



A COMPARATIVE ANALYSIS OF THE EFFECTS OF TRAMADOL, CLONIDINE, AND DEXMEDETOMIDINE ON POST-SPINAL ANESTHESIA SHIVERING

Anaesthesiology

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ABSTRACT

Introduction: Shivering following spinal anesthesia is a common and distressing complication. This study aimed to compare the efficacy and safety of tramadol, clonidine, and dexmedetomidine in treating post-spinal anesthesia shivering. **Methods:** This prospective, randomized, double-blinded study was conducted at the Pacific Institute of Medical Sciences. A total of 150 ASA I/II patients, aged 18-70, who developed shivering after spinal anesthesia were randomly allocated into three groups (n=50 each). Group T received tramadol (1 mg·kg⁻¹), Group C received clonidine (1 mcg·kg⁻¹), and Group D received dexmedetomidine (0.5 mcg·kg⁻¹). The primary outcomes were time to control shivering and recurrence rate. Secondary outcomes included hemodynamic changes, sedation scores, and adverse effects. **Results:** Dexmedetomidine was significantly faster in controlling shivering (5.5 ± 1.2 min) compared to tramadol (7.1 ± 1.5 min) and clonidine (9.9 ± 1.1 min) (p < 0.0001). The recurrence rate was lowest in the dexmedetomidine group (6%) compared to clonidine (12%) and tramadol (26%). Dexmedetomidine and clonidine caused a significant but transient decrease in heart rate and blood pressure. Vomiting was most frequent with tramadol (16%), while hypotension and bradycardia were more common with dexmedetomidine (26% and 16%, respectively). **Conclusion:** Dexmedetomidine is the most effective agent for treating post-spinal anesthesia shivering due to its rapid onset and low recurrence rate. Although associated with a higher incidence of transient hypotension and bradycardia, its beneficial sedative properties and overall efficacy make it a superior clinical choice compared to tramadol and clonidine.

KEYWORDS

INTRODUCTION

Shivering is an oscillatory, involuntary muscular activity and a common problem for patients undergoing procedures with spinal anesthesia. It is a natural physiological response to a decrease in body temperature, as the body attempts to generate metabolic heat to restore homeostasis¹. Typically, the human core body temperature is maintained within a narrow thermoneutral zone of 36.5–37.5 °C¹. When the core temperature falls below this range, thermoregulatory responses like vasoconstriction and shivering are activated¹. The neurological mechanism driving shivering is mediated by spinal α-motor neurons, with the control center located in the preoptic nucleus of the anterior hypothalamus².

The incidence of shivering following spinal anesthesia is reported to be as high as 30–60%³. This shivering can increase heat production by up to 600% and triple oxygen consumption⁴. Such physiological stress can lead to adverse metabolic consequences, including hypoxemia, hypercarbia, and lactic acidosis, as well as increased intraocular and intracranial pressure^{4,5}. In patients with coronary artery disease, the increased myocardial demand from shivering can be particularly detrimental⁵.

Numerous pharmacological and non-pharmacological strategies have been explored for the treatment of shivering⁷. Non-pharmacological methods include using blankets, warming intravenous fluids, and employing external warmers¹. A wide array of drugs has been investigated, including pethidine, tramadol, nefopam, ketamine, dexmedetomidine, clonidine, and magnesium sulphate, among others⁷. Pethidine, once considered a first-line treatment, is now often avoided in many institutions due to its side effects⁸.

The objective of this prospective, randomized, double-blinded control study was to compare the efficacy, recurrence rate, hemodynamics, and complications of tramadol, clonidine, and dexmedetomidine in the treatment of shivering following spinal anesthesia.

MATERIALS AND METHODS

The study was conducted at Pacific Institute of Medical Sciences after receiving approval from the Institutional Ethical Committee. Written,

informed consent was obtained from all patients prior to their inclusion in the study.

Patient Selection And Randomization

Patients included in the study were between the ages of 18 and 70 years, classified as American Society of Anesthesiologists (ASA) physical status I or II, and were scheduled for elective surgery under spinal anesthesia. Any patient who developed shivering during their procedure was considered for inclusion. Exclusion criteria were an ASA status of III or higher; pre-existing cardiac, hepatic, or renal disease; a known allergy to any of the study medications; pregnancy; or patient refusal to participate.

A total of 150 patients who developed shivering were randomly divided into three equal groups of 50.

- **Group T** received tramadol 1 mg·kg⁻¹.
- **Group C** received clonidine 1 mcg·kg⁻¹.
- **Group D** received dexmedetomidine 0.5 mcg·kg⁻¹.

Group allocation was performed using a computer-generated random envelope method to ensure proper randomization.

Study Protocol And Blinding

To maintain the double-blind nature of the study, the assigned study drug was prepared by a primary anesthesiologist who was not involved in patient assessment. This anesthesiologist opened the sealed envelope, prepared the medication by adding it to a 100 mL bag of normal saline, and then handed it to a second anesthesiologist. This second anesthesiologist, who was blinded to the drug being administered, infused the solution over 10 minutes and was responsible for all subsequent monitoring and data collection.

Monitoring And Data Collection

Standard intraoperative monitoring was implemented for all patients, including continuous electrocardiogram, noninvasive blood pressure, and oxygen saturation. Axillary temperature was also recorded. To standardize environmental factors, the operating room temperature was consistently maintained at 22°C, and no external warming devices were used. All intravenous fluids were administered at room

temperature.

Spinal anesthesia was performed using a 25-gauge Quincke spinal needle, with the goal of achieving a sensory block to at least the T10 dermatome, as required by the surgical procedure. Shivering intensity was graded on a 1-4 scale as described by Wrench. Patients were treated and included in the analysis if they developed shivering of at least Grade 2.

Following drug administration, hemodynamic monitoring was continued for two hours. The primary outcomes measured were the time required to control shivering, the rate of shivering recurrence, and the incidence of adverse effects (nausea, vomiting, dry mouth). Patient sedation was assessed using the Filos et al. sedation scale.

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 17.0 (IBM Corporation, Armonk, NY, USA). Continuous variables were analyzed using a One-Way Analysis of Variance (ANOVA) with post-hoc testing. Categorical data were analyzed using the Chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 385 patients scheduled for elective surgery under spinal anesthesia were assessed for eligibility for this study. From this pool, 235 patients were excluded as they either did not meet the inclusion criteria or declined to participate. The remaining 150 patients who developed post-spinal anesthesia shivering were randomized into three equal treatment groups of 50 patients each: Group T (Tramadol), Group C (Clonidine), and Group D (Dexmedetomidine). All randomized patients completed the follow-up and were included in the final statistical analysis, as illustrated in the CONSORT flow diagram (Figure 1).

Consort Flow Diagram

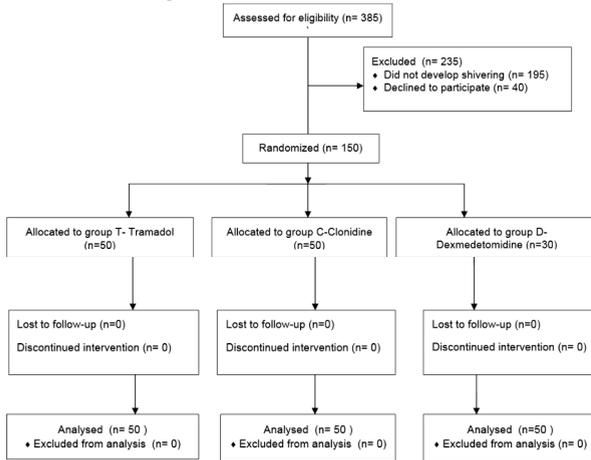


Figure 1: Consort Flow Diagram

The demographic profiles of the three groups were well-matched, with no statistically significant differences found in terms of age, weight, height, ASA physical status, gender distribution, or the mean duration of anesthesia (p > 0.05 for all comparisons). These characteristics are detailed in Table 1. Baseline hemodynamic variables and mean axillary temperature were also comparable across all groups before the intervention.

Table 1: Demographic Characteristics

Patient characteristics	Group T (n=50)	Group C (n=50)	Group D (n=50)	p-Value
Age (years)	37.4 ± 6.3	36.8 ± 5.9	35.8 ± 6.8	0.596
Weight (kg)	66.7 ± 7.5	68.7 ± 8.3	67.3 ± 7.6	0.578
ASA physical status (I/II)	23/27	25/25	20/30	0.891
Gender (M/F)	20/30	22/28	20/30	0.912
Mean duration of anesthesia (min)	62.4 ± 3.8	64.5 ± 4.4	63.3 ± 4.4	0.157

Primary Outcomes: Efficacy Of Shivering Control

Dexmedetomidine demonstrated the fastest onset of action, controlling shivering in a mean time of **5.76 ± 1.14 minutes**. This was significantly faster than both tramadol (6.72 ± 1.27 min) and clonidine, which was the slowest (9.48 ± 0.95 min) (p < 0.0001) (Table 2).

Table 2: Mean Time To Control Shivering

Parameter	Group T (Tramadol)	Group C (Clonidine)	Group D (Dexmedetomidine)	p-Value
Mean Time to Control Shivering (min)	6.72 ± 1.27	9.48 ± 0.95	5.76 ± 1.14	<0.000

The recurrence of shivering was lowest in the dexmedetomidine group (6%), followed by clonidine (12%), and was highest in the tramadol group (26%). The treatment failed to control shivering in 3 patients in the clonidine group and 2 patients in the tramadol group, necessitating the use of rescue pethidine.

Table 3: Recurrence Of Shivering By Treatment Group

Treatment Group	Number of Patients with Recurrence (n)	Recurrence Rate (%)
Group D (Dexmedetomidine)	3	6%
Group C (Clonidine)	6	12%
Group T (Tramadol)	13	26%

Secondary Outcomes: Hemodynamic Changes, Sedation, and Adverse Effects

Significant hemodynamic changes were observed post-intervention. Dexmedetomidine and clonidine caused a marked reduction in heart rate and blood pressure, while the tramadol group remained hemodynamically more stable. For blood pressure, this effect was most pronounced in the first 20 minutes, after which the differences were no longer statistically significant. For heart rate, the differences persisted for 30 minutes before becoming non-significant. The detailed variations are presented in Tables 4, 5, and 6.

Table 4: Variations In Heart Rate (beats/min) After Study Drug Administration

Time (min)	Group T (Tramadol)	Group C (Clonidine)	Group D (Dexmedetomidine)	p-Value	Intergroup Comparison (p < 0.05)
0	76.1 ± 5.1	75.5 ± 5.8	76.4 ± 4.9	0.781	NS
10	77.2 ± 4.2	69.1 ± 3.9	65.3 ± 3.1	<0.0001	T vs C: <0.001 T vs D: <0.001 C vs D: <0.001
20	75.8 ± 5.5	68.5 ± 4.8	62.1 ± 4.2	<0.0001	T vs C: <0.001 T vs D: <0.001 C vs D: <0.001
30	74.5 ± 4.1	69.9 ± 4.5	64.8 ± 4.8	<0.0001	T vs C: <0.001 T vs D: <0.001 C vs D: <0.001
40	73.8 ± 4.5	72.5 ± 4.2	72.9 ± 5.0	0.358	NS
50	74.0 ± 4.7	73.1 ± 4.0	73.5 ± 5.2	0.512	NS
60	74.2 ± 4.9	73.8 ± 4.1	74.0 ± 5.1	0.899	NS

Values are presented as mean ± SD. NS = Not Significant.

Table 5: Variations In Systolic Blood Pressure (mmHg) After Study Drug Administration

Time (min)	Group T (Tramadol)	Group C (Clonidine)	Group D (Dexmedetomidine)	p-Value	Intergroup Comparison (p < 0.05)
0	112.1 ± 9.8	110.8 ± 8.9	111.5 ± 9.2	0.795	NS
10	110.5 ± 8.1	101.3 ± 9.1	95.4 ± 10.1	<0.0001	T vs C: <0.001 T vs D: <0.001 C vs D: p=0.008
20	109.8 ± 8.8	98.1 ± 8.2	91.9 ± 9.4	<0.0001	T vs C: <0.001 T vs D: <0.001 C vs D: p=0.002
30	108.5 ± 9.2	106.5 ± 9.5	105.9 ± 9.9	0.418	NS
40	109.1 ± 9.1	107.8 ± 9.8	107.2 ± 9.1	0.567	NS
50	109.0 ± 9.3	108.1 ± 10.0	107.9 ± 9.5	0.782	NS

60	108.9 ± 9.5	108.5 ± 10.1	108.2 ± 8.9	0.915	NS
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Values are presented as mean ± SD. NS = Not Significant.

Table 6: Variations In Diastolic Blood Pressure (mmHg) After Study Drug Administration

Time (min)	Group T (Tramadol)	Group C (Clonidine)	Group D (Dexmedetomidine)	p-Value	Intergroup Comparison (p < 0.05)
0	74.2 ± 5.1	75.1 ± 6.1	74.8 ± 4.9	0.711	NS
10	73.1 ± 6.5	68.2 ± 7.1	64.9 ± 6.8	<0.0001	T vs C: p=0.001 T vs D: <0.001
20	72.5 ± 4.5	66.9 ± 5.9	61.8 ± 6.5	<0.0001	T vs C: <0.001 T vs D: <0.001 C vs D: p=0.002
30	71.9 ± 5.8	70.8 ± 6.9	69.5 ± 5.1	0.214	NS
40	72.8 ± 5.5	71.5 ± 6.5	70.9 ± 6.1	0.301	NS
50	73.5 ± 5.2	72.2 ± 6.0	71.8 ± 6.8	0.422	NS
60	74.1 ± 5.1	73.1 ± 6.2	72.9 ± 7.3	0.689	NS

Values are presented as mean ± SD. NS = Not Significant.

Sedation was most prominent in the dexmedetomidine group, where 35 patients (70%) were drowsy but responsive to verbal stimuli (Score 2) and 12 patients (24%) were arousable only to physical stimuli (Score 3). In contrast, the tramadol group had the highest number of alert patients (Table 7) (Figure 2). No patient in any group became unarousable (Score 4).

Table 7: Distribution Of Sedation Scores By Treatment Group (N=150)

Sedation Score	Group T (Tramadol) n (%)	Group C (Clonidine) n (%)	Group D (Dexmedetomidine) n (%)
1 (Alert)	20 (40%)	8 (16%)	3 (6%)
2 (Drowsy, responds to verbal)	27 (54%)	32 (64%)	35 (70%)
3 (Drowsy, responds to physical)	3 (6%)	10 (20%)	12 (24%)
4 (Unarousable)	0 (0%)	0 (0%)	0 (0%)

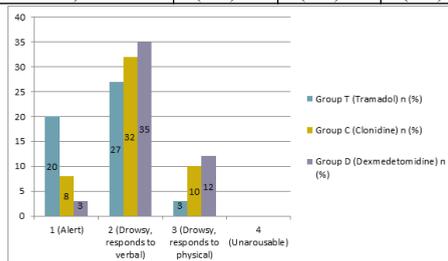
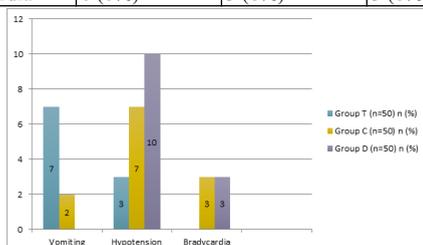


Figure 2: Distribution of Sedation Scores by Treatment Group

The incidence of adverse effects is shown in Table 8. Vomiting was most common in the tramadol group (16%). Hypotension and bradycardia were significantly more frequent in the dexmedetomidine and clonidine groups (Table 8) (Graph 3). All adverse hemodynamic events were transient and responded appropriately to standard treatment.

Table 8: Incidence of Adverse Effects by Treatment Group

Adverse Effect	Group T (n=50) n (%)	Group C (n=50) n (%)	Group D (n=50) n (%)
Vomiting	7 (14%)	2 (4%)	0 (0%)
Hypotension	3 (6%)	7 (14%)	10 (20%)
Bradycardia	0 (0%)	3 (6%)	3 (6%)



Graph 3: Incidence of Adverse Effects by Treatment Group

DISCUSSION

This prospective, randomized, double-blinded control study was designed to compare the efficacy and safety of tramadol, clonidine, and dexmedetomidine for the treatment of post-spinal anesthesia shivering. The principal finding of our study is that dexmedetomidine was the most effective agent, demonstrating a significantly faster onset of action and the lowest rate of shivering recurrence compared to both clonidine and tramadol. This suggests that for the acute management of shivering in a perioperative setting, dexmedetomidine offers superior clinical efficacy.

Our findings are consistent with a growing body of literature that supports the use of α2-adrenergic agonists for shivering control. Dexmedetomidine, with its high affinity for the α2 receptor, likely exerts its anti-shivering effect by modulating thermoregulatory control at the hypothalamic level, thereby reducing the shivering threshold⁹. The superiority of dexmedetomidine over clonidine in our study, both in terms of speed and recurrence, can be attributed to its higher receptor affinity and specificity. The results align with studies by Mittal et al. who, in a similar comparison, concluded that dexmedetomidine at a dose of 0.5 mcg·kg⁻¹ had a faster onset in controlling shivering than tramadol¹⁰. Our finding that tramadol was more effective than clonidine is also supported by the work of Bansal et al., who reported that tramadol was superior in suppressing shivering¹¹. The overall findings of our study, where dexmedetomidine was superior, are in broad agreement with the conclusions of Venkatraman et al.¹², who also found dexmedetomidine to be more effective than tramadol and clonidine.

While tramadol was faster than clonidine in controlling shivering, it was associated with the highest rate of recurrence (26%). This finding is consistent with previous research. For instance, Bansal et al. reported a recurrence rate of 30% with tramadol and 26% with clonidine¹¹. Similarly, Mittal et al. noted that the recurrence of shivering was doubled in their tramadol group compared to their dexmedetomidine group¹⁰. This suggests that while tramadol's mechanism—inhibiting the reuptake of serotonin and norepinephrine¹³—is effective for initial control, its effect may be less sustained compared to α2-agonists in this context.

A critical aspect of this study was the evaluation of the drugs' side effect profiles. The most significant hemodynamic changes—hypotension and bradycardia—were observed in the dexmedetomidine and clonidine groups. These effects are well-documented consequences of α2-agonist-induced sympatholysis. In our study, while the incidence of hypotension (26%) and bradycardia (16%) was highest in the dexmedetomidine group, these events were transient and responded appropriately to standard management. This rate of adverse effects is comparable to other studies. For example, Kim et al. reported bradycardia in 16.6% of patients receiving a higher dose of dexmedetomidine (1 mcg·kg⁻¹) for shivering¹⁴. This suggests that with vigilant monitoring, the drug can be used safely. The hemodynamic effects were most pronounced in the first 20-30 minutes, after which the values began to return towards baseline, indicating a predictable and manageable clinical course.

Another key secondary outcome was sedation. Dexmedetomidine provided a superior level of sedation compared to the other two agents, with the majority of patients becoming comfortably drowsy but easily arousable. This can be a desirable clinical effect, reducing patient anxiety and improving the overall perioperative experience. This aligns with the findings of Bozgeyik et al., who observed that in addition to preventing shivering, dexmedetomidine was superior in increasing the level of sedation without significant side effects during arthroscopy¹⁵. Tramadol, in contrast, was associated with a higher level of alertness and a significantly higher incidence of vomiting (16%). This side effect is a major disadvantage of tramadol and can be distressing for patients, potentially limiting its clinical utility despite its efficacy in controlling shivering.

Limitations

This study has several strengths, including its prospective, randomized, and double-blinded design, which minimizes bias. The sample size of 150 patients provided adequate statistical power to detect significant differences between the groups. However, some limitations should be acknowledged. First, the study was conducted at

a single institution, which may limit the generalizability of our findings to other populations or settings. Second, we used axillary temperature for monitoring, whereas core temperature measurement would have provided a more precise assessment of the patients' thermal state. Finally, this study used fixed doses of each drug; future dose-ranging studies could help determine the optimal balance between efficacy and side effects for each agent.

CONCLUSION

Based on the findings of this study, dexmedetomidine appears to be the most favorable option for the treatment of post-spinal anesthesia shivering. Its rapid onset, low recurrence rate, and beneficial sedative properties outweigh the manageable risk of transient hypotension and bradycardia. While tramadol is effective, its high rate of recurrence and incidence of vomiting make it a less ideal choice. Clonidine, being the slowest and offering no significant advantages over dexmedetomidine, appears to be the least effective of the three agents in this comparison.

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