

## COMPARISON OF ORAL TRAMADOL AND ORAL CLONIDINE AS A PREMEDICATION TO PREVENT PERIOPERATIVE SHIVERING IN PATIENTS UNDERGOING SURGERY UNDER SUBARACHNOID BLOCK

Arun Kumar Ajjappa<sup>1</sup>, M. Lingaraj<sup>2</sup>

<sup>1</sup>HOD, Department of Anaesthesiology, SSIMSRC, Davangere.

<sup>2</sup>Post Graduate, Department of Anaesthesiology, SSIMSRC, Davangere.

---

### ABSTRACT

---

#### BACKGROUND

Perioperative shivering, in patients undergoing surgery under central neuraxial blockade is a common complication. Prophylactic measures to reduce shivering are quintessential to decrease the morbidity and mortality.

#### AIMS

This randomised prospective study seeks to compare the efficacy of oral clonidine and tramadol, as premedication, in prevention of shivering in patients undergoing surgery under spinal anaesthesia.

#### METHODS AND MATERIAL

The patients were randomly allocated into two groups (50 patients each). Group C received oral clonidine 100 µg; Group T received oral tramadol 50 mg. Number of patients having shivering, their grades and duration, hemodynamic changes were recorded.

#### STATISTICAL ANALYSIS

Data were analysed using appropriate statistical software, Student's t-test when appropriate

**RESULTS** In group I and II, 39 patients (78%) and 28 patients (56%) did not shiver, respectively. No drug showed any statistically significant advantage over the other.

#### CONCLUSION

Oral clonidine and tramadol were comparable in respect to their effect in decreasing the incidence, intensity and duration of shivering when used prophylactically in patients who underwent surgery under subarachnoid blockade.

#### KEYWORDS

Tramadol, Clonidine, Hypothermia, Shivering.

---

**HOW TO CITE THIS ARTICLE:** Ajjappa AK, Lingaraj M. Comparison of oral tramadol and oral clonidine as a premedication to prevent perioperative shivering in patients undergoing surgery under subarachnoid block. J. Evid. Based Med. Healthc. 2016; 3(46), 2287-2291. DOI: 10.18410/jebmh/2016/505

---

**INTRODUCTION:** Shivering is distressing for the patients undergoing surgery under both regional and after general anaesthesia. The main causes for shivering intra/post-operatively are temperature loss, decreased sympathetic tone and systemic release of pyrogens.<sup>1</sup> Shivering increases expenditure of cardiac and systemic energy.<sup>2</sup> Shivering is a potential serious complication resulting in an increased oxygen consumption and raised carbon dioxide production: ventilation and cardiac output: adverse postoperative outcomes such as wound infection, surgical bleeding and morbid cardiac events.

It causes arterial hypoxemia, lactic acidosis, increased intraocular pressure and increased intracranial pressure and interferes with the pulse rate and blood pressure and ECG monitoring.<sup>3-5</sup> Perioperative hypothermia is a primary cause of which occurs due to neuraxial anaesthesia induced inhibition of thermoregulatory mechanism. Shivering occurs as a thermoregulatory response to hypothermia or muscle activity with tonic or clonic patterns and various frequencies have been noted.<sup>5</sup> Regional anaesthesia produces vasodilatation, which facilitates core to peripheral redistribution of heat. It also increases sweating threshold and decreases vasoconstriction and shivering threshold<sup>6</sup>. Intra- and post-operative management of shivering are usually done by external heating (Forced air warming, warming blankets, warmed fluids) or pharmacological interventions. Various drugs from different groups like opioids, 5-hydroxytryptamine receptor (5-HT<sub>3</sub>) antagonists, N-methyl D-aspartate (NMDA) receptor antagonists, cholinomimetics and biogenic amines have been used in the literature.<sup>7-10</sup>

---

*Financial or Other, Competing Interest: None.  
Submission 14-05-2016, Peer Review 31-05-2016,  
Acceptance 06-06-2016, Published 08-06-2016.*

*Corresponding Author:*

*Dr. M. Lingaraj,*

*#F-12, Shubh Residency, Lalgeri Cross, Brahmpur, Gulbarga.*

*E-mail: lingu19111977@gmail.com*

*DOI: 10.18410/jebmh/2016/505*

---

Shivering under neuraxial anaesthesia is a common problem faced by anaesthetists; therefore, a comparative study was conducted using commonly available drugs like oral clonidine and oral tramadol to assess their efficacy when used prophylactically to control shivering under neuraxial blockade.

**METHODS:** After Institutional Ethical Committee approval and informed consent, 100 patients of ASA grade 1 and 2, belonging to either sex, aged between 18 and 65 years, undergoing lower abdominal or lower limb surgery were included in the study. Exclusion criteria included Patients with allergy to the drug used in the study; Patients who received other vasodilators 24 hours prior to surgery; Patients who have ischaemic heart disease, cerebrovascular events, thyroid dysfunction and autonomic neuropathy pregnant women.

Patients were randomly allocated to two groups by computer generated numbers: group C and group T Patients were premedicated with tab clonidine 100 mcg 1.5 hours before surgery in group C and cap tramadol 50 mg 2 hours before surgery in group T. Anaesthesiology Department technicians who were not involved in the study prepared these trial preparations. They recorded the group randomisation separately, such that the anaesthesiologist recording the data and caring for the patient was unaware of what the preparation contained or which group the patient belonged to.

Following a detailed pre-anaesthetic checkup along with relevant investigations, patients were brought to the operation theatre (OT) and relevant monitoring like pulse oximetry, non-invasive blood pressure, capnography, electrocardiography attached.

- Intravenous access using 18G cannula will be established.
- All the patients were preloaded with Ringer lactate 10 mL/kg before giving neuraxial blockade.
- All preloading fluids and drugs were stored and administered at room temperature.

Subarachnoid anaesthesia was instituted at the L3 – L4 spinal interspaces, with 0.5%, hyperbaric bupivacaine. Heart rate, noninvasive blood pressure, respiratory rate, SpO<sub>2</sub> recorded every 5 min. from the baseline (when SAB was given) till the end of surgery and every 15 min. postoperatively.

Patients wore cotton surgical drapes and no means of active warming were used until deemed essential. The ambient temperature was measured by a wall-mounted thermometer. The ambient temperature was maintained at 21°C – 24°C, with constant humidity. The grades of shivering were recorded at a period of every 10 min. from baseline till the end of surgery and every 15 min. postoperatively as per grades similar to those used by Wrench et al.<sup>11</sup> Perioperatively if shivering occurred; it was treated in the same manner in all the groups with reassurance, warming blanket. If the shivering is grade 3 and above severity, inj. Pethidine 25 mg intramuscularly was administered.

Side effects such as nausea, vomiting, hypotension, bradycardia, dry mouth, sedation, skin rash and headache, if present were recorded. Hypotension was treated with i.v. incremental bolus dose of mephentermine 3 mg and a further i.v. infusion of Ringer lactate. If patients developed nausea and vomiting, i.v. metoclopramide 10 mg was administered.

Grades	Muscle group involved
Grade 0	No shivering observed
Grade 1	One or more of piloerection; peripheral cyanosis without other cause, but without visible muscular activity
Grade 2	Visible muscle activity confined to one muscle group
Grade 3	Visible muscle activity in more than one muscle groups
Grade 4	Gross muscular activity involving the entire body

*Table 1: Grading of shivering as per WRENCH*

**STATISTICAL ANALYSIS:** After completion of the study, observations obtained were tabulated and analysed using Statistical Package for Social Sciences (SPSS version 17). To calculate the sample size, we hypothesised that keeping Type I (alpha) error at 5% and Type II (beta) error at 20%, the study drugs would be able to reduce the incidence of shivering by 15% and using the variability of data as a standard deviation (SD), 50 patients per study group was arrived. Student t-test was used to compare different groups among themselves. A p < 0.05 was considered to be statistically significant.

**RESULTS:** A total of 100 patients were enrolled in the present study and were randomised into two groups of 50 each. Both the groups were comparable with respect to age, weight, duration of surgery. The mean age of the patients in group C was 39.38±11.98 years; and patients in Group T 36.48 ± 11.22 years.

Parameter	Group C	Group T
Age (years)	39.38±11.98 years	36.48±11.22 years
Duration of surgery	77.2±32.89 min.	75.6±42.09 min.
Weight (kg)	71.1±10.3	68.90±9.21
Range of OT TEMP	21-24°C	21-24°C

**Table 2: Demographic Profile and Other Characteristics of Patients in Two Groups**

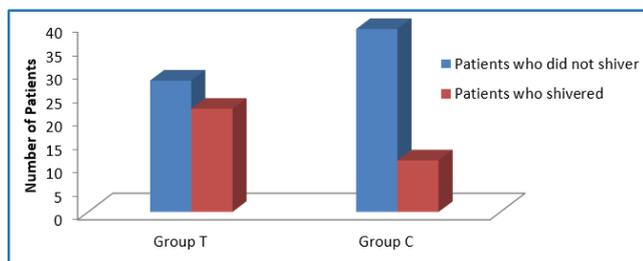
**Hemodynamic Parameters:** the hemodynamic parameters were comparable in both the groups with respect to heart rate, systolic and diastolic blood pressure

Parameter	Group T	Group C
Heart rate/min	73.5±9.40	71.0±9.76
Systolic blood pressure (mmHg)	116.6±14.52	114.9±11.45
Diastolic blood pressure (mmHg)	68.2±7.20	66.5±7.08

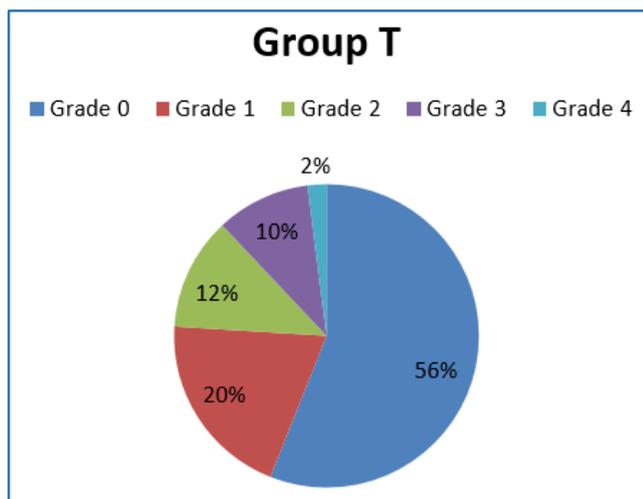
**Table 3: Hemodynamic Parameters of the Patients During the Observation Period**

**Shivering:** In Group T, 28 patients (56%) did not shiver while 22 patients (44%) did. Of which 10 patients had grade I shivering, 6 had Grade II shivering, 5 had Grade III shivering and 1 patient had Grade IV shivering All three patients experienced Grades 1-4 shivering, during the observation period. In the group C, 39 patients (78%) did not experience shivering, but 16 patients (22%) experienced different grades of shivering.

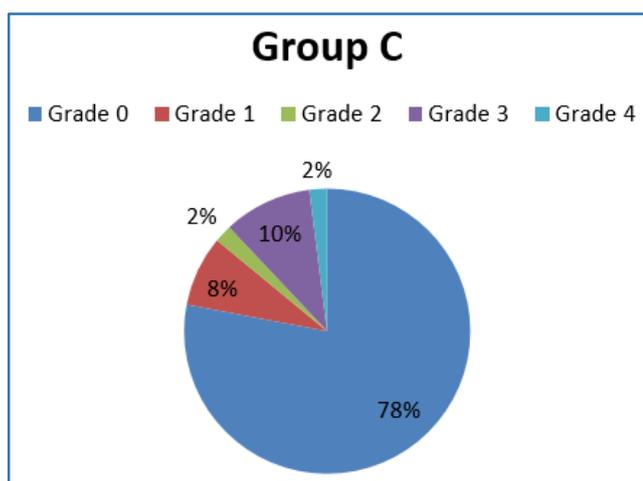
**Shivering in Both the Groups:**



**Figure 1: Shivering in Group T and Group C**



**Figure 2: Shivering in Group T**



**Figure 3: Shivering in Group C**

**Shivering Characteristics in Two Groups:** The mean onset of shivering in both the groups were comparable: Group C: 59.09±1.03 mins, Group T: 57.72±1.66 mins.

The incidence of shivering (t=1.299, df=6, p =.242) and onset of shivering (t=1.322, df=34, p=.195) in both groups was not statistically significant.

**DISCUSSION:** Regional anaesthesia, either central neuraxial block or peripheral nerve block is a safe and very popular technique used for various surgeries. However, 40% to 70% of patients undergoing regional anaesthesia develop shivering, though it is also found to occur after general anaesthesia.<sup>1-2</sup> The mechanism which leads to shivering after regional anaesthesia is not clear, but the probable mechanisms could be decrease in core body temperature secondary to sympathetic block; peripheral vasodilatation; increased cutaneous blood flow, which leads to increased heat loss through skin; cold temperature of operation theatre; rapid infusion of cold IV fluids; and effect of cold anaesthetic drugs upon the thermosensitive receptors in the spinal cord.<sup>7,10</sup> 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.<sup>11,12</sup> The present study was designed to standardise these possible compounding factors, while reflecting the common practice in our institution.

In the present study, the factors that influence the occurrence of shivering, like temperature of IV fluids and drugs, were not tightly controlled, but this should not affect the validity of our study. After randomisation, both groups were subjected to similar degrees of influence of these factors. Pharmacological methods to treat shivering include Pethidine, tramadol, doxapram, ketanserine, nefopam, alfentanil, doxapram, etc.

A limitation of this study is that we could not measure the core body temperature. For measurement of core body temperature, the probe needs to be put in the oesophagus or near the tympanic membrane. Both these are uncomfortable and unacceptable who has been given spinal anaesthesia. Rectal temperature monitoring was a possibility but was not tried.

In the present study, we compared the efficacy of clonidine and tramadol for treatment of shivering after spinal anaesthesia in patients undergoing various elective surgeries. Clonidine is a centrally acting selective α<sub>2</sub> agonist. Clonidine exerts its anti-shivering effects at three levels: Hypothalamus, locus coeruleus and spinal cord. At the hypothalamic level, it decreases thermoregulatory threshold for vasoconstriction and shivering, because hypothalamus has high density of α<sub>2</sub> adrenoceptors and hence is effective in treating the established post-anaesthetic shivering.<sup>13,14</sup> It also reduces spontaneous firing in locus coeruleus — a pro-shivering centre in pons.<sup>15</sup> At the spinal cord level, it activates the α<sub>2</sub> adrenoceptors and release of dynorphin, norepinephrine and acetylcholine.<sup>15</sup> The depressor effects of these neurotransmitters at dorsal horn modulate cutaneous thermal inputs.<sup>16</sup>

Clonidine is highly lipid-soluble and easily crosses the blood-brain barrier.<sup>17</sup> Due to these merits, interaction at the  $\alpha_2$  adrenoreceptors at spinal and supraspinal sites occurs within central nervous system. Clonidine is highly lipid-soluble and easily crosses the blood-brain barrier.<sup>16</sup> Due to these merits, interaction at the  $\alpha_2$  adrenoreceptors at spinal and supraspinal sites occurs within the central nervous system.<sup>17</sup>

Tramadol is an opioid analgesic with opioid action preferably mediated via  $\mu$  ( $\mu$ ) receptor with minimal effect on kappa and delta binding sites. Tramadol also activates the monoaminergic receptors of the descending neuraxial inhibiting pain pathway. The anti-shivering action of tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both.<sup>18-20</sup>

Few studies in literature have evaluated the effectiveness of prophylactic use of pharmacologic agents for the control of shivering under neuraxial anaesthesia. Rama Wason et al<sup>21</sup> observed that prophylactic use of intravenous ketamine, clonidine and tramadol were effective in preventing shivering during neuraxial anaesthesia without causing any major untoward side-effects. No drug showed any statistically significant advantage over the other. No major haemodynamic changes were seen with prophylactic use of test drugs. This study used parenteral drug formulations prophylactically, where as in our study oral formulations were used to evaluate the effectiveness of the drugs for the control of shivering prophylactically. In a similar study by Anurag Tiwari et al in their study evaluated the effective of oral clonidine and tramadol prophylactically in patients who underwent TURP under subarachnoid blockade. They concluded that both drugs were comparable in respect to their effect in decreasing the incidence, intensity, and duration of shivering. This study unlike our study involved patients undergoing TURP under subarachnoid blockade.

**CONCLUSION:** Oral clonidine and tramadol were comparable in respect to their effect in decreasing the incidence, intensity and duration of shivering when used prophylactically in patients who underwent surgery under subarachnoid blockade.<sup>22</sup>

## REFERENCES

- De Whitte J, Sessler DI. Perioperative shivering: physiology and pharmacology. *Anaesthesiology* 2002;96(2):467-484.
- Sessler DI, Ponte J. Shivering during epidural anaesthesia. *Anesthesiology* 1990;72(5):816-821.
- Bhatnagar S, Saxena A, Kannan TR, et al. Tramadol for postoperative shivering: a double blind comparison with Pethidine. *Anaesth Intensive Care* 2001;29(2):149-154.
- Katyal S, Tewari A. Shivering: anesthetic considerations. *J Anaesth Clin Pharmacol* 2002;18(4):363-376.
- Sessler Daniel I. Temperature monitoring. In: Millar RD, Textbook of anaesthesia. Churchill Livingstone Inc, New York 1994;5<sup>th</sup> edn:1367-1389.
- Glosten B, Hynson J, Sessler DI, et al. Preanaesthetic skin-surface warming reduces redistribution hypothermia caused by epidural block. *Anesth Analg* 1993;77(3):488-493.
- Chan AM, Ng KF, Tong EW, et al. Control of shivering under regional anaesthesia in obstetric patients with tramadol. *Can J Anesth* 1999;46(3):253-258.
- Capogna G, Celleno D. IV clonidine for post-extradural shivering in parturients: a preliminary study. *Br J Anesth* 1993;71(2):294-295.
- Shukla U, Malhotra K, Prabhakar T. A comparative study of the effect of clonidine and tramadol on post-spinal anaesthesia shivering. *Indian J Anaesth* 2011;55(3):242-246.
- Chaturvedi S, Domkondwar G. Control of shivering under regional anaesthesia using tramadol. *Asian Archives of Anaesthesiology and Resuscitation* 2002;57:491-496.
- Wrench IJ, Cavill G, Ward JE, et al. Comparison between alfentanil, Pethidine, and placebo in the treatment of postoperative shivering. *Br J Anaesth* 1997;79(4):541-542.
- Ikeda T, Sessler DI, Tayefeh F, et al. Meperidine and alfentanil do not reduce the gain or maximum intensity of shivering. *Anesthesiology* 1998;88(4):858-865.
- Delaunay L, Bonnet F, Liu N, et al. Clonidine comparably decreases the thermoregulatory threshold for vasoconstriction and shivering in humans. *Anesthesiology* 1993;79(3):470-474.
- Joris J, Banache M, Bonnet F, et al. Clonidine and ketanserin both are effective treatment for post anaesthetic shivering. *Anesthesiology* 1993;79(3):532-539.
- Powell RM, Buggy DJ. Ondansetron given before induction of anesthesia reduces shivering after general anesthesia. *Anesth Analg* 2000;90(6):1423-1427.
- Alojado ME, Ohta Y, Kemmotsu O. The effect of clonidine on the activity of neurons in the rats dorsal raphe nucleus in vitro. *Anesth analg* 1994;79(2):257-260.
- Timmermans PB, Brands A, van Zwieten PA. Lipophilicity and brain disposition of clonidine and structurally related imidazolidines. *Naunyn Schmiedeberg Arch Pharmacol* 1977;300(3):217-226.
- Klimecsha W, Tong C, Eisenach JC. Intrathecal alpha-2 adrenergic agonist stimulate acetylcholine and norepinephrine release from the spinal cord dorsal horn in sheep. An in vivo microdialysis study. *Anesthesiology* 1997;87(1):110-116.
- Mathews S, Al Mulla A, Varghese PK, et al. Post anaesthetic shivering: A new look at tramadol. *Anaesthesia* 2002;57(4):387-403.
- Tsai YC, Chi KS. A comparison of tramadol, amitriptyline and meperidine for post-epidural anaesthetic shivering in parturients. *Anesth Analg* 2001;93:1288-1292.

21. Rama Wason, Nikhil Jain, Poonam Gupta, et al. Randomized double-blind comparison of prophylactic ketamine, clonidine and tramadol for the control of shivering under neuraxial anaesthesia. *Indian J Anaesth* 2012;56(4):370-375.
22. Anurag Tewari, Ira Dhawan, Vidhi Mahendru, et al. A comparative study evaluating the prophylactic efficacy of oral clonidine and tramadol for perioperative shivering in geriatric patients undergoing transurethral resection of prostate. *Journal of Anaesthesiology Clinical Pharmacology* 2014;30(3):340-44.