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COMPARISON OF PROPHYLACTIC USE OF KETAMINE AND TRAMADOL FOR THE PREVENTION OF SHIVERING DURING SPINAL ANESTHESIA

Original Research

Zahoor Rahman[1]*, Chanda Naseem[2], Shah Faisal[3], Fazal Wadood[4]
[1]Student of MS-AHS, Faculty of Allied Health Sciences, Superior University Lahore, Pakistan.
[2]Assistant Professor, Superior University, Lahore, Pakistan.
[3]Emergency Care Technologist, Peshawar Institute of Medical Sciences, Peshawar, Pakistan.
[4]Assistant Professor, Khyber Teaching Hospital, Peshawar, Pakistan.
Corresponding Author: Zahoor Rahman, Student of MS-AHS, Faculty of Allied Health Sciences, Superior University Lahore, Pakistan, zahoorrahman662@gmail.com
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ABSTRACT

Background: Post-spinal anesthesia shivering is a frequent and distressing complication that may impair postoperative recovery, increase oxygen consumption, and induce cardiovascular instability. It affects up to 70% of patients receiving regional anesthesia, particularly during abdominal or lower limb surgeries. Effective pharmacologic management is essential to reduce its physiological burden and enhance patient comfort. Ketamine and tramadol have both demonstrated anti-shivering properties through distinct mechanisms, yet their comparative effectiveness remains under-explored.

Objective: To compare the prophylactic efficacy and safety of intravenous ketamine and tramadol in preventing shivering during spinal anesthesia.

Methods: This randomized comparative study included 110 adult patients (aged 18–60 years) undergoing elective lower abdominal or lower limb surgery under spinal anesthesia. Patients were randomly assigned to receive either intravenous ketamine 0.25 mg/kg (n=55) or tramadol 0.5 mg/kg (n=55) immediately after spinal block with 3 mL of 0.5% hyperbaric bupivacaine. Shivering intensity was recorded using a validated 5-point scale at baseline, and at 5, 10, 15, and 20 minutes post-administration. Core temperature was monitored tympanically. Adverse effects such as hypotension, hallucinations, and gastrointestinal disturbances were documented.

Results: At 20 minutes, 81.8% of ketamine patients and 89.1% of tramadol patients exhibited no shivering (score 0). However, moderate to severe shivering (scores 5–8) was more common in the tramadol group (25.5%) than in the ketamine group (1.8%). At 10 minutes, 65.5% of ketamine patients had no shivering compared to 78.2% in the tramadol group. Ketamine showed superior control during early intraoperative periods with fewer adverse events.

Conclusion: Both ketamine and tramadol effectively reduced intraoperative shivering during spinal anesthesia. Ketamine offered more consistent control with fewer moderate to severe cases, suggesting it as the preferable agent, especially in high-risk patients.

Keywords: Anesthesia, Drug Therapy, Ketamine, Perioperative Care, Postoperative Complications, Spinal Anesthesia, Tramadol.

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INTRODUCTION

Regulation of body temperature is a fundamental physiological process critical to maintaining homeostasis, as various biochemical functions—including enzymatic activity, membrane stability, and cellular metabolism—are optimized within a narrow thermal range. Even minimal deviations can significantly disturb internal equilibrium, with systemic consequences that may affect patient safety and clinical outcomes. Among the body's intrinsic responses to hypothermia, shivering stands out as a prominent thermoregulatory mechanism characterized by involuntary, rhythmic muscle contractions. This response is primarily triggered by a drop in core body temperature and is commonly observed in the perioperative setting, particularly during spinal anesthesia (1,2). The central control of thermoregulation resides in the anterior hypothalamus, which maintains body temperature between 36.5°C and 37.5°C. A subtle decrease of just 0.2°C to 0.4°C is sufficient to activate compensatory mechanisms such as vasoconstriction and shivering (3). In patients undergoing spinal anesthesia, the incidence of shivering is notably high, ranging from 40% to 70%, especially during procedures involving the abdomen or lower extremities (4,5). Several physiological disruptions contribute to this phenomenon, including redistribution of heat from the core to the periphery, altered hypothalamic responses, inhibition of vasomotor tone due to spinal blockade, and the release of inflammatory cytokines induced by surgical trauma (5–7). While often considered a minor discomfort, intraoperative shivering can have serious clinical implications. It markedly increases metabolic demands, raising oxygen consumption by up to 600%, which in turn elevates cardiac workload and predisposes patients—especially those with compromised cardiovascular function—to lactic acidosis, arterial desaturation, myocardial ischemia, and overall hemodynamic instability (5,6,8). In addition, shivering can interfere with monitoring accuracy, particularly in electrocardiography and pulse oximetry, potentially masking critical clinical changes (9,10).

Although external warming techniques and warmed intravenous fluids are helpful, they are not always sufficient or practical in the intraoperative setting, making pharmacologic intervention a cornerstone of shivering management. Numerous agents have been explored, including opioids like pethidine and fentanyl, α2-agonists like clonidine, and serotonin antagonists such as ondansetron. However, in recent years, non-opioid alternatives such as tramadol, ketamine, and dexmedetomidine have gained favor due to their effectiveness and more favorable side-effect profiles (5,11). Tramadol, a synthetic analgesic, acts through weak μ-opioid receptor agonism combined with serotonin and norepinephrine reuptake inhibition, providing both analgesic and anti-shivering effects without substantial respiratory depression. Nevertheless, isolated cases of paradoxical reactions have been reported (4,10,12). Ketamine, on the other hand, is an NMDA receptor antagonist that offers potent sympathomimetic effects, which help mitigate core temperature redistribution and support cardiovascular stability. Its efficacy in preventing shivering at sub-anesthetic doses is well-established, making it a compelling alternative (13–15). Despite the growing use of both agents, a clear consensus on the superior option remains elusive, particularly in terms of efficacy, hemodynamic stability, and overall safety. Therefore, this study seeks to comparatively evaluate tramadol and ketamine for the prophylaxis of shivering during spinal anesthesia, with the objective of identifying the more effective and clinically advantageous agent for routine intraoperative use.

METHODS

A comparative experimental study was conducted at Health Net Hospital, Peshawar, over a six-month duration to evaluate and compare the prophylactic efficacy of ketamine and tramadol in preventing intraoperative shivering during spinal anesthesia. Following approval from the institutional ethical review board and the acquisition of informed written consent, a total of 110 adult patients scheduled for elective lower abdominal or lower limb surgeries under spinal anesthesia were enrolled. Patients were randomly assigned into two groups of 55 each using a computer-generated randomization table to ensure unbiased allocation. Participants included in the study were between 18 and 60 years of age, classified as American Society of Anesthesiologists (ASA) physical status I to III. Exclusion criteria comprised patients with documented hypersensitivity to either of the study drugs, those presenting with baseline fever, thyroid dysfunction, seizure disorders, or psychiatric illness, and patients who were receiving sedatives or vasodilators preoperatively, as these factors could independently alter thermoregulatory responses.

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All patients received spinal anesthesia using 3 mL of 0.5% hyperbaric bupivacaine administered at the L3–L4 interspace with a 25-gauge spinal needle under strict aseptic precautions. Upon confirmation of successful spinal blockade, patients in Group K were administered intravenous ketamine at a dose of 0.25 mg/kg, while patients in Group T received intravenous tramadol at 0.5 mg/kg. The selection of drug dosage was based on prior evidence demonstrating optimal efficacy at these sub-anesthetic and low analgesic doses with minimal adverse effects. Standard perioperative monitoring included continuous electrocardiography, non-invasive blood pressure, heart rate, peripheral oxygen saturation (SpO_2), and core temperature. Tympanic temperature measurement was utilized as a non-invasive and practical method to monitor core body temperature at baseline and at 10-minute intervals for up to 60 minutes following spinal anesthesia. Shivering was evaluated using a validated five-point scale ranging from 0 (no shivering) to 4 (gross muscle activity involving the entire body), providing a standardized framework for assessment across all time points. Adverse events such as nausea, vomiting, bradycardia, hypotension, hallucinations, and respiratory depression were recorded throughout the intraoperative period. All patients were monitored by trained personnel, and observers were blinded to group assignments to ensure objectivity in data collection. Emergency protocols were in place for the management of any adverse effects observed during the study.

RESULTS

A total of 110 patients were enrolled in the study and equally divided into two groups: Ketamine (n=55) and Tramadol (n=55). The demographic profile revealed that the majority of participants were in the 20–30 years age group (42.7%, n=47), followed by 31–40 years (37.3%, n=41), while both 41–50 and 51–60 age groups comprised 10.0% each (n=11). Gender distribution showed a predominance of male patients, with 68.2% (n=75) male and 31.8% (n=35) female. Initial assessment of shivering scores at baseline demonstrated that in the Ketamine group, 63.6% (n=35) experienced mild to moderate shivering (score 3–5), and no patient reported a severe score of 8. In contrast, the Tramadol group exhibited a broader distribution of shivering severity, with 54.5% (n=30) scoring between 3–5 and 25.5% (n=14) scoring in the higher range (6–8), including three patients with the highest score of 8. At five minutes post spinal anesthesia, 78.2% of patients in the Ketamine group had shivering scores ranging from 0–2, with 30.9% (n=17) showing complete absence of shivering. In the Tramadol group, 78.2% of patients also fell in the 0–2 range, but a higher proportion (43.6%, n=24) had no shivering. However, the Tramadol group demonstrated more cases with scores of 5–6 compared to Ketamine. At ten minutes, the Ketamine group showed further improvement, with 65.5% (n=36) experiencing no shivering, and only one patient reporting a moderate score (3). In the Tramadol group, 78.2% (n=43) had no shivering, though one patient still exhibited a higher score (4).

By fifteen minutes, 80% (n=44) of the Ketamine group reported no shivering, and only 5.5% (n=3) had scores ranging from 2–3. In the Tramadol group, 90.9% (n=50) had complete resolution of shivering, with the remaining 9.1% (n=5) experiencing only mild symptoms (score 1–2). At twenty minutes post anesthesia, 81.8% (n=45) in the Ketamine group were shivering-free, 16.4% (n=9) had mild shivering (score 1), and one patient (1.8%) had moderate shivering (score 3). In comparison, 89.1% (n=49) of Tramadol patients had no shivering, and the remaining 10.9% (n=6) had only mild symptoms (score 1). No patient in the Tramadol group experienced moderate or severe shivering at this point. By the end of the study, 81.8% of patients in the Ketamine group had no shivering (score 0), while in the Tramadol group, this figure was higher at 89.1%. Notably, the Ketamine group demonstrated superior efficacy in preventing higher-grade shivering throughout the observation period, with fewer patients progressing to moderate or severe scores compared to Tramadol. In terms of safety and hemodynamic tolerance, both agents demonstrated distinct side-effect profiles. In the Ketamine group, mild hypotension was observed in 3 patients (5.5%), and 4 patients (7.3%) reported transient hallucinations, which resolved without intervention. Nausea and vomiting occurred in 2 (3.6%) and 1 (1.8%) patient, respectively. Notably, no patient in this group experienced respiratory depression. Conversely, in the Tramadol group, nausea was reported in 5 patients (9.1%) and vomiting in 3 (5.5%). Hypotension was observed in only 1 patient (1.8%), and no hallucinations or respiratory depression were noted. Overall, while both drugs were well-tolerated, Ketamine showed slightly more neuropsychiatric side effects, whereas Tramadol was more likely to cause gastrointestinal discomfort. No major hemodynamic instability or serious adverse event requiring withdrawal from the study was recorded in either group.Here is the merged table with an appropriate title:

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Table 1: Demographic Distribution of Study Participants by Age and Gender

Age Group (Years)	Frequency	Percent	Cumulative Percent	Gender	Gender Percent
20–30	47	42.7%	42.7%	Male	68.2%
31–40	41	37.3%	80.0%	Female	31.8%
41–50	11	10.0%	90.0%	—	—
51–60	11	10.0%	100.0%	—	—

Table 2: Agent * Shivering Base Line Crosstabulation

		Shivering								Total
		1	2	3	4	5	6	7	8	
Agent	Ketamine	1	2	5	18	17	10	2	0	55
	Tramadol	1	3	10	10	13	7	8	3	55
Total		2	5	15	28	30	17	10	3	110

Table 3: Agent * Shivering Afte 5 Minutes Crosstabulation

		Shivering							Total
		0	1	2	3	4	5	6	
Agent	Ketamine	17	15	11	7	4	1	0	55
	Tramadol	24	12	7	7	2	2	1	55
Total		41	27	18	14	6	3	1	110

Table 4: Agent * Shivering after 10 Minutes Crosstabulation

		Shivering					Total
		0	1	2	3	4	
Agent	Ketamine	36	14	4	1	0	55
	Tramadol	43	5	5	1	1	55
Total		79	19	9	2	1	110

Table 5: Agent * Shivering after 15 Minutes Crosstabulation

		Shivering				Total
		0	1	2	3	
Agent	Ketamine	44	8	2	1	55
	Tramadol	50	4	1	0	55
Total		94	12	3	1	110

Table 6: Agent * Shivering after 20 Minutes Crosstabulation

		Shivering			Total
		0	1	3	
Agent	Ketamine	45	9	1	55
	Tramadol	49	6	0	55
Total		94	15	1	110

Table 7: Adverse Effects Comparison Between Ketamine and Tramadol

Adverse Effect	Ketamine (n=55)	Tramadol (n=55)
Nausea	2 (3.6%)	5 (9.1%)
Vomiting	1 (1.8%)	3 (5.5%)
Hypotension	3 (5.5%)	1 (1.8%)
Hallucinations	4 (7.3%)	0 (0.0%)
Respiratory Depression	0 (0.0%)	0 (0.0%)

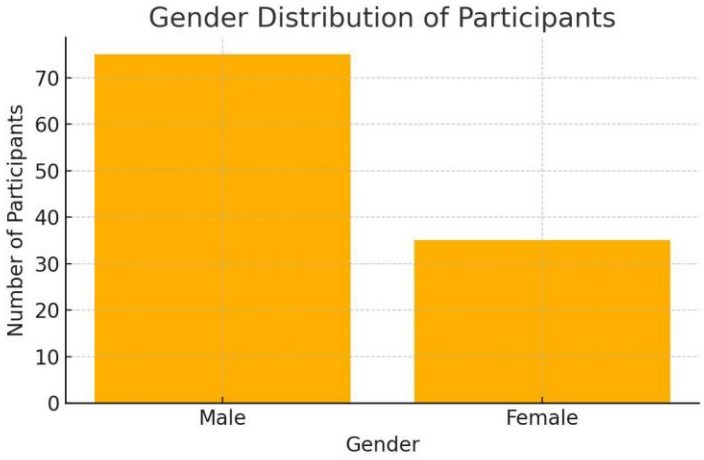

Figure 1 Gender Distribution of Particiants

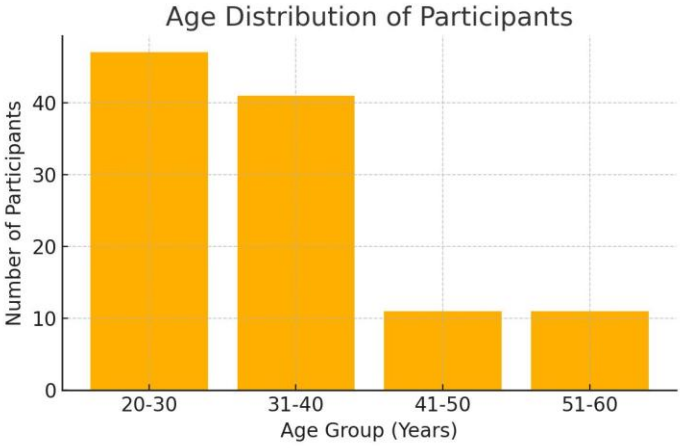

Figure 2 Age Distribution of Participants

DISCUSSION

This study evaluated and compared the prophylactic efficacy of ketamine and tramadol in preventing intraoperative shivering during spinal anesthesia. The findings demonstrated that both agents were effective in reducing the incidence and severity of shivering, although their response profiles differed. Ketamine exhibited a more consistent and controlled anti-shivering effect, with 81.8% of patients remaining shiver-free and a notably low proportion of moderate to severe cases. Tramadol, while showing a slightly higher rate of complete shivering resolution at certain time points (89.1%), displayed a broader variability in shivering scores and a higher frequency of moderate to severe shivering during the earlier intraoperative intervals. The superior performance of ketamine in minimizing shivering severity may be attributed to its unique pharmacodynamic action. As an N-methyl-D-aspartate (NMDA) receptor antagonist, ketamine not only reduces afferent thermal input but also promotes peripheral vasoconstriction and sympathetic activation, thereby stabilizing thermoregulatory mechanisms and mitigating core-to-peripheral heat redistribution (16,17). In contrast, tramadol, which acts as a weak μ-opioid receptor agonist and a serotonin-norepinephrine reuptake inhibitor, exerts its anti-shivering effect through modulation of central monoaminergic pathways (18). However, the interindividual variability in metabolic response to tramadol may account for its fluctuating effectiveness, as influenced by polymorphisms in CYP2D6-mediated metabolism and serotonergic tone.

Comparative literature supports the findings of this study, where ketamine has been shown to offer effective prophylaxis against spinal anesthesia-induced shivering with the added advantage of cardiovascular stability (13–15). Tramadol remains a widely accepted option due to its safety and tolerability profile, particularly its negligible respiratory depression, but previous trials have similarly noted variability in response and a slightly higher incidence of gastrointestinal side effects (19-21). From a safety perspective, both drugs were well tolerated, although adverse effect profiles varied. Ketamine was associated with a higher incidence of hallucinations and transient neuropsychiatric symptoms, which resolved spontaneously. Conversely, tramadol was more commonly associated with nausea and vomiting (22,23). Notably, neither group experienced severe hemodynamic instability or respiratory depression, underscoring the suitability of both agents in routine clinical use for shivering prevention.

The strengths of this study lie in its randomized comparative design, standardized dosing protocols, and objective shivering assessment using a validated scoring scale. However, several limitations merit attention. The absence of ambient operating room temperature documentation may have influenced the incidence and severity of shivering. In addition, the use of tympanic thermometry, although non-invasive and practical, might not have provided the most accurate representation of core temperature compared to esophageal or bladder probes. The study also lacked subgroup analysis based on patient comorbidities or gender, which could offer more nuanced insights into drug response variability. Future studies should aim to incorporate multimodal temperature monitoring, stratify patients by physiological and pharmacogenetic profiles, and extend follow-up to include postoperative shivering and recovery quality. Investigating the combined or synergistic effects of low-dose pharmacologic agents may also present a valuable direction in enhancing intraoperative

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thermoregulation while minimizing side effects. Overall, the study reinforces the clinical utility of both ketamine and tramadol in preventing spinal anesthesia-related shivering. Ketamine's stability in efficacy and supportive hemodynamic profile make it particularly valuable in settings requiring tighter thermoregulatory control, while tramadol remains a favorable alternative where neuropsychiatric tolerance is a concern.

CONCLUSION

This study concluded that both ketamine and tramadol are effective pharmacologic options for preventing intraoperative shivering during spinal anesthesia. Ketamine demonstrated more consistent efficacy and favorable hemodynamic stability, making it particularly suitable for patients with higher perioperative risk. Tramadol, while slightly more variable in response, maintained a strong safety profile and remains a reliable alternative. The selection of either agent should be individualized based on patient characteristics, surgical setting, and potential side-effect considerations, supporting their valuable role in enhancing intraoperative comfort and safety.

AUTHOR CONTRIBUTION

Author	Contribution
Zahoor Rahman*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Chanda Naseem	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Shah Faisal	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Fazal Wadood	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

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