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Evaluation of Anti-Shivering Mechanisms of Ketamine and Tramadol in Patients Undergoing Spinal Anesthesia

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Abstract

Background: Perioperative shivering is a common complication during spinal anesthesia, affecting patient comfort and increasing metabolic and cardiovascular stress. Effective prophylactic interventions are necessary to reduce shivering and improve perioperative outcomes. Ketamine and tramadol are pharmacologic agents known to prevent shivering through distinct central mechanisms.

Objective: To evaluate and compare the anti-shivering mechanisms of ketamine and tramadol in patients undergoing spinal anesthesia, focusing on incidence, severity, onset, duration of effect, and safety profiles.

Methodology:
A prospective, randomized study was conducted at Lady Reading Hospital, Peshawar from January to June 2025**.** A total of 204 patients aged 18–60 years, ASA I–II, undergoing elective surgery under spinal anesthesia, were enrolled using non-probability convenient sampling**.** Patients were randomly assigned to receive either low-dose ketamine (Group K, n=102**)** or tramadol (Group T, n=102) intravenously immediately after spinal anesthesia. Perioperative shivering was graded using a four-point scale (0–3), and hemodynamic parameters and adverse effects were recorded. Data were analyzed using SPSS Version 25.0, with Chi-square and t-tests applied; $p \leq 0.05$ was considered significant.

Results
The mean age of participants was 38.5 ± 12.3 years**,** with 59.8% males and 40.2% females. In Group K, 76.5% of patients did not experience shivering, compared to 70.6% in Group T. Severe shivering was rare in both groups (2% vs 3.9%). Ketamine

had a faster onset (3.8 ± 1.2 min) and longer duration (68.4 ± 12.3 min) of anti-shivering effect than tramadol (onset 6.2 ± 1.5 min, duration 60.5 ± 10.7 min). Minor adverse effects were observed, with ketamine causing mild sedation and occasional hallucinations, and tramadol associated with nausea and vomiting. No serious complications occurred in either group.

Conclusion

Both ketamine and tramadol are effective and safe for preventing perioperative shivering in patients undergoing spinal anesthesia. Ketamine demonstrates a slight advantage in terms of faster onset and longer duration**,** making it a preferred choice when rapid and sustained anti-shivering action is required. Both agents improve patient comfort and perioperative outcomes, supporting their use as prophylactic interventions against shivering.

Introduction

Shivering is a frequent and distressing complication during and after spinal anesthesia, with an incidence reported between 40% and 70% depending on the patient population and surgical type [1]. It is characterized by involuntary, oscillatory muscular activity that increases metabolic rate, oxygen consumption, and carbon dioxide production, potentially leading to cardiovascular and respiratory stress [2]. Beyond physiological disturbances, shivering causes discomfort, increases postoperative pain perception, and may interfere with monitoring and surgical procedures, highlighting its clinical significance [3]. The development of shivering during spinal anesthesia is multifactorial, primarily due to impaired thermoregulation caused by sympathetic blockade. Spinal anesthesia blocks afferent thermal signals from the lower body and disrupts efferent sympathetic responses, leading to peripheral vasodilation and redistribution of heat from the core to the periphery [4]. This redistribution lowers core body temperature, triggering shivering as a compensatory mechanism to maintain thermal homeostasis [5]. Additionally, factors such as operating room temperature, infusion of cold intravenous fluids, and the duration of surgery may exacerbate hypothermia and increase shivering risk [6].

The hypothalamus serves as the central thermoregulatory center, maintaining body temperature within a narrow physiological range [7]. Even minor deviations in core temperature activate thermoregulatory effectors, including shivering, to generate heat and restore balance [8]. Spinal anesthesia reduces the shivering threshold due to peripheral vasodilation and impaired thermoregulatory signaling, increasing susceptibility to hypothermia-induced shivering [9]. Clinically, uncontrolled shivering can increase myocardial oxygen demand, interfere with electrocardiographic monitoring, and prolong recovery time, particularly in elderly patients or those with cardiovascular comorbidities [10]. Several pharmacological strategies have been employed to prevent or treat shivering, with ketamine and tramadol emerging as commonly used agents due to their distinct mechanisms and safety profiles. Ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist, exhibits anti-shivering properties by modulating central thermoregulatory pathways and reducing the shivering threshold [11]. Additionally, its sympathomimetic effects help maintain hemodynamic stability during spinal anesthesia, which is advantageous in patients susceptible to hypotension or bradycardia.

Tramadol, a synthetic opioid, exerts anti-shivering effects through central modulation of monoaminergic pathways. By enhancing serotonergic and noradrenergic transmission in the hypothalamus, tramadol lowers the shivering threshold and reduces involuntary muscular activity [12]. It also provides analgesic benefits, contributing to overall patient comfort. While tramadol is generally well-tolerated, side effects such as nausea and dizziness may occur and should be considered when selecting an anti-shivering agent. Comparative studies have highlighted the effectiveness of both drugs in preventing shivering during spinal anesthesia. Ketamine

has been shown to significantly reduce the incidence and severity of shivering at low doses without major adverse effects [13]. Tramadol has demonstrated comparable efficacy, although the onset of action may be slightly delayed relative to ketamine [14]. The choice between ketamine and tramadol may depend on patient comorbidities, side effect profiles, and institutional protocols, making further investigation into their mechanisms and comparative efficacy clinically important [15].

Understanding the pharmacologic basis and effectiveness of these agents is essential for optimizing perioperative management. Evaluating how ketamine and tramadol modulate central thermoregulation, their onset and duration of action, and potential adverse effects can guide anesthesiologists in selecting the most appropriate prophylactic strategy for shivering [16]. Moreover, such insights can improve perioperative comfort, reduce metabolic stress, and enhance overall patient satisfaction, particularly in high-risk populations [17].

Despite existing studies, there remains a need to clarify the mechanisms by which ketamine and tramadol exert anti-shivering effects in patients undergoing spinal anesthesia. Investigating these mechanisms and their comparative efficacy can contribute to evidence-based guidelines, helping clinicians prevent shivering while maintaining hemodynamic stability and minimizing adverse effects [18]. This study therefore aims to evaluate the anti-shivering mechanisms of ketamine and tramadol, assess their effectiveness, and provide insights to optimize anesthetic care during spinal procedures [19].

Methodology:

Study Design

A prospective, comparative, randomized study was conducted to evaluate the anti-shivering effects of ketamine and tramadol in patients undergoing spinal anesthesia.

Study Setting

The study was conducted at Lady Reading Hospital (LRH), Peshawar, in the Department of Anesthesia, which serves as a tertiary care referral center for both elective and emergency surgical procedures.

Study Duration

The study was carried out over a period of 6 months, from January 2025 to June 2025.

Sampling Technique

A non-probability convenient sampling technique was used to select patients based on availability and eligibility according to inclusion and exclusion criteria.

Sample Size

A total of 204 patients were included in the study. The sample size was calculated using Cochran’s formula with a 95% confidence level and 5% margin of error.

Inclusion Criteria

Patients aged 18–60 years undergoing elective surgeries under spinal anesthesia.
Both male and female patients.
Patients classified as American Society of Anesthesiologists (ASA) physical status I and II.
Patients willing to provide **written informed consent** for participation in the study.

Exclusion Criteria

Patients with known hypersensitivity to ketamine, tramadol, or other anesthetic agents
Patients with pre-existing neurological or psychiatric disorders

Patients with cardiovascular instability, severe hypertension, or ischemic heart disease. Patients who had received opioids or other anti-shivering medications within 24 hours prior to surgery.

Ethical Consideration

Ethical approval was obtained from the Institutional Research and Ethical Committee of LRH, Peshawar. Written informed consent was obtained from all participants after explaining the purpose, procedures, potential benefits, and risks of the study. Patient confidentiality and anonymity were maintained throughout the study. The study adhered to the principles outlined in the **Declaration of Helsinki** for research involving human subjects.

Data Collection Procedure

After obtaining informed consent, patients were randomly assigned into two groups: Group K (ketamine) and Group T (tramadol). Standard spinal anesthesia was administered using 0.5% hyperbaric bupivacaine. Patients in Group K received low-dose ketamine intravenously, while those in Group T received tramadol intravenously, immediately after the induction of spinal anesthesia.

Perioperative shivering was monitored and graded using a validated shivering scale at regular intervals. Hemodynamic parameters, including heart rate, blood pressure, and oxygen saturation, were recorded throughout the procedure. Any adverse effects, such as nausea, vomiting, or sedation, were also documented. All data were collected using structured proformas prepared for this study.

Data Analysis

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) Version 25.0. Quantitative variables such as age, duration of surgery, and hemodynamic parameters were presented as mean ± standard deviation (SD), while qualitative variables such as gender, ASA status, and incidence of shivering were presented as frequencies and percentages.

Result:

Age-wise distribution of patients

Age Group (years)	**Group K (Ketamine) n (%)**	**Group T (Tramadol) n (%)**	**Total n (%)**
18–30	28 (27.5)	30 (29.4)	58 (28.4)
31–40	32 (31.4)	30 (29.4)	62 (30.4)
41–50	24 (23.5)	26 (25.5)	50 (24.5)
51–60	18 (17.6)	16 (15.7)	34 (16.7)
Total	102 (100)	102 (100)	204 (100)

Gender-wise Distribution

Gender	**Group K (Ketamine) n (%)**	**Group T (Tramadol) n (%)**	**Total n (%)**
Male	62 (60.8)	60 (58.8)	122 (59.8)
Female	40 (39.2)	42 (41.2)	82 (40.2)
Total	102 (100)	102 (100)	204 (100)

Incidence and severity of shivering

Shivering Grade	**Group K (Ketamine) n (%)**	**Group T (Tramadol) n (%)**	**Total n (%)**
0 (None)	78 (76.5)	72 (70.6)	150 (73.5)
1 (Mild)	14 (13.7)	16 (15.7)	30 (14.7)

2 (Moderate)	8 (7.8)	10 (9.8)	18 (8.8)
3 (Severe)	2 (2.0)	4 (3.9)	6 (2.9)
Total	102 (100)	102 (100)	204 (100)

Parameter	**Group K (Ketamine) Mean ± SD**	**Group T (Tramadol) Mean ± SD**
Onset of anti-shivering (min)	3.8 ± 1.2	6.2 ± 1.5
Duration of effect (min)	68.4 ± 12.3	60.5 ± 10.7

Adverse effect

Adverse Effect	**Group K (Ketamine) n (%)**	**Group T (Tramadol) n (%)**
Nausea	6 (5.9)	12 (11.8)
Vomiting	2 (2.0)	8 (7.8)
Sedation	10 (9.8)	4 (3.9)
Hallucinations	2 (2.0)	0 (0)
No adverse effect	82 (80.4)	78 (76.5)

Discussion:

Shivering is a frequent complication associated with spinal anesthesia, causing patient discomfort and increasing perioperative metabolic demand. In this study, we evaluated the anti-shivering effects of ketamine and tramadol in 204 patients undergoing elective surgeries under spinal anesthesia. The results demonstrated that both ketamine and tramadol were effective in preventing perioperative shivering, with ketamine showing a slightly better overall efficacy.

The age distribution in our study indicated that most patients were between 31 and 40 years of age, with a mean age of 38.5 ± 12.3 years. This aligns with previous studies suggesting that shivering can occur across all adult age groups undergoing spinal anesthesia, although younger and middle-aged adults may report discomfort more readily due to increased awareness of involuntary muscle activity [20]. Gender distribution was comparable between groups, with 59.8% males and 40.2% females. Previous research has shown no significant gender-related differences in the incidence of shivering under spinal anesthesia, which corroborates our findings [21].

The primary outcome of this study was the incidence and severity of perioperative shivering. In Group K (ketamine), 76.5% of patients did not experience shivering, compared to 70.6% in Group T (tramadol). Severe shivering was rare in both groups, affecting only 2% in the ketamine group and 3.9% in the tramadol group. These results are consistent with previous clinical trials reporting that low-dose ketamine effectively prevents shivering by blocking NMDA receptors, thereby reducing central thermoregulatory activity [22,23]. Tramadol, through its modulation of serotonergic and noradrenergic pathways, also demonstrated significant anti-shivering effects, although its onset of action was slightly slower compared to ketamine [24].

Analysis of the onset and duration of anti-shivering effect revealed that ketamine produced a faster response (3.8 ± 1.2 minutes) and longer duration (68.4 ± 12.3 minutes) than tramadol (onset 6.2 ± 1.5 minutes, duration 60.5 ± 10.7 minutes). This suggests that ketamine may be more suitable for surgeries where rapid onset of anti-shivering action is desirable. Similar findings were reported in previous studies where ketamine demonstrated a prompt and prolonged effect due to its central NMDA receptor antagonism and sympathomimetic properties, which help maintain core body temperature and reduce heat redistribution [25,26]. Tramadol, while effective, may require slightly more time to achieve optimal central modulation of shivering pathways, consistent with the results of other comparative trials [27].

Both drugs were generally well-tolerated, with minor differences in adverse effect profiles. Ketamine was associated with mild sedation and occasional hallucinations, whereas tramadol was more frequently associated with nausea and vomiting. No serious complications were observed in either group. This safety profile is consistent with previous research suggesting that low-dose ketamine can be safely used for shivering prophylaxis without significant hemodynamic compromise, while tramadol's gastrointestinal side effects should be monitored [28,29].

The findings of this study support the use of both ketamine and tramadol as effective pharmacological interventions for the prevention of shivering during spinal anesthesia. The slightly superior efficacy of ketamine in terms of faster onset and longer duration may offer clinical advantages, especially in procedures requiring rapid thermoregulatory control. Moreover, understanding the mechanisms underlying their anti-shivering effects provides insight for anesthesiologists in tailoring patient-specific prophylactic strategies. By reducing the incidence and severity of shivering, patient comfort and overall perioperative outcomes can be improved, particularly in patients with cardiovascular or respiratory comorbidities [30].

Conclusion:

Both ketamine and tramadol are effective in preventing perioperative shivering in patients undergoing spinal anesthesia. Ketamine demonstrated a slightly superior efficacy compared to tramadol, with a faster onset and longer duration of anti-shivering effect. Both agents were generally safe and well-tolerated, with ketamine associated with mild sedation and occasional hallucinations, while tramadol more commonly caused nausea and vomiting. The study highlights that ketamine may be preferable in situations where rapid and sustained anti-shivering action is desired, whereas tramadol remains an effective alternative, especially for patients where ketamine use may be contraindicated. Overall, both drugs provide significant perioperative comfort and reduce physiological stress associated with shivering, contributing to improved patient outcomes during spinal anesthesia.

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