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**Original Research Article**

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## Comparison of clonidine and tramadol for the control of shivering under spinal anaesthesia

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E-mail: [dr.prerna@yahoo.co.in](mailto:dr.prerna@yahoo.co.in)**Abstract**

**Objectives:** This study aimed to evaluate the relative efficacy of intravenously administered clonidine and tramadol for control of intraoperative shivering following spinal anaesthesia.

**Materials and Methods:** A prospective, randomized, clinical controlled study was conducted on 60 ASA grade-I & II patients of either sex, aged 18-40 years, scheduled for elective lower abdominal and lower limb surgeries, under spinal anaesthesia. Patients who developed post spinal intraoperative shivering of grades 3 or 4, lasting for minimum period of 2minutes were included in the study, and randomly allocated to one of the two groups, group C (n=30), received Inj. clonidine 50µg i.v., and group T (n=30), received Inj. tramadol 50mg i.v. when shivering was observed. Time taken for control of shivering, response rate, recurrence rate, and side effects were observed.

**Results:** The response rate was significantly higher in tramadol group than clonidine group at 1min, 2mins, and 3mins and 5mins intervals and comparable in both groups at 15 mins. The average time taken for disappearance of shivering was higher in clonidine group i.e.  $5.76 \pm 0.88$ mins as against  $3.16 \pm 0.84$ mins in tramadol group (P=0.038). Patients with incomplete response and recurrence were more in clonidine group. Side effects like hypotension, bradycardia, sedation and dry mouth were observed in clonidine group patients, and nausea and vomiting in tramadol group, but were controllable.

**Conclusion:** Tramadol is better as compared to clonidine for control of intraoperative shivering under spinal anaesthesia due to rapid onset, higher response rate, lesser recurrence, lesser sedation and lesser hemodynamic alterations.

**Keywords:** Shivering; Spinal anaesthesia; Clonidine; Tramadol.

**1.Introduction**

Regional anaesthesia (spinal anaesthesia) is widely used as a safe anaesthetic technique for both elective and emergency operations. Shivering is known to be a frequent event, reported in 40 to 70% of patients undergoing surgery under regional anaesthesia.[1][2]

Prolonged impairment of thermoregulatory autonomic control under anaesthesia along with the cold environment of operating rooms and cold infusion fluids, contributes to a fall in core body temperature, and hence cause shivering.[3] Other known causes of shivering include transfusion

reactions, drug reactions, pre-existing high grade fever or bacteremia, or infusion of contaminated intravenous fluids (fungal growth in dextrose containing fluids).

Shivering is a potentially serious event, resulting in increased metabolic rate; oxygen consumption may increased by 200% - 500% along with a linear increase in carbon dioxide (CO<sub>2</sub>) production[4]; ventilation and cardiac output; and adverse postoperative outcomes, such as wound infection; increased surgical bleeding; and morbid cardiac events. It can cause arterial hypoxemia, lactic

acidosis, increased intraocular pressure (IOP), increased intracranial pressure (ICP); and interferes with pulse rate, blood pressure (BP); and creates difficulty in electrocardiographic (ECG) monitoring.[5]

Various methods are available to control shivering during anaesthesia, which include non-pharmacological methods (like covering the patient with blankets, application of radiant heat and warming the operating room, use of warm local anaesthetic solution or warm intravenous fluids) and pharmacological methods using drugs like opioids (pethidine, nalbuphine, or tramadol), ketanserin, propofol, granisetron, doxapram, physostigmine, clonidine, and nefopam, but debate on an 'ideal anti-shivering drug' continues.[3][6]

Tramadol hydrochloride is a synthetic opioid with opioid action preferably mediated via  $\mu$  ( $\mu$ ) receptor. It has a modulatory effect on central monoaminergic pathways, and thus inhibits the neuronal uptake of noradrenaline/serotonin and encourages hydroxytryptamine secretion which resets the body temperature regulation centre and has shown to be effective in controlling post spinal shivering.[7]

Clonidine is an  $\alpha_2$ -adrenoceptor agonist. It exerts its anti-shivering effects at three levels: Hypothalamus, locus coeruleus and spinal cord. At hypothalamus it decreases the thermoregulatory threshold for vasoconstriction and shivering[8][9], at locus coeruleus -a pro-shivering centre in pons, it reduces spontaneous firing, and at the spinal cord level, it activates the  $\alpha_2$ -adrenoreceptors and release of dynorphine, norepinephrine and acetylcholine.[10] Clonidine is highly lipid-soluble and easily crosses the blood-brain barrier.[11] Due to these merits, interaction at the  $\alpha_2$ -adrenoreceptors at spinal and supraspinal sites occurs within the central nervous system.[12]

Although, both the drugs are being used for control of shivering but comparative studies regarding relative efficacy of two drugs have shown contrasting findings, while some workers[13] are of the view that Clonidine offers a better relief against shivering, others[14] report in favour of Tramadol. In view of these contrasting findings, this study was conducted to compare the relative efficacy of tramadol and clonidine for control of intraoperative shivering under spinal anaesthesia.

## 2. Material and Methods

This study was conducted in Dhiraj hospital, in department of Anesthesiology. After obtaining approval of the ethics committee and obtaining

written informed consent from patients, 60 American Society of anaesthesiologists grade-I & II (ASA I & II) patients of either sex, aged between 18 to 40 years, scheduled for elective lower abdominal and lower limb surgeries, under spinal anaesthesia, who developed intraoperative shivering post spinal anaesthesia of grade 3 or 4 lasting for minimum period of 2 minutes were included in this prospective randomized clinical controlled study. Patients with history of fever, known sensitivity to drugs to be used, shivering even before administering spinal anaesthesia, requirement of supplementation with general anaesthesia were excluded from the study.

### 2.1 Preoperative management

Detailed pre-anaesthetic check up of all the patients posted for surgery was done a day prior to surgery. All the patients were kept nil by mouth for more 8 hours prior to surgery.

On the day of surgery the patients were brought to the operation theatre (OT), i.v. line secured, standard monitors attached and baseline parameters recorded. Baseline temperature was recorded using a mercury thermometer in the axilla. All the patients were pre-loaded with Ringer lactate 10 ml/kg before giving neuraxial blockade. All the fluids and drugs were stored and administered at room temperature, and ambient temperature of the operating room was maintained at 22°C–25°C. Spinal anaesthesia was performed with a 23 or 25 gauge Quincke spinal needle, in a sitting position, at the L3–4/4–5 interspace (midline approach) with bupivacaine (0.5%, heavy) in a dose of 3.5 mL, to achieve a desirable level at T8–10 dermatome, in accordance with the surgical procedure. After induction of spinal anaesthesia, patients were observed for the occurrence of shivering. All patients who developed intraoperative shivering post-spinal anaesthesia of grade 3 or grade 4, lasting for minimum period of 2 minutes were included in the study. They were randomly allocated to two groups: Group C ( $n=30$ ) received inj. clonidine 50 $\mu$ g i.v., and Group T ( $n=30$ ) received inj. tramadol 50mg i.v. Grading of shivering was done as per wrench<sup>[15]</sup>, which is as follows: Grade 0: No shivering, Grade 1: One or more of the following: Piloerection, Peripheral vasoconstriction, peripheral cyanosis with, but without visible muscle activity, Grade 2: Visible muscle activity confined to one muscle group, Grade 3: Visible muscle activity in more than one muscle group, Grade 4: Gross muscle activity involving the whole body. The study drug was administered slowly IV as per the allotted group. The attending anaesthetist recorded the time in minutes at which shivering started after spinal anaesthesia (onset of

shivering), grade of the shivering, time to disappearance of shivering after drug administration and response rate (whether shivering ceased after treatment within 15 minutes or not). Treatment that stopped shivering was considered successful. Duration of surgery was noted. Recurrence of shivering was also observed until the patient left the operation theatre. Patients who did not respond or in whom recurrence of shivering occurred were treated with additional dose of Clonidine (50µg IV) or Tramadol (50mg IV) in the respective groups, if required. Pulse rate, blood pressure, Axillary temperature, SpO<sub>2</sub> were also monitored throughout. If the systolic arterial pressure (SAP) decreased more than 20% below the pre-anaesthetic value, was considered as significant hypotension which was treated with intravenous inj. mephenteramine 6mg in increments. Significant bradycardia (HR <60beats/min) was treated with atropine sulphate 0.6mg intravenously. Sedation score was assessed with a four-point scale as per filios[16]: Awake and alert; Drowsy, responsive to verbal stimuli; Drowsy, arousable to physical stimuli; Unarousable.

Side-effects and complications such as nausea, vomiting, hypotension, bradycardia, allergic reactions and sedation if present, were recorded. If patients develop nausea and vomiting, metoclopramide 10 mg i.v. was administered.

## 2.2 Statistical Methods

Observation and results were evaluated and compared between the two groups using Graph Pad Prism ® computer software version 6.04. Numerical variables were presented as mean & standard deviation (SD) while categorical variables were presented as percent. As regard numerical variables; unpaired student – t test was done. And for categorical variables; chi-square test was done. p value < 0.05 was considered significant.

## 3. Results

There were no statistically significant differences between the two groups in terms of demographic characteristics namely age, sex, weight, ASA status, duration of surgery and grade of shivering as shown in **Table 1**.

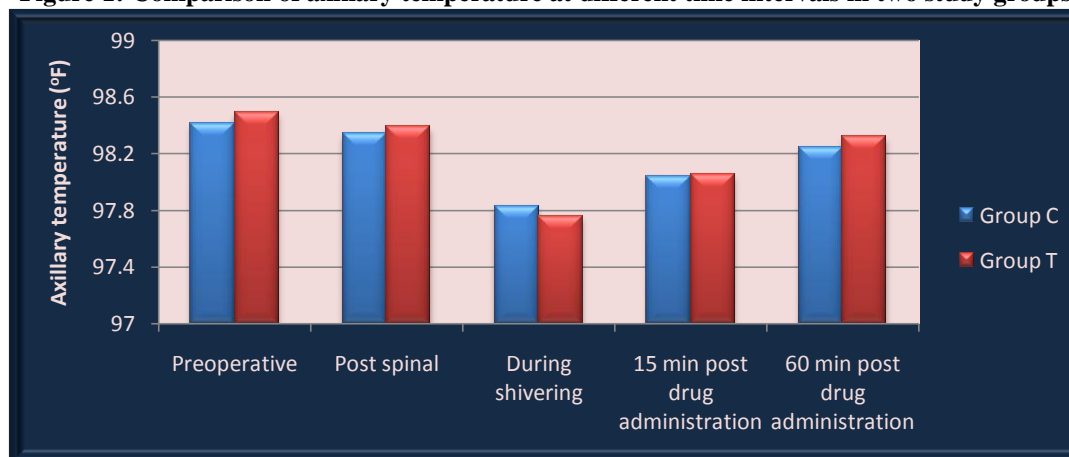
**Table 1: Demographical profile of the patients of both the groups**

Groups	Group C	Group T	P value
Age in years (mean ± SD)	30.6 ± 1.32	30.7 ± 1.22	> 0.05
Sex (male/female)	25/5	22/8	> 0.05
Weight in Kg (mean ± SD)	51.53 ± 1.01	49.53 ± 0.97	> 0.05
ASA grade I/II	9/21	12/18	> 0.05
Duration of surgery in mins (mean ± SD)	76.67 ± 4.16	77.0 ± 3.81	> 0.05
Grade of shivering (III/IV)	15/15	18/12	> 0.05

No statistically significant differences between the two groups in terms of demographic characteristics namely age, sex, weight, ASA status, duration of surgery and grade of shivering ( p > 0.05).

The axillary temperature in both groups fall significantly during shivering compared with the baseline values (p>0.001), but the values between two groups did not differ significantly. (Figure 1)

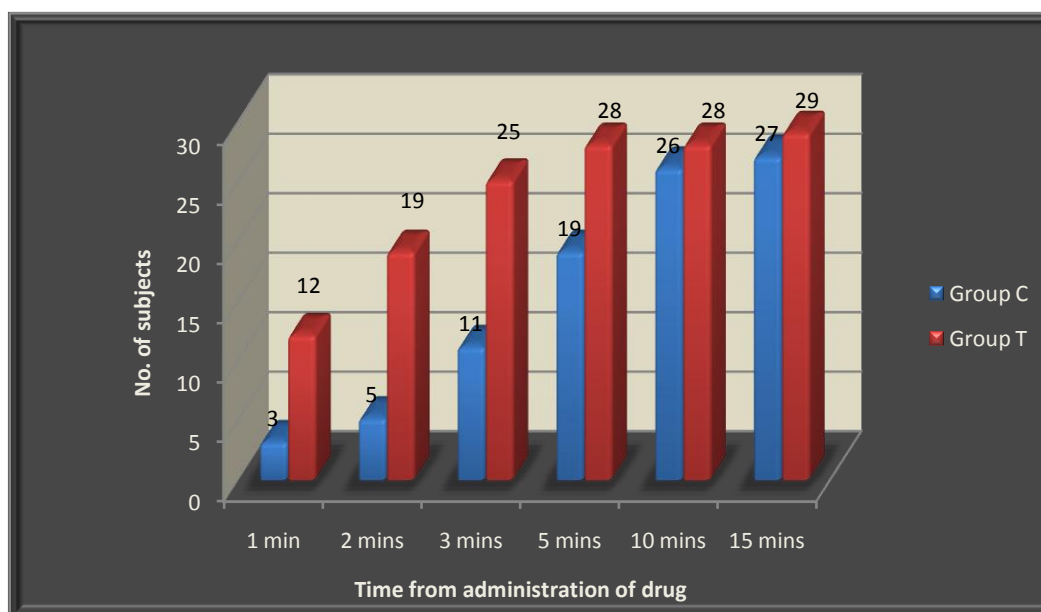
**Figure 1: Comparison of axillary temperature at different time intervals in two study groups**



The axillary temperature in both groups fall significantly during shivering compared with the baseline values, but the values between two groups did not differ significantly.

The 'response with relation to time' rate was higher in group T than Group C. (Figure 2)

**Figure 2: Comparison of response rate in study groups**



Response rate i.e. response to drug (cessation of shivering) with relation to time, was observed significantly higher in Tramadol group as compared to Clonidine. ( $p < 0.05$ )

The time taken for control of shivering was less in Tramadol group i.e.  $3.16 \pm 0.84$ mins than in Clonidine group i.e.  $5.76 \pm 0.88$ mins and difference was statistically significant. ( $P=0.038$ ) (Table 2)

Patients with incomplete response to drug were more in group C i.e. in 3 (10%) patients than in group T i.e. in 1 (3.3%) patients. (Table 2)

**Table 2: Comparison of average time taken for control of shivering, incomplete response and recurrence in study groups.**

Event	Group C	Group T	P value
Time taken for control of shivering in mins (mean $\pm$ SD)	$5.76 \pm 0.88$	$3.16 \pm 0.84$	0.038 (significant)
Incomplete response (%)	10	3.3	0.30
Recurrence (%)	13.3	6.6	$> 0.05$

With tramadol the time taken for control of shivering, patients with incomplete response and recurrence were less than with clonidine.

The recurrence of shivering occurred in 4 patients (13.3%) among group C and only 2 patients (6.6%) in group T. (Table 2)

Side effects like hypotension, bradycardia and dry mouth were seen in Clonidine group, and nausea and vomiting were seen in Tramadol group, but all were controllable. The sedation score was higher in group C than group T. (Table 3)

**Table 3: Side effects**

Complications	Group C		Group T	
	No. of patients	%	No. of patients	%
Nausea	0	0	5	16.6
Vomiting	0	0	1	3.3
Hypotension	4	13.3	0	0
Bradycardia	2	6.6	0	0
Dry mouth	1	3.3	0	0
Sedation score 2 or more	18	60	6	20

Complications like hypotension, bradycardia, and dry mouth were observed in Clonidine group and nausea and vomiting in Tramadol group. The sedation score was higher in group C than group T.

#### 4. Discussion

Shivering is an involuntary, oscillatory muscular activity, occurs as a thermoregulatory response to hypothermia in an attempt to augment the metabolic heat production.

There are three principal reasons for hypothermia under spinal anaesthesia. First, spinal anaesthesia leads to an internal redistribution of heat from the core to the peripheral compartment. Second, loss of thermoregulatory vasoconstriction below the level of the spinal block. Last, there is altered thermoregulation under the central neuraxial block, characterized by a decrease in shivering thresholds.[17]

Unfortunately it presents as a common peri-operative problem causing hypertension, tachycardia and increase metabolic demands. Various risk factors associated with shivering include type and duration of anaesthesia, level of sensory blockade, age of patient, and temperature of operating room and infusion fluids.[1]

There are many non-pharmacological and pharmacological methods used to prevent heat loss and decrease shivering. Non-pharmacological methods include radiant heat warmers, warming the operation theatre, blankets, warm IV fluids and using anaesthetic drugs at body temperature.[13] The present study was designed to standardise these possible compounding factors, while reflecting the common practice in our institution. The temperature in the operating room was maintained constant at 22°C to 25°C. IV fluids and drugs were given at room temperature.

Our study did not control tightly the various factors such as the temperature of drugs and intravenous fluids. However, this should not have affected the validity of our comparisons, because first, the current study focused on the response after treatment, rather than the incidence of shivering, and second, by randomization, both groups had been subjected to a similar degree of influence of these factors.

Our study was designed to compare the efficacy of Clonidine, an  $\alpha_2$  adrenoceptor agonist, with that of Tramadol, an opioid analgesic for control of intraoperative shivering after spinal anaesthesia in patients undergoing lower limb and lower abdominal surgeries.

According to the study by Mohta *et al*[18], three doses of Tramadol i.e. 1, 2, and 3mg/kg were effective for prophylaxis of post anaesthetic shivering. Since the adverse effects, nausea in particular, are dose dependent and therefore

considerably more likely to appear if the loading dose is high[19]. So in our study we choose the dose of Tramadol as 50mg.

Clonidine is an established antishivering drug[8][20][21], in addition, clonidine also has well known sedative effects. In antishivering studies, the sedative effects of Clonidine were noticed when a dose of 3 $\mu$ g/kg was used[22][23]. Other studies have shown that lower doses were also effective in the reduction of shivering[8][9][20][24][25], so to minimise adverse effects, we decided to administer Clonidine in a dose of 50 $\mu$ g. This lower dosage of Clonidine used in the present study was effective in the prevention of shivering, but still had sedative effects.

In our study, both groups were comparable with regard to demographic characteristics i.e. age, sex, weight, ASA grade, duration of surgery and grade of shivering. (**Table 1**)

With respect to axillary temperature the two groups did not differ from each other significantly. But a significant fall ( $p < 0.001$ ) in axillary temperature was observed in both groups during shivering compared with the baseline values. This is in accord with the observations made in study done by Bansal and Jain[26] and in study done by Bhaarat and co-workers[27]. (Figure 1)

Shivering is so distressing to the patients that quick response to antishivering agent is appreciated. Keeping this in mind we compared these two drugs in respect of 'response with relation to time' rate. (**Figure 2**)

Our result showed the superiority of Tramadol over Clonidine for control of intraoperative shivering post spinal anaesthesia, as the time taken for control of shivering was less in Tramadol group and showed statistically significant difference from Clonidine group.

It was  $5.76 \pm 0.88$ mins and  $3.16 \pm 0.84$ mins in Clonidine and Tramadol group respectively ( $P=0.038$ ) (Table 2), and was comparable to the previous study by Bansal and Jain[26], Reddy *et al*[28] and Talakoub *et al*[29].

Patients of both the groups, in whom shivering continued to occur even after 15mins of drug administration were categorised as patients with incomplete response. Patients with incomplete response to drug were more in group C than in group T. (**Table 2**)

In 4 patients (13.3%) among group C and only 2 patients (6.6%) in group T were occurred recurrence of shivering (**Table 2**). Though this difference was not statistically significant but the recurrence was more with clonidine.

In our study there was no significant difference in the pulse rate, systolic and diastolic blood pressure between the two groups in their baseline values. During shivering there was minimal rise in pulse rate (approximately 10% from baseline value) and blood pressure (approximately 6-7%) in both the groups. And after drug administration, a propensity toward minor fall in hemodynamic parameters was observed in both groups with a higher fall in pulse rate and blood pressure in Clonidine group compared with the Tramadol group at various time intervals. Bansal and Jain[26] study observation supports our findings.

Hypotension, bradycardia and dry mouth were seen in 4 patients (13.3%), 2 patients (6.6%) and 2 patients (6.6%) respectively, of the Clonidine group while none of the patient among Tramadol group developed so. (Table 3)

There was statistically significant difference in the sedation score[26] among both groups, with higher score in group C than group T. (Table 3)

None of the patient among clonidine group complained of nausea or vomiting while in tramadol group 16.6% patients complained of nausea and 3.3% patient had vomiting (Table 3). Our finding were comparable to Bhaarat and co-workers[27] and Joshi et al[30] study.

To conclude, Tramadol Hydrochloride and Clonidine both are effective for control of shivering under spinal anaesthesia. But Tramadol Hydrochloride is better as compared to Clonidine due to rapid onset, higher response rate, more effective control, lesser recurrence, less sedation and hemodynamic alterations, though nausea and vomiting is more in Tramadol group, still controllable.

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