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Original Article

Using ondansetron as an oral premedication drug for prevention of postanesthesia shivering

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Abstract

Introduction
Postanesthesia shivering (PAS) is one of the most common complications after surgeries. There are two methods to reduce the shivering, including pharmacological and nonpharmacological methods.

Aim
This study compared the efficacy and safety of 4-mg oral ondansetron premedication on preventing PAS, perioperative core body temperature changes, and hemodynamic stability.

Patients and methods
This prospective, observational study consisted of 100 adult patients scheduled for general surgery or interventional structural heart disease. The patients were randomized into two groups of 50 patients each. Group I received 4 mg of oral ondansetron, and group II received an oral placebo 60–90 min before the operation. All patients were assessed for perioperative hemodynamic changes, core body temperature changes, and PAS.

Results
Regarding the efficacy of the preoperative administration of oral ondansetron, this study reports the valuable preventive effect on shivering for ondansetron group (8.1%) compared with control group (44.3%), and there was a highly significant difference between both groups according to the incidence and scoring of shivering. On the contrary, we found no significant difference between groups according to heart rate, systolic blood pressure, and diastolic blood pressure. However, reduction in systolic blood pressure and diastolic blood pressure was recorded in both groups after induction, which came back up at the end of surgery. In addition, tympanic temperature reduction was recorded intraoperatively and came back up during the recovery period, with no statistically significant differences between groups.

Conclusion
Oral ondansetron premedication adequately decreases PAS compare with placebo. Ondansetron does not have any significant effect on the core or peripheral temperature.

Keywords: PAS, perioperative, ondansetron

Introduction

Postoperative shivering is one of the most common complications after surgeries, which is seen among 40–65% of patients, and includes involuntary movements of one or more groups of muscles. Shivering can cause many adverse effects such as increased oxygen consumption, carbon dioxide production, heart rate (HR), and blood pressure, resulting in exacerbation of ischemic heart disease, as well as increased intracranial pressure, pain at the surgical site, and a sense of discomfort to the patient [1]. General anesthesia facilitates the redistribution of the temperature from the central tissues to the peripheral tissues. Owing to anesthesia, core temperature regulation responses like the vasoconstriction threshold are controlled, and most anesthetic drugs cause peripheral vasodilatation [2].

Shivering could be the result of hypothermia readjustment of body core temperature during surgery, or because of fever and shivering, which could lead to activation of the

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inflammatory response and cytokine release [3]. There are two methods to reduce the shivering, including pharmacological and nonpharmacological methods. Nonpharmacological methods involve the use of moisturizers, prevention of hypothermia using warm blankets, and warm and moist oxygen inhalation [1].

Ondansetron is a 5-hydroxytryptaminergic (5-HT3) receptor antagonist. Although some studies have reported 5-HT3 may be an effective receptor in postanesthesia shivering (PAS) pathway, the results remain controversial [4].

Aim

The aim of the study is to evaluate the efficacy of ondansetron as an oral premedication drug in the prevention of PAS.

Patients and Methods

Patients

Inclusion criteria were as follows: 100 patients with BMI less than 30 kg/m^2, between 20 and 60 years with ASA I–II planned for general surgery or interventional structural heart disease were enrolled in a double-blind comparative study, after obtaining approval of the written informed consent from patients between November 2016 and March 2018.

Exclusion criteria were as follows: known allergy to the study drugs and contraindications to the study drugs. Patients with a thyroid disorder, cardiopulmonary disorders, severe hemorrhages, using a large number of irrigation fluids, neuromuscular diseases, and fever were excluded as well. Preoperatively, 100 patients were randomly divided into two groups:

(1) Group I: ondansetron group (N = 50) received 4-mg ondansetron.
(2) Group II: control group (N = 50) received a placebo drug.

The placebo and ondansetron were administrated orally with sips of water ~60–90 min before the operation.

On arrival to the operating room, monitors were attached. Baseline HR, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded. After preoxygenation for 3 min with 100% oxygen, anesthesia was induced with propofol at 2 mg/kg or dose sufficient for the loss of verbal commands. Direct laryngoscopy and intubation were facilitated with atracurium at 0.5 mg/kg. Anesthesia was maintained with isoflurane in 40% air and 60% oxygen. The patients were mechanically ventilated to maintain normocapnia ($ETCO_2$ between 35 and 40 mmHg). The supplemental neuromuscular blockade was achieved with atracurium at 0.1 mg/kg. After completion of the surgery, the residual neuromuscular block was antagonized with appropriate doses of neostigmine (0.05 mg/kg) and atropine (0.01 mg/kg), and extubation was performed when respiration was adequate.

The following data were recorded: (a) core body temperature: for all patients, the core temperature was measured and recorded through tympanic temperature using QQcute IT-121 (Shenzhen Xianda Information Technology Co., Ltd., Shenzhen, Guangdong, China) infrared thermometer before administration of medication (baseline) and after induction of anesthesia, and then every 15-min interval till the end of surgery, after the patient's entrance to the postanesthetic care unit (PACU), and before the patient's exit from the PACU. (b) PAS: it was carried out using Bedside Shivering Assessment Score[5] as follows:

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

In case of scores 3–4 for more than 4-min duration, the prophylaxis was considered ineffective, and intravenous bolus of pethidine 20 mg was administrated, and then titration as requirements.

(C) Hemodynamic parameters: HR (beats/min) was assessed using lead II ECG waves. Systolic arterial blood pressure and diastolic arterial blood pressure were measured in mmHg and recorded at the following times: premedication, after induction of general anesthesia, at the end of surgery, after the patient entrance to PACU, and before the patient exit from PACU.

Results

Table 1 shows no statistically significant difference between the groups according to demographic data.

Table 2 shows no statistically significant difference between the groups according to tympanic temperature as mean ± SD.

Table 3 shows no statistically significant difference between the groups according to systolic blood pressure.

Table 4 shows no statistically significant difference between the groups according to diastolic blood pressure.

Table 5 shows no statistically significant difference between the groups according to HR.

Table 6 shows statistically highly significant difference between groups according to Bedside Shivering Assessment Score.

Discussion

General anesthesia facilitates the redistribution of the temperature from the central tissues to the peripheral tissues. Owing to anesthesia, core temperature regulation responses like the vasoconstriction threshold are controlled, and most anesthetic drugs cause peripheral vasodilatation [2]. Shivering could be the result of hypothermia readjustment of body core temperature during surgery, or because of fever and shivering, which could lead to activation of the inflammatory response and cytokine release [3].

Table 1: Comparison between groups according to demographic data

Demographic data	Group I ($n=50$)	Group II: Control ($n=50$)	$t/\chi^{2\#}$	*P*
Age (years)				
Mean±SD	31.45±9.84	33.56±9.70	1.323	0.138
Range	18-54	19-59		
Sex				
Female	17 (34.7%)	26 (52.6%)	3.340	0.092
Male	33 (65.3%)	24 (47.4%)		
BMI (kg/m^2)				
Mean±SD	24.87±1.45	24.98±1.48	0.254	0.615
Range	22.6-27.2	23-27.3		
ASA				
ASA I	37 (74.5%)	30 (60.8%)	1.162	0.141
ASA II	13 (25.5%)	20 (39.2%)		

Table 2: Comparison between groups according to tympanic temperature (deg.)

Tympanic temperature	Group I ($n=50$)	Group II ($n=50$)	*t*-Test	*P*
Baseline	18.94±0.34	18.92±0.32	0.225	0.636
At induction	18.31±0.42	18.31±0.29	0.313	0.59
After 15 min	17.89±0.31	18.07±0.29	1.271	0.187
After 30 min	17.72±0.28	17.84±0.31	2.13	0.286
After 45 min	17.49±0.31	17.65±0.27	1.221	0.132
After 60 min	17.31±0.20	17.41±0.35	0.411	0.211
After 75 min	17.30±0.15	17.24±0.37	1.772	0.186
After 90 min	17.18±0.21	17.90±0.22	1.238	0.193
End of surgery	17.32±0.26	17.19±0.32	1.72	0.121
Entrance to PACU	17.41±0.27	17.33±0.33	0.539	0.344
Exit from PACU	18.16±0.32	18.02±0.30	1.715	0.211

PACU, postanesthetic care unit.

Table 3: Comparison between groups according to systolic blood pressure (mmHg)

Systolic blood pressure	Group I ($n=50$)	Group II ($n=50$)	*t*-Test	*P*
Baseline				
Mean±SD	120.58±7.85	120.82±11.22	0.031	0.861
Range	109-135	100-135		
After induction				
Mean±SD	104.76±9.41	104.54±8.16	0.03	0.862
Range	90-130	90-117		
End of surgery				
Mean±SD	118.18±6.69	117.99±7.34	0.037	0.847
Range	107-130	99-125		
Entrance to PACU				
Mean±SD	127.52±4.41	121.91±5.07	0.753	0.142
Range	115-135	105-130		
Exit from PACU				
Mean±SD	120.18±3.73	121.57±8.09	2.357	0.126
Range	110-125	110-135		

PACU, postanesthetic care unit.

In this study, there were no significant demographic differences between both groups according to age, sex, BMI, and ASA group. Our results showed that the tympanic temperature significantly decreased from preoperative to postoperative; besides, there were no significant differences in tympanic temperature trend between ondansetron and control groups in the perioperative period. In other words, the tympanic temperature was decreased in both groups even after ondansetron was administered. This implies that ondansetron probably acts by a central inhibitory mechanism and modifying thermoregulatory inhibition [5]. In this study, regarding HR, SBP, and DBP, there was no significant difference between both groups. However, we found a reduction in SBP and DBP in both groups after induction, which came back up at the end of surgery.

This was the same result reported by Gupta *et al.* [5]. In this study, the effect of ondansetron on postoperative shivering incidence was studied. Our results showed that ondansetron (4 mg oral 60–90 min preoperative) significantly prevents PAS compare with control without affecting the core-to-peripheral redistribution of heat during general anesthesia. This suggests that ondansetron, a 5-HT3 antagonist, has a role in the prevention of PAS. This study reports the valuable preventive effect on shivering for ondansetron group (8.0%) compared with control group (44.0%), and there was a highly significant difference between both groups according to incidence and scoring of shivering, as shown in Table 6.

Other studies have shown that ondansetron can effectively reduce PAS compare with control group [6]. Tie *et al.*[7] showed that ondansetron has a preventive effect on PAS without a paralleled adverse effect of bradycardia. Even in coronary artery bypass graft patients, it was demonstrated that ondansetron is more effective in preventing shivering after off-pump coronary artery bypass graft than meperidine [8]. Nevertheless, controversies over ondansetron effect in PAS are still continuing.

Browning *et al.*[9] showed that prophylactic ondansetron does not prevent shivering or decrease shivering severity during cesarean delivery under combined spinal-epidural anesthesia. In a trial, administration of two different doses of intravenous ondansetron, 6 and 12 mg, significantly attenuates spinal-induced shivering compared with the control saline group [10]. Others have depicted the preventive effect of ondansetron on PAS after general anesthesia in gynecological surgery [11]. Prophylactic ondansetron (4 mg) significantly decreased shivering in patients undergoing spinal anesthesia without significant adverse effects [12]. The mechanism through which ondansetron suppresses shivering is supposedly through 5-HT3 antagonism. Ondansetron probably acts by a central inhibitory mechanism on postanesthetic shivering through 5-HT3 pathways by changing thermoregulatory set points. Clinically, our result indicated that ondansetron effect on body temperature is similar to control, which emphasizes its central effect. Various receptors like μ-agonist meperidine

Table 4: Comparison between groups according to diastolic blood pressure (mmHg)

Diastolic blood pressure	Group I ($n=50$)	Group II ($n=50$)	*t*-Test	*P*
Baseline				
Mean±SD	78.43±6.52	77.79±6.61	0.456	0.5
Range	69-90	65-88		
After induction				
Mean±SD	69.04±5.43	70.29±6.25	1.216	0.138
Range	60-80	60-80		
End of surgery				
Mean±SD	77.36±6.51	77.23±4.52	0.026	0.871
Range	60-85	70-83		
Entrance to PACU				
Mean±SD	82.77±4.33	81.61±3.32	0.382	0.376
Range	75-90	75-85		

PACU, postanesthetic care unit.

Table 5: Comparison between groups according to heart rate (/min)

Heart rate	Group I ($n=50$)	Group II ($n=50$)	*t*-Test	*P*
Baseline				
Mean±SD	77.58±8.90	75.62±6.76	1.006	0.085
Range	62-92	63-87		
After induction				
Mean±SD	74.52±8.47	73.34±7.26	1.09	0.298
Range	57-90	58-87		
End of surgery				
Mean±SD	79.71±6.95	79.06±5.91	0.498	0.481
Range	69-96	69-90		
Entrance to PACU				
Mean±SD	80.63±7.49	79.92±4.80	0.618	0.587
Range	65-104	70-85		
Exit from PACU				
Mean±SD	77.56±4.79	77.87±3.79	0.242	0.623
Range	70-91	67-87		

PACU, postanesthetic care unit.

Table 6: Comparison between groups according to shivering score

Shivering score (BSAS score)	Group I ($n=50$)	Group II ($n=50$)	χ^2	*P*
1	46 (92.0%)	28 (56.0%)	33.052	<0.00
2	2 (4.0%)	14 (28.0%)		
3	1 (2.0%)	3 (6.0%)		
4	1 (2.0%)	5 (10.0%)		
Total number of patients with shivering	4 (8.0%)	22 (44.0%)		

BSAS, Bedside Shivering Assessment Score.

is a considerably effective drug in treating shivering. However, the action of meperidine is in part mediated by non-μ-opioid receptors and also has central anticholinergic activity [13].

Conclusion

Preoperative administration of oral ondansetron adequately prevents PAS incidence compared with placebo. Ondansetron does not have any significant effect on tympanic temperature.

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Conflicts of interest

There are no conflicts of interest.

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