

Original Research Article

Prophylactic ondansetron eight milligrams vs. four milligrams against post spinal anaesthesia shivering

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ABSTRACT

Background: Shivering is one of the commonly encountered adverse affect after spinal anaesthesia. Shivering can be very discomforting to the patient and hampers operative maneuvering. Pharmacological therapies have been studied for control and management of shivering. One such drug is ondansetron, a 5-HT₃ antagonist. Aim of current study is to evaluate the efficacy of prophylactic administration of ondansetron 8 mg vs. 4 mg for prevention of shivering.

Methods: A prospective, randomized, and double blind study was conducted on 100 patients, from either gender, aged 20-60 years, of the American society of anesthesiologists grade I or II, scheduled for various surgeries under spinal anesthesia. The patients were randomly divided into two groups of 50 each to receive either ondansetron 8 mg (group E) or ondansetron 4 mg, (group F) as slow intravenous infusion prior to spinal anesthesia. The primary end point were intraoperative shivering and secondary outcomes included hypotension, adverse reaction, cardiac dysrhythmia's.

Results: A total of 10 patients in group E (20%) and 20 (40%) patients in group F experienced shivering (p=0.029). Incidence of nausea was similar in both groups, total of 8 (16%) patients in group E and 5 (10%) in group B had hypotension (p=0.27). 1 (2%) patient in group E experienced bradycardia.

Conclusions: Prophylactic administration of ondansetron 8 mg has better efficacy in prevention of spinal anaesthesia induced shivering with minimal side effects as compared to 4 mg dosage.

Keywords: Spinal Anesthesia, Shivering, Dysrhythmias

INTRODUCTION

Shivering is a very common complication of intra operatively owing to pain and post anesthesia hypothermia. It is distressing for both patient and clinicians. Shivering is defined as the involuntary and oscillatory muscular activities that increase the metabolic rate by two to three folds to maintain the core temperature, with the increment of heat production.^{1,2} Neuraxial (epidural and spinal anesthesia) and general anesthesia are associated with a significant incidence of

shivering, and the incidence is 40%-60% in regional anesthesia and up to 60% during general anaesthesia.^{3,4} Shivering can be associated with adverse effects attributed to increasing the oxygen demand by 200-500% with carbon dioxide retention. Shivering can cause arterial hypoxia, increase cardiac output, the risk of myocardial ischemia, increase in intra ocular pressure and can be disastrous in patient with intrapulmonary shunts. Besides it the associated musculoskeletal activity interferes with the electrocardiogram, blood pressure, and pulse oximetry.⁵

With increasing awareness of its undesirable aftermath, effective prevention of postanesthesia shivering (PAS) is being imperative. Several modalities are available to decrease the incidence of shivering. These include pharmacological and non pharmacological methods. Non-pharmacological methods includes specialized equipment's which works by supplying heat there by prevents development of shivering and warming the administered fluid, but it is not a perfect way these equipment's are costly and at times availability constrains are encountered.⁶⁻⁸ Many drugs have been shown to be effective on prevention of PAS, such as opioids, α 2-agonist, anticholinergic, CNS stimulant, corticosteroid, however their usage has found limited value in practical set up owing due to their adverse drug profile.⁹

Ondansetron, a 5 TH3 receptor antagonist, is widely used antiemetic. Studies have demonstrated the efficacy of this drug to affect the body temperature and shivering in by maintaining balance of nor-epinephrine and 5-hydroxytryptamine (5-HT) in the preoptic-anterior hypothalamus.^{10,11} Consistently, several studies have demonstrated ondansetron can prevent PAS, which made ondansetron a promising drug for postoperative complications including PAS, nausea and vomiting.¹²

Ondansetron 8 mg has shown efficacy in prophylaxis against shivering but has been associated with adverse effects (nausea, hypotension, cardiac rhythm disturbances). Current study is an attempt to investigate the efficacy of ondansetron 4 mg (lower dose) for prevention of shivering with acceptable tolerability.

METHODS

Current study was a prospective, randomized, and double blind study undertaken at our tertiary care centre during the period from June 2018 to June 2020.

Inclusion criteria

Inclusion criteria for current study were; patients in the age group of 20-60 years, patients with ASA grade I or II and surgeries under spinal anaesthesia.

Exclusion criteria

Exclusion criteria for current study were; patients with hypersensitivity to ondansetron, patients with cardiovascular, renal or thyroid disease, contraindication to spinal anaesthesia and patients who did not give their consent for the study.

Procedure

All patients were visited on the day prior to surgery and explained in detail about the anesthetic procedure and necessary consents obtained. The study patients were randomly divided into two groups using computer generated numbers and divided into 2 groups. Group E

received ondansetron 8 mg in 100 ml of saline and group F received ondansetron 4 mg in 100 ml of saline as slow intravenous (IV) infusion over 15 minutes before spinal anaesthesia. To ensure double blinding, a third party administered study drug. All the patients were preloaded with 500 ml of lactated Ringer's solution. Patients' peripheral oxygen saturation, blood pressure (systolic, diastolic, and mean arterial pressure), and electrocardiogram were monitored. Basal values were recorded. Intraoperatively, temperature monitored using the temperature probe placed in axilla. Spinal Anaesthesia were administered to all study patients in the sitting position, and dural puncture was performed at L3-L4 subarachnoid space. A volume of 3-3.5 ml of hyperbaric bupivacaine 0.5% was injected intrathecally, as per the height of the patient, after confirmation of spinal needle placement. The volume of the local anesthetic and use of vasopressors was determined by the attending anesthesiologists, which was not affected by inclusion in the study. A blanket was used to cover the chest and upper limb of the patients. All the preloading fluids and drugs were given at room temperature. ambient temperature of operation theater was maintained between 21°C and 23°C.

Intraoperatively shivering was recorded at interval of 5 minutes, using Wrench scale. Scaling was done by attending anaesthesiologist on a scale of 0 to 4 with grade 0: no shivering, grade 1: one of the following: piloerection, peripheral vasoconstriction, and peripheral cyanosis but without muscle activity, grade 2: muscular activity confined to one muscle group, grade 3: shivering involving more than one muscle group, and grade 4: gross muscle activity involving whole body.

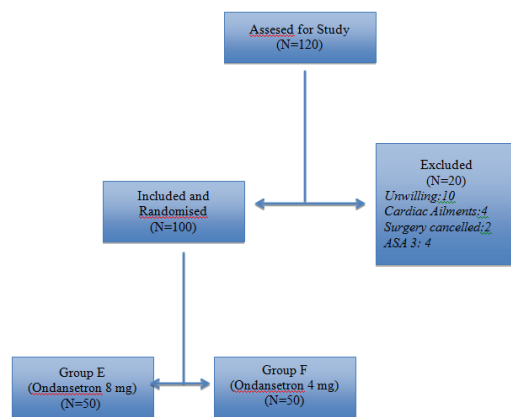


Figure 1: CONSORT flow chart.

Study protocol adopted included use of pethidine (0.5 mg/kg), if shivering grade was 3/4 as rescue agent. For secondary end point vital parameters were monitored throughout the procedure. Patients were assessed for nausea, dizziness, and observed for vomiting. Hypotension (systolic blood pressure <100 mmHg or fall >20% baseline values) was treated with injection ephedrine 6 mg IV, up to a maximum of 30 mg, heart rate

<50 bpm was considered as bradycardia and treated with injection atropine 0.6 mg IV.

The sample size calculation was done on basis of study by Powell et al in which incidence of post anaesthesia shivering was reported to be 15% (ondansetron 8 mg). Student's t test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups, $p < 0.05$ was considered as statistically significant.

RESULTS

Total 100 patients were studied. Ondansetron 8 mg group E had 50 patients and ondansetron 4 mg group F also had 50 patients (Figure 1). There was no statistical difference in the demographical profile of study patients (Table 1). No statistical disparity was elicited between groups pulse rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, temperature, and duration of surgery. About 20 (40%) patients in group F and 10 (20%) patients in group E experienced shivering ($p=0.028$) (Table 2-3). In group E 8 (16%) and group F 5 (10%) subjects experienced hypotension ($p=0.27$) (Table 4). The mean ephedrine dosage for group E was 4.5 ± 0.57 mg and for group F was 4.5 ± 0.58 mg. One (2%) study patient in group E developed bradycardia. Incidence of nausea was similar with both formulations.

Table 1: Demographical comparison.

Demography	Group E (n=50)	Group F (n=50)
Age (in years)	33±13.6	32±13.6
Sex (F:M)	30:20	27:23
Weight (kgs)	51.5±5	53.5±6

Table 2: Shivering score.

Shivering Grade (n=50)	Group E (ondansetron 8 mg) N (%)	Group F (ondansetron 4 mg) N (%)
0	40 (80)	30 (60)
1	6 (12)	10 (20)
2	2 (4)	5 (10)
3	1 (2)	3 (6)
4	2 (4)	2 (4)
Total	50 (100)	50 (100)

Table 3: Incidence of shivering.

Shivering (n=50)	Group E (ondansetron 8 mg)	Group F (ondansetron 4 mg)	P value
Present	10	20	0.028
Absent	40	30	
Total	50	50	

Table 4: Adverse reaction.

Adverse reaction (n=50)	Group E N (%)	Group F N (%)	P value
Hypotension	8 (16)	5 (10)	0.278
Dizziness	0 (0)	0 (0)	-
Arrhythmias	0 (0)	0 (0)	-
Bradycardia	1 (2)	0 (0)	-
Nausea	2 (4)	2 (4)	-
Anaphylaxis	0 (0)	0 (0)	-

DISCUSSION

Neuraxial anaesthesia offers advantages over general anaesthesia ranging from post operative pain relief to reduction in intravenous/oral analgesics. Since its conduct includes intrathecal instillation of local anaesthetic agent, which has its own share of issues of causing, post anaesthesia shivering, hypotension and bradycardia. The incidence of spinal anaesthesia-induced hypotension is 20-80%.¹⁴ Hypotension after the administration of the spinal anaesthesia is mainly caused due to sympathetic blockade with a parasympathetic overdrive and the BJR.¹⁴ BJR is a cardio-inhibitory reflex producing bradycardia, hypotension, and cardiovascular collapse, which occurs due to activation of the left ventricular mechanoreceptors from sudden decrease in the left ventricular volume and is mediated by serotonin receptors.¹⁵ The etiology of shivering is not clearly understood till date. Factors chiefly responsible for shivering in patients undergoing surgery are intraoperative temperature loss, increased sympathetic tone, pain, and systemic release of pyrogens. The best way to avoid the intraoperative and postoperative shivering induced complications is to prevent shivering either by supplying external heat or by interfering at CNS level (thermoregulation at pre optic hypothalamic axis).

Numerous authors have worked to identify and devise prophylactic and treatment strategies for the post spinal anaesthesia shivering (PAS), hypotension and bradycardia. These strategies include Supplying external heat by blowers, usage of warm body fluids, lower leg compression, intravascular preloading and coload of crystalloids and colloids and administration of pharmacologic vasopressors.¹⁶ Recently ondansetron have been studied in spinal anaesthesia induced hypotension, shivering and bradycardia. Ondansetron a 5-HT₃ antagonist is widely used in the prevention and treatment of post-operative nausea and vomiting.¹³⁻¹⁵ Due to its antagonistic effect on 5-HT₃ receptor (serotonergic antagonism) it may be considered for attenuating spinal anaesthesia induced shivering (lowering the human thermal set range thereby reducing metabolic cold defenses and discomfort associated with postoperative hypothermia), hypotension and bradycardia. Ondansetron 8 mg slow infusion dose has been studied to alleviate post spinal shivering, bradycardia and hypotension. This study was carried out to compare the efficacy of ondansetron 8

mg with 4 mg preparation, in an attempt to arrive to a more tolerable dosage regimen.

After due extrapolation of data, over all incidence of shivering and hypotension after prophylactic administration of ondansetron was 30% and 13%. This clearly states about the efficacy of ondansetron for prevention of shivering (40-60%) and hypotension (20-80%).^{1,14} In current study, it was found that the incidence of shivering with ondansetron 8 mg dosage was 20% (n=10, p=0.029) and hypotension was 16% (n=8) however with ondansetron 4 mg dosage shivering was encountered in 40% (n=20) and hypotension in 10% (n=5, p=0.27). The safety profile with respect to incidence of nausea, vomiting, dysarrhythmias and bradycardia did not prove any better tolerability of 4 mg dosage. Ephedrine requirement in both group was also similar (mean dose 4.5±0.57 mg). Powell and Buggy compared two doses of ondansetron (4 mg vs. 8 mg) with placebo group for prevention of shivering.¹⁷ They found out that incidence of shivering was 15% in group which used 8 mg, 33% in group which used 4 mg, and 57% in saline group. The results in 8 mg group and placebo group are consistent to our finding. However the comparison of 8 mg vs. 4 mg can be derived from our study which points towards better efficacy of ondansetron 8 mg in prevention of shivering. Shah et al conducted study to evaluate efficacy of prophylactic administration of ondansetron for the prevention of spinal anesthesia induced hypotension in elderly patients. They included 100 patients and recorded that hypotension was present in 23 (46%) patients in group A (ondansetron 8 mg), whereas it was present in 34 (68%) patients in group B (placebo) (p=0.026). Bradycardia was recorded in 3 (6%) versus 11 (22%) patients in group A and B, respectively (p=0.021).¹⁸ The author concluded that intravenous administration of 8 mg of ondansetron 5 minutes before subarachnoid block is effective in decreasing frequency of hypotension and bradycardia in elderly patients. Marashi et al carried out a comparison of two different doses of intravenous ondansetron with placebo for assessment of post spinal hypotension.¹⁹ The study was conducted with sample size of 70 in each group. One group received saline, the second group received 6 mg of ondansetron, and the third group received 12 mg ondansetron. Their study demonstrated efficacy of Ondansetron in prevention of hypotension. The dosage and drug administered found that 12 patients in the control group had hypotension and none of the patients in ondansetron group experienced hypotension (p=0.04). Results of this study is comparable to one conducted by us which showed reduced incidence of Post spinal hypotension.

CONCLUSION

It was concluded that prophylactic use of 8 mg ondansetron IV is effective in reducing the incidence of post anaesthesia shivering, hypotension and bradycardia effectively as compared to 4 mg ondansetron dosage.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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