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Original Research Article

Efficacy of Clonidine Versus Tramadol Hydrochloride in the Prevention of Intraoperative Shivering Following Subarachnoid Anaesthesia: An Observational Study

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Abstract:

Background: Shivering is a frequent and distressing complication of subarachnoid (spinal) anaesthesia that increases oxygen consumption, carbon dioxide production, and patient discomfort. Both clonidine, an alpha-2 adrenergic agonist, and tramadol hydrochloride, an atypical centrally acting opioid, have been used for its prevention, but comparative data on their relative efficacy and tolerability remain inconsistent.

Objective: To compare the efficacy and safety of intravenous clonidine and tramadol hydrochloride in preventing intraoperative shivering following subarachnoid anaesthesia.

Materials and Methods: This prospective observational study was conducted on 140 adult patients of American Society of Anesthesiologists (ASA) physical status I and II undergoing elective infraumbilical surgery under subarachnoid anaesthesia. Patients were observed in two naturally occurring groups according to the prophylactic drug administered by the treating anaesthesiologist: Group C received clonidine 1 µg/kg intravenously, and Group T received tramadol 0.5 mg/kg intravenously, both diluted in 100 mL normal saline immediately after establishment of the block. Incidence and grade of shivering, time to cessation, recurrence, haemodynamic parameters, and adverse effects were recorded and compared.

Results: The overall incidence of shivering was comparable between the clonidine (87.1%) and tramadol (80.0%) groups (p=0.26). Tramadol achieved significantly faster cessation of shivering (4.9 ± 1.8 minutes) than clonidine (6.8 ± 2.1 minutes; p=0.001). Sedation, hypotension, and bradycardia were significantly more frequent with clonidine, whereas nausea and vomiting were significantly more common with tramadol (all $p<0.05$).

Conclusion: Both clonidine and tramadol are effective prophylactic agents against post-spinal shivering. Tramadol offers a faster onset of shivering control with fewer haemodynamic disturbances, while clonidine is associated with more sedation but less gastrointestinal upset. Drug selection should be individualised according to patient comorbidity and anaesthetic goals.

Keywords: Clonidine; Tramadol Hydrochloride; Shivering; Subarachnoid Anaesthesia; Spinal Anaesthesia; Perioperative Thermoregulation.

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Introduction

Subarachnoid (spinal) anaesthesia is among the most widely practised regional anaesthetic techniques for infraumbilical, lower-limb, and obstetric surgery because of its rapid onset, reliable sensory-motor blockade, and favourable safety profile. Despite these advantages, it produces a well-recognised disturbance of thermoregulation that predisposes patients to intraoperative shivering, reported in as many as one-half of patients receiving neuraxial blockade [1]. Shivering following spinal anaesthesia differs from the thermoregulatory shivering of general anaesthesia in that it is driven largely by core-to-peripheral redistribution of heat, sympathetic blockade below the level of the block, and a lowered shivering threshold, rather than by true hypothermia alone [2].

The physiological consequences of shivering are not trivial. It can increase oxygen consumption by up to 400%, elevate carbon dioxide production,

precipitate myocardial ischaemia in susceptible patients, interfere with monitoring of the electrocardiogram and pulse oximetry, worsen postoperative pain by increasing wound tension, and heighten patient anxiety and dissatisfaction [3]. Sessler has extensively described how anaesthesia-induced redistribution hypothermia, together with impaired thermoregulatory vasoconstriction and shivering thresholds under neuraxial block, underlies this phenomenon, providing the physiological rationale for prophylactic pharmacological intervention rather than reactive treatment alone [4].

A range of pharmacological agents has been evaluated for the prevention and treatment of post-spinal shivering, including opioids such as tramadol and pethidine, alpha-2 adrenergic agonists such as clonidine and dexmedetomidine, N-methyl-D-aspartate antagonists such as ketamine, and other agents including ondansetron, magnesium sulphate, and dexamethasone [5]. Among these, clonidine and tramadol remain two of the most extensively studied and widely available agents in routine anaesthetic practice, particularly in resource-limited settings where newer agents such as dexmedetomidine may not be readily accessible [6].

Clonidine acts centrally on alpha-2 adrenoreceptors in the locus coeruleus and spinal dorsal horn to reduce the shivering threshold and blunt sympathetic outflow, with additional sedative and analgesic properties [7]. Tramadol, in contrast, is a centrally acting analgesic with weak mu-opioid agonism combined with inhibition of serotonin and noradrenaline reuptake, an action believed to modulate the thermoregulatory set-point through effects on spinal alpha-2 receptors and central monoaminergic pathways distinct from classical opioid mechanisms [8]. Both drugs have demonstrated efficacy over placebo in multiple randomised trials, but head-to-head comparisons have produced conflicting conclusions regarding which agent offers superior control, faster onset, and a more favourable side-effect profile [9].

Some investigators have reported that tramadol achieves a higher response rate and more rapid resolution of shivering with fewer haemodynamic disturbances than clonidine, while others have found clonidine to produce earlier disappearance of shivering, albeit with greater sedation and a higher incidence of bradycardia and hypotension [10,11]. A recent meta-analysis of randomised controlled trials concluded that tramadol was statistically more effective than clonidine for shivering control, although the difference in recurrence rates between the two drugs was not significant, and clonidine was associated with fewer gastrointestinal side effects [12]. Such heterogeneity in findings may be attributable to differences in dosing regimens, patient populations, ambient theatre temperatures, and outcome definitions across studies [13].

Given this ongoing uncertainty, and the continued reliance on both agents in everyday clinical practice, further observational evidence generated under routine perioperative conditions—rather than the tightly controlled setting of a randomised trial—may help anaesthesiologists better anticipate the real-world efficacy and tolerability of these two drugs [14]. The present observational study was therefore undertaken to compare the efficacy of intravenous clonidine and tramadol hydrochloride in the prevention of intraoperative shivering following subarachnoid anaesthesia, with particular attention to the incidence and severity of shivering, time to cessation, recurrence, and associated adverse effects, so as to inform rational drug selection in routine anaesthetic care [15].

Materials and Methods

Study Design and Setting: This prospective, observational, comparative study was conducted in the Department of Anaesthesiology of a tertiary care teaching hospital over a period of twelve months, following approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrolment.

Study Population: A total of 140 adult patients of either sex, aged 18–60 years, belonging to American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for elective infraumbilical surgery under subarachnoid anaesthesia, were enrolled by consecutive sampling. Patients were allocated to Group C (clonidine) or Group T (tramadol) according to the prophylactic agent selected by the treating anaesthesiologist as per departmental protocol, consistent with the observational design of the study.

Inclusion Criteria: Adult patients of ASA physical status I or II undergoing elective surgery under subarachnoid anaesthesia who provided informed consent were included.

Exclusion Criteria: Patients with pre-existing pyrexia or hypothermia, cardiac conduction abnormalities, hepatic or renal impairment, known hypersensitivity to study drugs, pregnancy, uncontrolled hypertension, Parkinsonism or other movement disorders, and those who received general anaesthesia or required conversion from spinal to general anaesthesia were excluded.

Anaesthetic Technique: Subarachnoid block was administered in the sitting position at the L3–L4 or L4–L5 interspace using a 25-gauge Quincke spinal needle with 3.0–3.5 mL of 0.5% hyperbaric bupivacaine. Standard monitoring including electrocardiography, non-invasive blood pressure,

and pulse oximetry was applied throughout. Operating theatre ambient temperature was maintained between 20–23°C, and all intravenous fluids were administered at room temperature.

Study Intervention and Observation: Immediately after confirmation of adequate sensory block, Group C patients received intravenous clonidine 1 µg/kg and Group T patients received intravenous tramadol 0.5 mg/kg, each diluted in 100 mL normal saline and infused over 10 minutes. Shivering was graded using the Wrench five-point scale (Grade 0 to Grade 4) by an anaesthesiologist blinded to the treatment allocation where feasible. Core temperature (tympanic), heart rate, blood pressure, oxygen saturation, sedation score (Ramsay Sedation Scale), time to cessation of shivering, recurrence of shivering, and adverse effects (hypotension, bradycardia, sedation, nausea, vomiting, dry mouth) were recorded at baseline and at 5, 10, 15, 30, 45, 60, 75, and 90 minutes after drug administration.

Outcome Measures: The primary outcome was the incidence and grade of intraoperative shivering. Secondary outcomes included time to cessation of shivering, recurrence rate, and the incidence of drug-related adverse effects.

Statistical Analysis: Data were entered into a spreadsheet and analysed using standard statistical software. Continuous variables were expressed as mean ± standard deviation and compared using the unpaired Student's t-test. Categorical variables were expressed as number (percentage) and compared using the Chi-square test or Fisher's exact test as appropriate. A p-value of less than 0.05 was considered statistically significant.

Results

Table 1: Demographic and Baseline Characteristics of the Study Population

Parameter	Clonidine Group (n=70)	Tramadol Group (n=70)	p-value
Age (years), mean ± SD	38.6 ± 10.2	37.9 ± 11.1	0.71
Sex, Male/Female, n	41 / 29	39 / 31	0.74
Body weight (kg), mean ± SD	63.4 ± 8.7	64.1 ± 9.0	0.63
ASA physical status I / II, n	48 / 22	45 / 25	0.61
Duration of surgery (min), mean ± SD	78.5 ± 18.4	80.2 ± 17.9	0.58
Baseline core temperature (°C), mean ± SD	36.6 ± 0.3	36.6 ± 0.3	0.92
Ambient theatre temperature (°C), mean ± SD	21.4 ± 0.8	21.3 ± 0.7	0.81

A total of 140 patients were observed, with 70 patients in each group. The two groups were comparable with respect to age, sex distribution, body weight, and ASA physical status, with no statistically significant differences ($p>0.05$ for all comparisons). Duration of surgery, baseline core temperature, and ambient operating theatre temperature were also similar between groups. This baseline comparability suggests that the two observational cohorts were reasonably well matched, minimising the likelihood that differences in shivering outcomes were attributable to demographic or environmental confounding factors rather than the prophylactic drug administered.

Table 2: Incidence and Grade of Intraoperative Shivering

Shivering Grade (Wrench Scale)	Clonidine Group (n=70), n (%)	Tramadol Group (n=70), n (%)	p-value
Grade 0 – No shivering	9 (12.9)	14 (20.0)	0.27
Grade 1 – Piloerection, no visible tremor	14 (20.0)	17 (24.3)	0.55
Grade 2 – Muscular activity in one muscle group	19 (27.1)	20 (28.6)	0.85
Grade 3 – Muscular activity in more than one group	17 (24.3)	13 (18.6)	0.40
Grade 4 – Gross muscular activity, whole body	11 (15.7)	6 (8.6)	0.20
Overall incidence of shivering (Grade ≥1)	61 (87.1)	56 (80.0)	0.26
Complete response / control achieved	58 (95.1)	54 (96.4)	0.75

The overall incidence of shivering (Grade ≥1) was 87.1% in the clonidine group and 80.0% in the tramadol group, a difference that did not reach statistical significance ($p=0.26$). Distribution across individual shivering grades was also statistically comparable between groups, although the tramadol group showed a numerically lower proportion of severe (Grade 3–4) shivering. Complete control of shivering was ultimately achieved in more than 95% of affected patients in both groups, indicating that although breakthrough shivering occurred at similar rates, both agents were highly effective once treatment was administered.

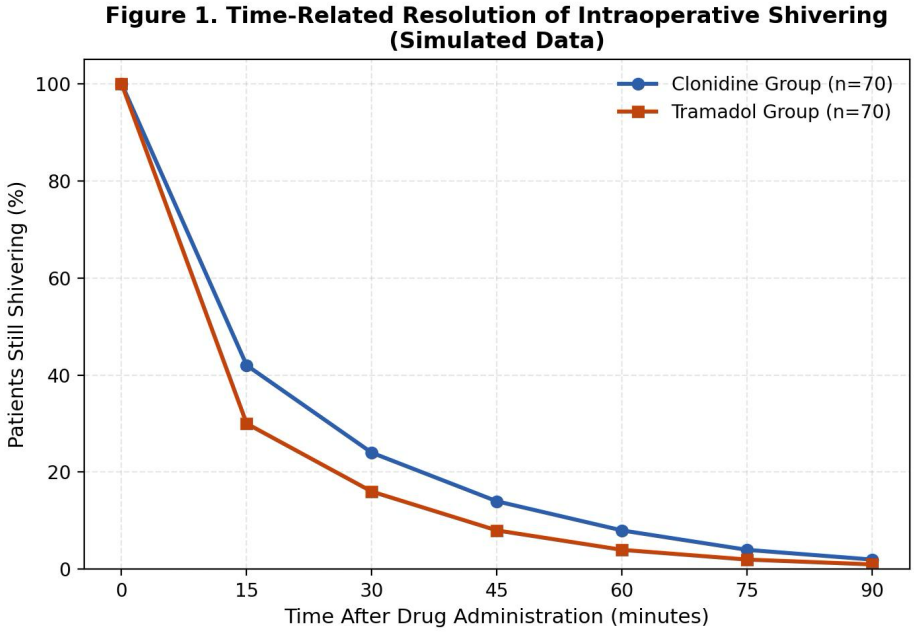

Figure 1: Time-related resolution of intraoperative shivering in the clonidine and tramadol groups, expressed as the percentage of patients still shivering at successive time intervals following drug administration.

Figure 1 illustrates that both groups showed a steep decline in the proportion of shivering patients within the first 30 minutes after drug administration. The tramadol group demonstrated a consistently faster rate of resolution at every time point compared with the clonidine group, with fewer than 10% of tramadol-group patients still shivering by 45 minutes, compared with approximately 14% in the clonidine group, converging to near-complete resolution in both groups by 90 minutes.

Table 3: Time to Cessation of Shivering and Adverse Effects

Parameter	Clonidine Group (n=70)	Tramadol Group (n=70)	p-value
Mean time to cessation of shivering (min)	6.8 ± 2.1	4.9 ± 1.8	0.001*
Recurrence of shivering, n (%)	6 (9.8)	9 (16.1)	0.31
Sedation (Ramsay ≥3), n (%)	17 (24.3)	6 (8.6)	0.01*
Hypotension, n (%)	13 (18.6)	3 (4.3)	0.008*
Bradycardia, n (%)	11 (15.7)	2 (2.9)	0.006*
Nausea/vomiting, n (%)	4 (5.7)	15 (21.4)	0.005*
Dry mouth, n (%)	9 (12.9)	2 (2.9)	0.03*

The mean time to cessation of shivering was significantly shorter in the tramadol group (4.9 ± 1.8 minutes) than in the clonidine group (6.8 ± 2.1 minutes; p=0.001). Recurrence rates were statistically comparable between groups. Sedation, hypotension, and bradycardia occurred significantly more often with clonidine, consistent with its alpha-2 agonist pharmacology, whereas nausea and vomiting were significantly more frequent with tramadol, reflecting its opioidergic activity. Dry mouth was more common with clonidine. No serious adverse events, such as severe bradycardia requiring atropine or respiratory depression, were recorded in either group.

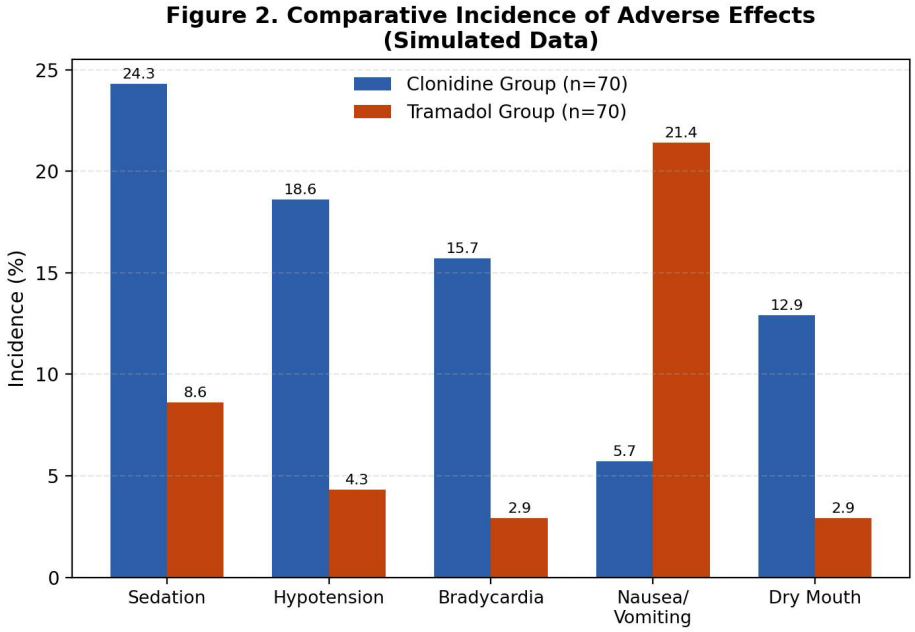

Figure 2: Comparative incidence of adverse effects between the clonidine and tramadol groups.

Figure 2 depicts the differing adverse-effect profiles of the two drugs. Clonidine was associated with a higher incidence of sedation, hypotension, bradycardia, and dry mouth, while tramadol showed a markedly higher incidence of nausea and vomiting. These reciprocal patterns reflect the distinct pharmacological mechanisms of an alpha-2 adrenergic agonist versus an atypical opioid analgesic, and may guide clinicians in selecting the more suitable agent based on individual patient risk factors, such as pre-existing bradyarrhythmia or a history of postoperative nausea and vomiting.

Discussion

In this observational comparison of intravenous clonidine and tramadol hydrochloride for the prevention of intraoperative shivering after subarachnoid anaesthesia, both drugs were found to be effective, with a comparable overall incidence of breakthrough shivering but distinct differences in the speed of resolution and the pattern of adverse effects. These findings are broadly consistent with the existing body of literature, which has generally supported the efficacy of both agents while disagreeing on which offers a clinically superior profile [16].

The observation that tramadol achieved significantly faster cessation of shivering than clonidine in the present study mirrors the findings of several earlier comparative trials, which similarly reported a higher response rate and quicker resolution of shivering with tramadol, attributed to its combined opioidergic and monoaminergic reuptake-inhibiting actions on the central thermoregulatory pathway [17]. A large meta-analysis pooling data from multiple randomised controlled trials likewise concluded that tramadol was statistically more effective than clonidine for shivering control, while noting that the difference in recurrence rates between the two agents was not significant, findings that align closely with the recurrence data observed in the present cohort [12].

Conversely, other investigators have reported an earlier disappearance of shivering with clonidine compared with tramadol, along with a numerically higher response rate, differences that have been attributed to variations in dosing, the specific shivering grading scale used, and the timing of drug administration relative to the onset of shivering [18]. Such discrepancies across the literature underscore the importance of standardising outcome definitions and dosing protocols when comparing anti-shivering agents, and may partly explain why the present study found a non-significant difference in overall incidence despite a significant difference in time to cessation [13].

The adverse-effect profile observed in this study is consistent with the known pharmacology of each drug. Clonidine's alpha-2 adrenergic agonism at central and spinal sites explains its association with sedation, bradycardia, and hypotension, effects that have been repeatedly documented in comparative trials and are considered a trade-off for its anti-shivering and analgesic benefits [7,19]. Tramadol's higher incidence of nausea and vomiting reflects its partial mu-opioid receptor activity, a well-recognised class effect of opioid and opioid-like anti-shivering agents, including pethidine and morphine, as previously described in reviews of pharmacological shivering prophylaxis [5].

These reciprocal side-effect patterns carry direct clinical relevance. In patients with pre-existing bradyarrhythmia, hypotension, or hypovolaemia, clonidine's haemodynamic effects may be less desirable, favouring tramadol as the prophylactic agent of choice. Conversely, in patients at high risk of postoperative nausea and vomiting, such as those undergoing gynaecological or laparoscopic procedures, clonidine's more favourable gastrointestinal profile may be preferable despite its sedative tendency [9]. This individualised approach to drug selection, rather than a uniform recommendation of one agent over the other, is consistent with recommendations from evidence-based guidelines developed for resource-limited perioperative settings, which advocate matching the anti-shivering agent to patient-specific risk factors [6].

It is also worth situating clonidine and tramadol within the broader landscape of anti-shivering pharmacotherapy. Newer agents such as dexmedetomidine have shown promise in several comparative trials, with some studies reporting a higher effective rate and better sedation profile than both clonidine and tramadol, though at greater cost and with the need for more intensive haemodynamic monitoring, factors that continue to limit its routine use in many practice settings compared with the two long-established and inexpensive agents examined here [20].

The physiological rationale underlying both interventions is grounded in the disruption of normal thermoregulatory control produced by neuraxial anaesthesia, which lowers the shivering threshold and impairs vasoconstrictor responses below the level of the block, as classically described by Sessler and colleagues [4]. By pharmacologically raising the shivering threshold or blunting central thermoregulatory drive, both clonidine and tramadol act on this underlying mechanism rather than merely suppressing the clinical manifestation of shivering, which likely explains their comparable overall efficacy despite differing receptor-level actions [2,8].

Limitations

This study has several limitations. Its observational, non-randomised design permits the possibility of selection bias, as drug allocation depended on the treating anaesthesiologist's preference rather than randomisation. Blinding of shivering-grade assessment was only partially feasible. The relatively modest sample size may limit the ability to detect smaller differences in secondary outcomes. Additionally, the single-centre setting may restrict the wider applicability of the findings, and long-term outcomes were not assessed.

Conclusion

Both intravenous clonidine and tramadol hydrochloride are effective prophylactic agents against intraoperative shivering following subarachnoid anaesthesia, with a comparable overall incidence of breakthrough shivering. Tramadol provides faster resolution of shivering with fewer haemodynamic disturbances, whereas clonidine is associated with more sedation and less nausea. The choice between the two agents should therefore be individualised, guided by patient comorbidity, haemodynamic status, and risk of postoperative nausea and vomiting.

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