

# Oral Clonidine Premedication to Prevent Perioperative Shivering in Elderly Patients Undergoing Surgery Under Subarachnoid Block

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## Abstract :

**Aims :** To assess whether prophylaxis with oral clonidine prevents perioperative shivering in elderly patients undergoing surgery under subarachnoid block.

**Materials and Methods :** Prospective randomized placebo controlled study. After considering inclusion and exclusion criteria and obtaining informed consent from the patients, subjects are allocated into group X or group Y, by randomization technique.

**Group X :** Patients received premedication with clonidine orally in a dose of 2mcg/kg.

**Group Y :** Patients received premedication with placebo. The study drugs containing clonidine and placebo prepared in double blind fashion by a collaborator not involved in data recording. Appropriate code number assigned, the same collaborator administered the drug, while blind observer collected the data.

All patients received the premedication 90 minutes before the anticipated time for SAB. Subarachnoid block upto T9-T10 dermatome level achieved with 0.5% Bupivacaine Heavy. Operation theatre maintained at a constant humidity and temperature of around 22±1°C. No means of active rewarming used. Pre warmed (upto the body temperature of 37°C) intravenous and irrigating fluids used perioperatively. HR, NIBP, respiratory rate, SpO<sub>2</sub> and body temperature (rectal thermistor probe) recorded every 5 minutes intraoperatively and then every 15 minutes for the rest of the post-operative period. In all cases, shivering recorded by the same attending anaesthesiologist at a period of 0,1,5,10,15,30,45,60 & 90 minutes from the baseline as per grade wrench.

Perioperatively if shivering occurred, patients were treated in the same manner in both groups with reassurance and warming blanket. The associated conditions like bradycardia & hypotension (fall in systolic blood pressure >20% of the baseline) appropriately treated with atropine and normal saline or mephenteramine in the titrated doses respectively.

**Results:** Incidence of shivering was significantly less in patients who were given oral clonidine when compared with that of the placebo group (6.6% v/s 40% respectively; P value of <0.001). Clonidine did not lead to any collateral clinically significant side effects.

**Conclusion:** We conclude that as a prophylaxis, oral clonidine 150 µg is effective in reducing the incidence, severity and duration of perioperative shivering in elderly patients undergoing surgery under spinal anaesthesia.

**Keywords:** Perioperative shivering, elderly patients, Clonidine, spinal anaesthesia.

## Introduction

In the elderly patients when the incidence of other coexisting disease also tends to increase, anaesthetic management of such patients thus becomes complicated. Regional anaesthesia is a safe and popular anaesthetic technique for various surgeries. Around 40-60% of

patients under regional anaesthesia develop shivering.<sup>1</sup> Perioperative shivering during spinal anaesthesia is a common complication in patients undergoing surgery and is secondary to peripheral vasodilatation from sympathetic blockade or cold irrigating fluids. Regional anaesthesia has been known to be associated with greater heat loss than general anaesthesia.<sup>2</sup>

Elderly patients are especially at risk of hypothermia under anaesthesia, as low core temperatures may not initiate autonomic protective responses.<sup>3</sup> Shivering can be very unpleasant and physiologically stressful for the patient. It may be associated with a number of

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deleterious sequelae, including sympathetic stimulation induced increased oxygen consumption<sup>4</sup> (more than 200%) and carbon dioxide production.<sup>5</sup>

Many physical and pharmacological interventions are used to decrease the incidence and to reduce the severity of post anesthetic shivering. Clonidine, a centrally acting  $\alpha$  2-selective agonist, has been used intravenously as an adjunct to general anesthesia to decrease shivering and oxygen consumption.

Pharmacologically oral clonidine virtually undergoes complete absorption and the peak concentration occurs after 90 minutes after administration.<sup>1</sup> The anatomic target of its anti-shivering effect can be found at three levels at hypothalamus, pons and spinal cord. It is highly lipid-soluble and easily crosses the blood-brain barrier.<sup>6</sup> These merits make it to interact at the  $\alpha$  2 adrenoreceptors at spinal and supraspinal sites within the central nervous system.<sup>7</sup>

### **Aims And Objectives**

To assess the role of oral clonidine as prophylaxis in prevention of perioperative shivering in patients undergoing surgery under subarachnoid block.

### **Materials And Methods**

**Source of Data :** The present study was undertaken at SSIMS AND RC, Davangere during the period December 2012-September 2014. Institutional Ethical Committee approval was obtained. Informed written consent was obtained by participating patients. In the present randomised controlled prospective study a total of 60 patients aged between 55-75 years of ASA grade I, II or III undergoing surgery under regional anaesthesia were included.

### **Inclusion criteria**

1. Patients undergoing elective surgery under subarachnoid block
2. Age between 55-75 years
3. ASA grade I, II and III

### **Exclusion criteria**

1. Allergic to the drug used in the study
2. Patients who received other vasodilators, 24 hrs prior to surgery
3. Patients who had ischemic heart disease, cerebrovascular events, thyroid dysfunction and autonomic neuropathy
4. Who did not give valid informed consent

### **Method**

After considering inclusion and exclusion criteria and obtaining informed consent from the patients, subjects

are allocated into group X or group Y, by randomization technique.

Group X- 30 patients who received 2mcg/kg clonidine orally. Group Y- 30 patients who received placebo orally

The study drug containing clonidine and placebo prepared in double blind fashion by a collaborator not involved in data recording. Appropriate code number were assigned, the same collaborator administers drug, while blind observer collected the data. All patients received premedication 90 minutes before the anticipated time for subarachnoid block.<sup>21</sup> Preoperative condition of the patient was assessed. The baseline heart rate, blood pressure and mean arterial pressure was recorded and noted.

### **Anaesthetic management :**

Ambient temperature was noted. Baseline vital parameters were recorded. IV access was obtained with 18 G cannula and IV fluids started. The volume of the local anaesthetic, volume of preloading fluid, use of vasopressors were determined by the attending anaesthesiologist, and was not affected by inclusion in the study. A standard double layered blanket was used to cover the chest and upper limb of the patient. All the preloading fluids and drugs were given at room temperature. Oxygen at rate of 5 Litre/min was administered through face mask to all the patients. Monitoring of NIBP, pulse oximetry and ECG was done throughout the procedure. Baseline preoperative rectal temperature using rectal thermistor was noted in all the patients.

Sub arachnoid block upto T9-10 dermatome level achieved with 3ml 0.5% bupivacaine (H). A total of 60 cases fitting the above criteria were studied. They were randomly divided into one of the two groups,

Group X 30 patients receiving 2mcg/kg clonidine orally.

Group Y 30 patients receiving placebo orally.

### **Parameters compared**

Baseline HR, SBP, DBP, SPO<sub>2</sub>, respiratory rate, and temperature was noted, and also during shivering at regular intervals. All the patients were assessed for shivering grades, its appearance and disappearance, haemodynamic status, and complications if any. Patients were observed at intervals of 5 minutes intraoperatively and postoperatively every 15 minutes for 1 hr. Wrench scale<sup>14</sup> was used to assess the degree of shivering.

### **Sedation**

Sedation characteristics were noted and graded according to the Ramsay's sedation scores.

### **Statistical analysis**

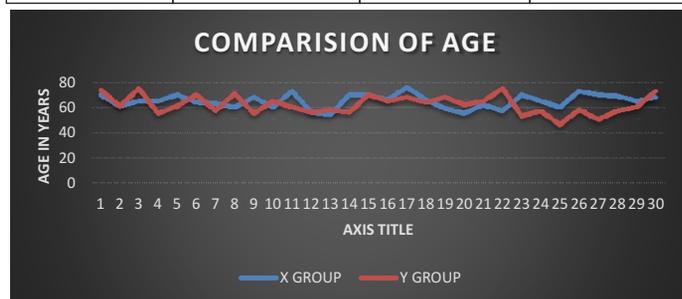
Statistical analysis was done using SPSS software 16.0. Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Student's T Test has been used to find the significance of study parameters between two groups of patients, Chi-square/ 2x3 Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Student t-test for paired comparisons. P<0.01 was considered statistically significant.

**Results :**

**Demographic profile:** There is no significant difference in the age and weight distribution between the two groups. Samples were matching by ASA grading also. Analysis was done by chi square test.

Demographic profile in both the group. All patients who were subjected to bronchoscopy from department of Otolaryngology in our hospital between November 1<sup>st</sup> 2011 and October 31<sup>st</sup> 2014 were studied retrospectively. Case records were reviewed with respect to the clinical presentation, duration of symptoms, clinical signs, imaging findings, complications, diagnosis and treatment of tracheobronchial foreign body. All patients were admitted in intensive care unit. Vitals including oxygen saturation were monitored. Oxygen by mask was given for those with respiratory distress. All patients were kept nil per oral for 6 hours before procedure. High risk informed written consent was taken from patient

	X GROUP	Y GROUP	P VALUE
AGE(YR)	62.17±7.616	64.9±5.772	0.053
WT(KG)	62±6.43	59.76±5.34	0.495
ASA 1	6	4	0.283
2	24	26	



Comparison of age (years) distribution of patients in year Heart rate.

The patients in the clonidine group had lower heart rate compared to the control group throughout the study, but

it did not cause any clinically significant hemodynamic aberrations.

**SBP :** There's no statistically significant difference in SBP and DBP among the two groups.

**Shivering :** Incidence of shivering was significantly less in Group X (6.66%) when compared with that of the Group Y (40%). In the study group, 28 patients (95%) did not experience shivering. Of the 2 patients who shivered, one had grade 1 shivering that progressed to grade 2. The second patient experienced shivering of grade 1 only. In the placebo group, 18 patients (60%) had no shivering, while 12 patients (40%) experienced various grades of shivering, ranging from grade 1 to grade 3. Many patients progressed from low to high grades of shivering. On comparison, a P value <0.01 was observed, thus implying a statistically significant variance regarding the incidence amongst them. We observed that 15 (37.5%), 11 (27.5) and 10 (25) patients in the control group experienced grades 1, 2 and 3 of shivering respectively at various time intervals during the study period.

The variation was significant throughout the period of study, especially at 30, 45 and 60 minutes intervals, where the P value <0.01 was observed; while at 5, 10, 15 and 90 minutes' intervals, the P value was <0.05.

It was observed that shivering started earlier (in 5 min) and persisted for a longer duration in control group (range 5-90 min); while in the patients who were administered prophylactic oral clonidine, its onset was delayed and was of a shorter duration (range 15-60 min). All the patients who experienced grade 2-3 of shivering had tachycardia and increased blood pressure recording. P value is significant for the clonidine group for stopping shivering. Analysis was done by independent T test.

	X (study)	Y (study)
Shivering	2 (6%)	12 (40%)

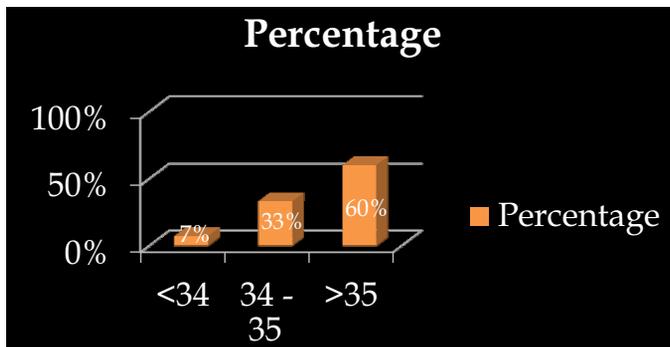
Incidence of shivering

**Temperature :**

The rectal temperature showed statistically significant variation, especially in the later part of the study (P< 0.01). There was no statistical variance when the blood pressure, respiratory rate and SpO2 were compared. There is no statistically significant difference in temperature between the two groups. Analysis done by independent samples T Test.

In control group: 12 patients developed shivering, out of them 10 (83%)patients developed shivering at temperatures between 34 and 35 degrees and 2 (17%) patients developed below 34degrees.

Comparison of Mean temperature in the two groups (in centigrade)



Comparison of incidence of shivering with respect to temperature

### Discussion :

In this study most of the patients in X group, about 80% belong to 50 - 70 years age group and only 3% belong to below 50 years age group, in Y group also most of the patients about 87% belong to 50 - 70 years age group and no patients below 50 years age group.

In our study oral clonidine was effective in providing prophylaxis against shivering in surgery under subarachnoid blockade. The incidence of shivering in patients who were given oral clonidine was only 6.66% as compared to 40% in the control group ( $P < 0.01$ ). This is comparable to Mao<sup>29</sup>, who also found an incidence of 4% when patients were given clonidine as compared to 44% in the control group. It was observed that shivering started earlier (in 5 min) and persisted for a longer duration in control group (15-30 min); while in the patients who were administered prophylactic oral clonidine, its onset was delayed and was of a shorter duration (10-20 min). We found that the lowest mean temperature was at 30 and 40 min in control and clonidine groups respectively.

Two patients who received clonidine developed shivering at temperature below 34 degrees and in the remaining 28 patients, 10 (36%) patients did not develop shivering even at temperatures below 35 degrees. In control group out of 12 patients who developed shivering 10 (83%) patients developed shivering at temperatures between 34 and 35 degrees and 2 (17%) patients developed below 34°C. This shows that clonidine decreases the threshold of temperature for shivering. The 6.6% patients who shivered in the clonidine group experienced only Grade I and/or II of shivering as compared to the control group in which the patients experienced shivering ranging from Grade I to III. It was observed that shivering had early onset and persisted longer in control group, while in the clonidine group

shivering had a delayed onset and persisted for a shorter duration. This is in concordance with various studies, which showed that clonidine reduces the incidence, severity and duration of perioperative shivering.<sup>14</sup>

There was no significant variation in the blood pressure of the patients of the two groups ( $P = 0.242$ ) though two patients in clonidine and one in placebo group required mephenteramine. There is no statistically significant difference ( $P = 0.235$ ) in HR between the two group.

Maintaining strict normothermia can prevent shivering during regional anesthesia.<sup>30</sup> Most of the morbidity and mortality is associated with the cardiovascular system, with myocardial infarction, cardiac arrest, heart failure or cardiac dysrhythmias occurring in up to 2.5% of patients.<sup>15,16</sup> The cardiovascular system could be adversely affected by perioperative reduction in core temperature and metabolic demands. Hypothermia causes bradycardia, reduced cardiac output and peripheral vasoconstriction.

The metabolic cost of shivering is an increase in oxygen consumption. We therefore undertook the study as these patients are predisposed to shivering and any therapeutic effect of our study might prove beneficial for such patients. Oral clonidine is easily available and economical and its salient attributes are its high safety profile, particularly in geriatric patients. It has a potential to prevent perioperative morbidity associated with shivering and leads to shorter hospital stay.

### Conclusion :

Oral clonidine is easily available and economical and it's salient and high safety profile, particularly in geriatric patients. It has a potential to prevent perioperative morbidity associated with shivering and leads to shorter hospital stay.

Clonidine decreases the threshold of temperature for shivering. As like in other studies in this study also it is shown that patients who received clonidine had lesser incidence of shivering and also at lower temperatures when compared to group who received placebo with no significant difference in side effects like hypotension and bradycardia.

Clonidine in a dose of 2mcg/kg oral premedication can control shivering in patients undergoing surgery under regional anaesthesia with minimal side effects.

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