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COMPARATIVE EFFICACY AND HEMODYNAMIC EFFECTS OF INTRAVENOUS TRAMADOL VERSUS INTRAVENOUS CLONIDINE FOR CONTROL OF POST-SPINAL ANESTHESIA SHIVERING: A RANDOMIZED STUDY

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ABSTRACT

Background: Post-spinal anesthesia shivering is a common perioperative complication with an incidence ranging from 40% to 70%. It increases metabolic demand, oxygen consumption, carbon dioxide production, and may precipitate cardiovascular instability. Various pharmacological agents have been used for its management, among which clonidine and tramadol are widely studied. However, comparative data regarding their efficacy, onset time, hemodynamic effects, and adverse profile remain inconsistent. The present study aimed to compare intravenous clonidine and intravenous tramadol for the control of post-spinal anesthesia shivering.

Materials and Methods: This prospective, randomized comparative study included 64 patients (ASA I–II, aged 18–45 years) who developed grade III or higher shivering following spinal anesthesia. Patients were randomized into two groups: Group T received intravenous tramadol (0.5 mg/kg) and Group C received intravenous clonidine (0.5 µg/kg). The primary outcome was time to cessation of shivering. Secondary outcomes included response rate within 15 minutes, hemodynamic changes, sedation score (Filos scale), and adverse events. Statistical analysis was performed using independent t-test and Chi-square/Fisher's exact test, with $p < 0.05$ considered significant.

Results: Time to cessation of shivering was significantly shorter in the tramadol group compared to the clonidine group (3.17 ± 0.78 min vs 5.47 ± 3.19 min; $p = 0.0002$). Complete control within 15 minutes was achieved in 100% of tramadol patients and 93.8% of clonidine patients ($p = 0.154$). Heart rate reduction was significantly greater in the clonidine group ($p = 0.02$). Sedation was significantly higher with clonidine (65.6% vs 15.6%; $p = 0.0001$). Bradycardia and hypotension occurred only in the clonidine group.

Conclusion: Intravenous tramadol provides faster control of post-spinal anesthesia shivering with comparable overall efficacy and better hemodynamic stability compared to clonidine. Tramadol may be preferred in patients where cardiovascular stability is essential.

Keywords: Post-spinal anesthesia; Shivering; Tramadol; Clonidine; Hemodynamic stability.

INTRODUCTION

Shivering is a frequent and distressing complication observed during and after spinal anesthesia, with a reported incidence ranging from 40% to 70%.[1,2] It is defined as an involuntary, oscillatory muscular activity that augments metabolic heat production in response to perioperative hypothermia or thermoregulatory impairment.[3] Although often

considered benign, shivering can significantly increase oxygen consumption (up to 100–600%), carbon dioxide production, and catecholamine release, thereby precipitating myocardial ischemia, lactic acidosis, raised intracranial and intraocular pressures, and interference with routine intraoperative monitoring.[4,5] Regional anesthesia impairs central thermoregulation by redistributing core heat to the periphery and inhibiting vasoconstrictive responses below the level of block, thus predisposing patients to hypothermia and subsequent shivering.[6,7]

The pathogenesis of post-spinal anesthesia shivering is multifactorial and involves a combination of core hypothermia, altered afferent thermal inputs, and decreased threshold for vasoconstriction and shivering due to sympathetic blockade.[6] Clonidine, a selective α_2-adrenergic agonist, exerts anti-shivering effects by reducing central thermoregulatory thresholds and inhibiting noradrenergic transmission in the locus coeruleus.[8] Tramadol, an atypical opioid analgesic, suppresses shivering through weak μ-opioid receptor agonism and inhibition of serotonin and norepinephrine reuptake, modulating thermoregulatory control at the hypothalamic level.[9] Both agents have been widely used for the treatment of post-spinal shivering, but their comparative efficacy and safety profiles remain variable across studies, particularly with respect to hemodynamic stability and adverse effect patterns.[10,11]

Given the clinical implications of shivering and the pharmacological differences between clonidine and tramadol, a direct comparison of their efficacy, onset of action, hemodynamic effects, and adverse events is clinically relevant. While several studies have evaluated these agents independently, there remains inconsistency in reported onset time, recurrence rates, and incidence of side effects such as hypotension, bradycardia, nausea, and sedation.[8,10] Therefore, the present study was undertaken to comparatively evaluate intravenous clonidine and intravenous tramadol for control of post-spinal anesthesia shivering, with particular emphasis on efficacy, hemodynamic stability, time to cessation, and adverse effect profile.

MATERIALS AND METHODS

This prospective, randomised, comparative study was conducted at a tertiary care teaching hospital between May 2017 and December 2018 after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrollment. A total of 64 patients aged 18–45 years, belonging to American Society of Anesthesiologists (ASA) physical status I and II, scheduled for elective or emergency surgeries under spinal anesthesia and developing intraoperative shivering were included. Patients with ischemic heart disease, uncontrolled hypertension, renal or hepatic dysfunction, thyroid disorders, uncontrolled diabetes mellitus, psychological illness, chronic alcohol or drug abuse, or known hypersensitivity to clonidine or tramadol were excluded. Sample size was calculated using Win PEPI software based on previous literature comparing efficacy rates of clonidine and tramadol, with 32 patients allocated to each group.

Patients were randomised using block randomisation (block size 8) into two equal groups. Group T (Tramadol group) received intravenous tramadol 0.5 mg/kg, and Group C (Clonidine group) received intravenous clonidine 0.5 μg/kg upon development of grade III or higher shivering according to Wrench criteria. Standard monitoring, including electrocardiography, non-invasive blood pressure, pulse oximetry, and axillary temperature, was instituted. All patients were preloaded with Ringer's lactate (10 mL/kg) and received spinal anesthesia using 0.5% hyperbaric bupivacaine at the L3–L4 or L4–L5 interspace. Operating room temperature was maintained between 21°C and 23°C. Hemodynamic parameters and temperature were recorded preoperatively, during shivering, and 5 minutes after administration of the study drug. Sedation was assessed using the Filos sedation scale. If shivering persisted beyond 15 minutes, rescue medication was administered.

The primary outcome measure was time to cessation of shivering following drug administration. Secondary outcomes included response rate within 15 minutes, recurrence of shivering, changes in heart rate and blood pressure, sedation score, and incidence of adverse events such as nausea, vomiting, hypotension, and bradycardia. Continuous variables were analyzed using independent sample t-tests, while categorical variables were compared using Chi-square or Fisher's exact test as appropriate. A p-value of <0.05 was considered statistically significant. Statistical analysis was performed using SAS version 20.0, and data were compiled using Microsoft Excel 2016.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Tramadol (n=32)	Clonidine (n=32)	p-value
Age (years), mean ± SD	33 ± 8.2	32 ± 7.5	0.612
Weight (kg), mean ± SD	54 ± 6.9	57 ± 7.1	0.090
Male, n (%)	13 (40.6)	18 (56.3)	0.215
Female, n (%)	19 (59.4)	14 (43.8)	
ASA I, n (%)	18 (56.3)	16 (50.0)	0.615

ASA II, n (%)	14 (43.8)	16 (50.0)	
Time to onset of shivering (min), mean ± SD	23.6 ± 6.3	21.4 ± 5.6	0.130
Grade III shivering, n (%)	19 (59.4)	20 (62.5)	0.798
Grade IV shivering, n (%)	13 (40.6)	12 (37.5)	

The baseline demographic and clinical characteristics of patients in both groups were comparable. The mean age of patients in the tramadol group was 33 ± 8.2 years, while in the clonidine group it was 32 ± 7.5 years, with no statistically significant difference (p = 0.612). Mean body weight was also similar between groups (54 ± 6.9 kg vs 57 ± 7.1 kg; p = 0.09). The gender distribution did not differ significantly, with males constituting 40.6% in the tramadol group and 56.3% in the clonidine group (p = 0.215). ASA physical status classification and the distribution of shivering grades (III and IV) were comparable between the two groups (p > 0.05). Additionally, the mean time to onset of shivering following spinal anesthesia was similar (23.6 ± 6.3 minutes vs 21.4 ± 5.6 minutes; p = 0.13), confirming homogeneity between groups at baseline.

Table 2: Comparison of Hemodynamic and Temperature Parameters

Parameter	Time Point	Tramadol (Mean ± SD)	Clonidine (Mean ± SD)	p-value
Axillary Temperature (°F)	Preoperative	97.6 ± 0.56	97.48 ± 0.64	0.188
	During shivering	96.66 ± 0.64	96.70 ± 0.69	0.810
	5 min post-drug	96.98 ± 0.65	97.02 ± 0.62	0.802
Heart Rate (beats/min)	Preoperative	80.09 ± 6.59	79.47 ± 5.66	0.688
	During shivering	91.47 ± 7.45	92.91 ± 7.34	0.439
	5 min post-drug	86.88 ± 7.35	81.00 ± 13.00	0.020
Systolic BP (mmHg)	Preoperative	117.56 ± 7.56	114.75 ± 7.87	0.150
	During shivering	126.50 ± 7.73	124.19 ± 7.18	0.220
	5 min post-drug	120.63 ± 7.30	118.81 ± 7.00	0.312
Diastolic BP (mmHg)	Preoperative	80.06 ± 6.05	77.25 ± 6.85	0.080
	During shivering	85.38 ± 5.51	82.69 ± 6.57	0.080
	5 min post-drug	83.50 ± 5.22	81.06 ± 6.06	0.090

Hemodynamic variables and axillary temperature measurements were recorded preoperatively, during shivering, and five minutes after administration of the study drug. In both groups, axillary temperature decreased during shivering and showed a slight increase after drug administration; however, intergroup differences were not statistically significant at any time point (p > 0.05). Heart rate increased during shivering in both groups and decreased following treatment. A statistically significant reduction in heart rate was observed five minutes after drug administration in the clonidine group compared to the tramadol group (p = 0.02). Systolic and diastolic blood pressures rose during shivering and returned toward baseline after treatment, with no significant intergroup differences at any measurement interval (p > 0.05). Overall, hemodynamic parameters remained comparable except for a greater reduction in heart rate in the clonidine group.

Table 3: Efficacy Outcomes

Outcome	Tramadol (n=32)	Clonidine (n=32)	p-value
Time to cessation of shivering (min), mean ± SD	3.17 ± 0.78	5.47 ± 3.19	0.0002
Shivering controlled within 15 min, n (%)	32 (100)	30 (93.8)	0.154
Rescue medication required, n (%)	0 (0)	2 (6.3)	0.154

The primary efficacy outcome, time to cessation of shivering, was significantly shorter in the tramadol group compared to the clonidine group (3.17 ± 0.78 minutes vs 5.47 ± 3.19 minutes; p = 0.0002). This indicates a faster onset of anti-shivering action with tramadol. Regarding overall response rate within 15 minutes, all patients (100%) in the tramadol group achieved complete control of shivering, whereas 93.8% of patients in the clonidine group responded within the same duration. The difference in response rates was not statistically significant (p = 0.154). Two patients in the clonidine group required rescue medication due to persistence of shivering beyond 15 minutes.

Table 4: Sedation Profile (Filos Sedation Scale)

Sedation Score	Tramadol (n=32)	Clonidine (n=32)	p-value
Score 1 (Awake, alert), n (%)	27 (84.4)	11 (34.4)	0.0001
Score 2 (Drowsy, responsive), n (%)	5 (15.6)	21 (65.6)	

Assessment of sedation using the Filos sedation scale demonstrated a significantly higher incidence of sedation in the clonidine group. In the tramadol group, 84.4% of patients remained fully awake and alert (Score 1), compared to only 34.4% in the clonidine group. Conversely, 65.6% of patients in the clonidine group exhibited mild sedation (Score 2), compared to 15.6% in the tramadol group. This difference was highly statistically significant (p =

0.0001), indicating a greater sedative effect associated with clonidine administration.

Table 5: Adverse Events

Adverse Event	Tramadol (n=32)	Clonidine (n=32)
Nausea, n (%)	4 (12.5)	1 (3.1)
Vomiting, n (%)	2 (6.3)	0 (0)
Dizziness, n (%)	1 (3.1)	2 (6.3)
Hypotension, n (%)	0 (0)	2 (6.3)
Bradycardia, n (%)	0 (0)	4 (12.5)

The incidence of adverse events varied between the two groups. Nausea was more frequently observed in the tramadol group (12.5%) compared to the clonidine group (3.1%). Vomiting occurred in 6.3% of patients receiving tramadol and was not observed in the clonidine group. Dizziness was reported in both groups, with slightly higher occurrence in the clonidine group (6.3% vs 3.1%). Hypotension and bradycardia were observed exclusively in the clonidine group, affecting 6.3% and 12.5% of patients, respectively. These findings suggest that tramadol is more commonly associated with gastrointestinal side effects, whereas clonidine is more likely to cause hemodynamic alterations such as bradycardia and hypotension.

DISCUSSION

Post-spinal anesthesia shivering remains a clinically significant problem due to its metabolic and hemodynamic consequences.[10] In the present study, intravenous tramadol demonstrated a significantly shorter time to cessation of shivering compared to clonidine (3.17 ± 0.78 min vs 5.47 ± 3.19 min; p = 0.0002), while overall response rates within 15 minutes were comparable (100% vs 93.8%; p = 0.154). These findings align with the randomized controlled trial by Shukla et al., who reported a mean cessation time of 2.54 ± 0.76 minutes with clonidine and 5.01 ± 1.02 minutes with tramadol, though in their study clonidine acted faster.[11] Conversely, Attal et al.[13] observed a shorter mean cessation time with tramadol (3.16 ± 0.84 min) compared to clonidine (5.76 ± 0.88 min; p = 0.038), which closely mirrors the results of the present study.[12] Similarly, Jain et al. reported successful shivering control in 96.7% of clonidine-treated patients and 86.7% of tramadol-treated patients, though clonidine required a longer time to achieve complete cessation. These inter-study variations may be attributed to differences in dosing regimens and patient populations.[13]

Hemodynamic stability is a critical determinant when selecting anti-shivering agents. In our study, heart rate reduction was significantly greater in the clonidine group at 5 minutes post-administration (p = 0.02), while systolic and diastolic blood pressures were comparable between groups. Bradycardia was observed in 12.5% of patients receiving clonidine and none in the tramadol group. These findings are consistent with Vyas et al., who reported bradycardia in 6.7% and hypotension in 13.3% of patients receiving clonidine, whereas nausea occurred in 36.7% of tramadol recipients.[14] Wang et al. in a meta-analysis of 14 randomized trials (n = 960) concluded that clonidine was associated with a higher incidence of hypotension and bradycardia compared to tramadol, while tramadol had significantly higher rates of nausea and vomiting. Our adverse event profile corroborates this trend, with nausea occurring in 12.5% of tramadol patients versus 3.1% in the clonidine group, and hypotension and bradycardia occurring exclusively in clonidine recipients.[15]

Sedation was significantly higher with clonidine in our study (65.6% with Filos score 2 vs 15.6% in tramadol group; p = 0.0001). This finding is pharmacologically plausible due to central α_2-adrenergic agonism. Shukla et al. also reported higher sedation levels in clonidine-treated patients (25% exhibiting sedation score ≥2) compared to tramadol.[11] Similarly, Banerjee et al. observed significantly greater sedation and hemodynamic alterations in patients receiving prophylactic clonidine compared to tramadol. Although sedation may be beneficial in certain operative settings, excessive sedation may delay recovery and warrants cautious use.[16]

Overall efficacy outcomes in our study demonstrated that tramadol achieved rapid shivering control without significant hemodynamic compromise. These findings support the conclusions of multiple comparative trials indicating that tramadol provides effective anti-shivering action with a favourable cardiovascular profile.[16,17] While clonidine remains an effective alternative, its association with bradycardia, hypotension, and higher sedation rates may limit its routine use, particularly in patients with borderline hemodynamic status.

The present study demonstrates that intravenous tramadol offers faster control of post-spinal anesthesia shivering with comparable overall efficacy and a more stable hemodynamic profile compared to clonidine. Although clonidine produces significant sedation and may reduce heart rate more profoundly, tramadol appears preferable in clinical settings where rapid shivering cessation and cardiovascular stability are priorities. These findings reinforce existing evidence while contributing region-specific comparative data to the literature.

Limitations

The study has certain limitations. The sample size was relatively small and conducted at a single

centre, which may limit generalizability. Core temperature monitoring was not employed, and axillary temperature was used instead, which may not accurately reflect central thermoregulation. Additionally, long-term postoperative outcomes were not evaluated. Future multicentric studies with larger sample sizes and standardized temperature monitoring methods are recommended to further validate these findings.

CONCLUSION

The present study demonstrates that intravenous tramadol provides significantly faster cessation of post-spinal anesthesia shivering compared to intravenous clonidine, while achieving comparable overall response rates. Tramadol was associated with minimal hemodynamic alterations, whereas clonidine produced a greater reduction in heart rate and a higher incidence of sedation, bradycardia, and hypotension. Although both drugs were effective in controlling shivering, tramadol exhibited a more favorable cardiovascular safety profile.

Based on these findings, intravenous tramadol may be preferred for the management of post-spinal anesthesia shivering, particularly in patients where hemodynamic stability is a priority. Clonidine remains a viable alternative but should be used cautiously in patients at risk of bradycardia or hypotension.

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