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Original Research Article

To Determine and Compare the Efficacy of Tramadol, Ketamine, and Dexamethasone in the Control of Intra-operative Shivering after Central Neuraxial Blockade (SA)

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Abstract

Background: Intraoperative shivering is a common complication of spinal anesthesia (SA), often resulting from disrupted thermoregulatory control. Shivering can increase metabolic demands, interfere with surgical monitoring, and compromise patient comfort and safety. Various pharmacological agents have been studied for their management, but their comparative efficacy remains inadequately addressed.

Objective: "This study aims to evaluate and compare the efficacy of tramadol, ketamine, and dexamethasone in managing intraoperative shivering following spinal anesthesia."

Methods: "A prospective, randomized, double-blinded study was conducted on 300 patients undergoing elective and emergency surgeries under SA". Participants were divided into three groups (100 each) and administered tramadol, ketamine, or dexamethasone as anti-shivering agents. Shivering severity was graded on a 4-point scale, and outcomes were assessed at 0-, 5-, and 15-minutes post-intervention. Primary endpoints included shivering cessation, while secondary endpoints included the onset of action, hemodynamic parameters, and rescue drug requirements.

Results: The groups were comparable in demographic and anthropometric characteristics. All three agents effectively reduced shivering, with dexamethasone showing the fastest onset and highest success rate. Ketamine demonstrated comparable efficacy to tramadol but was associated with mild psychomimetic effects in some patients. Rescue drug requirements were minimal, and hemodynamic parameters remained stable across groups.

Conclusion: Dexamethasone emerged as the most effective agent for intraoperative shivering management due to its rapid onset and high success rate, followed by ketamine and tramadol. These findings support its preferential use in resource-constrained settings to improve intraoperative patient comfort and outcomes.

Keywords: Dexamethasone, Ketamine, Intraoperative shivering, Spinal anesthesia, Tramadol

Introduction

Spinal anesthesia (SA) is a commonly employed treatment for both elective and emergency surgical procedures. Shivering is one of the most often reported consequences of central neuraxial blockade, attributable to disruptions in thermoregulatory control [1]. Patients are susceptible to hypothermia and shivering during spinal anesthesia since it inhibits tonic vasoconstriction and redistributes core heat from the trunk to peripheral tissues. Data training is currently up to October 2023. A reflexive, repetitive skeletal muscle response to core hypothermia that enhances metabolic heat generation is termed PSS (PSAS). "PSAS elevates O2 consumption, CO2 production, plasma catecholamines, and cardiac output, potentially disrupting the monitoring of ECG, blood pressure, and oxygen saturation [2]."

Shivering during anesthesia can be efficiently managed using anti-shivering drugs, both non-pharmacological and pharmacological strategies. "A

variety of pharmacological agents, including opioids, 5-hydroxytryptamine receptor (5-HT3) antagonists, N-methyl D-aspartate (NMDA) receptor antagonists, cholinomimetics, and biogenic amines, are employed to manage intra-operative shivering [1].” Although spinal anesthesia is commonly used, post-spinal shivering (PSS) is a potential consequence often observed after surgery in impoverished countries due to insufficient resources for sustaining normothermia. In emerging nations, it has been seen to vary from 8.15% to 11.6% [3,4]. Hypothermia, characterized by "heat redistribution from the core" to the periphery during the intraoperative phase due to vasodilation and diminished "thermoregulatory vasoconstriction below the spinal block level," is associated with a high incidence of PSS. Research reveals that the kind of anesthesia used, the patient's age and gender, and the nature of the surgical procedure all influence the occurrence of PSS [5].

Untreated PSS may lead to significant adverse effects, especially in people with diminished cardiac reserves and arterial hypoxia, such as exacerbation of surgical-site discomfort, protracted wound healing, increased metabolic demand, elevated oxygen consumption, and hemostatic dysfunction. Non-pharmacological methods such as radiant heat or warm humidified anesthetic gases are employed to reduce the occurrence of PSS. These non-pharmacological therapies are costly and exhibit limited accessibility [6]. This study aimed to assess and compare the effectiveness of tramadol, ketamine, and dexamethasone in controlling intra-operative shivering after spinal anesthesia.

Materials and Methods

Study Design

“Prospective, Randomized Double-Blinded Study”

Study Site

“Department of Anesthesiology and Critical Care, Darbhanga Medical College & Hospital, Laheriasarai, Darbhanga, Bihar”

Study Duration: 2 Years

Source of Data

Patient undergoing elective and emergency surgeries under regional anesthesia (SA) at “Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar.”

Ethical Consideration

The study protocol received approval from the institutional ethics council of DMCH, Laheriasarai, and adhered to the “International Conference on Harmonisation Guidelines for Good Clinical Practice and the Declaration of Helsinki.” Informed permission was obtained from patients before surgery. The Participant Information Sheet (PIS) was delivered and elucidated to patients in their native language. Subsequently, consent was obtained by the acquisition of their signature or thumbprint on the informed consent form. The data were acquired from the hospital record system after the requisite authorization from the relevant authorities.

Sample Size

With medium (0.25) effect size, 0.05 alpha error probability, 95% power, and 2 degrees of freedom, the minimum sample was found to be 248. Expecting a 20% attrition rate, the minimum sample size was calculated to be around 300 with 100 patients in each group.

Sample selection criteria

Inclusion criteria

- Patients of either sex
- “Patients of ASA Grade I and II”
- Patients of 21-60 years of age
- Patients scheduled for lower abdominal or lower limb surgeries under SA in an emergency as well as routine cases.

Exclusion criteria:

- Patients other than ASA grade 1 and 2
- “Patients with thyroid or neuromuscular disease, patients on narcotics/sedatives, with history of febrile illness, patients who require blood transfusion during surgery, or patients with an initial body (core) temperature >38°C or <36.5°C”
- Patients having sub-arachnoid block failure
- History of allergy to agents to be used.”

Intervention

“Details of the group and the drug were sealed within envelopes, which were randomly picked and administered by the anaesthesiologist unrelated to the study.”

Study Technique

“Every patient underwent pre-anesthetic check-up where detailed history was obtained from them or their attendants. Patients were physically examined, and routine and special investigations (as required) were carried out.”

Study Protocol

Preoperative preparation included fasting for 6–8 hours, with no preoperative medication. Upon arrival in the operating room, an 18G/20G venous cannula was inserted for intravenous access. Spinal anesthesia was preceded by preloading with 10

ml/kg of Ringer's lactate, maintained at 6 ml/kg/hr. Blood pressure fluctuations of about 10% were noted, with medications administered for significant changes. ASA monitoring criteria were followed, including heart rate, ECG, blood pressure, SpO2, and temperature (both surface and core).

"An intrathecal block was administered at the L3–L4 or L4–L5 interspace with 12.5–17.5 mg hyperbaric bupivacaine (0.5%) via a 25G Quincke's needle". The anesthetic dose was tailored to the patient's height and weight. After the block, the needle site was sterilely covered, and the patient was positioned supine. Shivering occurrence and intensity were monitored during the procedure and for 90 minutes post-injection using a four-point scale:

- **"None (Grade 0):** no shivering noted on palpation of the masseter, neck, or chest wall."
- **"Mild (Grade 1):** shivering localized to the neck and/or thorax only"
- **"Moderate (Grade 2):** shivering involved gross movement of the upper extremities (in addition to neck and thorax)"
- **"Severe (Grade 3):** shivering involved gross movements of the trunk, upper and lower extremities."

Shivering was monitored and treated with appropriate medication, with severity assessed at 0-, 5-, and 15 minutes post-treatment. The response was categorized as "Null" (no change in shivering intensity), "Improvement" (decreased intensity), or "Success" (no shivering present), with the absence of shivering considered successfully treated. The primary endpoint of the study was the cessation of post-spinal shivering within 15 minutes after medication, while secondary endpoints included the onset of action, heart rate, arterial pressure, the reappearance of symptoms, and the dose of rescue medication (pethidine) if required.

Statistical Analysis

Data from patients undergoing surgery under spinal anesthesia were organized in tabular format using Microsoft Excel 365 and subsequently uploaded to SPSS version 24 for advanced statistical analysis. Continuous variables, including age, BMI, start of action, duration of action, blood pressure, and heart rate, were reported as mean ± SD (standard deviation). The statistical significance of the differences in continuous data across group A (tramadol), group B (ketamine), and group C (dexamethasone) was assessed using One-way ANOVA. Categorical data, such as shivering grade, result, age group, gender, kind of operation, and frequency of rescue medicine usage, were presented as percentages and frequencies, and thereafter analyzed using the chi-square test. A p-value below 0.05 was established as the threshold for statistical significance.

Results

Table 1 compares the age distribution among Groups A (Tramadol), B (Ketamine), and C (Dexamethasone). Most patients across all groups were in the 41–50 age range, with 37% in Group A, 36% in Group B, and 42% in Group C. The proportions of patients in the 21–30, 31–40, and 51–60 age groups were also similar across groups. The differences in age distribution were not statistically significant ($p = 0.97$), indicating that the groups were comparable in terms of age demographics.

Table 1: Comparison of Age between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)

Age Group	Number of Patients (%)			P-Value (Chi-square test)
	Group A (N = 100)	Group B (N = 100)	Group C (N=100)	
21-30	10	12	9	0.97
31-40	26	27	25	
41-50	37	36	42	
51-60	27	25	24	

Table 2 compares the gender distribution across Groups A (Tramadol), B (Ketamine), and C (Dexamethasone). "Male patients were slightly more prevalent in all groups, with percentages ranging from 54% in Group B to 62% in Group C. Female patients constituted 41% in Group A, 46% in Group B, and 38% in Group C. The differences in gender distribution were not statistically significant ($p = 0.51$)", indicating a comparable gender balance among the groups.

Table 2: Comparison of Gender between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)				
Gender	**Number of Patients (%)**			**P-Value (Chi-square test)**
	Group A (N = 100)	**Group B (N = 100)**	**Group C (N=100)**	
Male	59	54	62	0.51
Female	41	46	38	

Table 3 compares the anthropometric parameters (weight, height, and BMI) between Groups A (Tramadol), B (Ketamine), and C (Dexamethasone). "The mean weight ranged from 62.14 kg in Group A to 64.09 kg in Group B, height from 1.63 m in Group A to 1.65 m in Group B, and BMI from 22.96 kg/m² in Group B to 23.21 kg/m² in Group A. None of the differences were statistically significant ($p > 0.05$ for all parameters), indicating that the groups were comparable in terms of baseline anthropometric characteristics."

Table 3: Comparison of Anthropometric Parameters between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)				
Parameters	**Parameters in Mean ± SD**			**P-Value (One Way ANOVA)**
	Group A (N = 100)	**Group B (N = 100)**	**Group C (N=100)**	
Weight in kg	62.14 ± 8.28	64.09 ± 7.11	63.42 ±9.05	0.23
Height in meter	1.63 ± 0.13	1.65 ± 0.12	1.64 ± 0.17	0.61
BMI in kg/m^2	23.21 ± 2.45	22.96 ± 2.03	23.07 ± 2.23	0.73

Table 4 compares the ASA status of patients in Groups A (Tramadol), B (Ketamine), and C (Dexamethasone). The distribution of ASA I and ASA II patients was similar across all groups, with ASA II being slightly more prevalent: 57% in Group A, 53% in Group B, and 59% in Group C. ASA I patients accounted for 43%, 47%, and 41% in Groups A, B, and C, respectively.

Table 4: Comparison of ASA Status between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)				
Gender	**Number of Patients (%)**			**P-Value (Chi-square test)**
	Group A (N = 100)	**Group B (N = 100)**	**Group C (N=100)**	
ASA I	43	47	41	0.68
ASA II	57	53	59	

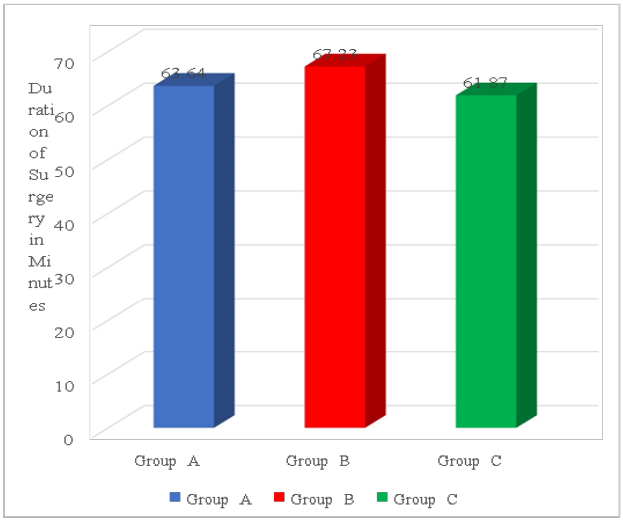

Figure 1: Comparison of Duration of Surgery between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)

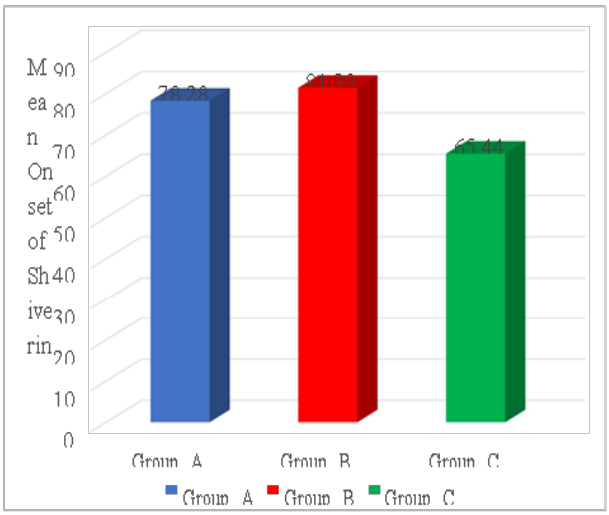

Figure 2: Comparison of Onset of Shivering between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)

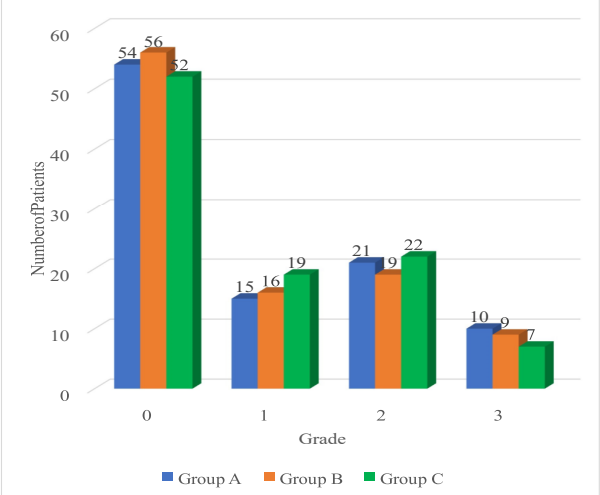

Figure 3: Comparison of Grade of Shivering between Group A (Tramadol), B (Ketamine), and C (Dexamethasone) at Baseline

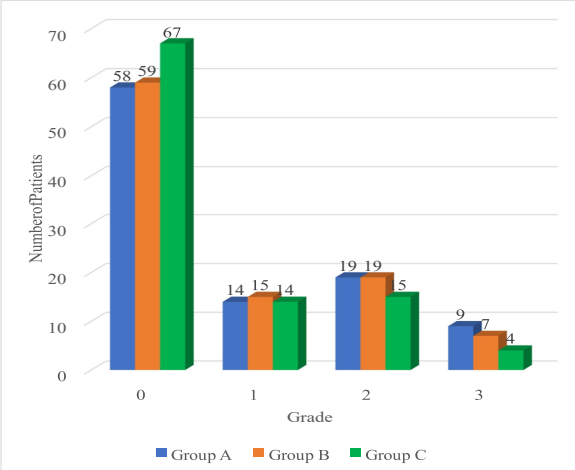

Figure 4: Comparison of Grade of Shivering between Group A (Tramadol), B (Ketamine), and C (Dexamethasone) at 5 Minutes

Table 5 compares the grade of shivering at 15 minutes among Groups A (Tramadol), B (Ketamine), and C (Dexamethasone). Group C showed the highest percentage of patients with no shivering (Grade 0, 82%) compared to Group A (64%) and Group B (60%). Lower grades of

shivering (Grades 1 and 2) were also less frequent in Group C (9% and 7%) compared to Groups A and B, while severe shivering (Grade 3) was minimal across all groups but lowest in Group C (2%). The differences in shivering grades were statistically significant ($p = 0.03$), indicating that Dexamethasone is the most effective at reducing shivering within 15 minutes.

Table 5: Comparison of Grade of Shivering between Group A (Tramadol), B (Ketamine), and C (Dexamethasone) at 15 Minutes

Shivering Grade	Number of Patients (%)			P-Value (Chi-square test)
	Group A (N = 100)	Group B (N = 100)	Group C (N=100)	
0	64	60	82	0.03
1	13	15	9	
2	17	19	7	
3	6	6	2	

Table 6 evaluates the treatment response at 15 minutes among patients in Groups A (Tramadol), B (Ketamine), and C (Dexamethasone). Group C demonstrated the highest success rate (30%) compared to Group A (10%) and Group B (4%). Conversely, Group C had the lowest percentage of patients with no response (9%) compared to Group A (23%) and Group B (25%). The proportion of patients showing improvement was relatively comparable across groups: 67% in Group A, 71% in Group B, and 61% in Group C. The differences were statistically significant ($p < 0.0001$), highlighting Dexamethasone's superior efficacy in achieving a successful response within 15 minutes.

Table 6: Comparison of Response to Treatment between Group A (Tramadol), B (Ketamine), and C (Dexamethasone) at 15 Minutes

Response	Number of Patients (%)			P-Value (Chi-square test)
	Group A (N = 100)	Group B (N = 100)	Group C (N=100)	
Null	23	25	9	<0.0001
Improvement	67	71	61	
Success	10	4	30	

Table 7 compares the rescue pethidine doses among groups receiving Tramadol (A), Ketamine (B), and Dexamethasone (C). “Group C had the lowest mean dose (54.28 mg), followed by Group A (68.85 mg) and Group B (71.57 mg), with significant differences across groups ($p < 0.0001$). Tukey's post hoc analysis revealed a statistically significant lower dose in Group A compared to Group B ($p = 0.03$) and in Group C compared to both Group A and Group B ($p < 0.0001$).” This indicates that Dexamethasone (Group C) effectively reduced the need for rescue pethidine compared to Tramadol and Ketamine.

Table 7: Comparison of Dose of Rescue Pethidine Dose between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)

	Group A	Group B	Group C
Number of Patients (N)	100	100	100
Mean Pethidine Dose in mg	68.85	71.57	54.28
Standard Deviation (SD)	7.48	7.97	6.79

P Value	<0.0001
Tukey's Post Hoc (A-B)	0.03
Tukey's Post Hoc (A-C)	<0.0001
Tukey's Post Hoc (B-C)	<0.0001

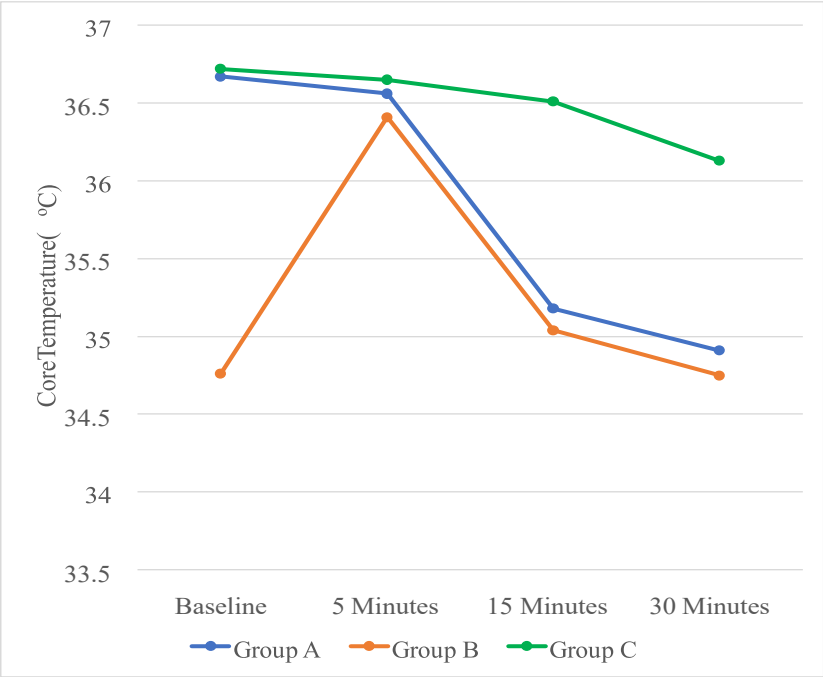

Figure 5: Comparison of Core Temperature between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)

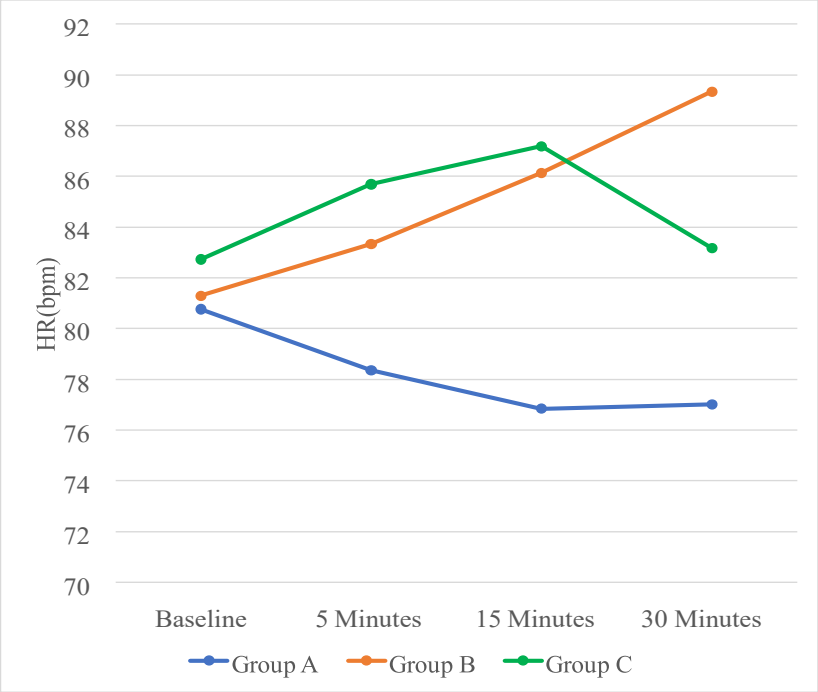

Figure 6: Comparison of HR between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)

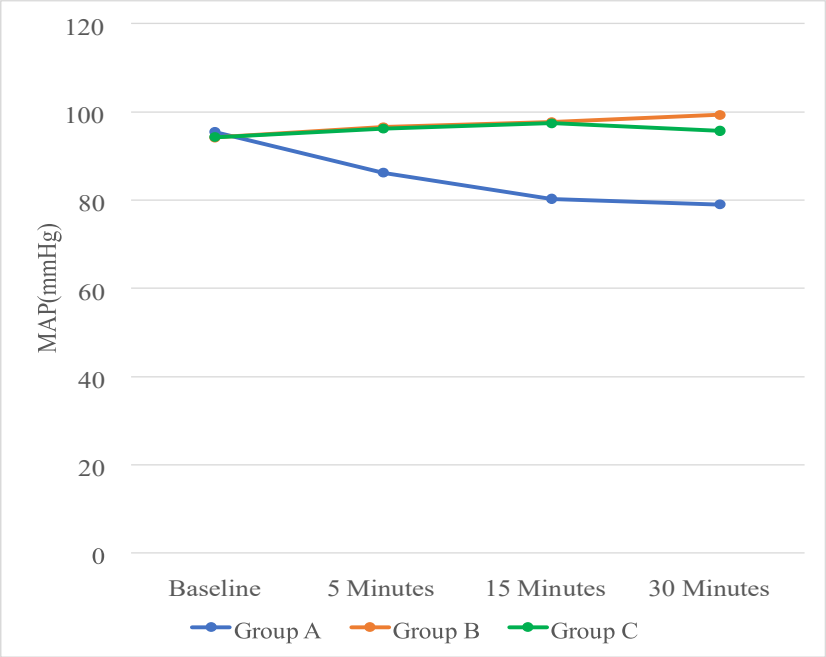

Figure 7: Comparison of MAP between Group A (Tramadol), B (Ketamine), and C (Dexamethasone)

Discussion

This prospective, randomized, double-blinded study evaluated and compared the efficacy of tramadol, ketamine, and dexamethasone in controlling intra-operative shivering after central neuraxial blockade (spinal anesthesia). The findings demonstrated that dexamethasone was the most effective in minimizing shivering, ensuring stable hemodynamics, and reducing the drop in core body temperature. Most participants were male, aged 31–50 years, with ASA II status. The dexamethasone group exhibited a significantly shorter duration of surgery, earlier onset of shivering, and lower shivering severity compared to tramadol and ketamine groups ($p=0.03$).

Furthermore, dexamethasone required fewer rescue pethidine doses and showed a more stable profile for HR, SBP, and DBP ($p<0.0001$). These outcomes align with previous studies demonstrating dexamethasone's anti-inflammatory properties and its ability to reduce the core-to-skin temperature gradient, likely by modulating immune responses and cytokine release during spinal anesthesia.

Various studies corroborate dexamethasone's effectiveness in controlling post-spinal shivering (PSS). For instance, a study by Destaw B et al. (2020) [7] reported shivering rates of 44% and 22% in dexamethasone and pethidine groups, respectively ($p=0.064$). Similarly, Hossain S et al. [8] observed that dexamethasone (0.15 mg/kg) reduced shivering incidence by 55% compared to 15% with placebo during ENT surgeries under general anesthesia (GA). Khosravi et al. [9] demonstrated a decrease in shivering rates from 31% to 12% with dexamethasone (0.15 mg/kg) compared to placebo. Contrastingly, studies by El Bakry AE et al. [10] and Gholami et al. [11] noted no statistically significant differences between dexamethasone and pethidine in shivering incidence. Differences in outcomes may be attributed to variations in methodology, concurrent use of other anti-shivering agents, and population characteristics. Notably, Vinthai G et al. [12] found dexamethasone to be more effective and safer than ketamine and tramadol for PSS management.

Despite its effectiveness, the use of dexamethasone for PSS prevention must consider potential adverse effects associated with prolonged corticosteroid use, such as HPA axis suppression, metabolic imbalances, and osteoporosis. However, short-term, high-dose corticosteroid administration (<7 days) is unlikely to cause significant systemic effects. Strengths of this study include its unique focus on eastern India (Bihar) and the direct comparison of three drugs in a single study design. However, limitations such as the small sample size, single-center design, and lack of plasma concentration correlation with anti-shivering and hemodynamic outcomes should be addressed in future research. The findings reinforce the utility of dexamethasone as an effective and safe alternative for preventing intra-operative shivering.

Conclusion

This study comprehensively evaluated and compared the efficacy of tramadol, ketamine, and dexamethasone in controlling intra-operative shivering following spinal anesthesia (SA). The findings demonstrated that all three drugs were effective in managing post-spinal shivering, with differences in their onset of action, duration, and side effect profiles. Tramadol exhibited a reliable

reduction in shivering severity with a balanced onset and duration of action. Ketamine showed rapid onset with potential psychotropic side effects, while dexamethasone provided prolonged relief with minimal side effects. These results support the selection of anti-shivering agents based on individual patient needs, emphasizing a tailored approach for optimal intra-operative care.

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