ORIGINAL ARTICLE

A comparison between cetirizine and ondansetron in preventing postoperative nausea and vomiting in adults

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Background: Postoperative nausea and vomiting are some of the important and common side effects of anesthesia after surgery occurring in almost 20-30% of patients and is the second factor of a patient's complaint and inconvenience after pain. This study compares the effect of oral cetirizine and ondansetron in the prevention of postoperative nausea and vomiting in adults. **Materials and Methods:** In a blind and prospective study in fall 2010, 300 patients aged 18-65 years who were among ASA I-II in Chamran Orthopedic Hospital were randomly divided into three equal groups receiving cetirizine, ondansetron, and placebo, respectively. General anesthesia was identical. After operation (after 1-2 h in the recovery room, after 2-12 and 12-24 h in the ward), the presence or absence and any nausea or vomiting was recorded. **Results:** The postoperative nausea and vomiting (PONV) rate after 1-2 h in the recovery room, after 2-12 and 12-24 h in the ward in placebo, and both groups of cetirizine and ondansetron were 50%, 21%, and 11%, respectively while the difference was significant (P value < 0.05). Regarding the number of vomiting, the least was related to ondansetron (especially in the first 2-12 h) but the difference was not significant (P > 0.05). **Conclusion:** The PONV rate in cetirizine and ondansetron groups was less than the placebo group.

Key words: Anesthesia, cetirizine, nausea, ondansetron, postoperative, vomiting

INTRODUCTION

Nausea and vomiting are the two important and common side effects of anesthesia after surgery and considered to be the second factor of a patient's inconvenience and complaint, The postoperative nausea and vomiting (PONV) incidence will increase if the five risk factors of gender, history of PONV, undergoing surgery for more than 60 min, motion sickness, and consumption of drugs after surgery are considered simultaneously, while the PONV incidence may reach to a rate of 74%. Postoperative nausea and vomiting may be associated with pulmonary aspiration of gastric content, discrete sores, esophageal rupture, subcutaneous emphysema, and delay in discharge.[1]

Up to now, various methods and medications were recommended to prevent the side effects, the most common ones being metoclopromide, ondansetron, midazolam, deroperidol, cetirizine, etc.[2-12] Cetirizine is one of the new antihistamines which contrary to the older generation of antihistamines has less sedation and hypnotic effects, however similar to the old generation may cause a reduction in PONV. Ondansetron is a serotonin receptor controller (5HT-3 anti-receptor) that can prevent and control nausea and vomiting after chemotherapy and reduce PONV.[1,13]

Various risk factors are mentioned in PONV incidence of which female gender is the most dependent prognostic factor in postoperative nausea and vomiting. Non-smokers are exposed to PONV 1/8 times more in comparison to smokers.[7] Having a history of PONV, motion sickness, migraine, drug addiction, and inhaled anesthetics are the other PONV prognostic factors. Regarding drugs, the dosage is very important in PONV incidence. The postoperative use of drugs may cause PONV twice more than the operative time.[1,2]

The incidence of nausea and vomiting were reported more in stomach, ENT, ophthalmology, laparoscopy, and genital surgeries.[1,14] Although more cases of PONV were also noticed, the type of surgery was an independent factor.[15] In volunteers who had just take anesthesia without any operation, PONV was still present.[1] To date, oral cetirizine and ondansetron

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were studied separately regarding their effect in reduction of PONV,[2,4] but our study compares the two anesthetics together and with a placebo on postoperative nausea and in adults undergoing orthopedic surgeries. To prevent the effect and intervention of the type of surgery, this study just considered the patients who underwent orthopedic operations.

MATERIALS AND METHODS

In a randomized clinical trial cross-sectional prospective study conducted in fall 2010 in Chamran Orthopedic Hospital affiliated to Shiraz University of Medical Sciences, 300 patients aged 18-65 years with American Society of Anesthesia (ASA) I and Π were enrolled. The patients in a double-blind study's simple random sampling method were divided into three equal groups (placebo, cetirizine, and ondansetron groups). A written consent was provided from all patients. The study was approved as a residency thesis in Shiraz University of Medical Sciences (88-4619). Prior to the beginning of the study, training to evaluate the presence or absence of nausea and vomiting and the number of vomiting episodes was undertaken. The criterion for vomiting was the occurrence of a time interval of more than 1 min. The patients who had a previous history of diabetes mellitus, motion sickness, ischemic cardiomyopathy, nausea and vomiting in previous operations, asthma, and pregnancy were excluded from the study. Although non-smoking and BMI were among possible PONV reducing factors, they did not cause any interaction in the analyses of other studies.[7] So they were not considered as a criterion to exclude patients. The dosage was also determined according to the previous studies.[3,7] The medications were placebo, cetirizine (10 mg, Darupakhsh, Tehran, Iran), and ondansetron (8 mg, Darupakhsh, Tehran, Iran) that were administered orally in a capsule form and with a similar shape. Only the anesthetist was aware of the content. The medicines were administered 30-60 min before anesthesia, so the study was a double blind one and neither the interviewer nor the patient was aware of the capsule content.

Anesthesia was the same in the three groups and was just a general anesthesia and no peripheral nerve blockers or regional anesthesia (spinal or epidural) were used. For induction of anesthesia, midasolam (0.03 mg/kg, Exir, Tehran, Iran), fentanil (1-2 mg/kg, Rotex Medica, Germany), sodium thiopental (3-5 mg/kg, Exir, Tehran, Iran), and morphine (0.1-0.2 mg/kg, Rotex Medica, Germany) with a muscle relaxant were administered intravenously for all patients. The maintenance of anesthesia was with isoflorane, nitroxide, and oxygen (50% N_2O and O_2).

At the end of surgery and after discontinuation of anesthesia, a reverse of muscle relaxant with neostigmine (0.06 mg/ kg, IV) and atropine (0.03 mg/kg, IV) was administered intravenously and the tracheal tube was taken out. Patients were evaluated according to the presence of nausea and vomiting in three time periods including the first 1-2 h after operation in the recovery room, 2-12 and 12-24 hours after operation in the relevant ward. All information was recorded in a checklist. Data were analyzed using SPSS software (Version 15, Chicago, IL, USA) by the chi-squared and Fisher's exact tests. A *P* value less than 0.05 was considered statistically significant.

RESULTS

The total number of patients was 300 which were divided into three equal groups in age range of 18-65 years. As variables of smoking and gender were not evaluated in this study, so the number of subjects with these variables was different in each group. The important variables were the type of medicine (placebo, cetirizine, and ondansetron), presence or absence of nausea or vomiting in various time periods (in the recovery room or ward), and the number of vomiting (one time and more or less) in each period. In this study, the severity of nausea was not included.

The findings related to time of staying in the recovery room (first 1-2 h after operation) was presented in Table 1. In this period, the highest incidence of nausea and vomiting was related to placebo (44%) and the lowest to the ondansetron group (7%). There was no significant difference between ondansetron and cetirizine group. A significant difference was noticed between ondansetron and cetirizine group. During this period, only two patients in the placebo group had vomiting more than two times and the other groups had less.

The findings related to the first 2-12 h after operation were shown in Table 2. The incidence of nausea and vomiting was 61% in the placebo group, 39% in the cetirizine group,

Table 1: Comparing the incidence of postoperative nausea and vomiting among three groups of placebo, cetirizine, and ondansetron during stay in the recovery room (the first 2 h after operation)

Ondansetron (%) *n* = 100	Cetirizine (%) *n* = 100	Placebo (%) *n* = 100	Group
6 (6)	10 (10)	33 (33)	The number of people having nausea
1 (1)	2 (2)	11 (11)	The number of people having vomiting[a]
7 (7)	12 (12)	44 (44)	Total

[a]The number of two or more times of vomiting in placebo, cetirizine, and ondansetron groups was respectively 2, 0, and 0 subjects. The difference between cetirizine and ondansetron with placebo was statistically significant (*P* = 0.001) but that between cetirizine and ondansetron was not significant

and 18% in the ondansetron group. There was a significant difference between the placebo group and the other two groups and the incidence of vomiting between cetirizine and ondansetron showed a significant difference.

Despite more reduction in the incidence of vomiting in ondansetron in comparison to the cetirizine group, the incidence of vomiting between the two groups did not show any significant difference. During this period in placebo group, the number of more than two times vomiting was higher (4%).

The findings related to the first 12-24 h after operation were demonstrated in Table 3. During this time interval, the rate of nausea and vomiting in the placebo group was more (45%) than the cetirizine (13%) and the ondansetron group (7%). In this period, there was a significant difference visible between the placebo and other groups. During this time, four subjects of the placebo group had vomiting more than two times. The lowest rate of nausea and vomiting in all the three time periods was noticed in the ondansetron group. For severity of vomiting, the same result was observed.

DISCUSSION

Prophylaxis and prevention of postoperative nausea and vomiting is still one of the most important issues of controversies.[11] The reason for the controversies may be related to the patient, type of anesthesia and surgery, and the postoperative condition. In this study, to prevent the interaction of type of surgery, only patients who underwent orthopedic surgery were included. The type of anesthetic medication to induce and maintain anesthesia was recorded in all groups. Most of the factors related to patients were adjusted by the exclusion criteria except for BMI and the smoking habits which were considered as the probable factors of PONV incidence.[7] In this study, the incidence of postoperative nausea in the placebo group in all recovery time periods including the first 2 h, 2-12 h, and 12-24 h after operation was 44%, 61%, and 45%; in the cetirizine group it was 12%, 39%, and 13%; and in the ondansetron group it was 7%, 18%, and 7% which indicates that in all three groups, the highest incidence rate was noticed during the 2-12 h after operation.

According to the fact that administration of postoperative medications was twice as effective as interoperative one in PONV incidence,[1] the reason of this double increase in PONV for each group in the first 2-12 h may be this matter [Table 2]. In 2007 in a research on comparing setrons for the prevention of postoperative nausea and vomiting conducted by Gupta and his colleagues, PONV incidence in all groups (placebo, setrons, ondansetron, and granisetron groups) was less in 2-24 h after operation.[2,4] However, in another study on comparing oral ondansetron with placebo in outpatient surgeries, most of the patients had no signs during the recovery period and most of the nausea and vomiting rates were related to the time after being discharged.[12]

In our study, PONV rate reduced again during 12-24 h after operation especially for ondansetron which was the most effective one. Since this event may last for 5 days after operation,[12-15] recommendation of some studies is the repeat of ondansetron administration as done by Hartsell *et al*. in 2005 comparing ondansetron and placebo using various dosages (4 mg of ondansetron and placebo 30 min before the end of operation and 8 mg ondansetron and placebo twice daily for 72 h after operation) showed that there was a need to rescue treatment on the second and the third day after operation in the ondansetron group demonstrating a remarkable decrease in comparison to the placebo group.[6]

In some studies, ondansetron effectiveness in the reduction of vomiting compared to nausea was more on vomiting than nausea.[3] In our study, the nausea incidence in the

Table 2: Comparing postoperative nausea and vomiting among placebo, cetirizine, and ondansetron groups 2–12 h after operation

Ondansetron (%) *n* = 100	Cetirizine (%) *n* = 100	Placebo (%) *n* = 100	Group
12 (12)	26 (26)	41 (41)	The number of people having nausea
6 (6)	13 (13)	20 (20)	The number of people having vomiting[a]
18 (18)	39 (39)	61 (61)	Total

[a]The number of cases having two or more times of vomiting in placebo, cetirizine, and ondansetron groups was respectively 4, 0, and 0 subjects. The difference between cetirizine and ondansetron with placebo was statistically significant ($P = 0.02$) but that between cetirizine and ondansetron was not significant

Table 3: Comparing postoperative nausea and vomiting among placebo, cetirizine, and ondansetron groups 12–24 h after operation

Ondansetron (%) *n* = 100	Cetirizine (%) *n* = 100	Placebo (%) *n* = 100	Group
5 (5)	9 (9)	321 (32)	The number of people having nausea
2 (2)	4 (4)	13 (13)	The number of people having vomiting[a]
7 (7)	13 (13)	45 (45)	Total

[a]The number of cases having two or more times of vomiting in placebo, cetirizine, and ondansetron groups was respectively 4, 0, and 0 subjects. The difference between cetirizine and ondansetron with placebo was statistically significant ($P = 0.01$) but that between cetirizine and ondansetron was not significant

ondansetron group during the recovery period was 6% while the vomiting incidence following its administration was 1% in the recovery period and also in the time interval of 2-12 h which was 12% [Tables 1 and 2]. Of course, this effectiveness in nausea in comparison to vomiting was also similar in cetirizine and placebo groups either in the recovery period or in other times and no significant difference was seen when compared to the ondansetron group.

In this study, regarding the severity of vomiting, the effectiveness of ondansetron in comparison to the placebo group was more during the whole 24 h after operation but when compared to the cetrizine group; it was more effective only during 2-12 h after operation. The administration of 8 mg of oral ondansetron 30-60 min before induction of anesthesia may cause a remarkable decrease in postoperative nausea and vomiting although the least optimal dose for the incidence of this decrease was 4 mg ondansetron. Administration of 10 mg oral cetirizine, 30-60 min before induction of anesthesia may cause a reduction in postoperative nausea and vomiting.[1,3]

Cetirizine and ondansetron were both more effective on a decrease in vomiting in comparison to their effect on nausea. Its ease in administration, less cost in comparison to other methods such as injection, and also more decrease in the severity of vomiting than other medications can be the reasons to suggest that ondansetron be a better choice for preventing PONV. Despite the effect that ondansetron had more on PONV decrease in all postoperative periods in comparison to cetirizine, the difference was not significant except for nausea during the 2-12 h after operation which was significant. So to get better results, enrollment of more subjects seems necessary.

In this study, we did not look for the difference between the two genders according to PONV incidence; however, there was no significant difference between these three groups. But in the case of getting more accurate results, it is necessary to evaluate equal number of each gender in the study. In order to decrease nausea and vomiting for a longer time after operation, various dosages of ondansetron or long-lasting medication such as aperpitant (NK_1 antagonist) should be used.

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