ORIGINAL ARTICLE

Comparative Study Of Efficacy Of Prophylactic Low Dose Ketamine And Ondansetron For Prevention Of Shivering During Spinal Anesthesia

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Abstract

Hypothermia in common during regional anesthesia and may as nearly as severe during general anesthesia. Preoperative shivering is common problem during regional anesthesia and is distressing to the patient as patient are awake or minimally sedated. Various drugs have been used to prevent the preoperative shivering. This study was undertaken to evaluate comparative efficacy of low dose ketamine and ondansetron as prophylactic to prevent shivering during spinal anesthesia. Methods: This was a clinical trial, in this, patients were randomly divided into two groups of 30 each. Group O: 30 patient received inj. ondansetron 4mg just after spinal anesthesia. Group K: 30 patient received inj. Ketamine 0.25 mg/kg just after spinal anesthesia. The temperature of operating room was maintained at 240C-260C. During surgery, shivering score was recorded at 10 minutes interval. The data so abstained was evaluated using chi-square test with Yates correction. Results: Both the groups were comparable in age, weight, sex distribution and surgical duration. The incidence of shivering in group O was higher than group K and the difference was statically significant. No significant side effects were seen in either of the groups. The prophylactic administration of low dose ketamine (0.25mg/kg) and ondansetron (4mg) produces significant anti shivering effect in patient undergoing spinal anesthesia without side effect. Ketamine (0.25mg/kg) is significantly more effective than ondansetron (4mg) for shivering during spinal anesthesia.

Key Words

Shivering, Ketamine, Ondansetron, Spinal anesthesia

Introduction

Hypothermia is common during regional anesthesia and may be nearly as severe as during general anesthesia (1). Perioperative shivering is a common problem during anaesthesia. Shivering-like tremor in volunteers given neuraaxial anesthesia is always preceded by core hypothermia and vasoconstriction above the level of the block (2). Shivering during neuraxial anesthesia can sometimes be treated by warming sentient skin. This augments cutaneous thermal input to the central regulatory system and thus increases the degree of core hypothermia tolerated. Because the entire skin surface contributes 20% to thermoregulatory control and the lower body contributes about 10%, sentient skin warming is likely to compensate for only small reduction in core temperature. Apart from physical warming, many drugs have also been used for prevention of shivering. The normal human core temperature ranges from 36.50C to 37.50C (3).

Thermal inputs are integrated at the level of the anterior hypothalamus, which compares peripheral information with a threshold value, or, the set-point. Temperatures

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higher than this set point will trigger responses to cool the body, while temperatures lower than this set point will activate reflexes to warm the body (4).

Both general and regional anaesthesia is known to affect the efficiency of this homeostatic system and may result in different degrees of perioperative hypothermia. Regional anaesthesia also decreases this threshold by 0.50C, triggering vasoconstriction and shivering above level of block (5). This reduction in threshold is proportional to the number of spinal segments blocked, advanced age and high-level spinal blockade (6).

Perioperative hypothermia and shivering is one of the frequent, undesirable and unpleasant complications of both general and regional anaesthesia. The incidence of shivering is up to 40-60% even in regional anaesthesia (7).

Shivering causes increased metabolic activity and increased oxygen consumption up to 100%. It also cause arterial hypoxia and has been shown to correlate with increased risk of myocardial ischemia. It also increases intracranial and intraocular pressure. The other effects are increase in cardiac output, peripheral resistance, carbon dioxide production, lactic acidosis. Moreover it also interferes with ECG and oxygen saturation monitoring (pulse oximetry) (8).

The most reliable method and gold standard of core temperature monitoring is tympanic temperature monitoring by using tympanic probe-(9). Nasopharyngeal, esophageal, and bladder temperature measurements provide the best combination of accuracy and precision. It is recommended using these sites when appropriate rather than subjecting the tympanic membrane to possible trauma when monitoring temperature during anesthesia and surgery.

Perioperative hypothermia and shivering is usually prevented by physical methods like surface warming, and pharmacologically by drugs like pethidine, tramadol, and clonidine etc.(10).

Recently ketamine and ondansetron have been tried to prevent shivering during anaesthesia with good results. Ketamine a competitive NMD A receptor antagonist has a role in thermoregulation at various levels. NMDA receptor modulates noradrenergic and serotoninergic neurons in locus coeruleus. It is used as antishivering agent in dose of 0.5-0.75mg/kg IV. But even in these doses it causes side effects i.e. drowsiness, hallucination and delirium (11).

Ondansetron is 5HT 3 receptor antagonist, primarily used to prevent emesis. Recently it has also been tried successfully for prevention of shivering in dose of 8mg IV without any side effects (12).

As there are very few studies in relation to use of prophylactic ketamine and ondansetron for prevention of shivering during spinal anaesthesia and there is no comparative study evaluating use of low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia. So the present study was conducted to evaluate and compare the relative efficacy and safety of low dose ketamine (0.25mg kg-1) and ondansetron (4mg) for prevention of shiver during spinal anaesthesia.

To evaluate and compare the relative efficacy and safety of low dose ketamine (0.25mg/kg) and ondansetron (4mg) for prevention of shivering during spinal anesthesia.

Material and Method

This study was conducted in the Department of Anaesthesiology and Intensive Care Unit Govt. Medical College Jammu. After obtaining informed written consent and approval from hospital ethics committee, the study was conducted on 60 patients of age 18-70 years of either sex, 30 in each group of ASA physical status I and II undergoing elective lower abdominal surgical procedures (general and gynaecological surgery).

The exclusion criteria were

1. Patients with thyroid disorder.
2. Patients with severe cardiopulmonary disease.
3. Pregnancy.
4. Uncooperative patients.

The selected patients were randomly allocated to two groups each containing 30 patients according to the study drug; Ondansetron 4 mg group (Group O) and Ketamine 0.25 mg/kg group (Group K).

All the patients were premedicated with 0.20 mg/kg of oral diazepam before coming to the operation room. Routine standard monitoring was used in all patients. The temperature of the operating room was maintained at 240C - 260C. Before the spinal anesthesia procedure, each patient was preloaded with 15 ml/kg of Ringer Lactate solution. Subarachnoid anesthesia was instituted at either L3/4 or L4/5 interspace with 3ml of 0.50% hyperbaric Bupivacaine. Nasopharyngeal temperature

Table.1 Showing Demographic Variables

Group	Age	BMI	Sex Ratio (M/F)	Surgical Duration	Median level of sensory block
Group [O]	50.5	22±1.4	12/18	105	T_{10}
Group [K]	51.4	22±1.39	13/17	103	T_{10}
P value	0.59	0.32	0.69	0.90	0.70

Table. 3 Comparative evaluation of Shivering score score between 30-60 minutes between Group [O] and Group [K] was done using Chi-square test with Yates correction

Group	Shivering Score ≥ 3	Shivering Score < 3	Total
Group [O]	2	28	30
Group [K]	0	30	30
Yates correction = 0.04 and p value = 0.05, statistically significant.			

monitored every 10 minutes till the end of surgical procedure. The intravenous fluids kept at room temperature were infused.

Just after the intrathecal injection, one of the study drug was given as an iv bolus. During surgery, shivering score was recorded at 10 minute interval. Shivering was graded using a scale similar to that validated by Tsai and Chu. In which Grade 0: no shivering, Grade 1; piloerection or peripheral vasoconstriction but no visible shivering, Grade 2: muscular activity in only one muscle group, Grade 3: muscular activity in more than one muscle group but not generalized and Grade 4: shivering involving the whole body. If 15 minutes after spinal anesthesia and concomitant administration of a prophylactic dosed of one of the study drugs, the patients shivered to atleast Grade 3, shivering was considered significant and prophylaxis as ineffective and Tramadol 0.50 mg/kg iv was given as rescue drug. Side effects such as hypotention, nausea and vomiting, and hallucinations were recorded.

Results

Patient characteristics such as age, sex, weight, male / female ratio, duration of surgery and median level of sensory block was similar between the two groups and

Table. 2 Comparative evaluation of Shivering score at 0-30 minutes between Group [O] and Group [K] was done using Chi-square test with Yates correction

Group	Shivering Score ≥ 3	Shivering Score < 3	Total
Group [O]	1	29	30
Group [K]	0	30	30
Yates correction = 3.67 and p value = 0.057, statistically non-significant.			

Table. 4 Comparative evaluation of Shivering score score between 60-90 minutes between Group [O] and Group [K] was done using Chi-square test with Yates correction

Group	Shivering Score ≥ 3	Shivering Score < 3	Total
Group [O]	3	27	30
Group [K]	1	29	30
Yates correction = 0.06 and p value = 0.05, statistically significant.			

Table. 5 Comparative evaluation of Shivering score score between 90-120 minutes between Group [O] and Group [K] was done using Chi-square test with Yates correction

Group	Shivering Score ≥ 3	Shivering Score < 3	Total
Group [O]	3	27	30
Group [K]	1	29	30
p value = 0.05, statistically significant.			

difference between them was found non-significant ($p>0.05$).

Discussion

In this study, the comparative efficacy and safety of prophylactic low dose of ondansetron and ketamine (with different mechanism of action) for prevention of shivering during spinal anaesthesia. The median level of sensory block after 15 minutes of spinal anesthesia was comparable (upto 110) in both study groups. Hemodynamic parameters like heart rate, systolic BP, diastolic BP and mean arterial pressure were monitored every 10 minutes throughout intra-operative period. There

was no difference among the two groups in relation to hemodynamic parameters.

The results of the study were consistent with the study of Shakya S *et al,* who evaluated the role of prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anesthesia.

Results were also consistent with the study of Sagir O *et al* (11), who evaluated the role of prophylactic ketamine and granisetron for control of shivering during spinal anesthesia.

There was a consistency of results with study of Kelsaka E *et al* (12), who evaluated the role of ondansetron and meperidine for prevention of shivering in patients undergoing spinal anesthesia.

In our study, nasopharyngeal temperature was measured, using non-invasive nasopharyngeal temperature probe. Nasopharyngeal temperature is one of the reliable sites for measurement of core temperature. The mean nasopharyngeal temperature decreased significantly after spinal anaesthesia in both the groups with respect Lo baseline values. This is expected because hypothermia occurs during spinal anaesthesia due to internal redistribution of body heat, heat loss to the environment and inhibition of centrally mediated thermoregulatory control. The nasopharyngeal temperature decreased significantly in Group O than in Group K which may be due to vasoconstrictive action of ketamine.

Ondansetron is a specific 5HT3 receptor antagonist. The mechanism of action could be related to the inhibition of serotonin uptake on the preoptic anterior hypothalamic region. 5HT3 receptors may also influence both heat production and heat loss pathways. In our study low dose of ondansetron was used and the incidence of shivering was only 10%.

Ketamine is competitive receptor antagonist of N-methyl-D-aspartic acid (NMDA) has a role in thermoregulation in various levels.

Ketamine probably controls shivering by non-shivering thermogenesis either influencing the hypothalamus or by the beta adrenergic effect of norepinephrine. The shivering was seen only in 1 patient. In our study ketamine was found to be more effective in prevention of shivering. The hypotensive episode was also found to be less in ketamine as compared to ondansetron. Ketamine has sympathetic stimulation and vasoconstrictive effect which explains less incidence of hypotention. The other significant finding in our study' was that no hallucination was seen with 0.25 mg/kg of ketamine.

Conclusion

The prophylactic administration of low dose ketamine (0.25mg/kg) and ondansetron (4 mg) produces significant antishivering effect in patients undergoing spinal anesthesia wilhout any significant side effects. Ketamine (0.25mg/kg) is significantly more effective than ondansetron (4mg) during spinal anesthesia.

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