Original Article

PROPHYLACTIC LOW DOSE KETAMINE IN PREVENTING PERI-OPERATIVE SHIVERING DURING SPINAL ANESTHESIA IN ORTHOPEDIC PATIENTS: A PROSPECTIVE RANDOMIZED DOUBLE-BLIND STUDY

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ABSTRACT

Background: After spinal anesthesia, shivering is reported to occur in 36 - 85 % of the cases. Physical techniques like external heating or pharmaceutical interventions are often used to avoid peri-operative hypothermia and shivering. This study aimed to assess the effectiveness of low dose ketamine in preventing peri-operative shivering during spinal anesthesia in orthopedic patients

Material and Methods: This was a prospective randomized double-blinded study done at the Department of Anesthesia and Pain Management, The Indus Hospital, and Health Network Raiwind Campus Lahore for four months. 60 patients were incorporated. Group 1 patients (n=30) were given a low dose of ketamine (0.2 mg/kg iv) after spinal anesthesia while group 2 patients (n=30) were given 5ml of saline after spinal anesthesia. Axillary/frontal temperature was measured at 0, 15, and 30 minutes after spinal anesthesia.

Results: In group 1, shivering was observed in 1 (3.33%), 1 (3.33%) and 3 (10%) patients after 0, 15 and 30 minutes respectively while in group 2, shivering was observed in 0 (00), 6 (20%) and 11 (36.67%) patients after 0, 15 and 30 minutes respectively (p=0.006). In group 1, rescue maneuver was used in 4 (13.33%) patients while group 2 rescue maneuver was used in 14 (46.67%) patients. This difference was statistically significant (p=0.005)

Conclusion: Our study concludes that prophylactic Low dose ketamine is effective in preventing peri-operative shivering during spinal anesthesia in orthopedic patients as compared to the placebo group.

Key Words: Ketamine, Shivering, Spinal anesthesia

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INTRODUCTION

In humans, thermal stimuli are processed at the anterior hypothalamus level. The typical core temperature of the human body is 36.5°C–37.5°C, with a 0.2–0.4°C inter-threshold range. If the temperature drops below this threshold, responses to warm the body are triggered.[1] Vaso-dilation caused by regional anesthesia enables heat transfer from the core to the periphery, resulting in vasoconstriction and shivering above the block level.[2] Shivering is described as a

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perceptible fasciculation or tremor lasting more than 15 seconds in the Jaw, face, trunk, head, or extremities.[3] After spinal anesthesia, shivering is reported to occur in 36 – 85 % of cases.[4,5] The thermoregulation system is affected by spinal anesthesia because it inhibits tonic vasoconstriction, which is important for the regulation of temperature.[6] Although the specific cause of shivering during spinal anesthesia is unknown, hypotheses have been proposed to explain it.[7-9] The heat is transferred internally from the core to the peripheral region. Increased heat loss from body surfaces exceeds metabolic heat generation due to the lack of temperature regulation vasoconstriction below the blockage. There is a 0.5° C reduction in vasoconstriction and a small rise in the sweating threshold, indicating altered temperature regulation.[10]
Shivering during regional anesthesia is impacted by a variety of different parameters, including the number of spinal segments blocked, old age, a high degree of the spinal blockade, and the usage of ingredients in spinal anesthesia, all of which may have an impact on the regulatory systems. One of the most common unpleasant adverse effects of surgery is perioperative hypothermia and shivering. Because of its ability to impede norepinephrine absorption into postganglionic sympathetic nerve terminals, ketamine plays a function in thermoregulation.[11,12] By inhibiting norepinephrine absorption into postganglionic sympathetic nerve terminals and directly stimulating central sympathetic nerves, redistribution of heat might be reduced by ketamine to the periphery from the core.[13] After regional anesthesia, ketamine was beneficial in the prevention and treatment of shivering, although patients had hallucinations.[11,14] This study was piloted to determine the role of prophylactic low dose ketamine i.e 0.25mg/kg in preventing peri-operative shivering with fewer hallucinations during spinal anesthesia in orthopedic patients.

MATERIAL AND METHODS

This was a prospective randomized double-blinded study done at the Department of Anesthesia and Pain Management, The Indus Hospital, and Health Network Raiwind Campus Lahore for four months (**March-June**). Study approval was taken from the hospital's ethical and research committee. The inclusion criteria for our study were ASA 1 patients of both genders having age ranged from 18 to 60 years enrolled for orthopedic surgery under spinal anesthesia while the exclusion criteria were patients having >30 kg/m2 BMI with uncontrolled hypertension, patients having coronary problems, patients having high intracranial and intraocular pressure, patients not willing for spinal anesthesia and patients having known psychiatric problems. The sample size was calculated according to a previous study by considering intraoperative shivering as the main outcome.[20] In this previous study, the intra-operative incidence of shivering was 42.5% in the saline group while it was 2.5% in the Ketamine group.
In the above study, the incidence of intraoperative shivering in the saline group was 42.5% and incidence in the ketamine group was 2.5%. By taking the difference of 40%, power of 80%, and 95% confidence interval, the sample size needed was 21 in each group. Therefore, a total of 30 patients were incorporated in each group to allow for withdrawal or dropout. They were categorized into groups 1 and 2. Randomization was done by the lottery method. Consent form in written was taken from all the patients. 30 patients were included in each group. Group 1 patients were given intravenous pre-filled syringe group 1 drug i.e 5ml low dose of ketamine (0.25mg/kg diluted to form 5ml) after spinal anesthesia while group 2 patients were given pre-filled syringe group 2 drug i.e 5ml of saline after spinal anesthesia. A standard dose of 2ml of 0.75% bupivacaine at L3/4 or L5/4 interspace was injected. Axillary/frontal temperature was measured at 0,15 and 30 minutes after spinal

anesthesia. The operating room temperature was maintained at 24-26 C°. by adjusting air conditioners. The presence of mild to moderate shivering was observed at 0,15 and 30min according to. The Bedside Shivering Assessment Scale (Table 1) and recorded. Rescue drug tramadol 20 mg was given in case of mild to moderate shivering. Data were analyzed statistically by using SPSS version 23. For qualitative data mean (SD) was calculated while for quantitative data, frequency (percentages) were calculated. For comparison of shivering between the two groups, the Chi-square test was used.

Table 1: The Bedside Shivering Assessment Scale

Score	Definition
0	None; no shivering noted on palpation of the masseter, neck or chest wall
1	Mild: Shivering localized to the neck and/or thorax only
2	Moderate: shivering involves gross movement of the upper extremities (in addition to neck and thorax)
3	Severe: shivering involves gross movements of the trunk and upper and lower extremities

RESULTS

In this study, a total of 60 patients were included. There were 24 (80%) males and 6 (20%) females in group 1 while in group 2, there were 21 (70%) males and 9 (30%) females. (Figure 1) The mean (SD) age in group 1 was 37.24 (12.79) years while in group 2, the mean age was 37.43 (12.54) years. (Table 2) In group 1, shivering was observed in 1 (3.33%), 1 (3.33%) and 3 (10%) patients after 0, 15 and 30 minutes respectively while in group 2, shivering was observed in 0 (00), 6 (20%) and 11 (36.67%) patients after 0, 15 and 30 minutes respectively (p=0.006). (Table 3) In group 1, rescue maneuver was used in 4 (13.33%) patients while group 2 rescue maneuver was used in 14 (46.67%) patients. This difference was statistically significant (p=0.005) (Figure 2)

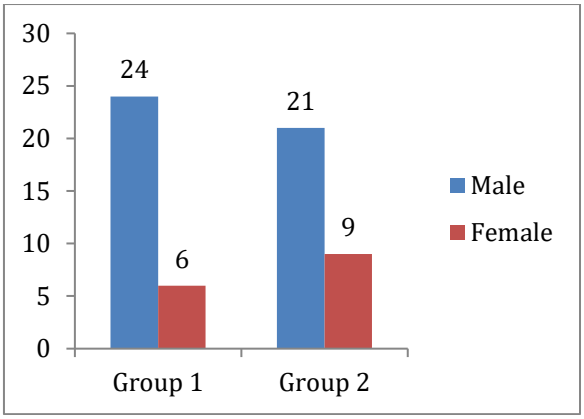

Figure 1: Gender wise distribution of patients in both the groups

Table 2: Age-wise distribution of patients in both the groups

Parameter	Group 1 (Years)	Group 2 (Years)
Mean age	37.24	37.43
Standard deviation	12.79	12.54

Table 3: Comparison of shivering in both the groups

Shivering	Group 1 N (%)	Group 2 N (%)
Shivering at 0 minutes	1 (3.33%)	0 (00)
Shivering at 15 minutes	1 (3.33%)	6 (20%)
Shivering at 30minutes	3 (10%)	11 (36.67%)

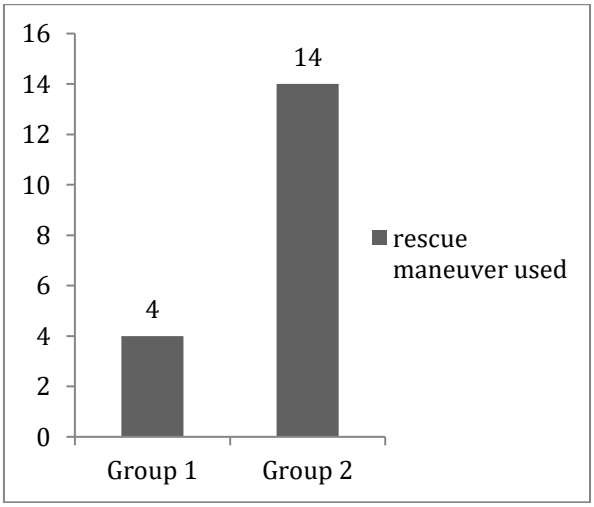

Figure 2: Rescue maneuver used in both the groups

DISCUSSION

A rise in metabolic activity, increased oxygen use (by 300–400%), and increased carbon dioxide generation are all associated with shivering. It induces arterial hypoxemia and lactic acidosis, as well as increased intraocular and intracranial pressures, as well as elevated cardiac activity, and peripheral vascular resistance.[15,16] Physical techniques like external heating[15] or pharmaceutical interventions are often used to avoid peri-operative hypothermia and shivering.[17-19] According to the literature, ketamine has been used in various studies for the treatment of shivering in various doses.[20, 21] In our study, in group 1, shivering was observed in 1 (3.33%), 1 (3.33%), and 3 (10%) patients after 0, 15 and 30 minutes respectively while in group 2, shivering was observed in 0 (00), 6 (20%) and 11 (36.67%) patients after 0, 15 and 30 minutes respectively (p=0.006).

In accordance with our study, a previous study by Kose et al. reported that there were few cases of shivering in patients treated with ketamine as compared to the placebo group.[22] While its function in thermoregulation has been linked to its anti-shivering effects, the precise mechanism by which ketamine works to counteract this effect is yet unknown. Another study was done by Shakya et al. also reported that shivering can be reduced effectively with ketamine after spinal anesthesia than saline.[20] Ketamine's vasoconstrictive characteristics reduce heat redistribution from the core to the periphery, limiting the drop in temperature that comes with spinal anesthesia. In addition to its effects on the periipheri, Ketamine has also been observed to have a central effect on thermoregulation at several levels, such as the hypothalamus and the locus coeruleus.[1,23] In group 1, rescue maneuver was used in 4 (13.33%) patients while group 2 rescue maneuver was used in 14 (46.67%) patients (p=0.005). In our study, a significant reduction in shivering was observed, in group 1patients as compared to group 2, by following them for two hours. This shows that ketamine has also anti-shivering ability post-operatively. Due to the huge volume of distribution and accumulation of ketamine after prolonged infusions, side effects such as abnormal liver function tests or psychomimetic problems might be developed.[24]

One of the recognized adverse effects of ketamine is hallucination, which has only been recorded in high dosages.[25] A previous study reported that a low dosage of ketamine effective in treating post-anesthetic shivering.[25] With the dosage utilized in our research, none of the patients had any side effects. The major limitation of our study was that shivering was not graded. The second limitation of our study is the small sample size.

CONCLUSION

Our study concludes that prophylactic Low dose ketamine is effective in preventing peri-operative shivering during spinal anesthesia in orthopedic patients as compared to the placebo group. No significant side effects were observed in our study. The ability of ketamine to minimize postoperative shivering should be studied in future trials and the ideal dose should be determined.

Abbreviations:

SPSS **(**statistical package for the social sciences)
SD (Standard deviation)
BSAS (Bedside shivering assessment scale).

AUTHOR'S CONTRIBUTION

FIK: Conception, design of work acquisition & analysis of data
TA: Writing research findings
UT: Outline of article & literature review
SKRR: Performa making
AS: Outline of article & literature review
SA: Data collection

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