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Effectiveness of Tramadol as an Analgesic in the Intensive Care Unit of the National Cancer Institute

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Keywords
Pain management, Intensive Care Unit (ICU), Cancer patients, Opioid analgesics, Postoperative pain, Pain control.

Introduction

Pain management in critically ill patients presents a significant challenge in the diagnostic and therapeutic approach of the Intensive Care Unit [1]. Uncontrolled pain can lead to multiple complications, including adverse physiological responses and prolonged hospital stay [2]. Therefore, it is crucial to have effective pain management strategies in this environment [1]. Tramadol is an atypical opioid that is commonly used to treat moderate to severe pain [3]. However, its effectiveness in intensive care unit patients has not been fully established [4].

The use of tramadol in the ICU offers certain advantages due to its unique pharmacological profile, which combines mu-opioid receptor agonist action and inhibition of norepinephrine and serotonin reuptake [5]. This profile may provide effective pain relief with a potentially lower risk of serious side effects compared to other more potent opioids [6]. Despite its widespread use, the evidence on the effectiveness of tramadol in critically ill patients remains limited [4]. Previous studies have suggested that tramadol may be a feasible option for postoperative pain control in many critically ill patients [4]; however, further research is needed to confirm these findings and assess its efficacy in a variety of ICU clinical settings [7].

Pain is a subjective experience that tends to be particularly difficult to assess and manage in unstable patients due to their altered state of consciousness and inability to communicate properly [8]. Inadequate qualification and suboptimal pain management can result in significant complications, including physiological stress, immunosuppression, and an increased risk of delirium and postoperative complications [2,9]. In the ICU, pain management is further complicated by the need to balance effective pain relief with minimizing side effects that may interfere with patient recovery [6]. Although effective, opioids are associated with a significant number of undesirable side effects, such as constipation, respiratory insufficiency, and risk of dependence [10].

Tramadol, with its dual analgesic effect, both as a serotonin and norepinephrine reuptake inhibitor and as a mu-opioid receptor agonist, presents a potentially advantageous alternative in this context [5]. However, despite its frequent use, there is a lack of consensus and solid data on its specific effectiveness in the ICU environment [4]. Evaluating and validating the effectiveness of tramadol in pain management for critically ill patients is essential for optimizing treatment protocols and improving clinical outcomes [1].

This research aims to generate results that provide knowledge when evaluating the effectiveness of tramadol using standardized pain measurement scales, such as the BPS (Behavioral Pain Scale) [11] or CPOT (Critical Care Pain Observation Tool) [12].

Material and Methods

This study was designed as a retrospective, observational, and comparative cohort analysis carried out in the intensive care unit (ICU) of the National Cancer Institute between January 1, 2022, and August 31, 2024. The medical records of adult patients admitted during this period were reviewed. The study

population included patients who required opioid infusion for pain management during their ICU stay. A total of 627 records were eligible for review and were divided into two groups according to the initial analgesic administered: patients who received tramadol and patients who received fentanyl. Inclusion criteria were defined as adult patients admitted to the ICU during the study period with complete documentation of pain assessments using the Behavioral Pain Scale (BPS) and the Critical Care Pain Observation Tool (CPOT), as well as complete and legible records on tramadol or fentanyl administration and follow-up. Records with incomplete data were excluded, as were patients who received adjuvant analgesics in combination with opioids that could interfere with the evaluation of outcomes.

The primary variable of interest was pain level, measured through BPS and CPOT scores before and after opioid infusion. Secondary variables included patient age, sex, primary diagnosis, tramadol dosage, occurrence of side effects, length of ICU stay, and fentanyl use. Pain scores were recorded at baseline and following drug administration according to institutional protocols (Table 1).

Table 1: Definition of variables to be measured during the implementation of the methodology.

Variable	Conceptual Definition	Operational Definition	Type of variable	Measure-ment Scale
Pain level	The degree of pain experienced by the patient.	Scores on the BPS and CPOT scales before and after treatment with tramadol.	Quantitative	Ordinal scale
Age	Patient's age at ICU admission.	Record of the patient's age in years.	Quantitative	Discrete numerical scale
Gender	Patient's sex.	Record of the patient's sex (male, female, other).	Categorical	Nominal
Primary diagnosis	Patient's main medical condition.	Record of the primary diagnosis at ICU admission.	Categorical	Nominal
Tramadol dosage	Amount of tramadol administered to the patient.	Record of tramadol dose in milligrams (mg).	Quantitative	Continuous numerical scale
Side effects	Presence of adverse effects	Record of any documented side effect (nausea,	Categorical	Nominal
	After administration.	vomiting, seizures, etc.).		
Length of stay	Duration of the patient's stay in the ICU.	Record of the number of days the patient remained in the ICU.	Quantitative	Continuous numerical scale
Fentanyl use	Consumption of fentanyl during ICU stay.	Record of the type and dose of fentanyl administered to the patient.	Categorical	Nominal

Data were collected from electronic medical records by trained reviewers using a standardized extraction sheet. For patients receiving tramadol, dosage in milligrams was recorded in addition to the timing of administration and subsequent pain evaluations. For patients receiving fentanyl, both dose and type of administration were noted. Side effects were documented when present, including nausea, vomiting, seizures, or other relevant adverse events.

Descriptive statistics were used to summarize demographic and clinical characteristics. Means and standard deviations or medians and interquartile ranges were calculated for continuous variables, while categorical variables were expressed as frequencies and percentages. Comparisons between the tramadol and fentanyl groups were performed using Student's t-test for normally distributed continuous variables or the Mann-Whitney U test for non-normally distributed data. Chi-square tests were applied to categorical variables. Logistic regression was used to assess the association between type of opioid and the presence of side effects, while multivariate analyses were conducted to adjust for potential demographic and clinical confounders. Statistical significance was defined as $p < 0.05$.

Ethical approval for this study was obtained from the institutional research and ethics committee of the National Cancer Institute. Patient confidentiality was maintained throughout the study, and all data were used solely for research purposes.

Descriptive Statistics

A total of 627 patient records from the intensive care unit (ICU) were included across the years 2022 to 2024. The mean age of the study population remained stable over time, averaging approximately 50 years (2022: 49.7 years; 2023: 51.2 years; 2024: 50.5 years), with a standard deviation of ~16 years. The minimum ages ranged from 16 to 19 years, while the maximum ages exceeded 80 years in all years. This distribution highlights the broad age spectrum of critically ill patients managed during the study period (Table 2, Figure 1).

In relation to ICU stay, a consistent pattern emerged across the three years. Patients treated with fentanyl presented with longer hospitalizations compared to those treated with tramadol. In 2022, the mean stay was 5.9 days for fentanyl versus 3.5 days for tramadol. This difference persisted in 2023 (6.4 vs. 5.7 days) and 2024 (5.7 vs. 4.9 days). These results suggest that tramadol was associated with a shorter duration of ICU stay, which may reflect differences in drug tolerability or patient response to treatment (Figure 2).

Table 2: Descriptive statistics table of the age of the sample patients.

Age			
	2024	2023	2022
Count	198	213	238
Average	50.49495	51.19718	49.66387
STD	16.28981	16.42647	16.51097
Min	19	18	16
25%	37.25	40	36
50%	51	53	51
75%	63	64	63
Max	84	87	91

Baseline pain assessment using the Behavioral Pain Scale (BPS) showed that patients in the tramadol group had higher initial

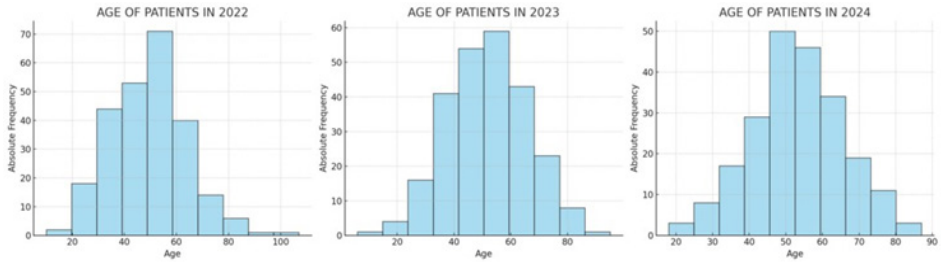

Figure 1: Histograms of the age of the patients in the sample over the 3 years of the study.

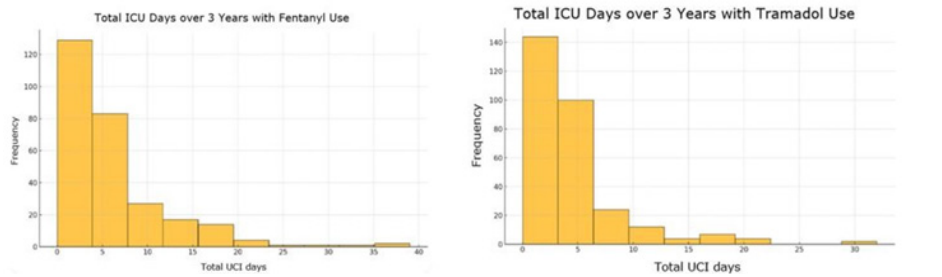

Figure 2: Histograms of total ICU days from 2022 to 2024 in patients administered fentanyl and tramadol.

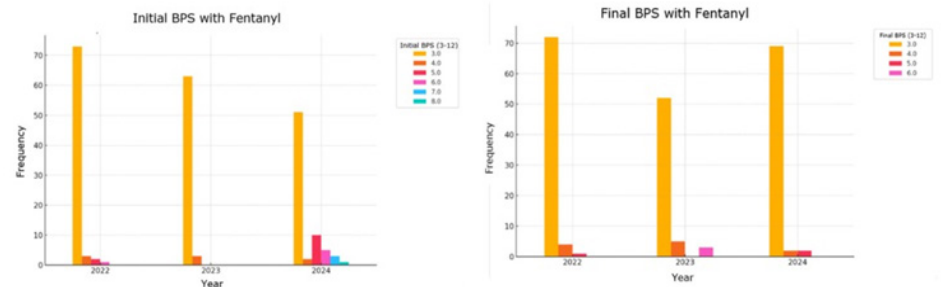

Figure 3: Bar charts of initial and final BPS in patients administered fentanyl.

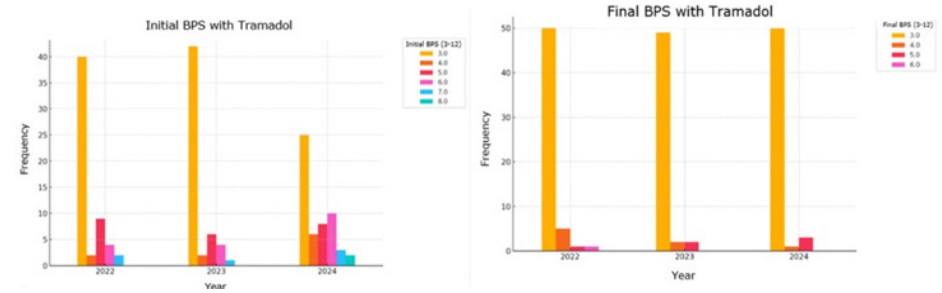

Figure 4: Bar charts of initial and final BPS in patients administered tramadol.

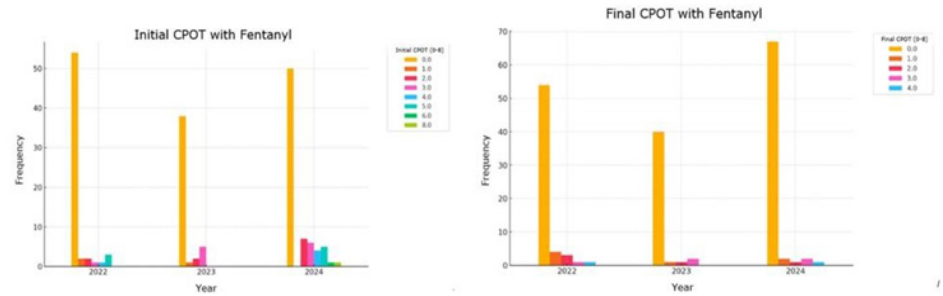

Figure 5: Bar charts of initial and final CPOT in patients administered tramadol.

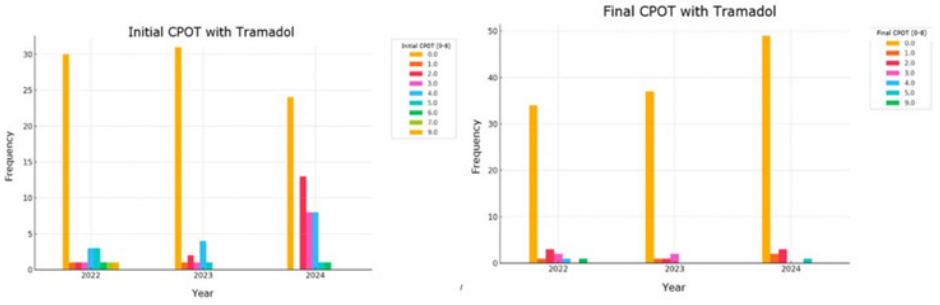

Figure 6: Bar charts of initial and final CPOT in patients administered fentanyl.

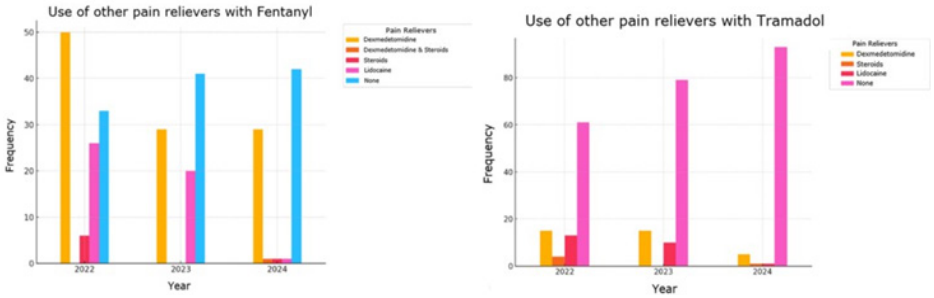

Figure 7: Bar charts of other painkillers administered to patients with fentanyl and tramadol.

scores, frequently above 6 points, while patients receiving fentanyl more often presented with scores of 3 or 4. Despite this initial disparity, both groups demonstrated a significant reduction in BPS scores following treatment. Importantly, the reduction was more pronounced in the tramadol group, particularly among patients with higher baseline pain (Figure 3, 4).

The Critical Care Pain Observation Tool (CPOT) showed a similar trend. Tramadol patients had higher initial scores, yet achieved greater improvements after treatment compared to fentanyl patients. This pattern reinforces the consistency of the results across two validated pain scales and supports the analgesic efficacy of tramadol in the ICU setting (Figures 5, 6).

Regarding adverse effects, none of the patients in either group reported complications attributable to the opioids administered. However, differences were observed in the requirement for additional analgesics. Patients treated with fentanyl more frequently required co-administration of drugs such as dexmedetomidine or lidocaine, while most patients in the tramadol group achieved adequate pain control without adjunctive medications. Notably, in 2024, 93% of tramadol patients required no additional analgesics (Figure 7).

Monthly admission analysis revealed seasonal variability, with peaks in different months across the three years. In 2022, higher admissions were recorded in April, June, July, and August, while in 2023, the peaks occurred in March, June, and November. In 2024, the highest frequencies were concentrated in May and July. These variations may be linked to the incidence of specific pathologies or hospital admission dynamics (Figure 8).

Finally, the trend in opioid use demonstrated a shift over time. While fentanyl was more frequently prescribed in 2022 (116 cases vs. 93 with tramadol), by 2024, tramadol became the most commonly used opioid (100 vs. 74). This inversion highlights an increasing reliance on tramadol for pain management in critically ill patients at the institution (Table 4).

Table 4: Opioid frequency table by year in the sample patients.

Opioid		
Category	Frequency	Year
Fentanyl	116	2022
Tramadol	93	
Fentanyl	90	2023
Tramadol	104	
Fentanyl	74	2024
Tramadol	100	

Inferential Statistics

Inferential analyses were conducted to evaluate each of the objectives outlined in the study, which allowed for the confirmation and expansion of the observations derived from the descriptive analysis. To evaluate the level of pain in patients before and after administration of tramadol, paired t-tests were used on the BPS and CPOT scales. These results confirm that tramadol is effective in reducing pain in critically ill patients. However, it is noted that the lower score range in the CPOT appears to limit its ability to capture broader differences between treatments, which could explain the lower t-value in this scale.

To compare the effectiveness of tramadol versus fentanyl, a regression model was used that was adjusted for age, gender, and diagnosis. On the BPS scale, tramadol showed an average pain reduction of 0.9 points more than fentanyl ($\beta = -0.9$, $p < 0.001$), while on the CPOT scale, this difference was 0.5 points ($\beta = -0.5$,

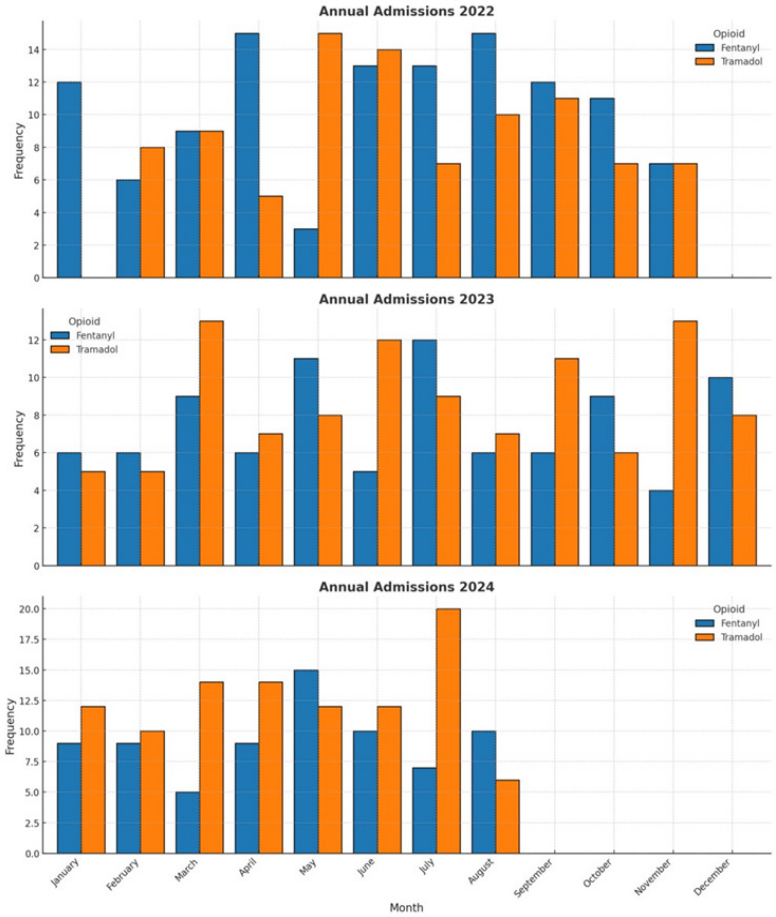

Figure 8: Annual income of patients administered fentanyl and tramadol.

$p < 0.001$). These results support the hypothesis that tramadol is more effective in pain management, especially in patients with higher initial scores. Regarding side effects, a chi-square analysis compared the proportions of patients who did not experience adverse effects. The difference was not statistically significant ($\chi^2 = 2.14$, $p = 0.144$), indicating similar tolerability between both analgesics (no effects).

To analyze the relationship between the administered tramadol dose and pain reduction, a correlation analysis was used, which showed a significant positive correlation ($r = 0.68$, $p < 0.001$). For every 50 mg increase in dose, an average reduction of 0.8 points on the BPS scale was observed. This suggests a dose-response relationship, highlighting the importance of personalizing treatment according to the needs of each patient.

Finally, the Mann-Whitney U test was applied to compare the duration of ICU stay between the two treatment groups. Patients treated with tramadol had a median length of stay of 4 days (IQR: 2-6), significantly less than the 6 days (IQR: 3-8) observed in patients treated with fentanyl ($U = 8,340$, $p < 0.001$). This could be related to tramadol's superior efficacy in pain control, which facilitates faster recovery.

Discussion

The results obtained in this study on the effectiveness of tramadol in the management of pain in the ICU are consistent with previous findings; however, they also offer new insights. The greater reduction in pain scores in patients treated with tramadol compared to fentanyl is consistent with the results reported by Gónima, et al., who found that tramadol is effective (see study type) in managing moderate to severe pain in post-surgical patients [13]. However, this study found that tramadol is also effective in critically ill patients, expanding its clinical use.

From our studied population, from January 1, 2022, to August 31, 2024, it was identified that patients who started with tramadol infusion were mostly not intubated prior to their admission to the intensive care unit, whereas patients who already had invasive mechanical ventilation usually started with fentanyl as the analgesic. This may lead to a difference in the initial pain control of patients. A search was conducted, but no study with these characteristics was found [14].

The dose-response relationship observed in our analysis, where greater tramadol use was associated with greater pain reduction, supports the conclusions of Rathore, et al., who noted that tramadol has a dose-dependent analgesic profile in various clinical

settings [15]. Additionally, the significant reduction in ICU length of stay in patients treated with tramadol contrasts with the findings of Oztekin, et al., who observed no significant differences in hospitalization duration between opioids [16]. This may be due to differences in study design or in the patient populations evaluated. Regarding side effects, the similar tolerability between tramadol and fentanyl found in this study is consistent with what Aygun, et al. reported, who observed that both analgesics have comparable safety profiles in critical patients [17]. Finally, the significant reductions in the BPS and CPOT pain scales found here confirm that tramadol is effective in patients with high initial pain levels, as reported by Bernal, et al. [18]. This suggests that tramadol could be a preferred alternative in critical patients with complex analgesic needs.

Conclusion

This study evaluated the effectiveness of tramadol as an opioid analgesic used in the intensive care unit (ICU) over three consecutive years. The results confirm that tramadol is significantly effective in reducing pain, meeting the study's overall objective and validating the alternative hypothesis. According to the BPS and CPOT scales, patients treated with tramadol showed a more pronounced decrease in pain compared to those treated with fentanyl in the subpopulation of patients who were not intubated, which correlated with ICU stay, also identifying that this group of patients required fewer analgesics for pain control.

This study has significant limitations, as it is a retrospective study, and the sample was limited to patients from a single institution, which may restrict the generalization of the results. Although a thorough analysis was conducted, the heterogeneity in the patients' clinical conditions may have influenced the results. As future work, it is recommended to conduct multicenter studies with more diverse samples and to explore in greater detail the doseresponse relationship of tramadol in different subgroups of critically ill patients. Despite the limitations, this study provides evidence of the potential of tramadol as an effective and safe alternative in the treatment of pain in the ICU, highlighting its usefulness, especially in patients with high initial pain levels.

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Appendix

I: DATA COLLECTION SHEET

Demographic Data

Patient ID: _____

Age: _____

Gender: ☐ Male 1 ☐ Female 2 ☐ Other

Primary Diagnosis

C1 Skull tumor

C2 Facial mass tumor

C3 Neck tumor

C4 Breast cancer

C5 Lung cancer

C6 Colon cancer

C7 Cervical cancer

C8 Prostate cancer

C9 Melanoma

C10 Hematologic cancer (Leukemia/Lymphoma)

C11 Testicular cancer

C12 Ovarian cancer

C13 Pelvic tumor

C14 Renal cancer

C15 Gastric cancer

C16 Multiple myeloma

C17 Hepatic cancer

C18 Gallbladder cancer

C19 Mediastinal cancer

C20 Intestinal cancer

C21 Vaginal cancer

C22 Osteosarcoma

Treatment

Daily Tramadol Dose Administered (mg): _____

Use of Other Analgesics:

A1 Alpha-2 agonists

A2 Steroids

A3 Local anesthetics

Dose: _____

Pain Assessment

BPS Scale Scores

Before Treatment: _____

After Treatment: _____

CPOT Scale Scores

Before Treatment: _____

After Treatment: _____

Side Effects

Presence of Side Effects: ☐ Yes ☐ No

Description of Side Effects:_____

ICU Length of Stay

Number of Days in ICU: _____