15
Duration of Surgery (minutes)	48.6 ± 12.4	46.8 ± 13.2

Values expressed as Mean ± SD or numbers. BMI: Body Mass Index; ASA: American Society of Anesthesiologists. No significant differences between groups (p>0.05 for all parameters).

Table 2: Visual Analogue Scale Scores at Different Time Intervals

Time Point	Group F (n=50)	Group T (n=50)	p-value
0 hours	1.86 ± 0.74	1.92 ± 0.68	0.674
2 hours	2.34 ± 0.82	3.76 ± 1.12	**<0.001***
4 hours	2.68 ± 0.94	3.92 ± 1.24	**<0.001***
6 hours	3.12 ± 1.08	4.28 ± 1.36	**<0.001***
12 hours	3.84 ± 1.22	4.42 ± 1.54	**0.038***
24 hours	4.12 ± 1.38	4.36 ± 1.62	0.425

*Values expressed as Mean ± SD. *Statistically significant (p<0.05). VAS scores range from 0 (no pain) to 10 (worst imaginable pain).*

Table 3: Rescue Analgesia Requirements

Parameter	Group F (n=50)	Group T (n=50)
Time to first rescue analgesia (hours)	4.82 ± 1.26	3.34 ± 0.98
Patients requiring rescue analgesia <4 hours	14 (28%)	28 (56%)
Total patients requiring rescue analgesia	32 (64%)	42 (84%)
Mean number of rescue doses (24h)	1.24 ± 0.86	1.88 ± 1.12

Values expressed as Mean ± SD or number (percentage). p<0.001 for time to first rescue analgesia; p=0.004 for patients requiring rescue analgesia <4 hours.

Table 4: Adverse Effects Profile

Adverse Effect	Group F (n=50)	Group T (n=50)
Nausea and Vomiting	9 (18%)	17 (34%)*
Pruritus	7 (14%)	4 (8%)
Excessive Sedation (Ramsay >4)	3 (6%)	2 (4%)

Respiratory Depression	0 (0%)	0 (0%)
Urinary Retention	1 (2%)	2 (4%)

*Values expressed as number (percentage). *p=0.048 statistically significant. All other comparisons p>0.05.*

Table 5: Patient Satisfaction Scores and Recovery Parameters

Parameter	Group F (n=50)	Group T (n=50)
Patient Satisfaction Score (0-10)	8.24 ± 1.12	7.16 ± 1.48
High Satisfaction (Score 8-10)	37 (74%)	26 (52%)
Time to First Ambulation (hours)	8.4 ± 2.6	9.8 ± 3.2
Hospital Length of Stay (days)	2.8 ± 0.9	3.1 ± 1.1

Values expressed as Mean ± SD or number (percentage). p<0.001 for patient satisfaction score; p=0.019 for high satisfaction rate; p>0.05 for recovery parameters.

Table 6: Hemodynamic Parameters

Time Point	Parameter	Group F	Group T
0 hours	Heart Rate (bpm)	82.4 ± 10.2	84.6 ± 11.4
2 hours	Heart Rate (bpm)	78.6 ± 9.8	80.2 ± 10.6
6 hours	Heart Rate (bpm)	76.8 ± 9.4	78.4 ± 10.2
0 hours	SBP (mmHg)	128.4 ± 12.6	126.8 ± 13.4
6 hours	SBP (mmHg)	122.6 ± 11.8	124.2 ± 12.4

Values expressed as Mean ± SD. bpm: beats per minute; SBP: Systolic Blood Pressure. No significant differences between groups at any time point (p>0.05).

DISCUSSION

The present prospective randomized controlled trial demonstrated that intravenous fentanyl provided superior postoperative analgesia compared to tramadol in patients undergoing appendectomy, as evidenced by significantly lower pain scores, prolonged duration of analgesia, reduced rescue analgesic requirements, and higher patient satisfaction scores. These findings contribute valuable evidence to the ongoing discourse regarding optimal analgesic selection for postoperative pain management in surgical populations and have important implications for clinical practice in the setting of appendectomy.(11)

The superior analgesic efficacy of fentanyl observed in this study aligns with several previous investigations examining opioid analgesics in various surgical contexts. Rawal et al. conducted a comparative study of fentanyl and tramadol for postoperative analgesia following abdominal surgery and reported significantly lower pain scores in the fentanyl group, consistent with the findings of the present investigation.(12) Similarly, Kumar and colleagues demonstrated that fentanyl provided more effective analgesia than tramadol following laparoscopic cholecystectomy, with patients receiving fentanyl experiencing significantly longer duration of analgesia and reduced requirement for supplemental analgesics.(13) The pharmacological basis for fentanyl's superior efficacy likely relates to its high affinity for μ-opioid receptors, rapid onset of action, and potent analgesic properties that enable effective suppression of nociceptive transmission at both spinal and supraspinal levels.

However, the literature also contains studies reporting contrasting findings regarding the comparative efficacy of these agents. Deshmukh et al. found no significant difference in analgesic efficacy between fentanyl and tramadol for postoperative pain management following gynecological surgeries, suggesting that the relative effectiveness of these agents may vary depending on the specific surgical procedure, patient population, and analgesic dosing regimen employed.(14) The discrepancy between studies underscores the importance of context-specific evaluation of analgesic strategies and highlights the value of procedure-specific research such as the present investigation focusing specifically on appendectomy patients. Variations in surgical trauma, inflammatory responses, and individual pain perception may contribute to differential analgesic requirements across different surgical procedures.

The significantly prolonged time to first rescue analgesia observed in the fentanyl group constitutes an important clinical finding with practical implications for postoperative care management. Extended duration of effective analgesia reduces nursing workload associated with frequent analgesic administration, decreases patient distress associated with recurrent pain episodes, and may contribute to improved sleep quality and overall recovery experience.(15) The mean time to rescue analgesia of 4.82 hours in the fentanyl group compared to 3.34 hours in the tramadol group represents a clinically meaningful difference that could influence decisions regarding timing of nursing assessments and anticipatory pain

management strategies. This finding suggests that fentanyl may offer practical advantages in terms of reduced frequency of analgesic administration and associated cost savings related to medication preparation and nursing time.

The adverse effect profile observed in this study revealed important differences between the two analgesic agents that merit consideration in clinical decision-making. The significantly higher incidence of nausea and vomiting in the tramadol group compared to the fentanyl group represents a clinically relevant finding, as postoperative nausea and vomiting constitute distressing complications that negatively impact patient satisfaction and may delay hospital discharge.(16) This observation contrasts with the traditional notion that tramadol exhibits a more favorable gastrointestinal side effect profile compared to pure opioid agonists. The mechanism underlying tramadol-associated nausea may relate to its serotonergic activity and potential effects on chemoreceptor trigger zone activation. Prophylactic antiemetic strategies may require greater emphasis when tramadol is selected as the primary analgesic agent.

Conversely, the trend toward higher incidence of pruritus in the fentanyl group, though not statistically significant in this study, represents a well-recognized adverse effect of μ-opioid agonists that clinicians should anticipate and manage appropriately. The mechanism of opioid-induced pruritus remains incompletely understood but likely involves both central and peripheral mediator release, including histamine-dependent and histamine-independent pathways.(17) The absence of respiratory depression in both groups, despite the use of potent opioid analgesics, likely reflects appropriate dosing, careful patient selection excluding those with significant comorbidities, and close postoperative monitoring. This safety finding provides reassurance regarding the use of these agents in the immediate postoperative period when administered at appropriate doses with adequate monitoring.

Patient satisfaction scores demonstrated significantly higher ratings in the fentanyl group, reflecting not merely superior pain control but the holistic patient experience encompassing comfort, functional ability, and perceived quality of care. The importance of patient satisfaction as a quality metric in healthcare delivery has gained increasing recognition, with regulatory bodies and accreditation organizations incorporating patient-reported outcomes into quality assessment frameworks.(18) The observed difference in satisfaction scores between groups likely reflects the superior analgesic efficacy of fentanyl, reduced incidence of nausea and vomiting, and potentially other unmeasured factors contributing to overall patient comfort. Healthcare systems increasingly recognize that effective pain management constitutes not merely a clinical obligation but an essential component of patient-centered care that influences patient perceptions of healthcare quality.

The favorable trends observed in secondary outcomes including time to first ambulation and hospital length of stay in the fentanyl group, though not achieving statistical significance, suggest potential benefits extending beyond immediate pain control. Early mobilization following surgery has been associated with reduced complications including venous thromboembolism, pulmonary complications, and ileus, while shorter hospital stays reduce healthcare costs and patient exposure to nosocomial infections.(19) The mechanistic link between superior analgesia and these secondary outcomes likely involves improved patient comfort enabling earlier ambulation, reduced opioid consumption minimizing side effects that impair mobility, and overall enhanced recovery facilitating earlier discharge readiness. Future studies with larger sample sizes and longer follow-up periods may clarify whether these trends translate into statistically significant differences with clinical and economic implications.

Cost-effectiveness considerations, though not formally assessed in this study, merit discussion in the context of analgesic selection. While fentanyl typically carries higher medication acquisition costs compared to tramadol, comprehensive economic analysis must account for multiple factors including total analgesic consumption, nursing time for medication administration, management of adverse effects, hospital length of stay, and long-term outcomes including chronic pain development.(20) The reduced rescue analgesic requirements, lower incidence of nausea and vomiting, and trends toward shorter hospital stay observed with fentanyl may offset higher medication costs when analyzed from a healthcare systems perspective. Formal cost-effectiveness analyses incorporating these multiple dimensions would provide valuable information for formulary decisions and institutional practice guideline development.

Several methodological strengths enhance the validity and clinical applicability of these findings. The prospective randomized controlled design with adequate sample size, standardized anesthetic and surgical protocols, validated outcome measures, systematic adverse effect monitoring, and comprehensive statistical analysis provides robust evidence regarding comparative analgesic efficacy. The single-center design enabled consistent implementation of study protocols and standardization of perioperative care, reducing confounding variables that might obscure treatment effects. The inclusion of patient-centered outcomes including satisfaction scores alongside traditional efficacy measures provides a comprehensive assessment of analgesic performance that reflects contemporary emphasis on patient-reported outcomes in clinical research.

Certain limitations of this investigation warrant acknowledgment and consideration in interpreting the results. The single-center design, while enabling protocol standardization, may limit generalizability to other healthcare settings with

different patient populations, surgical techniques, or perioperative care protocols. The study focused on appendectomy patients specifically, and extrapolation of findings to other surgical procedures should be undertaken cautiously given potential differences in surgical trauma, inflammatory responses, and pain characteristics across different operations. The relatively short 24-hour follow-up period, while appropriate for assessing acute postoperative analgesia, precludes evaluation of longer-term outcomes including chronic pain development, quality of life impacts, and late adverse effects. The single-dose study design, though clinically relevant for immediate postoperative analgesia, does not address questions regarding repeated dosing, cumulative effects, or alternative dosing regimens that might optimize analgesic outcomes.

Future research directions should address these limitations and explore several important questions that remain unanswered. Multicenter trials encompassing diverse healthcare settings and patient populations would enhance generalizability of findings and enable evaluation of how institutional factors influence analgesic outcomes. Comparative studies examining different doses of both agents could identify optimal dosing strategies that maximize analgesic benefit while minimizing adverse effects. Investigation of these analgesics in other common surgical procedures would expand the evidence base for analgesic selection across surgical specialties. Longer-term follow-up studies assessing outcomes including chronic pain development, functional recovery, quality of life, and healthcare resource utilization would provide comprehensive evaluation of analgesic strategies from both patient and healthcare system perspectives. Finally, pharmacogenetic studies examining how genetic polymorphisms in drug-metabolizing enzymes and opioid receptors influence analgesic response could advance precision medicine approaches to postoperative pain management.

CONCLUSION

This prospective randomized controlled trial demonstrated that intravenous fentanyl provided superior postoperative analgesia compared to tramadol in patients undergoing appendectomy, as evidenced by significantly lower pain intensity scores at early postoperative time points, prolonged duration of effective analgesia, reduced requirements for rescue analgesics, and higher patient satisfaction ratings. The fentanyl group also demonstrated a more favorable adverse effect profile with significantly lower incidence of nausea and vomiting, the most common distressing postoperative complication encountered in both groups. The hemodynamic stability observed in both groups confirmed the cardiovascular safety of these analgesic regimens when administered at appropriate doses with adequate monitoring. These findings support the preferential use of intravenous fentanyl over tramadol for postoperative pain management following appendectomy in appropriately selected patients without contraindications to opioid therapy. The superior pain control, extended analgesic duration, improved patient satisfaction, and acceptable safety profile associated with fentanyl make it an optimal choice for immediate postoperative analgesia in this common surgical population. Clinical practice guidelines and institutional protocols for postoperative pain management following appendectomy should consider incorporating these evidence-based findings to optimize patient outcomes and satisfaction while maintaining appropriate safety standards.

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