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ORIGINAL ARTICLE

Role of Pre-Medicational Ondansetron and Ketamine to Prevent Shivering During Spinal Anaesthesia: A Comparative Study

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ABSTRACT

Objective: Shivering is a common problem during anesthesia. Ketamine has been used for preventing shivering during anesthesia. Ondansetron (8 mg) has been recently evaluated for its peri-operative anti-shivering effect in patients undergoing spinal anesthesia. The objective of my study is to compare low dose Ondansetron with low dose Ketamine among patients undergoing spinal anesthesia in elective surgery in terms of frequency of shivering.

Patients and Methods: Patients undergoing elective general surgical procedures at Department of Anesthesiology, Holy Family Hospital, Rawalpindi, were inducted in the study. The study design was a randomized control trial and conducted from Jan 2016 to June 2016. Patients were included through a consecutive non-probability sampling. After spinal anaesthesia, patients were randomly assigned to receive Ketamine 0.25 mg/kg (group A) or Ondansetron 4mg (group B) by lottery method. During surgery, shivering was recorded at 10 min interval and recorded in terms of frequency.

Results: Out of the total 256 study participants, 128 patients in each group received the study drug (Ondansetron/ Ketamine) before surgery for prevention of shivering. Overall, there were 158 male and 98 female patients. The mean age of study population was 36 ± 11 yrs (range 21–40 yrs). Shivering occurred in 11 (4.3%) patients only. There was no significant difference between the gender distributions between the two groups (p=0.16). Patients pre-treated with Ketamine significantly experienced lesser shivering episodes than Ondansetron group (2 (1.6%) vs. 9 (7%), p=0.03).

Conclusion: The findings of our study suggest that the prophylactic administration of low dose Ketamine (0.25 mg kg^{-1}) and Ondansetron (4mg) produces anti-shivering effect in patients undergoing spinal anaesthesia. Ketamine (0.25 mg/kg) is significantly more effective than Ondansetron (4mg) during spinal anaesthesia.

Key words: Shivering, Ketamine, Ondansetron, Spinal Anesthesia.

Author`s Contribution
[1]Active participation in active methodology, Interpretation and discussion [2]Synthesis and Planning of the research, Conception, Review the Study, [3,4] Review and paper writing

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Introduction

Shivering is very unpleasant, physiologically stressful for the patient after surgery, and some patients feel the accompanying cold sensation to be worse than the surgical pain. Though the mechanism of origin of shivering is not clear, various hypotheses have been proposed to explain its occurrence.[1] Shivering occurs as a thermoregulatory response to hypothermia or muscle activity with tonic or clonic patterns, and various

frequencies have been noticed. However, in the postoperative period, muscle activity may be increased even with normothermia, suggesting that mechanisms other than heat loss with subsequent decrease in the core temperature contribute to the origin of shivering. These may be uninhibited spinal reflexes, sympathetic over-activity, postoperative pain, adrenal suppression, pyrogen release and respiratory alkalosis. [2]

Post Anesthesia Shivering (PAS) occurs in 40% of patients recovering from spinal anesthesia. Most of the times, it is preceded by central hypothermia and peripheral vasoconstriction indicating that it is almost always thermoregulatory mechanism, which even today is ill understood. Some shivering may not be thermoregulatory, thus making the management of PAS complex. The prime objective of this study was to understand physiology of PAS, organization of the thermoregulatory mechanism, and various measures for its prevention[3]. Shivering is an involuntary, repetitive activity of skeletal muscles mainly caused by intraoperative heat loss, increased sympathetic tone, pain, and systemic release of pyrogens. The median incidence of shivering related to regional anesthesia observed in a review of 21 studies is 55%.[4] Shivering increases oxygen consumption, lactic acidosis, carbon dioxide production, and metabolic rate by up to 400%. Therefore, shivering may cause problems in patients with low cardiac and pulmonary reserves. The best way to avoid these intraoperative and postoperative shivering-induced increases in hemodynamic and metabolic demands is to prevent shivering in the first place.[4] Post anesthetic shivering may cause discomfort to patients, and aggravate wound pain by stretching incisions and increase intracranial and intraocular pressure. Regional anesthesia produces vasodilatation, which facilitates core-to-peripheral redistribution of heat and the cool periphery is warmed at the expense of the core compartment. Thus, hypothermia from epidural anesthesia results from redistribution of heat from the core to the periphery.[5] Ondansetron, 5-HT3 receptor antagonist, is used antiemetic drug. It causes inhibition of serotonin reuptake on the pre-optic anterior hypothalamic region which might influence both heat production and heat loss pathways. Ketamine has sympathomimetic activity thus may contribute towards heat preservation model and thus prevent shivering.

Spinal anaesthesia is widely used as a safe anaesthetic technique for both elective and emergency operations. Shivering is known to be a frequent complication, reported in 40 to 70% of patients undergoing surgery under regional anaesthesia. Shivering is a potentially serious complication, resulting in wound infection; increased surgical bleeding; and morbid cardiac events.[6]

Patients and Methods

This prospective randomized trial was conducted at Holy Family Hospital, Rawalpindi for a period of 6 months from Jan 2016 to June 2016. A total of 256 elective general surgical patients, aged 20-40 years, having mild systemic diseases with no functional limitations were included in the study by consecutive non-probability sampling technique. Patients with concomitant co-morbid conditions like diabetes mellitus, hypertension, ischemic heart diseases, pulmonary, hepatic or renal diseases diagnosed on history and clinical examination were excluded from the study. Similarly, individuals suffering from illnesses in which regional anesthesia were contraindicated like coagulopathies, infection at injection site, hypovolemia and having history of allergic reactions/hypersensitivity for using ondansetron and ketamine were not included in the study. After taking approval from hospital ethical committee, patients were assessed for anesthesia fitness a day before surgery and no oral intake was advised for at least 8 hrs before surgery. Written informed consent was taken. Patients were randomly divided into group A and B of 128 individuals each by lottery method. All the patients were given premedication with 0.25mg Alprazolam oral tablet at night before surgery. In the operating room, routine standard monitoring protocols were followed in all patients. The temperature of operating room was maintained at 24-26°C with the help of air conditioner temperature setting. Before spinal anesthesia, each patient was preloaded with 10-15 ml/kg of the Ringer Lactate solution. Subarachnoid block was instituted at either L3-L4 interspace with 2 ml of 0.75% hyperbaric Bupivacaine in sitting position. Axillary temperature was measured with the help of axillary thermometer every 20 minutes till end of the surgical procedure.

The intravenous fluid at room temperature (24°C- 26°C) was infused and all the patients were covered with standard sterile surgical drapes. Just after the intrathecal injection, one of the study drugs (Ondansetron 4 mg/ Ketamine 0.25 mg/kg) was given as IV bolus. Shivering was measured as significant or not at 10 min interval per-operatively and recorded in terms of frequency.

Data was entered and analysed in SPSS (17.0). Mean ± standard deviation was calculated for quantitative variables like Age & BMI. Frequency and percentages were calculated for qualitative variables like gender and shivering. Chi- square or Fishers exact test was used to compare shivering in both groups. $p<0.05$ was taken as level of significance.

Results

Out of the total 256 study participants, 158 were male and 98 were female. Mean age of study population was approximately 36 ± 11yrs (range 21-40yrs) (Table 1).

Table 1: Baseline characteristics of study population

Total no. of patients		256
No. of patients in each group		128
Gender; n(%)	Males	158(61.72)
	Females	98(38.28)
Age (years); mean±SD		36 ± 11 (Range 21-40)
Shivering Frequency; n(%)		11 (4.3)

Patients were divided into two groups, 128 in each group. One group was given Ondansetron and second group was provided Ketamine before surgery for prevention of shivering. There were 58 (36.7%) males in Ketamine group in comparison to 100 (63.3%) males in Ondansetron group. Similarly, the female proportion in the study patients was 28.6% in Ondansetron group and 71.4% in Ketamine group. The mean Age (yrs) was not significantly different between the two groups. Patients pre-treated with Ketamine significantly experienced lesser shivering episodes than Ondansetron group; 2 (18.2%) vs. 9 (81.8%), p=0.03 (Table 2).

Table 2: Comparison of pre-operative Ketamine and Ondansetron in prevention of post-operative shivering (n=256)

Variables		Ketamine (n=128)	Ondansetron (n=128)	p-value
Gender; n(%)	Males	58 (36.7)	100 (63.3)	0.16
	Females	70 (71.4)	28 (28.6)	
Mean Age (years); mean±SD		30.02 ± 05.54	29.93 ± 05.80	0.9
Shivering; n(%)	Present	2 (18.2)	9 (81.8)	0.004
	Absent	126 (51.4)	119 (48.6)	

Discussion

Very few studies are available till date in relation to use of ketamine for prevention of shivering during general or regional anaesthesia probably because of its undesirable side effects like too much sedation, hallucination, nausea and vomiting. [10] In our study, very low dose of ketamine (0.25mg/kg) was used to minimize the side effect and we found that it was significantly effective and the shivering was observed only in 2 patients out of 40 (1.6%). In one study Dal et al. compared placebo, meperidine and ketamine 0.5 mg/kg for prevention of shivering after general anesthesia and found ketamine 0.5 mg/kg to be effective.[8] Although our study was performed on the patients to observe incidence of shivering after prophylactic use of ketamine during spinal anesthesia as compared to patients undergoing general anesthesia in Dal et al. study, our study is better because: first, a lower dose of ketamine (0.25 mg/kg) was used as compared to 0.5 mg/kg ketamine. In addition, in comparison to 30 patients who were given ketamine in this study we gave ketamine to 128 study participants. Shivering was graded using a scale that was validated by Gangopadhyay S et al.[9] The prophylactic drug was considered ineffective if the patient shivered to grade 3 and pethidine 0.5mg kg^{-1}IV was given to control the shivering. Sagir et al [10] and Shakya et al [7] used same protocol in their study. Ondansetron, which is a specific 5-HT3 receptor antagonist, influence both heat production and heat loss pathways.[11] The recommended dose of Ondansetron for prevention of postoperative nausea & vomiting is 4-8 mg in adult patients.[12] Kelsaka et al[13] compared the 8mg Ondansetron with Pethidine for prevention of shivering and found the same anti-shivering effect and the incidence of shivering was 8% in Ondansetron group. In study by Shakya et al [7], low dose of Ondansetron (4mg) was used and the incidence of shivering was only 10% in the Ondansetron group. In our study, shivering occurred in almost same frequency as given in literature i.e. 7% patients pre-medicated with Ondansetron in a dose of 4mg.

In present study, despite a higher age group in Ketamine treated patients, when the effectiveness of Ondansetron and Ketamine was compared, Ketamine was found to be more effective in prevention of shivering. 9 (7%) vs. 2 (1.6%), p=0.03). The side effects of the drugs, which although are not part of our study objectives, were also no more in Ketamine group as expected from its known pharmacologic properties.

Conclusion

The findings of our study suggest that the prophylactic administration of low dose Ketamine (0.25 mg kg-1) and Ondansetron (4mg) produces anti-shivering effect in patients undergoing spinal anaesthesia. Ketamine (0.25 mg/kg) is significantly more effective than Ondansetron (4mg) during spinal anaesthesia.

References

1. Torossian A. Perioperative thermal management in children. Anesthesiol Intensivmed Notfallmed Schmerzther. 2013; 48(4):278-80.
2. Pazderska A, O'Connell M, Pender N, Gavin C, Murray B, O'Dowd S. Insights into thermoregulation: a clinico-radiological description of Shapiro syndrome. J Neurol Sci. 2013; 329(1):66-8.
3. Crowley LJ, Buggy DJ. Shivering and neuraxial anesthesia. Reg Anesth Pain Med. 2008; 33(3):241–252.
4. Lenhardt R. The effect of anesthesia on body temperature control. Front Biosci (Scholar Ed). 2010; 2:1145-54.
5. Pitoni S, Sinclair HL, Andrews PJ. Aspects of thermoregulation physiology. Curr Opin Crit Care. 2011; 17(2):115-21.
6. Bilotta F, Pietropaoli P, La Rosa I, Spinelli F, Rosa G. Effects of shivering prevention on haemodynamic and metabolic demands in hypothermic postoperative neurosurgical patients. Anaesthesia. 2001; 56(6):519.
7. Shakya S, Chaturvedi A, Sah BP. Prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia. J Anaesthesiol Clin Pharmacol. 2010; 26(4):465-9.
8. Dal D, Kose A, Honca M, Akinci SB, Basgul E, Aypar U. Efficacy of prophylactic ketamine in preventing postoperative shivering. Br J Anaesth. 2005;95(2):189–92.
9. Gangopadhyay S, Gupta K, Acharjee S, Nayak SK, Dawn S, Piplai G. Ketamine, tramadol and pethidine in prophylaxis of shivering during spinal anaesthesia. J Anaesth Clin Pharmacol.2010; 26(1):59–63.
10. Sagir O, Gulhas N, Toprak H, Yucel A, Begec Z, Ersoy O. Control of shivering during regional anaesthesia: prophylactic ketamine and granisetron. Acta Anaesthesiol Scand. 2007; 51(1):44–49.
11. Ryan KF, Price JW, Warriner CB, Choi PT. Persistent hypothermia after intrathecal morphine: case report and literature review. Can J Anaesth. 2012; 59(4):384-8.
12. Elvan EG, Oç B, Uzun S, Karabulut E, Coşkun F, Aypar U. Dexmedetomidine and postoperative shivering in patients undergoing elective abdominal hysterectomy. Eur J Anaesthesiol. 2008 ; 25(5):357-64.
13. Kelsaka E, Baris S, Karakaya D, Sarihasan B. Comparison of ondansetron and meperidine for prevention of shivering in patients undergoing spinal anesthesia. Reg Anesth Pain Med. 2006; 31(1):40-5.