Comparison of ondansetron and tramadol for prevention of shivering in patients undergoing lower limb surgery under spinal anesthesia

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ABSTRACT

Introduction: Shivering is a common and unpleasant phenomenon in patients undergoing spinal anesthesia that leads to several complications. The purpose of this study was to compare the incidence and severity of shivering in patients who received ondansetron and tramadol preemptively for the prevention of intra-operative shivering. **Methods:** A prospective, observational, comparative study was conducted on 100 patients, of both genders, aged 18 to 60 years with an American Society Anesthesiology Physical Status I or II, undergoing lower limb surgeries under spinal anesthesia. Patients were randomly assigned to two study groups, ondansetron (Group ON) or tramadol (Group TM) according to the medication they received 30 minutes before spinal anesthesia. The incidence of peri-operative shivering, grades of shivering, skin temperature changes and adverse effects were observed. **Results:** Group TM had significantly less shivering than Group ON. In group ON, 37.5% had grade 1, 8.3% grade 2, and 4.1% grade 3 shivering. Group TM had 14.8% grade 1, with no higher-grade shivering. The difference in intensity was also significant. A significant drop in axillary temperature was observed at 75 and 90 minutes post spinal anesthesia. Complications were significantly higher in Group TM, with 25 patients experiencing nausea, vomiting, or sedation, compared to just one patient in Group ON. **Conclusions:** Tramadol was more effective than ondansetron in preventing intraoperative shivering, however, Ondansetron was better tolerated with lower incidence of nausea and vomiting.

Keywords: Ondansetron, prevention, shivering, spinal anesthesia, tramadol.

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INTRODUCTION

Spinal anesthesia (SA) is commonly used for both elective and emergency surgeries involving lower abdomen and lower limbs. SA inhibits tonic vasoconstriction and causes redistribution of core heat from the trunk (below the block level) to the peripheral tissues predisposing patients to hypothermia and shivering.[1] Perioperative shivering, is an involuntary, oscillatory muscular activity that augments metabolic heat production up to 600% above the basal metabolic level.[2] It is an unpleasant, discomforting phenomenon occurring during and after surgery with complications ranging from mild discomfort to generalized continuous muscle contraction with prevalence ranging between 40-80%.[3–5]

Shivering can be associated with increased adrenergic and sympathetic hyperactivity which causes a high metabolic rate, which in turn can lead to increased oxygen consumption, hypoxia and its sequelae.[6] Beside patients' discomfort, it is also associated with increased pain, bleeding, delayed wound healing as well as increased intracranial, intraocular pressure and lactic acidosis.[7] Effective treatment of post-operative shivering is imperative as there

is increasing evidence of significant benefits of maintaining normothermia in patients undergoing surgery.[8] Several studies have been conducted using both pharmacological and non-pharmacological methods for the management of perioperative shivering. Non-pharmacotherapy such as active cutaneous warming using electric heating, water-circulating garments, forced-air warmer and radiant heating has been effective in the management of shivering.[6] Non-pharmacological methods are effective in maintaining normothermia and controlling shivering once it begins, but these equipments are either unavailable or limited in our settings. Similarly pharmacological agents such as such as opioids, α2-agonists, anticholinergics, central nervous system stimulants, 5-HT3 antagonist and corticosteroids has been used for the management of perioperative shivering.[6,9] Ondansetron, a 5-HT3 antagonist, is a commonly used antiemetic drug during intraoperative as well as post-operative period.[10] There are different studies conducted demonstrating the anti-shivering effect of ondansetron following both general and regional anaesthesia.[11–13] Tramadol, a commonly used opioid in perioperative period is associated with a lower risk of respiratory depression, drug tolerance, and drug dependence, is also used for the treatment and prevention of shivering.[14,15] The mechanism of anti-shivering effect of tramadol is through serotonergic and noradrenergic receptors.[4] Various drugs have also been used successfully to control shivering after its occurrence but there are very few studies which have used preemptive pharmacological measures.

This study aimed to compare the incidence and severity of shivering in patients undergoing lower limb orthopedic surgeries, using two commonly used drugs in anesthesia practice, ondansetron and tramadol, administered preemptively for their anti-shivering properties.

METHODS

This is a prospective, observational, comparative study, conducted at Shree Birendra Hospital, Kathmandu, Nepal. The study was conducted after ethical clearance from Institutional Review Committee of Nepalese Army Institute of Health Sciences (NAIHS) (Ref.No.1143), from February to May 2025. Sample size was calculated based on similar study by Mushtaq et al. where the incidence of post-operative shivering was 31.4% with ondansetron and 8.6% with tramadol.[16] Considering confidence interval of 95% and power of study to be 80%, sample size was calculated to be 50 patients in each group. Patients aged 18 to 60 years undergoing elective lower limb orthopedic surgeries under SA with American Society of Anaesthesiology Physical Status (ASAPS) I and II were included in this study. Patients with known history of allergy to study drugs or any other opioids, severe renal or hepatic impairments, pregnant or lactating mothers were excluded from the study. Similarly, patients on medications known to reduce post-operatives shivering and patients with diseases associated with shivering or pyrexia, and any contraindication to regional anesthesia were also excluded from the study.

Written informed consent was obtained from all patients participating in the study. The temperatures in the operation theatre and post-operative ward were maintained at 24 degree Celsius (°C). Patients were taken in the operation theatre (OT) after confirming their identity and nil per oral (NPO) status. In the OT, monitors were attached and intravenous (IV) access was obtained. The iv fluids used in the peri-operative period were at room temperature. Patients received injection Ondansetron- 4mg or Tramadol-50mg, 30 minutes before administrating SA. The injections were given by the anesthesiologist/ anesthesia resident who were not a part of the study. Patients receiving iv ondansetron as prophylaxis were labelled as group ON, whereas, patients receiving iv tramadol were labelled group TM. Monitoring of heart rate, systolic and diastolic blood pressure, pulse oximetry and ECG were done throughout the procedure. Baseline preoperative skin temperature was also noted in all the patients using a skin probe kept in the axilla near the vicinity of axillary artery. Temperature was noted every 15 minutes intra-operatively and for two hours after surgery. Spinal anesthesia was delivered according to department protocol with bupivacaine heavy and when the desired level of block was obtained surgery was started.

The occurrences and intensity of shivering intra-operatively as well as during the post-operative period was assessed using the Crossley and Mahajan shivering scale.[17] (Table 1)

Table 1: Crossley and Mahajan shivering scale

Grading	Description
0	No shivering
1	No visible muscle activity, one or more of piloerection, peripheral vasoconstriction or peripheral cyanosis (other cause excluded)
2	Muscular activity in only one muscle group.
3	Moderate muscular activity in more than one muscle group, but not generalized shaking
4	Violent muscular activity that involves the entire body

Patients who had severe grades of shivering was managed with other warming measures. Incidence of side effects of the study drugs such as nausea, vomiting and sedation was also noted and managed as per the institutional protocol. Ramsay sedation score was used for assessing sedation.[18]

Data was collected using a proforma and statistical analysis was done using Statistical Package for Social Sciences (SPSS), version 16.0. Descriptive statistics was used to summarize demographic variables. Categorical data were expressed as frequencies and percentage and numerical data were expressed as mean±SD. Chi-square test was used to compare categorical variables. Mean shivering grades in both groups were compared using Student's t-test. P-value < 0.05 was considered statistically significant.

RESULTS

Among the 100 patients enrolled in this study, two patients in ON group were omitted from the study because of extended surgery time in one patient and hemodynamic instability in the other. Similarly, three patients were omitted in TM group due to extended surgery time in one and hemodynamic instability in two patients.

The two groups were comparable in terms of demographic profile (age, gender, weight), ASA PS status and duration of surgery. (Table 2)

Table 2: Demographic profile, ASA PS status and duration of surgery

	Group ON	Group TM	p-value
Total number of patients	48	47	
Age	38.96±13.33	42.11±13.8	0.261
Weight	66.67±6.72	68.55±7.25	0.192
Gender (Male/ Female)	38/10	30/17	0.98
ASA PS (ASA I/ASA II)	23/25	23/24	0.921
Duration of surgery (in minutes)	145.63±172.20	104.26±28.89	0.108

Shivering was significantly lower in Group TM (mean shivering grade 15±0.36) than in Group ON (0.67±0.36) with p-value of 0.000. On comparing the intensity of shivering, 37.5 % had grade 1, 8.3% had grade 2 and 4.1% had grade 3 and none of the patients had grade 4 in ON group. In TM group 14.8 % developed grade 1 shivering whereas there were no patients who developed shivering grades 2, 3 or 4. The difference between the two groups was found to be statistically significant with p-value of <0.001. Grades of shivering in each group are shown in Figure 1.

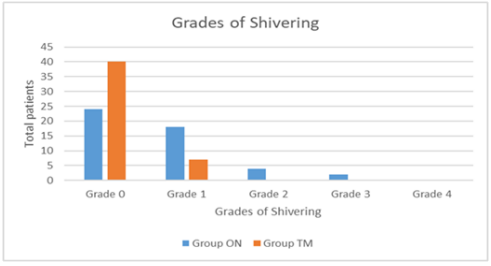

Figure 1: Bar diagram showing grades of shivering between two groups

Both groups were also comparable with respect to baseline axillary temperature but without statistical significance (p value 0.38). The drop in temperature was noted from 30 to 90 minutes after SA in both groups with significant drop in temperature between 75 minutes (p value 0.028) and 90 minutes (p-value=0.044).

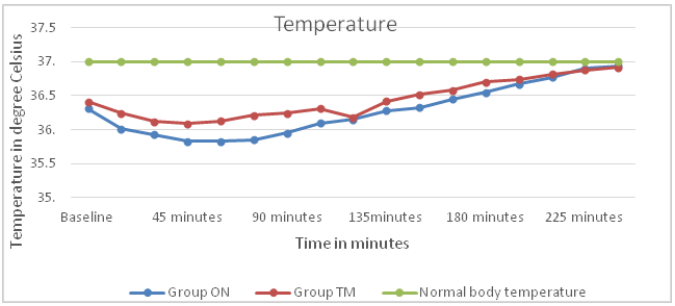

Figure 2: Line diagram showing axillary temperature changes during anesthesia between two groups

Sedation score was comparable between the two groups with p-value of 0.075. Most patients remained alert with the Ramsay Sedation score of 2 while only three patients in Group TM had a sedation score of 3.

The incidence of complications were higher more in Group TM than in Group ON with a p value of <0.001. Complications in ON group included nausea in one patient whereas in group TM 20 patients had nausea, one patient experienced nausea plus vomiting and four patients had nausea plus sedation.

DISCUSSION

Shivering occurs commonly during general and spinal anesthesia in the perioperative period. Mostly overlooked, shivering is a preventable complication of anesthesia. Besides causing discomfort to the patients shivering can lead to adverse effects including increased oxygen consumption, lactic acidosis, raised carbon dioxide production and increased left ventricular systolic work index.[19,20] Combating shivering after its occurrence results in slower heat recovery as the patient is deprived of important defense mechanisms against reduction of core temperature during anaesthesia; therefore shivering should be prevented, thereby offsetting hypothermia.[5]

This study demonstrated prophylactic use of both tramadol and ondansetron was effective in preventing shivering after spinal anesthesia. However, the incidence of shivering was lower in tramadol group as compared to ondansetron, but the incidence of adverse effects was higher in tramadol group. Both tramadol and ondansetron cause serotonin reuptake inhibition hence both have an important role in

shivering control.[20]

Effective shivering control with tramadol and ondansetron was noted in several studies and the anti-shivering effect of tramadol was also found to be superior to ondansetron.[16,20,21] In all these studies the study drug was given only after the occurrence of shivering whereas in our study preemptive medications were used. This superiority of tramadol suggests that the shivering process not only involves serotonin (5-HT3) but also noradrenaline.

Similar findings were observed in a study done by Lakhe et al. where the incidence of shivering decreased by 40% and 46.7% after prophylaxis with ondansetron and tramadol respectively.[22] The superiority of one drug over the other was also not found to be statistically significant in their study. The difference in results could be due to different time of administration of drug, their onset and duration of action as in their study the drugs were administered immediately after depositing the local anesthetics into the intrathecal space, while patients in our study received the study drug half an hour ahead of the procedure.

This study also compared the intensity of shivering in each group and though none of the patients had severe shivering (grade 4), in the ON group grades 1, 2 and 3 of shivering was observed in more patients than in TM group. Similar findings were observed in the study done by Mustaq et al. where higher grades of shivering were observed with ondansetron compared to tramadol.[16] However, Chagaleti et al. demonstrated that the severity of shivering was comparable between ondansetron and tramadol.[21,23]

Drop in axillary temperature was noted after 30 to 90 minutes after SA in both groups. It reached a minimum of 35.8°C in ON group and 36°C in TM group. The difference was statistically significant between the two groups at 75 minutes and at 90 minutes. Findings in our study were consistent with a study done by Lakhe et al, where significant drop in axillary temperature was also noted from 30 mins to 90 mins after SA.[22] Studies done by Chowdhury et al. and Mushtaq et al. also measured the axillary temperature at various intervals of time during anesthesia but no statistically significant change in temperature in either group was observed.[16,21] Chagaleti et al. observed no difference in reduction in core and skin temperatures intra-operatively when comparing tramadol and ondansetron.[23] However, Onyekwul et al., compared different doses of tramadol with normal saline and they observed significant reduction in tympanic temperature.[24] The probable mechanism of action of tramadol and ondansetron in thermoregulation could be attributed to inhibitory action of serotonin (5-HT) on the anatomic and physiologic pathways of both central and peripheral thermoregulation.[15,16]

In this study, though patients in TM group were more sedated than ON group, sedation score was comparable between the two groups and most patients remained alert throughout the anesthesia procedure. Similar findings were observed in the studies by Chagaleti et al. and Chaudary et al. where patients receiving tramadol had higher sedation score but the score was comparable with patient in ON group.[21,23] In contrast to our findings several study conclude that incidence of sedation with tramadol was significantly high[16,22,24] The tendency of tramadol to cause more sedation than ondansetron may be because of its partial agonist action at μ-opioid receptors.[16]

In our study, the incidence of complications such as nausea and vomiting was significantly higher with tramadol. Ondansetron is known to prevent nausea and vomiting, as it has powerful antiemetic effect. Similar findings were seen in several studies.[21,24–26] No significant difference in the occurrence of nausea and vomiting was however observed in studies conducted by Chagaleti et al.[23]

There are some limitations of this study. The main one being measurement of axillary temperature instead of the core body temperature. However, both the groups were exposed to the same environment. Pre-operative volume status and intraoperative hemodynamic changes were not considered which are important factors and could have also made a difference in the result.

CONCLUSIONS

This study concluded that preemptive tramadol and ondansetron were both effective in preventing peri-operative shivering in patients undergoing lower limb surgeries under spinal anesthesia with tramadol being superior to ondansetron. However, the use of tramadol could be limited due to complications like sedation and nausea and vomiting whereas ondansetron being an effective antiemetic could find more use.

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AUTHORS' CONTRIBUTIONS

MR designed the research, collected data, performed statistical analysis, and prepared the original draft of the manuscript. AS explained and interpreted the data and contributed to revision of the manuscript. PT and BRA were involved in the visualization, supervision and data analysis. KT reported and collected the data. All the authors have read and approved the final version of the manuscript.

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