

The Effect of Ondansetron and Meperedin on Preventing Shivering After Off-pump Coronary Artery Bypass Graft

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Abstract- One of the most common complications of operation and anesthesia is shivering. The purpose of this study was to compare the effectiveness of Ondansetron and Meperedine in preventing shivering after off-pump coronary artery bypass graft (OPCAB). In this double-blind randomized clinical trial, the sample consisted of 90 patients, who were candidates of CABG under general anesthesia. These patients were assigned to three groups, each containing 30 subjects: meperedine group (A), ondansetron group (B) and control group (C). Group (A) received 0.4 mg/Kg/IV of meperedine, group (B) received 8mg/IV of ondansetron and group (C) received Normal Saline. All these drugs were injected 15 minutes before the end of surgery. After the end of surgery, the intubated patients were transferred to the ICU and their body temperature was assessed through eardrum by a specialist who was blind to the research. The incidence of shivering in groups A, B, and C was 46.48%, 31.18%, and 60.83%, respectively ($P<0.01$). The incidence of shivering was 64.4% in males and 35.6% in females ($P=0.222$). Also, the amount of incidence of shivering up to 3 hours after surgery was 75.87 % ($P=0.064$). Bradycardia was 3.3% in group (A) and 0.0 % in group (B). Other variables (myoclonus, seizure and rash) showed no statistically significant difference ($P=0.353$). According to the findings, it was demonstrated that ondansetron is more effective in preventing shivering after Off-pump CABG than meperedine.

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Introduction

Shivering is one of the most common complications of surgery. The most common causes of shivering are pain and hypothermia. The factors causing shivering may include age, sex, weight, location and extent of surgery. The main cause of hypothermia after CABG is the induced-hypothermia during surgery. Hypothermia after coronary artery bypass graft (CABG) surgery ($<36^{\circ}\text{C}$) can cause complications such as increased mortality rate, increased weaning time, increased need for transfusion and increased discharge time (1). Many studies have compared the effects of various drugs on preventing post-operative shivering, but we decided to compare the effect of ondansetron and Meperedine on preventing shivering after Off-pump CABG (2). Meperedine is a synthetic drug that stimulates the μ receptors to exert their analgesic effect. It can prevent

hypothermia with peripheral vasoconstriction and central vasodilatation (3).

Drugs that lower shivering, can exert their effect by disturbing the central body temperature, so 5-HT antagonist receptors such as ondansetron can be effective in reducing shivering after surgery (4). Ondansetron was until recently considered the only antiemetic available, but studies indicated that 8mg of ondansetron used as a prophylaxis can reduce the shivering to 15% (5). The reason we chose ondansetron and meperedine from among a lot of useful drugs was that too few studies have been conducted on reducing shivering after CABG—especially off-pump CABG. Furthermore, these studies have reported confusing and controversial results so that, in some studies ondansetron have been recognized as a superior drug, while meperedine is reported to be superior in some other studies.

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Materials and Methods

After assessing the research topic in the Bioethics Committee and obtaining the informed written consent (with ASA level 1, 2, 3) of 90 patients, candidates for CABG were randomly assigned into 3 groups of 30. We analyzed the data using descriptive statistics via SPSS 11.5. Also, the comparisons among groups were performed using *Chi*-square and Fisher test.

These groups received ondansetron, meperidine and normal saline. Patients with myocardial failure (NYHA3, 4), dysrhythmia, muscular disease, Parkinson’s disease, fever (more than 37.5° c), patients receiving vasoconstrictor and alpha agonist, and addict patients were excluded. General anesthesia was induced with Thiopental (5mg/kg), Fentanyl (10mic/kg) and Pancoraniom (0/1mg/kg). Propofol infusion (50mic/kg/min) during surgery was used for maintenance of anesthesia. End tidal CO₂ during surgery was held between 30 to 36 mmHg. At the end of surgery, intubated patients were transferred to ICU and shivering scores were recorded by the anesthesiologist, who was not aware of the research groups.

Shivering was graded as follows (6):

0= Patient with no shivering.

1= whenever one of these symptoms is present: peripheral vasoconstriction, peripheral cyanosis without any other reason, and piloerection without muscle contraction.

2= Visible muscular activity that involved only one muscle group.

3= Visible muscular activity that involved more than one muscle group.

4= Intensive muscular activity that involved the whole body.

Evaluation of shivering was done after we were assured that the effects of neuromuscular blocker drugs were reversed. The mean arterial pressure and heart rate were evaluated before induction of anesthesia, before onset of surgery, and after extubation every 5-15 minutes. The most reliable method and gold standard of core temperature monitoring is tympanic temperature monitoring by using tympanic probe (7). Tympanic temperature measurements were recorded before surgery and during surgery every 5-15 minutes. Group (A) received meperidine (4mg/kg/iv), group (B) received ondansetron (8mg/IV) and group (C) or control group received Normal Saline. These drugs were administered 15 minutes before the end of surgery. If shivering with a score of 2 or higher existed, 25 mg of Meperidine was administered.

Results

In this study, 90 patients were assigned to 3 groups. There was no significant difference among the age, sex and surgery duration of groups (*P*=0.412). After analyzing the data via SPSS, *Chi*-square and Fisher test revealed that there was significant difference of shivering between groups (Table 1). This drug has also fewer side effects in addition to a lower incidence of shivering in group B compared to the common drug used to treat shivering, *i.e.*, meperidine.

The side effects of drugs used in this study such as bradycardia, convulsion, rash and myoclonus were assessed, too. There was no significant difference of these side effects between groups (Table 2).

Table 1. A comparison of the average of age, sex, surgery duration and shivering in 3 groups.

Variable	Meperidine Group	ondansetron Group	Control Group	P-Value
Age (Year)	10.916±63.93	10272±64.83	12.88 ±62.73	0.412
Sex (Male)	56.7	76.7	60	0.222
Sex (Female)	43.3	23.3	40	0.222
Surgery Duration (Min)	18.782y±123	17.42±143.17	18.789±142.50	0.064
Shivering	46.48	31.18	60.83	0.0

Table 2. A comparison of data in 3 groups.

Side Effect	Meperidine Group	ondansetron Group	Control Group	P-value
Convulsion	0.0	0.0	0.0	0.355
Bradycardia	3.3	0.0	6.7	0.355
Myoclonus	0.0	0.0	0.0	0.355
Rosh	0.0	0.0	0.0	0.355

Discussion

Perioperative hypothermia and shivering are among the frequent, undesirable and unpleasant complications of both general and regional anesthesia. The incidence of shivering is up to 40-60% even in regional anaesthesia (8). Apart from physical warming, many drugs have also been used for the prevention of shivering. This study compared the effect of ondansetron and Meperidine on preventing post-operative shivering after Off-pump CABG. Prevention and treatment of post-anesthesia shivering is an important aspect of patients care, as it may be associated with a number of deleterious sequelae, including sympathoadrenal stimulation, increasing oxygen consumption and carbon dioxide production. Thermal inputs are integrated at the level of the anterior hypothalamus, which compares peripheral information with a threshold value, or the set-point. Temperatures 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 (9). Both general and regional anesthetics are known to affect the efficiency of this homeostatic system and may result in different degrees of perioperative hypothermia. Regional anesthesia also decreases this threshold by 0.5°C, triggering vasoconstriction and shivering above the level of block. This reduction in threshold is proportional to the number of spinal segments blocked, advanced age and high-level spinal blockade (10). Shivering causes increased metabolic activity and increased oxygen consumption up to 100%. It also causes 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 an increase in cardiac output, peripheral resistance, carbon dioxide production, and lactic acidosis. Moreover, it interferes with ECG and oxygen saturation monitoring (pulse oximetry) (11).

In this study, post-anesthesia shivering was 46.48% in group (A) compared with 31.18% in group (B). Specific inhibition of 5-HT system, therefore, produced a dose-dependent reduction in shivering. Ondansetron, which is a specific 5-HT₃ receptor antagonist, is widely used as an antiemetic drug (12). The mechanism of action could be related to the inhibition of serotonin reuptake on the preoptic anterior hypothalamic region. 5-HT₃ receptors may also influence both heat production and heat loss pathways. The recommended dose of Ondansetron for prevention of postoperative nausea & vomiting is 4-8 mg in adult patients.

Information about the comparison of the two drugs is quite different. Robert and his colleagues, in their own study said that administration of 8mg ondansetron can reduce the shivering. Kelsaka *et al.*, compared the 8mg ondansetron with Meperidine for the prevention of shivering and found the same antishivering effect and the incidence of shivering was 8% in ondansetron group (13). In the study done by Kelsaka *et al.*, core temperature was preserved in Ondansetron group (8mg) and meperidine (0.4 mg kg⁻¹) in the control group during intraoperative period after spinal anesthesia. Yet, Komatso and his colleagues explicitly talked about the absence of any effect of ondansetron on reducing shivering (14). We can conclude that ondansetron is a better drug to preventing shivering.

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