Original Article

Prophylactic Use of Ketamine and Tramodol for the Prevention of Intra-Operative Shivering in Lower Limb Surgeries Done in Spinal Anesthesia

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ABSTRACT

Objective: To determine the efficacy of prophylactic intravenous ketamine in the prevention of shivering during spinal anesthesia for elective lower limb surgery.

Study Design: Comparative study.

Place and Duration of Study: This study was conducted at the Department of Anesthesia, Allied hospital, Faisalabad and Anesthesia Department, PIC, Lahore from 30th Oct. 2019 to 30th April 2020.

Materials and Methods: Vital monitoring was done using standard monitoring equipment on hourly basis and later more frequently during the spinal procedure till the next half an hour. Body temperature was noted before, during and after the procedure at regular interval to rule out any hypo- or hyperthermia. The room temperature was controlled and was kept between 24-26^{0}C along with humidification of the theatre. Patients were divided into three groups: first group receiving intravenous (IV) bolus normal saline (Group S, n = 30) or second group of intravenous ketamine 0.5mg/kg (Group K, n=30) and third group of tramodol 0.5mg/kg (Group T, no=30).

Results: No of patients who had intra operative shivering was found to be significantly less in Group K as compared to that in Group S. On further analysis of patients in the Group S, 18 patients had grade 2 shivering level and had to be injected with tramadol after shivering was observed. 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. 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 ($p>0.05$).

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

Key Words: Shivering, Intraoperative Shivering, Ketamine, Tramadol

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INTRODUCTION

Shivering in patients on operation tables is a very common situation face by surgeons and anesthetists.

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According to an estimate it is seen in around half of the surgeries done on regional anesthesia.[1] This could be a normal phenomenon as part of the thermoregulation system of the body due to hypothermia or as a result of chemokines produced in the body as a result of incisions done. This state of patient's body couldbe upsetting for the surgeon as well as for the anesthetist, with an extra stress for the patents as well. Studies have shown that it can increase the oxygen consumption, patient of heart disease can end up into serious complications like organ damage.[2]

Intra operative Shivering can have drastic effects on the surgical outcomes like prolonged recovery time and increase in the stay in hospital. Even during the surgical procedure, vital monitoring can be disturbed.[3,4]

In line to treat this emerging complication faced by the surgical team, various drug trials had been done worldwide to prevent and/or treat it; still there is no "gold standard" drug identified. Among these

medications, opiates family of drugs along with its adverse effects, are found to be most potent, pethedine being on the top of the list. The adverse effects like respiratory depression, hypotension, sedation, nausea, and vomiting make these drugs difficult to use.[5]

The aim of this study was to evaluate and compare the efficacy and safety of prophylactic ketamine for prevention of shivering in elective lower limb surgery done under spinal anesthesia. The drug with better control of shivering will be recommended.

MATERIALS AND METHODS

Department of Anesthesia, Allied hospital, Faisalabad and Anesthesia Department, PIC, Lahore from 30th Oct. 2019 to 30th April 2020. After the approval and informed patient's consent, 90 cases of age 18 to 60 years falling in the category of American Society of Anesthesiologist (ASA) grade I and II, of either sex, admitted for an elective procedure of orthopedic system using spinal approach of anesthesia were randomized into three groups (using the envelope randomization method).

All patients with a history of a drug therapy taken before the operation which can change the thermoregulation response of the body; all cases with history of alcohol abuse, hypothyroidism or hyperthyroidism, cardiopulmonary disease, psycho-logical disorders, a need for blood transfusion during surgery were excluded.

All patients were given ringer lactate before the start of the procedure as per protocol. Initially it was given at a rate of 10 ml per kg in 30 mins and later reduced to 6ml per kg per hr. Vital monitoring was done using standard monitoring equipment on hourly basis and later more frequently during the spinal procedure till the next half an hour. Body temperature was noted before, during and after the procedure at regular interval to rule out any hypo- or hyperthermia. The room temperature was controlled and was kept between 24-26^{0}C along with humidification of the theatre. Patients were divided into three groups: first group receiving intravenous (IV) bolus normal saline (Group S, n = 30) or second group of intravenous ketamine 0.5mg/kg (Group K, n=30) and third group of tramodol 0.5mg/kg (Group T, no=30).

After taking proper antiseptic measures, intrathecal injection was injected (hyperbaric bupivacaine (0.5%), 3ml) through 25 G Quincke spinal needle between L3-L4 or between L4-L5 interspaces. immediately after intrathecal injection. Treatment drugs were given in diluted form upto 2.5 ml as coded syringes by the primary investigator.

Presence of intra operative Shivering was reported by an observer. Shivering was graded using a scale similar to that validated by Tsai and Chu: [5] 0 for no shivering; 1 for piloerection or peripheral vasoconstriction but no visible shivering; 2 for muscular activity (only one muscle group); 3 for muscular activity in >1 group but not generalized; 4 for shivering involving whole body. During the procedure and during the surgery, the shivering score was noted after each 5 min intervals.

If during the surgery, 15 min after spinal anesthesia and/or along with the prophylactic dose of one of the study drugs, shivering of grade 3 or 4 noted, the prophylactic dose 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 injected. Hallucination was defined as false sensory experiences irrespective of what was seen, heard, tasted or felt by the patients. The level of sedation was also accessed by the anesthetist with 5-point scale: 1 for fully awake & oriented; 2 for drowsy; 3 for eyes closed but responding on command; 4 for eyes closed but responding on mild physical stimulus; 5 for eyes closed but non responding on mild physical stimulus.

Analysis of the data was done using the SPSS (20). Difference of the means of three groups in regard to age, weight and height were analyzed using variance (ANOVA test). The x2 test was used for the analysis of variables like gender, ASA class, shivering patients, number of patients required analgesics and number of patients with nausea and vomiting. A value of p of < 0.05 was taken as significant. Post hoc comparisons were done using Bonnferroni correction of significance 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 as shown in the Table no. 1. The preoperative vitals (mean arterial blood pressure and heart rate) and the temperatures were also statistically similar in the three groups. No of patients who had intra operative shivering was found to be significantly less in Group K as compared to that in Group S as shown in the Table no. 2). On further analysis of patients in the Group S, 18 patients had grade 2 shivering level and had to be injected with tramadol after shivering was observed.

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.

Table No.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 No.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				

DISCUSSION

Intra operative Shivering with regional anesthesia is commonly observed by surgeons and anesthetists in the operation theatre. It can be sometimes of the same intensity as that seen during general anesthesia.[6] This intra operative shivering can lead to significant discomfort for the patients and even for the surgeon; with significant worsening of the morbidity in the post-operative period. It can be prevented and managed with the use of skin surfaces warming devices, radiant heaters and/or some pharmological agents.[7]

Many other physiological changes in the body can also present as shivering or can be linked to shivering. Most important of these changes is the rise of oxygen consumption to upto 6 times the normal, depleting the cells of oxygen and ending up into cell and tissue death.[7-9] Additionally, shivering can result in increased heart rate, acidosis, increased intracranial tension, and increased carbon dioxide and stress hormone production. These complications can lead to cardiovascular and neurological deficits, as well as organ damage. Shivering can also disturb the intraoperative monitoring. thus leading to prolong recovery and hospital stay.[8,10-12]

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.[13] However, a "gold standard" drug treatment has not been defined so far with 100% efficacy because of the variety of unpredictable adverse effects like fall in blood pressure, sedation, nausea, itching, depression of respiration and vomiting. Some scientists have concluded that these effects can be due to NMDA receptor.[14]

As Ketamine antagonizes the NMDA receptors, it can be used as prophylactic drug to prevent these shivering episodes. Ketamine is easily available agent and has minimal effects on the cardiovascular or respiratory system. Some studies have shown that at a dose of 0.5mg/kg or less ketamine can have no significant sedation and it can prevent shivering.[15] Although the mechanism of ketamine in prevention of intra operative shivering is still not known, but its seems like it could be due to the thermoregulatory changes in the brain and in the body due to different mechanisms like decrease in the core and peripheral heat distribution and prevention of peripheral vasodilatation.[16]

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 IV to be effective in controlling shivering under neuraxial blockade.[17] Dalet al. witnessed significant results with ketamine 0.5 mg/kg i.v. to prevent shivering under general anesthesia.[18] Gangopadhyay et al. concluded that ketamine 0.5 mg/kg i.v. was effective in preventing shivering under spinal anesthesia. Ketamine is known to cause hallucinations, but none of the patients complained of hallucination in any of the groups.[19]

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.[20]

CONCLUSION

Prophylactic intravenous ketamine has a similar clinical efficacy compared to that of intravenous tramodol in preventing shivering during spinal anesthesia in elective

lower limb surgery. There were no significant changes in the hemodynamic parameters and adverse effects.

Author's Contribution:

Concept & Design of Study:	Mohsin Riaz Askri
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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