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Original Article

Effect of ondansetron for preventing postoperative nausea and vomiting after breast cancer surgery

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Abstract: Objective: To evaluate the preventive effect of preoperative administration of ondansetron on postoperative nausea and vomiting (PONV) in patients receiving breast cancer surgery. Methods: Data from 225 patients who received modified radical mastectomy from January 2019 to December 2020 were retrospectively reviewed. The patients were divided into an ondansetron group and a control group according to whether they received preoperative ondansetron or not. The incidence of PONV, visual analog scale (VAS) score, the rescue analgesics use and rescue antiemetic use, as well as the patient satisfaction degree about their PONV were compared between the two groups. Results: The ondansetron group showed lower total incidence of PONV, lower VAS score at 6 h post-operation as well as less rescue antiemetic use than the control group ($P<0.05$). Patients in the ondansetron group were more satisfied with their PONV condition than those in the control group ($P<0.05$). Conclusion: Preoperative administration of ondansetron can prevent PONV and relieve pain 2-24 hours after breast cancer surgery.

Keywords: Postoperative nausea and vomiting, breast cancer surgery, ondansetron, surgical pain

Introduction

Breast cancer is the most common malignant tumor in women. According to the national cancer statistics report in 2017, breast cancer was still the first killer threatening people's life in the world [1]. It is estimated that the number of people suffering from breast cancer worldwide will reach 2.64 million in 2030 [2]. Surgery is one of the most important treatments for breast cancer, and postoperative nausea and vomiting (PONV) is a common symptom in patients who have received breast cancer surgery [3, 4].

PONV usually occurs within 6-48 hours after breast cancer surgery [5, 6]. However, there are different opinions on prophylactic use of antiemetic drugs in breast cancer patients before surgery. For example, Pazoki et al. [7] suggested that prophylactic use of antiemetic drugs should be applied to middle and high-risk patients to prevent PONV. But some scholars considered that drugs have potential side effects, and some studies reported that the prophylactic use of antiemetic drugs were not albe to prevent PONV in patients undergoing surgery [8-10].

Currently, drugs including serotonin-3 receptor antagonists, neurokinin-1 receptor antagonists, glucocorticoids, butyryl benzenes, phenothiazines, benzamides, antihistamines and anticholinergics have been used for the prevention of PONV in clinic [11-15]. However, they have short acting duration, limited effects on postoperative vomiting and no effect for anti-nausea [16, 17]. The consensus guidelines for PONV recommend 5-HT3 receptor antagonists as the first-line drugs for the prevention and treatment of PONV [18]. Among them, ondansetron can effectively prevent and treat PONV [19, 20]. However, reports about the effectiveness of preoperative administration of ondansetron on PONV in breast cancer patients after surgery are limited. Therefore, the aim of this study was to investigate the preventive effect of ondansetron on PONV after breast cancer surgery with

the hope to provide more evidence for the use of ondansetron in clinic.

Materials and methods

Data collection

Data of 225 patients who received modified radical mastectomy at Cangzhou Central Hospital between January 2019 and December 2020 were retrospectively analyzed. The patients were assigned into a control group (n=111) and an ondansetron group (n=114) based on whether they received preoperative ondansetron or not. Patient baseline demographic and morphometric characteristics, surgery information, intraoperative and postoperative data were obtained from electronic medical records in our hospital. This study was approved by the Ethics Committee of Cangzhou Central Hospital (No.: ECZZX-2019.0112).

Inclusion criteria

Female patients who received modified radical mastectomy for the first time; patients who did not take targeted drugs for breast cancer treatment; patients aged over 18 years old; patients who had a physical status ranged one to three according to American Society of Anesthesiologists (ASA).

Exclusion criteria

Patients who had autoimmune diseases, malignant tumor or mental disorders; patients with severe defects in liver, kidney, heart or lung functions; patients with mental and cognitive dysfunctions; patients without complete clinical data.

Intervention method

All the patients received intravenous general anesthesia. After routine patient monitoring, anesthesia was induced by using 0.5 mg/kg lidocaine, 1.5 to 2.5 mg/kg propofol and 0.6 mg/kg rocuronium and maintained with 1.5% to 2.5% sevoflurane and 0.1 to 0.3 μg/kg/min remifentanil. The analgesic pump was used after surgery in the two groups.

Furthermore, the patients in the ondansetron group were injected with 8 mg of ondansetron (Lot number, 0110101EH; Qilu Pharmaceutical Co., Ltd) 10 min before anesthesia, while the control group didn't receive any drugs before anesthesia. In both groups, if patients had severe vomiting after surgery, they were intravenously given 10 mg metoclopramide.

Outcomes measurement

Primary outcomes

The incidence of PONV: The incidence of nausea and vomiting within 2 h, 6 h and 24 hours after operation was observed. The assessment scale for the incidence of PONV was as follows: 0 points, persistent severe nausea or vomiting; 1 point, moderate nausea or transient vomiting; 2 points, none or mild nausea with no active vomiting. A score of 0 or 1 point was considered as "PONV" and a score of 2 points was considered as "no PONV". All patients were assessed by primary nurse.

Pain score: Visual analog scale (VAS) was applied to assess the severity of pain at 6 h, 12 h and 24 h post-operation [21]. The pain was divided into three degrees: mild or no pain (0 point to 2 points), moderate pain (3-6 points) and severe pain (7-10 points).

Secondary outcomes

The use of rescue analgesics: If the VAS score was more than 3 points, 30 mg ketorolac was administered for rescue analgesia. If VAS score was over 6 points, 1 μg/kg fentanyl was injected. The use of rescue analgesics was recorded and analyzed.

The rescue antiemetic use: When patients complained about nausea or vomiting, 10 mg metoclopramide was administered as a rescue antiemetic. The use of metoclopramide was recorded and analyzed.

Patient satisfaction degree about the PONV condition: The verbal rating scale was used to assess the patients' satisfaction about prevention of PONV [22]. Zero points meant total dissatisfaction, and 10 points means the most satisfaction.

Statistical analysis

SPSS 25.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The measurement data were represented by mean ± SD, and independent samples t-test was used for inter-

Table 1. Baseline data

	Ondansetron group (n=114)	Control group (n=111)	t/χ^2	*P*
Age (years)	49.0±8.5	50.0±7.9	2.135	0.255
BMI	20.85±1.24	20.45±1.02	1.39	0.281
ASA classification			2.173	0.182
I	63 (59.4%)	69 (65.7%)		
II	16 (15.1%)	14 (13.3%)		
III	27 (25.5%)	22 (21%)		
Tumor stage			1.211	0.547
I	53 (46.5%)	57 (51.4%)		
II	47 (41.2%)	41 (36.9%)		
III	14 (12.3%)	13 (11.7%)	2.371	0.843
Smoking status	10 (8.8%)	13 (11.7%)	1.935	0.216
History of PONV	5 (4.4%)	4 (3.6%)	1.865	0.221
Motion sickness	6 (5.3%)	7 (6.3%)	1.376	0.142
Anesthesia time (min)	123.7±24.6	132.9±27.0	2.246	0.154
Pathological type			2.184	0.081
Invasive ductal carcinoma	57 (50%)	62 (55.9%)		
Ductal papillary carcinoma	47 (41.2%)	36 (32.4%)		
Invasive lobular carcinoma	10 (8.8%)	13 (11.7%)		

Note: BMI, body mass index; ASA, American Society of Anesthesiologists; PONV, postoperative nausea and vomiting.

Table 2. VAS scores before and after operation (scores, $\bar{x}\pm s$)

Group	Cases	Pre-operation	6 h post-operation	12 h post-operation	24 h post-operation
Ondansetron group	114	1.19±0.48	4.54±0.41	2.29±0.48	2.19±0.54
Control group	111	1.23±0.54	6.76±0.77	3.44±0.51	2.51±0.33
t	-	2.168	4.225	3.115	3.112
P	-	0.312	0.027	0.216	0.052

group comparisons, paired t-test for intra-group comparisons. The count data were expressed as percentage (%), and Chi square test was used for comparison. P<0.05 was considered as a statistically significant difference.

Results

Clinical characteristics

There was no statistical significance between the two group in terms of age, body mass index, ASA classification, tumor stage, smoking status, history of PONV, motion sickness, anesthesia time and pathological type (all P>0.05, **Table 1**).

Comparison of VAS scores between the two groups

The degree of pain in the two groups was assessed by VAS score. Before operation, there was no significant difference in VAS scores between the two groups. The VAS score was significantly lower in the ondansetron group than that in the control group at 6 h after operation (P<0.05). While there was no significant difference between the two groups at 12 h and 24 h after operation (P>0.05). See **Table 2**.

Comparison of the incidence of PONV between the two groups

The incidences of PONV during 0-2 h and 2-6 h post-operation were significantly lower in the ondansetron group than those in the control group (P<0.05). However, there was no significant difference in the incidences of PONV during 6-12 h and 12-24 h after surgery between the two groups (P>0.05). The total incidence of PONV at 24 h post-operation was significantly lower in the ondansetron group than that in the control group (P<0.001). See **Table 3**.

Table 3. Incidence of PONV

Group	Cases	0-2 h post-operation	2-6 h post-operation	6-12 h post-operation	12-24 h post-operation	Total incidence
Ondansetron group	114	13 (11.4%)	7 (6.1%)	8 (7%)	12 (10.5%)	40 (35.1%)
Control group	111	31 (27.9%)	21 (18.9%)	16 (14.4%)	13 (11.7%)	81 (73.0)
χ^2	-	6.939	5.522	1.185	6.212	32.47
P	-	0.011	0.023	0.116	0.127	<0.001

Note: PONV, postoperative nausea and vomiting.

Table 4. Use of rescue analgesics and antiemetics

Group	Cases	Use of rescue analgesics	Use of metoclopramide
Ondansetron group	114	60 (52.6%)	1 (0.8%)
Control group	111	61 (55%)	46 (41.4%)
χ^2	-	0.618	8.249
P	-	0.315	<0.001

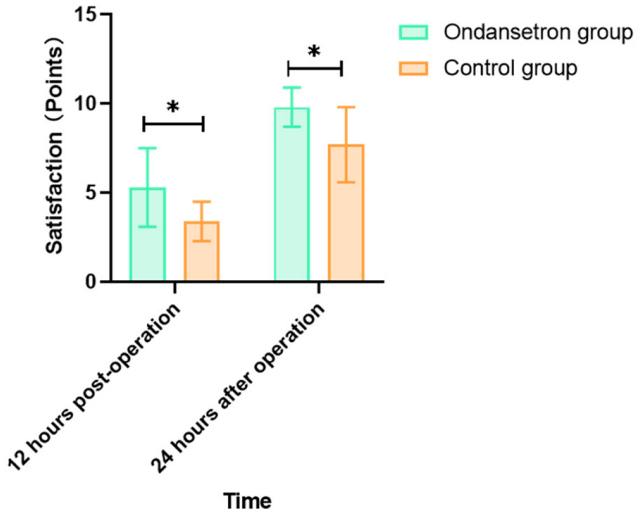

Figure 1. Comparison of the patient satisfaction between two groups after surgery. *P<*0.05*.

Comparison of rescue analgesics and antiemetic use between the two groups

The rescue analgesics use between two groups showed no obvious difference (P>0.05). However, the metoclopramide use in the ondansetron group was lower than that in the control group (0.8% vs. 41.4%; P<0.001). See **Table 4**.

Comparison of the patients' satisfaction between the two groups

As shown in the **Figure 1**, the ondansetron group had higher satisfaction about the PONV condition than the control group (P<0.05).

Discussion

PONV is one of the most common symptoms after breast cancer surgery [23, 24]. It is caused by many factors, including intraoperative hypotension, increased vagus nerve activity and visceral stimulation [25, 26]. In our study, the total incidence of PONV in all the participants was over 50% (53, 78%), which is higher than the previously reported incidence of PONV after other surgeries [27, 28]. This implies that a lot of breast cancer patients may suffer from PONV.

The mechanism of PONV has not been determined. In general, the reflex pathway of vomiting can be simplified as afferent integration efferent function [29]. PONV may be related to nerve conduction pathway network stimulated by bulbar vomiting center receiving stimulation signals from four main functional areas [30]. Ondansetron can inhibit the emetic reflex caused by vagus nerve excitation by selectively blocking the binding located in the central neurochemical receptor area and the afferent vagus nerve of the upper gastrointestinal tract [31]. A study has shown that ondansetron can reduce the level of motilin and restore gastrointestinal function [32]. In this study, our results showed that the incidence of PONV was still as high as 35.1%. This suggested that the 5-hydroxytryptamine (5-HT) pathway might be not the only mechanism of PONV, so this condition needs to be treated in combination with other drugs.

Pain is also a risk factor of PONV [33]. In our study, we found that VAS score was significantly decreased in the ondansetron group at 2 hours and 6 hours after surgery, which is consistent with other reports [34, 35]. The reason may be explained by blocking the sodium channels and peripheral 5-HT3 receptors related to

pain pathways [36], but further research is needed to study the molecular mechanism.

Undeniably, this study has some limitations. Firstly, this study was a single center with limited sample size, so the results may be biased. Secondly, due to the retrospective design, there was possible bias in pertinent information and heterogeneity of data acquisition. Therefore, further large clinical trials are needed to assess the effect of serotonin receptor antagonists on PONV in patients receiving breast cancer surgery.

In conclusion, preoperative ondansetron has certain effects on preventing PONV after breast cancer, and it could help the anesthetics to relieve pain within 2-6 hours after operation.

Disclosure of conflict of interest

None.

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