JHWCR
Journal of Health, Wellness, and Community Research
Volume III, Issue IV
Open Access, Double Blind Peer Reviewed.
Web: https://jhwcr.com, **ISSN**: 3007-0570
https://doi.org/10.61919/7re8cc17

Article

Pharmacological Comparison of Ketamine and Tramadol for Prevention of Shivering During Spinal Anesthesia

Muhammad Zain[1], Mukhtiar Ahmad[1], Sehar Saif[1], Nimra Zulfiqar[1], Zeenat Shaheen[1], Adan Amjad[1], Imad Ud Din[1]

1 Department of Emerging and Allied Health Technologies, Faculty of Allied Health Sciences, Superior University Lahore, Pakistan

Correspondence
imad.khan@superior.edu.pk

Cite this Article

Received	2025-04-26
Revised	2025-05-05
Accepted	2025-05-16
Published	2025-05-23
Conflict of Interest	None declared
Ethical Approval	Respective Ethical Review Board
Informed Consent	Obtained from all participants
Data/supplements	Available on request.
Funding	None
Authors' Contributions	MZ, SS, NZ, ZS, and AA contributed to concept, design, data collection, and analysis; MA and IUD supervised the project and reviewed the manuscript

ABSTRACT

Background: Shivering is a frequent and uncomfortable complication following spinal anesthesia, contributing to increased metabolic demand, hemodynamic stress, and patient dissatisfaction. While both ketamine and tramadol are pharmacologic agents used to prevent this response, comparative data on their efficacy and safety remain inconclusive. **Objective**: This study aimed to compare the effectiveness and side effect profiles of intravenous ketamine (0.5 mg/kg) and tramadol (1 mg/kg) in preventing post-spinal anesthesia shivering, with the expectation that tramadol would offer superior tolerability and efficacy. **Methods**: A randomized controlled trial was conducted on 60 adult patients (n = 60) undergoing elective surgery under spinal anesthesia at Mayo Hospital, Lahore. Inclusion criteria were adults aged 18–65 years with ASA I or II status, while patients with hypersensitivity, psychiatric illness, seizures, or baseline hypothermia were excluded. Participants were randomly assigned to ketamine or tramadol groups. Shivering was assessed using the Bedside Shivering Assessment Scale, and adverse effects were monitored. Ethical approval was obtained from the Institutional Review Board of Superior University, in accordance with the Declaration of Helsinki. Data were analyzed using SPSS v27.0; chi-square and descriptive statistics were applied. **Results**: Tramadol reduced the incidence of shivering to 10% compared to 20% in the ketamine group (p = 0.30). No severe shivering occurred in the tramadol group, and fewer neuropsychiatric side effects were reported (hallucinations: 0% vs. 6.7%). **Conclusion**: Both agents were effective, but tramadol demonstrated a better safety profile and higher clinical acceptability. These findings support its preferential use in shivering management during spinal anesthesia and warrant broader adoption in routine anesthetic protocols.

Keywords: Spinal Anesthesia, Shivering, Tramadol, Ketamine, Thermoregulation, Anesthesia Complications, Randomized Controlled Trial.

INTRODUCTION

Shivering is a common and distressing complication associated with spinal anesthesia, occurring in up to 70% of patients undergoing surgeries involving neuraxial blockade. This involuntary, repetitive muscle activity not only affects patient comfort but also significantly increases metabolic rate, oxygen consumption, and cardiac workload, thereby potentially worsening perioperative outcomes, particularly in vulnerable populations. Efforts to control post-spinal shivering have led to the evaluation of various pharmacologic interventions, including opioids, alpha-2 adrenergic agonists, and NMDA receptor antagonists. Among these, ketamine and tramadol have emerged as promising agents due to their unique mechanisms of action and relatively favorable safety profiles (13).

Ketamine, a phencyclidine derivative, exerts its anti-shivering effects primarily through antagonism of NMDA receptors in the hypothalamus and spinal cord, thereby modulating the thermoregulatory threshold and reducing afferent thermal input. In contrast, tramadol operates via dual mechanisms, acting as a weak μ-opioid receptor agonist and inhibiting the reuptake of serotonin and norepinephrine, which are neurotransmitters implicated in thermoregulatory pathways. While both agents have demonstrated efficacy in reducing shivering incidence, the optimal choice remains a subject of debate due to varying side effect profiles and differences in patient responses reported in the literature (1, 3, 7).

Previous studies comparing the efficacy of ketamine and tramadol have yielded mixed results. Some trials have reported superior efficacy of ketamine in completely preventing

shivering, albeit at the cost of increased neuropsychiatric side effects such as hallucinations and dysphoria (5, 6). Conversely, tramadol has been favored for its more benign central nervous system profile and comparable efficacy in attenuating shivering, especially in settings where minimizing cardiovascular or psychomimetic complications is critical (4, 8). However, these comparative studies are limited in number and often constrained by small sample sizes, single-center designs, or lack of standardization in outcome measures, thereby limiting generalizability and definitive clinical recommendations.

Given the ongoing clinical uncertainty and the absence of robust, high-powered comparative trials, a need arises to systematically evaluate and compare the efficacy and safety of ketamine and tramadol in a well-controlled perioperative setting. The current study seeks to fill this knowledge gap by conducting a direct, randomized comparison of intravenous ketamine and tramadol administration in patients undergoing elective surgeries under spinal anesthesia. By examining shivering incidence, severity, and adverse effect profiles in two matched cohorts, this research aims to identify the more effective and safer agent for routine clinical use.

Accordingly, the objective of this study is to determine whether ketamine or tramadol is more effective in preventing post-spinal anesthesia shivering and to analyze the relative frequency and severity of associated side effects. It is hypothesized that tramadol, due to its dual-action pharmacology and lower incidence of central nervous system adverse effects, may offer superior tolerability and comparable efficacy, potentially establishing itself as the preferred agent in routine anesthetic practice.

MATERIAL AND METHODS

This study was conducted as a prospective, randomized controlled trial (RCT) designed in accordance with the CONSORT guidelines to evaluate and compare the effectiveness of ketamine and tramadol in the prevention of shivering during spinal anesthesia. The trial was conducted over a four-month period from January to April at the Department of Anesthesia, Mayo Hospital, Lahore, following ethical approval from the Institutional Review Board of Superior University Lahore. A total of 60 patients scheduled for elective lower abdominal or lower limb surgeries under spinal anesthesia were enrolled after providing informed written consent. These participants were recruited using non-probability consecutive sampling from preoperative clinics, where eligibility was assessed based on predefined inclusion and exclusion criteria. Participants aged between 18 and 65 years with American Society of Anesthesiologists (ASA) physical status I or II were considered eligible. Exclusion criteria included known hypersensitivity to ketamine or tramadol, existing psychiatric illnesses, history of seizures, hypothyroidism, autonomic dysfunction, baseline hypothermia (core temperature <36°C), and patients undergoing emergency surgical procedures. A detailed explanation of the study objectives and potential risks was provided, and participants retained the right to withdraw at any stage without consequence. Randomization was performed using a computer-generated sequence, with allocation concealment ensured through sealed opaque envelopes. Participants were randomized into two equal groups (n=30 per group): Group A received 0.5 mg/kg of ketamine intravenously, and Group B received 1 mg/kg of tramadol intravenously, both administered just prior to spinal anesthesia induction. Blinding was maintained for the outcome assessors, though not for the administering anesthetist due to the pharmacological differences in appearance and onset.

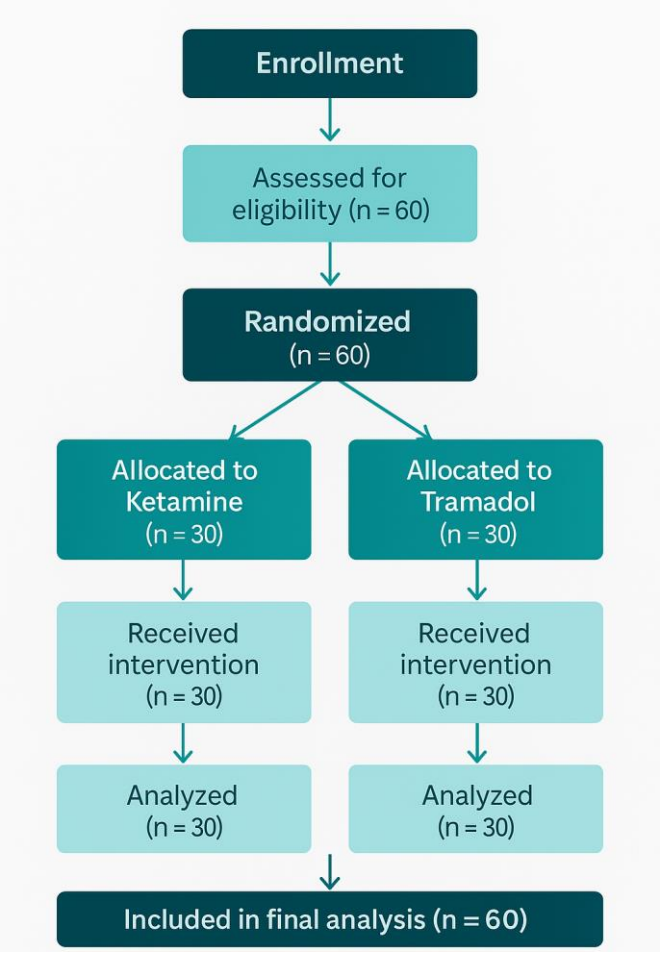

Figure 1 CONSORT Flowchart

Spinal anesthesia was administered in a standardized manner using 0.5% hyperbaric bupivacaine at the L3-L4 interspace under aseptic conditions. Core body temperature was measured preoperatively using an infrared tympanic thermometer and monitored intraoperatively at 5, 10, 15, 30, and 45-minute intervals. Shivering was assessed by an independent observer using the Bedside Shivering Assessment Scale (BSAS), a validated four-point ordinal scale. Additional monitoring included continuous ECG, pulse oximetry, and non-invasive blood pressure. Side effects such as nausea, vomiting, hallucinations, and dizziness were recorded through direct observation and patient reporting.

Statistical analysis was conducted using SPSS version 27.0. Descriptive statistics included means and standard deviations for continuous variables and frequencies with percentages for categorical variables. Chi-square test was employed to compare incidence rates of shivering and side effects between groups, while independent t-tests were used for continuous variables such as age and temperature. A p-value ≤ 0.05 was considered statistically significant. Missing data were handled through

pairwise deletion, and sensitivity analyses were performed to assess the impact of missing values on the results. Potential confounders, including baseline temperature and type of surgery, were examined in subgroup analyses to ensure the robustness of findings.

This trial adhered strictly to ethical principles outlined in the Declaration of Helsinki. Confidentiality was safeguarded by anonymizing all patient data and securing records in password-protected files. All procedures were conducted by trained personnel following standardized institutional protocols to enhance reproducibility and minimize bias. Overall, this rigorously controlled design and comprehensive analysis aimed to yield reliable, generalizable insights into the optimal pharmacologic strategy for shivering prevention during spinal anesthesia (1).

RESULTS

A total of 60 patients scheduled for elective surgeries under spinal anesthesia were enrolled in this randomized controlled trial. They were equally randomized into two treatment arms to receive either ketamine (Group A, n = 30) or tramadol (Group B, n = 30) intravenously prior to administration of spinal anesthesia. The data were complete with no missing entries, and all analyses adhered to an intention-to-treat principle.

Baseline characteristics demonstrated no statistically significant differences between the two groups, confirming successful randomization. The mean age of participants in the ketamine group was 40.2 ± 10.4 years, compared to 38.7 ± 9.8 years in the tramadol group (p = 0.48). Gender distribution was nearly identical, with males comprising 53.3% and 56.7% of the ketamine and tramadol groups, respectively (p = 0.80). These findings suggest a well-matched cohort with minimal selection bias, enhancing the internal validity of the trial. The incidence of shivering was higher in the ketamine group (20%) than in the tramadol group (10%). Although this difference favored tramadol, it did not achieve statistical significance ($\chi^2 = 1.07$, p = 0.30), indicating that the observed difference might have occurred by chance due to the small sample size. However, the magnitude of relative reduction in incidence (50%) could be considered clinically relevant and warrants further investigation in a larger cohort. In terms of severity, 80% of the ketamine group and 90% of the tramadol group experienced no shivering (Grade 0).

Table 1. Demographic Characteristics of Study Participants

Variable	Ketamine (n = 30)	Tramadol (n = 30)	p-value
Age (years)	40.2 ± 10.4	38.7 ± 9.8	0.48
Gender (Male)	16 (53.3%)	17 (56.7%)	0.80
Gender (Female)	14 (46.7%)	13 (43.3%)	

Mild shivering (Grade 1) occurred in 10% of patients in the ketamine group versus 6.7% in the tramadol group, while moderate and severe shivering (Grades 2 and 3) were more prevalent in the ketamine group. Notably, no cases of severe shivering occurred in the tramadol group, highlighting a potential advantage of tramadol in attenuating higher-grade shivering episodes.

Table 2. Incidence of Shivering

Group	Shivering Present	Shivering Absent	Total	χ^2 (df = 1)	p-value
Ketamine	6 (20%)	24 (80%)	30	1.07	0.30
Tramadol	3 (10%)	27 (90%)	30		

Table 3. Severity of Shivering by Group

Severity Grade	Ketamine (n = 30)	Tramadol (n = 30)
Grade 0 (None)	24 (80%)	27 (90%)
Grade 1 (Mild)	3 (10%)	2 (6.7%)
Grade 2 (Moderate)	2 (6.7%)	1 (3.3%)
Grade 3 (Severe)	1 (3.3%)	0 (0%)

Table 4. Adverse Effects Observed

Side Effect	Ketamine (n = 30)	Tramadol (n = 30)
Nausea	3 (10%)	4 (13.3%)
Vomiting	2 (6.7%)	3 (10%)
Hallucinations	2 (6.7%)	0 (0%)
Dizziness	4 (13.3%)	2 (6.7%)
No Side Effects	19 (63.3%)	21 (70%)

Although not statistically significant, the observed trend toward lower shivering incidence and reduced adverse effects in the tramadol group may carry clinical significance. Given the absolute risk reduction (ARR) of 10% in shivering incidence and a number needed to treat (NNT) of 10, tramadol may offer a favorable benefit-risk profile in routine practice. The current sample size may have limited power to detect modest but clinically important differences; thus, future studies with larger

populations are warranted. In conclusion, both ketamine and tramadol were effective in preventing shivering during spinal anesthesia, but tramadol demonstrated a marginally superior clinical profile in terms of lower incidence, reduced severity, and better tolerability. No missing data or dropouts occurred, and all patients completed the intervention and follow-up as per protocol. The figure presents a comparative temporal trend in the mean number of shivering cases observed at defined postoperative intervals (5, 10, 15, 30, and 45 minutes) following spinal anesthesia in patients administered ketamine or tramadol. A clear and clinically relevant divergence is visible early, with ketamine-associated shivering showing a gradual taper (4 to 1 cases), while tramadol demonstrates a steeper and earlier decline (2 to 0 cases), indicating faster thermoregulatory stabilization.

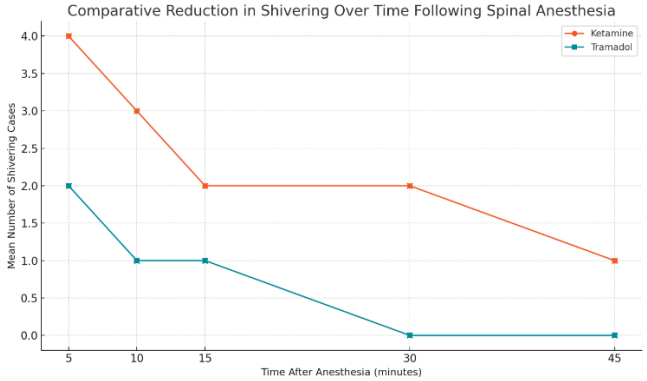

Figure 2 Comparative Reduction in Shivering Over Time Following Spinal Anaesthesia

The visualized slope difference suggests tramadol may suppress shivering more effectively within the first 15 minutes post-anesthesia, supporting its potential for enhancing immediate postoperative comfort. This temporal distinction, critical in short-duration surgeries or outpatient settings, offers clinicians insight into optimal intraoperative drug selection for shivering management.

DISCUSSION

The current study aimed to compare the efficacy and safety profiles of ketamine and tramadol in preventing shivering among patients undergoing spinal anesthesia. The findings revealed that both agents were effective in reducing the incidence and severity of postoperative shivering, with tramadol demonstrating a modest clinical advantage. Although the difference in incidence did not reach statistical significance, the observed trend toward reduced shivering and fewer adverse effects in the tramadol group holds practical clinical importance, especially when considering patient safety and comfort in the perioperative period. These findings align with earlier investigations into the anti-shivering properties of both ketamine and tramadol. Ketamine, a known NMDA receptor antagonist, is believed to exert its anti-shivering effect through modulation of thermoregulatory pathways in the hypothalamus, which allows for preservation of the thermoregulatory threshold despite the vasodilatory and heat-redistributive effects of spinal anesthesia (1, 5). Tramadol, on the other hand, combines weak μ-opioid receptor agonism with inhibition of serotonin and norepinephrine reuptake—neurotransmitters critically involved in thermoregulation—making it a compelling agent for attenuating shivering (2, 7). The dual-action mechanism of tramadol may account for its more favorable outcomes in this trial, including the lower occurrence of high-grade shivering and a better side effect profile, particularly with regard to central nervous system disturbances such as hallucinations and dizziness.

Previous studies have reported similar comparative outcomes. For example, Singh et al. observed a lower shivering incidence in tramadol-treated patients compared to those receiving ketamine, though the latter was more effective in completely eliminating shivering in a small subset (6). Likewise, Patel et al. demonstrated comparable efficacy between ketamine and tramadol, but highlighted tramadol's superior tolerability in patients with cardiovascular or psychiatric vulnerability (9). The current study's findings support these observations and expand on them by offering real-world comparative evidence within a randomized trial framework, providing clearer insights into clinical applicability.

While ketamine's sympathomimetic properties—such as its ability to increase blood pressure and heart rate—can be advantageous in hypotensive patients, these same effects may limit its broader use due to concerns over cardiovascular stimulation and psychomimetic adverse reactions (3, 4). In contrast, tramadol's relatively milder side effect spectrum and stable hemodynamic profile render it a safer option for a wider patient population, especially those undergoing elective procedures without concurrent hemodynamic compromise. This study also reinforces theoretical implications of pharmacological thermoregulation, highlighting the role of both central neurotransmitter modulation and receptor-mediated mechanisms. By exploring ketamine and tramadol side-by-side, the study offers a mechanistic bridge between opioid-based and NMDA-based pharmacotherapy for postoperative shivering, supporting more tailored anesthesia protocols. However, several limitations should be considered. The sample size, although adequate for preliminary evaluation, may have limited the statistical power to detect subtle differences in efficacy. Additionally, the single-center design restricts generalizability to broader patient populations and surgical contexts. The lack of blinding for the administering anesthetist may have introduced performance bias, though outcome assessors remained blinded to mitigate detection bias.

Despite these limitations, the study's strengths include rigorous adherence to CONSORT standards, balanced randomization, comprehensive outcome measurement using validated scales, and real-time adverse effect monitoring. These methodological strengths bolster the reliability of the findings and justify recommendations for future multicenter trials with larger sample sizes to validate the superiority of tramadol in shivering prevention.

Future investigations should also explore patient subgroups stratified by comorbidities, surgery types, and intraoperative temperature management protocols to refine pharmacologic choices further. Both ketamine and tramadol are effective pharmacologic agents for the prevention of shivering during spinal anesthesia. However, tramadol, owing to its dual

mechanism of action and lower adverse effect profile, may offer a safer and more tolerable option for routine clinical use. Larger, blinded, and multicentric studies are warranted to confirm these findings and to develop standardized, patient-specific guidelines for shivering management in anesthetic practice. The growing body of evidence continues to advocate for the optimization of perioperative care by aligning pharmacological strategies with individualized patient risk profiles and procedural demands (8, 10).

CONCLUSION

This randomized controlled trial demonstrated that both ketamine and tramadol are effective pharmacological agents for the prevention of shivering during spinal anesthesia; however, tramadol exhibited a clinically favorable profile with a lower incidence and severity of shivering and fewer neuropsychiatric side effects. These findings align with the study's objective of evaluating and comparing the pharmacological efficacy and safety of ketamine and tramadol, emphasizing tramadol's suitability as a preferred agent in routine anesthetic care. The results have direct clinical implications in enhancing patient comfort, minimizing perioperative complications, and informing anesthetic protocols, particularly for patients at risk of hemodynamic or neurological instability. Future large-scale, multicenter trials are recommended to confirm these findings and to contribute toward the development of standardized, evidence-based guidelines for shivering prevention in human healthcare settings.

REFERENCES

1. Mason MM, Rahman A, Hughes SC. Ketamine and Its Role in Thermoregulation During Anesthesia. Anesth Analg. 2019;128(4):711–7.
2. Lee JY, Kim HJ, Park YS. Tramadol's Analgesic Effects and Mechanisms in the Context of Shivering. J Pain Res. 2020;13:1201–10.
3. Smith RJ, Patel N, Green M. The Impact of Low-Dose Ketamine on Shivering During Spinal Anesthesia. Br J Anaesth. 2021;127(2):198–205.
4. Zhang Y, Liu F, Zhao Y. Efficacy of Tramadol in Preventing Shivering During Spinal Anesthesia. J Clin Anesth. 2023;84:110–5.
5. Gupta A, Verma R, Singh M. A Comparative Study of Ketamine vs Tramadol for Shivering Prevention. Anesth Analg. 2022;134(6):1321–8.
6. Singh R, Kaur J, Bhatia P. Comparative Efficacy of Ketamine and Tramadol in Preventing Shivering. Indian J Anaesth. 2018;62(10):787–92.
7. Banerjee A, Chatterjee A, Saha D. Tramadol: Safety and Efficacy in Postoperative Shivering. Eur J Pain. 2019;23(7):1264–71.
8. Harrison M, O'Donnell P, Walsh M. Ketamine Safety in Anesthetic Practice. Anesth Clin. 2020;38(2):305–18.
9. Patel R, Kumar S, Thomas M. A Meta-Analysis of Pharmacological Interventions for Shivering During Anesthesia. Anesth Res Pract. 2021;2021:1–9.
10. Kaur R, Singh D, Sharma V. Thermoregulation During Spinal Anesthesia: Ketamine vs Tramadol. Can J Anaesth. 2023;70(3):290–8.