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Ondansetron versus Pethidine for The Prevention of Postoperative Shivering

Medhat Noaman; Fouad Ibrahim Mohamed; Adel Al-Hady Ahmed Diab

Anesthesiology and Intensive Care Department, Faculty of Medicine, Al-Azhar University, New Damietta City, Egypt

Corresponding author
Adel Al-Hady Ahmed Diab

Anesthesiology and Intensive Care Department,

Faculty of Medicine,

Al-Azhar University, New Damietta, Egypt

Email: dr.adeldiab71@gmail.com

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Objective: The aim of the present study was to evaluate the effects of ondansetron for prevention of postoperative shivering.

Patients and Methods: The study was carried out on 40 patient ASA I or II scheduled for lower abdominal surgery. They were categorized into two equal groups Group I (Group P): Patients were receiving intravenous pethidine in a dose of 0.5 mg/kg. Group II (Group O): Patients were received intravenous ondansetron in a dose of 4 mg. just before induction of spinal block.

Results: The studied groups showed no significant difference regarding demographic data, or postoperative shivering. However, postoperative nausea, vomiting and sedation were significantly increased in pethidine when compared to ondansetron group.

Conclusion: Ondansetron is effective as Pethidine for prevention of postoperative shivering. However, side effects postoperative nausea & vomiting were significantly higher in pethidine group. Thus, ondansetron could be used as a safe and effective alternative for pethidine for postoperative shivering.

Keywords: Ondansetron; pethidine; postoperative shivering.

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Introduction

Postoperatively, and specifically after general anesthesia, shivering is a common and understandable complication. Its incidence ranged between 6.3- 66%, and the mechanism is not fully elucidated[1,2]. Shivering is associated with increased metabolic activity and consumption of oxygen. In addition, arterial hypoxia, lactic acidosis and interference with electrocardiogram monitoring could be associated with shivering. Thus, the prevention of shivering is an important especially in patients with low cardiopulmonary reserve[3].

There are different pharmacological agents used for prophylaxis or treatment of post-operative shivering (e.g., clonidine, ketamine, doxapram, tramadol, pethidine and other opioids)[4-6]. Pethidine is the most effective, however, it is associated with other side effects[7].

Inhibition of 5-hydroxytryptamine- 3 (5-HT3) system lead to reduction of shivering. However, shivering reduction could not be attributed solely to inhibition of 5-HT-3 system as there is a wide variety of neurotransmitter systems with anti-shivering effect [8]. Ondansetron, a 5-HT3 antagonist, is an anti-emetic, and could be prevent post-anesthesia shivering. However, it role as anti-shivering agent remains controversial. One meta-analysis reported that, ondansetron reduced the incidence of postoperative shivering with no cardiovascular side effects (e.g., Bradycardia) [9]

This study was designed to compare the effect of pethidine (standard treatment of post spinal shivering) and ondansetron in prevention of post-spinal shivering and determine which of these pharmacological interventions serves best to achieve therapeutic effect with minimal side effect.

Patient and methods:

They study protocol was approved by the Local Research and Ethical Committee approval and scheduled patients provided an informed written consent to participate in the study. The study included 40 patients who scheduled for lower abdominal surgery under spinal anesthesia. Their ages ranged from 21 to 60 years; and they were of American Society for Anesthesiologists (ASA) class I or II. The surgical procedures included Hernioplasty, appendicectomy and vaginal hysterectomy. Patients were randomly allocated by closed envelope into two equal groups: Group (P): 20 patients received pethidine in a dose of 0.5 mg/kg. iv just before induction of spinal block. Group (O): 20 patients received ondansetron in a dose of 4 mg. iv just before induction of spinal block.

Exclusion criteria were: any significant coexisting diseases (cardiopulmonary, renal, hepatic), patients with psychological disorder, temperature above 38ºC or below 36.5ºC, patients who might need blood transfusion, duration exceeds 180 minutes and patient refusal.

Oral diazepam 0.2mg/kg was used as a premedication at night and one hour before coming to the operation room. Standard monitoring was done including electrocardiogram, SPO_2, and non-invasive blood pressure. Subarachnoid blockade was achieved with 25 G disposable Quinke's spinal needle (Egemen) with 0.5% hyperbaric bupivacaine (Sunny Pivacaine) and the dose was adjusted according to patient height and body weight (average dose 15 mg at a rate of 0.2 ml/s.).

The primary outcome measure was shivering, defined as readily visible tremors of the face, trunk, or limbs lasting for a minimum of 15-s. Shivering was graded into 4 grades by a scale validated by Tsai and Chu[2].

The secondary outcome included intra-operative hemodynamic changes such as mean arterial pressure (MAP) and heart rate (HR). In addition, postoperative unwanted effects (e.g., hypotension, nausea and vomiting), and its management were documented.

Statistical analysis: numerical data expressed as mean±SD (standard deviation), while categorical data were expressed as frequency and percentage. Groups compared by independent samples student (t) test or Chi square test. All analyses were carried out using statistical package for social science (SPSS) version 18 (SPSS Inc., Chicago, Illinois, USA). P value < 0.05 was significant.

Results:

The two groups were comparable regarding distribution of age, weight, gender and ASA physical status (Table 1). Skin temperature was recorded every 5 minutes during intraoperative period for one hour. All patients in all the 2 groups had decrease in skin temperature from baseline value after spinal anesthesia. Temperature decreased more in ondansetron group than in pethidine groups. p value was found to be significant (<0.05) at 10 min till the remaining time of the study between pethidine and ondansetron groups (Table 2).

The incidence of shivering was not significantly different between group O and group P (15.0% vs 5.0%). There was significant increase of patients need pethidine in group O when compared to group P (30% vs 5.0%).

There is no significant difference between P and O groups regarding hypotension. However, nausea, vomiting and sedation were significantly increased in group P when compared to group O (20.0%, 20.0% and 85.0% vs 0.0%, 0.0% and 0.0% successively) (Table 3).

Table (1): Demographic characteristics in studied groups

	Group P	Group O	P value
Age (years) (mean±SD) Range	38.16±9.46; 25-70	38.53±9.48; 25-59	0.92(NS)
Sex (n,%) Male Female	 10(50%) 10(50%)	 12(60.0%) 8(40.0%)	 0.75(NS)
Weight (kg) (mean±SD) Range	71.43±7.04; 59- 84	73.66±7.63; 62- 85	0.38(NS)
ASA (n,%) I II	 11(55.0%) 9(45.0%)	 12(60%) 8(40.0%)	 0.74(NS)

Table (2): Comparison between groups regarding temperatures)

	Group P	Group O	P value
0 min	36.29±0.23	36.25±0.22	0.67
5 min	36.80±0.09	36.80±0.10	0.96
10 min	36.08±0.01	36.052±0.01	*0.002***
15 min	36.086±0.02	36.055±0.02	*0.03**
20 min	36.09±0.02	36.044±0.02	*0.004***
25 min	36.09±0.026	36.045±0.025	*0.001***
30 min	36.09±0.02	36.034±0.02	*0.001***
35 min	36.09±0.13	36.032±0.23	*0.008***
40 min	36.09±0.02	36.030±0.02	*0.008***
45 min	36.09±0.02	36.030±0.02	*0.001***
50 min	36.09±0.02	36.029±0.02	*0.008***
55 min	36.09±0.02	36.025±0.02	*0.001***
60 min	36.09±0.02	36.024±0.02	*0.008***

Table (3): Side effects among studied groups

	Group P	Group O	P value
Hypotension	2 (10.0%)	3(15.0%)	0.63
Nausea	4(20.0%)	0(0.0%)	*0.035**
Vomiting	4(20.0%)	0(0.0%)	*0.035**
Sedation	17(85.0%)	0(0.0%)	*<0.001**

Discussion

Postoperative shivering and hypotension are attributed to many factors including-but not limited to- patient age, surgery duration, operating room temperature and infusion solution. Hence, we excluded patients over the age of 60, as

For this reason, in our study patients over the age of 60 years were excluded, as advocated by Witte and Sessler [10]. In addition, temperature of operating theatre was preserved at 24^{o}C and administration of cold solution were prohibited.

According to researcher's best of knowledge, this is the one of earliest trials comparing Ondansetron to pethidine. Ondansetron was as effective as pethidine in prevention of postoperative shivering (no difference was found between groups). But, it was safer than pethidine as it is associated with significantly lower nausea, vomiting and sedation. Mahoori *et al.*[11] concluded that ondansetron (8mg) and pethidine have comparable effects on shivering and intravenous ondansetron (8mg) can control shivering and proposed that, this dose is the dose of choice for control of postoperative shivering. However, results of the present work proved that, a dose of 4mg of intravenous ondansetron could effectively control shivering.

Shakya et al.[12] proved the effectiveness and safety of low-dose ketamine and ondansetron (0.25 mg/kg and 4mg, respectively) in the prevention of post-anesthesia shivering when compared with placebo. In addition, Chagaleti and Athuru[13] studied ondansetron (4mg) versus tramadol and saline for prevention of post-operative shivering after caesarean Section with spinal anesthesia. They reported an incidence of postoperative shivering to be 20% in ondansetron group, 16.7% in the tramadol group and 53.3% in the saline group. In addition, Powell and Buggy[14] reported incidence of 57.0%, 33.0% and 15.0% after saline, ondansetron 4mg and 8mg respectively.

On the other side, Safavi et al. [15] studied 90 patients underwent spinal anesthesia, and reported that, ketamine (0.25 mg/kg) plus 37.5 µg/kg of midazolam is effective in prevention of postoperative shivering after spinal anesthesia such as ondansetron at dose of 8 mg. In addition, Browning et al.[16], found no significant difference between ondansetron 8 mg or saline in cesarean section regarding postoperative shivering. Also Kelsaka et al. [17] studied 75 patients, and compared ondansetron, pethidine and placebo. They found that pethidine and ondansetron had similar efficacy in prevention of postoperative shivering.

Finally, Chowdhury et al.[18] concluded that, IV opioid (tramadol) is superior than ondansetron for control of postoperative shivering. They added, ondansetron is effective for reduction of shivering with delayed onset than tramadol, but with better hemodynamic stability and significant reduction of postoperative nausea and vomiting.

Differences in the reported results in previous literature could be attributed to the heterogeneity in study design and dose of ondansetron used in previous works (the majority in previous studies use 8mg, with high safety profile as 4mg reported in the present work).

In conclusion, pethidine is significantly more effective in prevention of post-operative shivering. However, it is associated with significant increase of postoperative nausea, vomiting and sedation. Therefore, prophylactic ondansetron could be considered as an alternative for pethidine in reduction of postoperative shivering with high safety profile.

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