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A Comparative Study; Prophylactive Intravenous Ketamine and Tramodol in Preventing Intraoperative Shivering in Patients Undergoing Elective Lower Limb Surgery Under Spinal Anaesthesia

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ABSTRACT

Objective: The aim of this study was to evaluate the effectiveness of prophylactic intravenous ketamine in the prevention of shivering during spinal anesthesia for elective lower limb surgery and comparing it with intravenous tamodol.

Method: After ethical committee approval and informed consent, 90 patients of American Society of Anesthesiologist (ASA) grades I and II of either sex, aged 18-60 years scheduled for elective orthopedic surgery of lower limbs under spinal anesthesia were randomized into three equal groups (envelope randomization). Just after intrathecal bupivacaine injection, all patients received prophylactically intravenous drug as either normal saline (Group S, n=30) or ketamine 0.5mg/kg (Group K, n =30) or tramodol 0.5mg/kg (Group T, no=30) for shivering. The incidence and the degree of shivering, the effectiveness and the side-effects of ketamine and tramodol in preventing shivering during intraoperative period were recorded.

Results: The groups were comparable regarding demographic characteristics. The hemodynamic parameters and the temperatures were also similar in the three groups and active warming was not required during intraoperative period. The intraoperative shivering was significantly less in Group K than in the Group S ($p < 0.05$). In Group S, eighteen (18) patients reached grade 2 shivering and were subsequently treated with tramodol. In Group K, three (3) patients reached grade 2 shivering. In Group T, two (2) patients reached grade 2 shivering. At 30 min after anesthesia, there were no differences between the groups regarding the grade of shivering ($p>0.05$). None of the patients required a second dose of tramodol for grade 2 shivering within 30min period.

Conclusion: Prophylactic ketamine had a similar efficacy as compared to that of tramodol in preventing shivering during spinal anesthesia in elective lower limb surgery.

Keywords: Ketamine, Tramodol, Shivering.

INTRODUCTION

Intraoperative shivering occurs in 50-60% of patients undergoing regional anesthesia.[1,2] This may be normal thermoregulatory shivering in response to core hypothermia or may result from the release of cytokines by the surgical procedure. Intraoperative shivering is very unpleasant and physiologically stressful. It may also cause complications, especially in the patients with coronary artery disease, because of associated increase in oxygen consumption by 1-6%.[3,4] These complications can lead to cardiovascular and neurological deficits, as well as organ damage. Shivering if not treated, may detrimentally impact patient outcomes, prolong recovery, and prolong hospitalization. Intraoperative Shivering also interfere intraoperative monitoring like ECG, SpO_2 and blood pressure, which may pose patient safety issues.[8,10]

Different drugs have been evaluated for preventing and treating shivering, however, a "gold standard" drug treatment has not been defined. Among the drugs, opiates are most potent drugs used for shivering (especially the pethedine). However, the opiates are associated wide-ranging and unpredictable side effects, including respiratory depression, hypo-tension, sedation, itching, nausea, and vomiting. (12) So we conducted the present study to evaluate and compare the efficacy and safety of prophylactic intravenous ketamine for prevention of shivering in patients undergoing elective lower limb surgery under spinal anesthesia.

METHODS

After ethical committee approval and informed consent, 90 patients of American Society of Anesthesiologist (ASA) grades I and II of either sex, aged 18-60 years scheduled for elective orthopedic surgery of lower limbs under spinal anesthesia were randomized into three equal groups (envelope randomization). Patients with known history drug medications which likely to alter thermoregulation, patients with history of alcoholic, hypothyroidism or hyperthyroidism, cardiopulmonary disease, psychological disorders, a need for blood transfusion during surgery were excluded from the study. After insertion of 18G intravenous cannula in the left arm, a 10ml/kg of lactated ringer's solution was started before spinal anesthesia which was preheated to 37^{o}C in warmed cabinet and infused over 30 minutes. The infusion rate was then reduced to 6ml/kg/hr. Heart rate, mean blood pressure (MAP), and peripheral oxygen saturation were recorded using standard noninvasive monitors before intrathecal injection and thereafter recorded at 5min, 10min, 15min, 20min, 25min and 30 min. The body temperature was recorded before intrathecal injection and then 10min intervals during preoperative period. The ambient temperature was maintained at 24^{o}Cwith constant humidity. After appropriate patient position, strict septic and antiseptic precautions intrathecal injection of hyperbaric bupivacaine (0.5%), 3ml was injected using 25G Quincke spinal needle at L3-L4 or L4-L5 interspaces. The patients were randomly allocated to receive intravenous bolus of either normal saline (Group S, n=30) or ketamine 0.5mg/kg (Group K, n=30) or tramodol 0.5mg/kg (Group T, no=30) immediately after intrathecal injection. The treatment drugs were diluted to a volume of 2.5ml and presented as coded syringes by an anesthesiologist who was blinded to the group allocation. Supplement oxygen (5lit/min) was delivered via a mask during the operation. The presence of shivering was observed by an observer blinded to the study drug administered. Shivering was graded

using a scale similar to that validated by Tsai and Chu: (5) 0-noshivering; 1-piloerection or peripheral vasoconstriction but no visible shivering; 2- muscular activity in only one muscle group; 3-muscular activity in more than one muscle group but not generalized; 4- shivering involving whole body. During surgery shivering score was recorded at 5min intervals. If 15min after spinal anesthesia and concomitant of a prophylactic dose of one of the study drugs, grade 3 or 4 shivering was noted, the prophylaxis was regarded as ineffective and intravenous tramodol 25mg was administered. Side effects such as hypotension, nausea and vomiting, and hallucinations were recorded. Hypotension was defined as a decrease in mean arterial pressure of more than 20% from the baseline. If patients develop nausea and vomiting, intravenous metaclopramide 10mg was administered. Hallucinations as a side effect was defined as a false sensory experience, where the patient reported they saw, heard, smelled, tasted, and felt something that was non-existent. The attending anesthetist also assessed the degree of sedation on a five point scale: 1-fully awake and oriented; 2-drowsy; 3-eyes closed but rousable to command; 4- eyes closed but rousable to mild physical stimulation; and 5-eyes closed but unrousable to mild physical stimulation.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) Windows version 14. Mean differences between the three groups regarding age, weight and height were tested using analysis of variance (ANOVA). The x2 test was used to analyze the difference between gender, ASA class, the number of shivering patients, those who required analgesics and who had nausea and vomiting. A value of $p<0.05$ was taken as significant. Post hoc comparisons were performed using the Bonnferroni correction of the significances level. Power analysis showed that a sample size of 30 per group would be achieving 93% power in the x2 test with a significance level of 0.01 at group proportions of 0.6 and 0.1.

RESULTS

The demographic data and surgical characteristics were similar in each group (Table 1). The preoperative vitals (mean arterial blood pressure and heart rate) and the temperatures were also statistically similar in the three groups. The number of patients with intraoperative shivering was significantly less in Group K than in the Group S (Table 2). In Group S, 18 patients reached grade 2 shivering and were subsequently treated with tramodol. In Group K, 3 patients reached grade 2 shivering. In Group T, 2 patients reached grade 2 ($p<0.001$). At 30min after spinal anesthesia, there were no differences between the groups regarding grade of shivering (Table 2). None of the patients required a second dose of tramodol for grade 2 shivering within 30 min period after spinal anesthesia. Three patients in Group S, one patient in Group K and one patient in Group T had nausea ($p>0.05$). None of the patients had episodes of oxygen desaturation or respiratory depression during study. No hallucinations, tachycardia, hypotension or hypertension were seen in any of the patients.

DISCUSSION

Shivering during regional anesthesia is common and can be nearly as severe as that observed during general anesthesia.[6] Intraoperative shivering can be treated by skin surfaces warming, radiant heat application or pharmological agents. Shivering can be distressing to the patient and has been cited as one of the primary causes of discomfort during the

postoperative period.[7] Many physiological consequences are also associated with shivering. Among the most significant of these consequences is an increase in oxygen consumption by up to six times, which can cause rapid oxygen depletion, potentially leading to tissue death.[7,8,11] Additionally, shivering can result in increased heart rate, acidosis, increased intracranial tension, and increased carbon dioxide and stress hormone production.[8-10,12] These complications can lead to cardiovascular and neurological deficits, as well as organ damage. Shivering also interfere Intraoperative monitoring, which may pose patient safety issues.[8,10] Shivering if not treated during intraoperative may impact patient outcomes like prolong recovery and lengthen the period of hospital stay. Various methods have been used to prevent intraoperative shivering both pharmological and non-pharmological. Among drug 5HT3 receptor antagonist, α 2 receptor agonist, benzodiazepines and opiates have been evaluated for preventing and treating shivering.[8,10,12-14] However, a "gold standard" drug treatment has not been defined because varied actions of these drugs can result in wide-ranging and unpredictable side effects, including respiratory depression, hypotension, sedation, itching, nausea, and vomiting. The NMDA receptor is thought to play a role in the transmission of thermal signals to the brain and spinal cord.[16] Ketamine having antagonizing action on NMDA receptor is an inexpensive, widely available general anesthetic agent and Ketamine differs from other anesthetic agents as it produces a significant analgesic effect whilst rarely causing cardiovascular or respiratory depression.[15,17] Studies have shown that ketamine may prevent shivering at doses of 0.5mg/kg or less and this dose is much less than the dose used for induction in general anesthesia, ketamine 0.5mg/kg unlikely produce side effects associated with ketamine.[17] Though ketamine's role in preventing shivering is not fully understood, it appears that it is likely to affect thermoregulation through multiple mechanisms.[12,14] First, it is well documented that ketamine decreases core-to-peripheral redistribution of heat by preventing the vasodilatation that occurs with other anesthetic agents.[18]In addition, it is hypothesized that ketamine may prevent shivering by interfering with thermoregulatory control mechanisms in the brain.[10,12] Due to its unique properties, low cost, and wide availability, ketamine should be evaluated for its efficacy in preventing shivering.

In our study, we observed that in Group S (saline group) 18 patients (60%) reached Grade 2 shivering while only 2 patients (6.66%) in Group T (tramodol group) and 3 patients (10%) in Group K (ketamine group) reached grade 2 shivering. The incidences of side effects were comparative in Group T and Group K although groups did not differ significantly regarding patients characteristics. Studies investigating the anti-shivering role of ketamine and tramadol have shown similar results as our study. Sagir et al. also found ketamine 0.5 mg/kg i.v. to be effective in controlling shivering under neuraxial blockade.[19] Dalet al. witnessed significant results with ketamine 0.5 mg/kg i.v. to prevent shivering under general anesthesia.[21] Gangopadhyayet al.concluded that ketamine 0.5 mg/kg i.v. was effective in preventing shivering under spinal anesthesia.[22] Bilotta and co-authors also found that tramadol is promising drug in doses of 0.5 mg/kg and 0.25 mg/kg I, in controlling shivering under neuraxial blockade.[20.23] Tramadol has the potential to cause nausea and vomiting, but the incidence of nausea and vomiting in the study groups was comparable with the ketamine group. Similar results are reported in the literature.[23,24] Ketamine is known to

cause hallucinations, but none of the patients complained of hallucination in any of the groups.[19,21]

CONCLUSION

Prophylactic intravenous ketamine has a similar clinical efficacy compared to that of intravenoustramodol in preventing shivering during spinal anesthesia in elective lower limb surgery. There were no significant changes in the hemodynamic parameters and adverse effects.

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Table 1. Patient's characteristic of the three treatment groups.

	Group S	Group T	Group K
Age (yr)	43(18-60)	45 (18-60)	45 (20-60)
Sex (M/F)	23/7	23/7	24/6
Weight (kg)	67(6)	71(10)	65(9)
Height (cm)	164(6)	164(8)	162(9)
ASA I/II	25/5	26/4	26/4
Duration of surgery (min)	80.3(13.7)	78.0(12.5)	79.9(12.9)
Shivering grade 2	18	2	3
Data are given as mean (range), mean (SD) or absolute numbers.			

Table 2. No. of patients with different grades of shivering in the three treatment groups.

	Group S	Group T	Group K	P value
T5	18/4/2/6	30/0/0/0	30/0/0/0	<0.001
T10	10/2/12/6	27/1/2/0	25/2/3/0	<0.001
T20	23/1/6/0	28/1/1/0	25/5/0/0	<0.008
T30	28/2/0/0	30/0/0/0	28/2/0/0	0.088
T5- 5 min after anaesthesia, T10- 10 min after anaesthesia, T20- 20 min after anaesthesia, T30- 30 min after anaesthesia. P<0.01 between groups S and Group T, P<0.01 between groups S and Group K				