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COMPARISON OF THE EFFICACY AND POTENCY OF ORAL CLONIDINE AND TRAMADOL IN PERI-OPERATIVE SHIVERING IN GERIATRIC PATIENTS UNDERGOING TRANS-URETHRAL RESECTION OF PROSTATE UNDER SPINAL ANAESTHESIA

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ABSTRACT

Background: Shivering after subarachnoid block has various deleterious effects. Can be prevented and treated by various non pharmacological and pharmacological methods. Both of these act as synergistic to each other. **Objective:** To compare the efficacy, potency, hemodynamic effects and side effects of oral clonidine and tramadol in geriatric patients under spinal anaesthesia. **Methods:** A total of 150 patients undergoing TURP under spinal anaesthesia were randomly divided into GC (50) received oral clonidine 150microgram, GT (50) recieved oral tramadol 50mg, GP (50) recieved placebo preoperatively. In the intraoperative and postoperative period, grades and incidence of shivering were noted in all three groups and treated, if required. **Results:** Severity grades and incidence were low in group C and group T than group P however goup T had higher incidence and grades than group C. Both decreases incidence and grades of shivering and need of rescue doses. However, clonidine is better than tramadol but causes sedation. **Conclusion:** prophylactic oral clonidine and tramadol are effective in preventing shivering without side effects, with oral clonidine better than tramadol.

KEYWORDS: Shivering, tramadol, clonidine, TURP, subarachnoid block.

INTRODUCTION

In homoeothermic species, a thermoregulatory system coordinates and defenses against environmental temperature change to maintain internal body temperature within a narrow range, thus optimising normal body function. The processing of thermoregulatory response has three components: (A) Afferent thermal sensing, (B) Central regulation, and (C) Efferent response.

Shivering, an involuntary and oscillatory muscular activity, is a physiological response to core hypothermia in an attempt to raise the metabolic heat production of the human body1.Shivering is elicited when preoptic region of of hypothalamus is cooled. Efferent shivering pathways arises and descends from posterior hypothalamus. Increase in muscle tone during shivering is due to temperature induced changes in neuronal activity in mesencephalic reticular formation and dorsolateral pontine and medullary reticular formation. Synchronisation of motor neurons during shivering may be mediated by reticular inhibition through renshaw cells, a group of inhibitory interneurons 2. pre-existing high grade fever, infusionof contaminated fluids.

Causes of Perioperative Shivering

1) Perioperative hypothermia 2) Neuronal blockade induced inhibition of thermoregulatory mechanisms 3) Infusion of cold fluids, transfusion reactions, drug reactions, pre-existing high grade fever, infusion of contaminated fluids.

Neuronal blockade impairs regulation of body temperature, with the initial decrease in core body temperature, due to initial heat redistribution from core to periphery due to vasodilatation 3. Failure of vasoconstriction below the level of blockade promote ongoing heat loss, thus cannot reestablish core body temperature equilibrium. Shivering in these patients produce little amount of heat because it is restricted to the small muscle cephalad to block, as there is impaired perception of temperature in blocked dermatomes by the hypothalamus which senses elevation in skin temperature5. Shivering is associated with substantial adrenergic activation 5 and discomfort6.

Prevetion of Shivering

Maintaining normothermia may prevent shivering during regional anesthesia8.There are v arious methods available to control shivering during anesthesia, which include non-pharmacological and pharmacological methods.1Non Pharmacological Methods: 1) forced air

warming most effective8) 2) warming blankets 3) warm fluids 4) increasing the ambient temperature of operating room 5) preventing convective heat loss by insulation with surgical drapes and space blankets etc. Any method or combination of methods that maintain core body temperature above 36^{0C} is adequate.2Pharmacological Methods: Various pharmacological therapies aim to prevent or treat shivering include: opioid, ketamine, propofol, granisteron, doxapram, clonidine, tramadol, physostigmine, magnesium sulphate.

MATERIAL AND METHODS

This prospective randomised and double blind study entitled "To compare the efficacy and potency of Oral clonidine and tramadol in peri-operative shivering in geriatric undergoing trans-urethral resection of prostate under spinal anaesthesia", was conducted in SKIMS in the department of anaesthesia from 2015-2017 after approval from hospital ethical committee.

After taking approval of hospital ethical committee along with written informed consent, 150 male geriatric patients (ASA Grades I-III), scheduled for elective TURP under subarachnoid blockade (SAB) were enrolled in the study. Patients in the study were randomised to receive either oral clonidine, oral tramadol, or placebo.One day prior to surgery pre-anaesthetic visit was performed.Patients were kept overnight fasting, sedated with tablet Alprazolam (0.25 mg) on the night before surgery.Patients were randomly allocated in three groups (50 patients in each group). All received a sealed envelope of an oral formulation 90 min prior to surgery.

GROUP C received oral clonidine 150µg GROUP T received oral tramadol 50mg GROUP 3 received oral placebo tablets.

Group C	Group T	Group P
Clonidine 150mg	Tramadol 50mg	Placebo

Anaesthesiology department technicians who were not involved in study prepared these trial preparations. They recorded the group randomisation separately, such that anaesthesiologist recording data and caring for the patient was unaware of what preparation contained or which group patient belongs to.

All operations were performed in the operation theatre which was maintained at constant ambient temperature and humidity.On arrival to operation theatre intravenous line was established and ECG, pulse oximetery, non-invasive blood pressure and temperature probe attached and monitored. Under all asceptic precautions sub-arachnoid block was performed with bupivacaine (0.5%, hyperbaric) 2.5-3cc (12.5-15mg) in sitting position using 25gauge

Quincke's needle at L3-L4 intervertebral space. Patients were made supine following the block and block level upto T_9-$T_{10}$was achieved. Warmed (to body temperature) intravenous and irrigating fluids were used.Patients wore cotton surgical drapes and no means of active warming was used until deemed essential.

Heart rate, respiratory rate, non-invasive blood pressure,arterial oxygen saturation(SpO_2), skiin temperatures (axillary using temperature probes), were monitored and noted.The grades of shivering were observed by observer at a period of 0 minutes (before sub arachnoid block), 15 minutes, 30 minutes, 45 minutes, 60 minutes, 90 minutes after sub arachnoid block as per grades similar to those used by Wrech et al. Shivering if occurred was treated in all cases with reassurance, warm blanket, injection tramadol 1mg/ kg intravenously. Associated conditions such as nausea, vomiting, hypotension and bradycardia were recorded. Bradycardia (HR < 50) was treated with injection atropine 0.6 mg intravenous. Hypotension was treated with rapid infusion of fluids, head down position, and incremental doses of injection ephedrine 6 mg intravenously. Nausea and vomiting was treated with metaclopromide.

Inclusion Criteria: 100 Geriatric male patients (age > 60), ASA GRADE 1 to 3, scheduled for elective. TURP under sub- arachnoid block were enrolled in this study.

Exclusion Criteria: Patients with following features were excluded from the study, who were allergic to clonidine, obese, febrile, history of ischemic heart diseases, thyroid disease, cerebrovascular disease, severe diabetic autonomic neuropathy, contraindications to regional anaesthesia, renal insufficiency, pre-existing neurological and spinal disease.

RESULTS

A total of 150 patients were enrolled in the present study and were randomized into three groups of 50 each (n=50), Both the groups were comparable with respect to age, sex, weight, duration of surgery, type of surgery, volume of intravenous fluid administered and the duration of spinal block. The mean age and weight of the patients in group C was 65.8± 3.79years and68±7.29kgs and patients in Group T, 66.2 ± 3.58years68.5±6.28 patients in Group P, 66.9± 3.99 years67.1±8.63 respectively. group C had 33 ASAI,14 ASAII, 3 ASA III,group T had 36 ASAI,14 ASAII,0ASAIII andgroup P had 32 ASA I,17 ASAII,1 ASAIII patients respectively haemodynamic parameters heart rate, blood pressure,axillary temperature,oxygen saturation had no statistical significance. Duration of surgery were 37.6

minutes in group C, 40 minutes in group T and 38.9 minutes in group P. Both the drugs were found to be effective in reducing shivering.Complication rates were significantly higher in group T than in group C.3 patients in group C, 7 patients in group T and 2 patients in group P developed dizziness, nausea and vomiting.

3 patients in group C, 1 patient in group T and 2 patients in group P developed bradycardia.8 patients in group C, 6 patients in group T, and 2 patients in group P developed hypotension.

Showing incidence of shivering among various groups at various intervals of time

Patients who shivered at	Group C		Group T		Group P		P-value
	No.	%age	No.	%age	No.	%age	
0 Min	-	-	-	-	-	-	-
15 Min	3	6	5	10	11	22	0.043*
30 Min	2	4	3	6	10	20	0.015*
45 Min	4	8	4	8	14	28	0.005*
60 Min	1	2	4	8	12	24	0.002*
90 Min	2	4	3	6	7	14	0.212

Intergroup comparison based on shivering among various groups

Time interval	P-value		
	C vs T	C vs P	T vs P
0 Min	-	-	-
15 Min	0.712	0.043*	0.102
30 Min	0.646	0.014*	0.037*
45 Min	1.000	0.009*	0.009*
60 Min	0.362	0.001*	0.029*
90 Min	0.646	0.162	0.317

Showing grades of shivering among various groups

Grades of Shivering	Group C		Group T		Group P		P-value
	No.	%age	No.	%age	No.	%age	
Grade I	7	14	8	16	12	24	0.003*
Grade II	5	10	6	12	10	20	
Grade III	0	0	5	10	18	36	

Severity grades and incidence were low in group C and group T than group P, however, goup T had higher incidence and grades than group C.Both decreases incidence and grades of shivering and need of rescue doses. However, clonidine is better than tramadol but causes sedation.

DISCUSSION

Heart rate, systolic blood pressure, diastolic blood pressure were recorded at regular intervals between three groups. On comparison between three groups, no statistical significant difference was found (P > 0.05).

This result is in accordance with study concducted by Usha Shukla et al in 2011,[9] Claudia Stepelfeldt et al (2005),[10] Donal Buggy et al in 1997,[11] and Anurag Tewari et al in 2014,[12] Ebrahim Alijanpour et al in 2016,[13] in which they concluded that both clonidine and tramadol control postoperative shivering.Intraoprtively axillary temperature was recorded at regular intervals. In our study there was no statistically significant difference of axillary temperature between three groups, although there was fall in temperature during shivering among all groups compared with the baseline value.This is in accordance with studies conducted by Bhaarat et al in 2008,[14] Bansal and Jain in 2011,[15] Usha Shukla et al in 2011,[16] Anurag Tiwari et al in 2014.[17] we could not measure the core body temperature because probe needs to be put in the esophagus or near tympanic membrane which are uncomfortable and unacceptable in patients. In various studies, the prevalence of shivering in neuraxial blocks was suggested as 40-70%,[19] In our study the prevalence of shivering is 48%. Shivering was compared between three groups at arrival in operation theatre and at fifteen minute intervals after subarachnoid block for a period of 90 min.In group C 46 patients (92%) did not shiver while 4 patients (8%) did shiver. All the patients experienced shivering of grade 1and grade 2. None had grades 3 or 4.

In the group T, 5 patients (10%) experienced shivering while 45 patients (90%) did not shiver. All patients experienced grades 1-3 shivering. In the group P, 24 patients (48%) patients experienced shivering while 26 patients (52%) did not shiver. All experienced different grades of shivering (grade 1-4). On comparison of incidence of shivering among group C versus group P, and group T versus group P, a statistically significant variation was seen (P< 0.05) whereas group C versus group T has statistically insignificant variation. This is in accordance with study conducted by **Anurag Tiwari et al in 2014(16).**

The results of present study are consistent with those of study conducted by Mayo et al, **Tewari et al[12] Dhorigol et al[17] Vanderstappen et al[18]** Various studies have shown that tramadol can reduce the incidence, duration, and severity of postoperative shivering.[20,21,22] **Bilotta et al[23]** and **Chan et al[24]** found that 0.5-0.25mg/kg of intravenous tramadol are effective in controlling shivering after neuraxial blocks. **Gangopadhyay et al (25)** achieved

useful results regarding that 1mg/kg of intravenous tramadol was effective in controlling post-spinal shivering. However, **Mathew et al**[21] compared tramadol and saline administration in shivering prevention and found that the incidence of shivering in the tramadol group showed a significantly lower level than in the control group. **De Witte et al**[19] showed that high doses of tramadol administration were effective in preventing postoperative shivering in all patients.The patients from the three groups were observed for hypotension, bradycardia, nausea and vomiting. Cloniodine is known to cause hypotension and bradycardia, but in our study the incidence of hypotension and bradycardia in the study group was comparable with the placebo group, which is in accordance with other studies conducted by **Dhorigol et al (2010)**[17] **Sia et al (1998)**[26] **Tewari et al (2006)**[27]

Tramadol increases the chances of nausea and vomiting, but in our study, the rate of nausea and vomiting in the tramadol group has no significant difference when compared to placebo group. Similar results are reported in previous many studies28,[20] **Gangopadhyay et al**[25] observed significant number of cases of nausea and vomiting in tramadol as compared to placebo group; this high number of cases in the tramadol group can be explained by the fact they used tramadol at 1mg/kg intravenous as compared with 50mg oral in our study.

CONCLUSION

Prophylacticaly administered oral clonidine and tramadol can be effective in preventing perioperative shivering without side effects, with oral clonidine better than oral tramadol, after subarachnoid block in patients undergoing transurethral resection of prostate.Oral clonidine and tramadol are cheap and easily available than their intravenous counterparts. It might be rational to use them as a preventive medication before subarachnoid block to prevent post-subarachnoid block shivering.

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