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ORIGINAL ARTICLE

# A comparison between palonosetron and ondansetron in prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy

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**Abstract**

Postoperative nausea and vomiting (PONV) are common complications after anesthesia and surgery and is associated with adverse outcome. This study was designed to compare the effects of palonosetron and ondansetron in preventing PONV in patients with laparoscopic cholecystectomy. This prospective double-blind study included 60 female patients randomly assigned to the palonosetron group (n = 30) or the ondansetron group (n = 30). Palonosetron 0.075 mg was injected intravenously as a bolus in the palonosetron group. Ondansetron 8 mg was injected intravenously as a bolus in the ondansetron group. The incidences of nausea and vomiting and side effects was recorded after 30 min, 60 min, 2 hrs, 8hrs, 24 hrs postoperatively. The incidence of nausea and vomiting was maximal during immediate postoperative period particularly initial 4 hrs of postoperative period. The complete control of postoperative nausea and vomiting was seen in 30% patients of ondansetron group in first 12 hrs of postoperative period and 90% in palonosetron group. Safety profile was more with palonosetron. The effects of palonosetron and ondansetron in preventing PONV were compared in patients undergoing laparoscopic cholecystectomy and it was found that palonosetron was better in preventing postoperative nausea and vomiting.

**Key words:** Palonosetron, ondansetron, postoperative nausea and vomiting.

## Introduction

Postoperative nausea and vomiting (PONV) are common and distressing to patients. The PONV is a complication that delays recovery, prolongs hospital stays, and increases costs due to additional drug use.[1] Thus there have been many studies on methods and drugs to prevent PONV. The 5-Hydroxytryptamine ($5\text{-HT}_3$) receptor antagonist is being commonly used because it is more effective in PONV prevention and treatment than other antiemetics and has few side effects.[2] Among $5\text{-HT}_3$ receptor antagonists, ondansetron is the most widely used drug, granisetron and ramosetron are also used. Recently, palonosetron has been reported to be effective against chemotherapy-induced nausea and vomiting and effective in the prevention of PONV.[3-6]

Palonosetron is a newly developed $5\text{-HT}_3$ receptor antagonist. Its receptor-affinity is

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more potent than other antagonists. Its plasma half-life is very long.[7,8] However, studies comparing the effects of preventing PONV between palonosetron and other 5-$HT_3$ receptor antagonists are sparse. Thus, we compared the effects of palonosetron and ondansetron in PONV prevention in patients who underwent laparoscopic cholecystectomy.

## Materials and Method

The subjects of the present study were 60 American Society of Anesthesiologists physical status I and II female non-smoker patients aged 18 years and above, scheduled for laparoscopic cholecystectomy, with no history of PONV or motion sickness. Patients were excluded from the study if they had diseases in the major organs, were pregnant, vomited or taken antiemetics within 24 hrs before surgery. We launched the prospective study upon receiving approval from the Institutional Review Board of Jahurul Islam Medical College & Hospital, Bangladesh and received informed consent from the patients.

All patients were kept in the nothing per oral state for 8 hrs or longer. The patients did not receive premedication. General anesthesia was induced with propofol 2 mg/kg and fentanyl 1 µg/kg. Tracheal intubation was facilitated with suxamethonium bromide 2 mg/kg. Anesthesia was maintained with halothane 0.5 vol%, $O_2$-$N_2O$ 4 L/min ($FiO_2$ 0.5), and fentanyl 0.05-0.10 µg/kg intermittently. Heart rate and blood pressure were kept in the 20% range of baseline before anesthesia. When the surgery was over, neostigmine and atropine were used for reversing muscle relaxation. The patients were extubated with the return of consciousness and the stabilization of spontaneous breathing.

The patients were randomly assigned to the palonosetron group (n = 30) and the ondansetron group (n = 30). In the palonosetron group, palonosetron 0.075 mg (4 ml) was administered intravenously immediately before anesthesia induction. In the ondansetron group, ondansetron 8 mg (4 ml) was administered intravenously as a bolus injection immediately before anesthesia induction. After the surgery, if the patient wanted additional analgesics, ketorolac 30 mg was given 30 min, 60 min, 2 hrs, 8 hrs and 24 hrs after the surgery (recovery room), an anesthesiologist, blinded to group assignment, visited the patients and assessed whether or not the patients had nausea and vomiting. Nausea was defined as a subjectively unpleasant feeling associated with the awareness of the urge to vomit. Vomiting was defined as an actual physical phenomenon of the forceful expulsion of gastric contents from the mouth. Retching was defined as labored, spasmodic contractions of the respiratory muscle without expulsion of gastric contents. If the patient retched and had the symptoms of vomiting, it was counted as vomiting. Side-effects of 5-$HT_3$ receptor antagonists, which are headache, dizziness, drowsiness were also evaluated.

## Results

The study enrolled 60 patients until completion with no drop-outs. There were no significant differences between the two groups in patient characteristics and anesthesia time (Table 1).

The PONV incidence rates for each of the set times were similar in the two groups (Table 2). There was no difference in the total incidence rates of PONV in 0-24 hrs (43.3% for the ondansetron group, 16.7% for the palonosetron group). The incidence rate for vomiting was significantly lower in the ondansetron group than the palonosetron group (18% vs. 4%, $p < 0.05$). There was no difference in the use of additional antiemetics between the two groups.

There were postoperative side-effects such as headache, dizziness, and drowsiness, but they did not differ significantly between the ondansetron group and the palonosetron group (Table 3).

**Table 1. Patient characteristics and duration of anesthesia**

| Variables | Ondansetron Group (n = 30) | Palonosetron Group (n = 30) |
|---|---|---|
| Age, yrs | 36.2 ± 11.2 | 41.5 ± 12.1 |
| Weight, kg | 48.2 ± 8.3 | 52.1 ± 9.2 |
| Duration of anesthesia, min | 75.6 ± 15.8 | 78.9 ± 21.3 |

**Table 2. Incidence of postoperative nausea and vomiting (PONV)**

| Observation | Ondansetron Group (n = 30) | Palonosetron Group (n = 30) | *p* value |
|---|---|---|---|
| Postoperative 30 min | | | |
| Nausea, n (%) | 8 (26.7) | 3 (10.0) | 0.090 |
| Vomiting, n (%) | 4 (13.4) | 2 (6.7) | 0.380 |
| PONV, n (%) | 8 (26.7) | 3 (10.0) | 0.090 |
| Postoperative 60 min | | | |
| Nausea, n (%) | 4 (13.3) | 3 (10.0) | 0.680 |
| Vomiting, n (%) | 3 (10.0) | 2 (6.7) | 0.640 |
| PONV, n (%) | 4 (13.3) | 3 (10.0) | 0.680 |
| Postoperative 2 hrs | | | |
| Nausea, n (%) | 3 (10.0) | 5 (16.7) | 0.440 |
| Vomiting, n (%) | 2 (6.7) | 2 (6.7) | 0.990 |
| PONV, n (%) | 3 (10.0) | 5 (16.7) | 0.440 |
| Postoperative 8 hrs | | | |
| Nausea, n (%) | 5 (16.7) | 5 (16.7) | 0.990 |
| Vomiting, n (%) | 1 (3.4) | 2 (6.7) | 0.550 |
| PONV, n (%) | 5 (16.7) | 5 (16.7) | 0.990 |
| Postoperative 8 hrs | | | |
| Nausea, n (%) | 13 (43.3) | 5 (16.7) | 0.006 |
| Vomiting, n (%) | 6 (20.0) | 4 (13.4) | 0.480 |
| PONV, n (%) | 13 (43.3) | 5 (16.7) | 0.006 |

**Table 3. Incidence of adverse effects**

| Adverse effects | Ondansetron Group(n = 30) | Palonosetron Group (n = 30) |
|---|---|---|
| Headache, n (%) | 4 (13.3) | 2 (6.6) |
| Dizziness, n (%) | 1 (3.3) | 2 (6.6) |
| Drowsiness, n (%) | 2 (6.6) | 1 (3.3) |

## Discussion

PONV is a complication that causes discomfort and dissatisfaction in patients who undergo surgery. There are many methods for its prevention and treatment. Nevertheless, the incidence rate of PONV is 20-30%. It is affected by factors related to surgery, anesthesia, and the patient.[1] It was reported that among patients receiving inhaled anesthesia, female, a history of PONV or motion sickness, non-smoker, and postoperatively using opioid were the more important risk factors of PONV, and each additional risk factor increased the PONV incidence rate to 21, 39, 61, and 79%.[10]

The boundary of the present study was restricted to female who used opioids. These patients belonged to the high risk group since they had three of the risk factors listed by Apfel and had laparoscopic surgery, which is known for a high incidence of PONV.[10] So they were expected to have a high PONV incidence rate.[11,12] Thus on an ethical reasons, the study did not include a control group. Postoperative opioid use had caused PONV in many studies.[13,14]

Many types of 5-$HT_3$ receptor antagonists are being currently used to prevent PONV. It affects the receptors of 5-$HT_3$ in the mucous membrane of the stomach and the central chemoreceptor trigger zone and suppresses nausea and vomiting. Among them, ondansetron is the most widely used type.[15] Palonosetron is a second generation serotonin 5-$HT_3$ receptor antagonist. Unlike other antagonists, it has unique structural, pharmacological, clinical characteristics. Other antagonists directly compete with serotonin, but palonosetron has an indirect effect by its allosteric binding with 5-$HT_3$ receptors.[16] Also it suppresses the response induced by substance P, has negative cooperation with neurokinin-1 receptors by cross-talk, and creates an antiemetic effect.[17,18] These explain strong receptor-affinity of palonosetron and its long plasma half-life. However, the present study aimed at comparing the effects of two drugs.

Extensive literature was reviewed to find and use the method that best prevents PONV.[5,6,9,19-21] There have been many studies on optimal dose and usage of ondansetron. Generally an intravenous injection of 8 mg is suggested as appropriate.[19] There are reports that when using opioid-based IV-PCA, adding ondansetron decreases PONV.[20,21] Palonosetron 0.075 mg is reported to be more effective in PONV prevention than 0.025 mg and 0.050 mg.[5,6] The findings of these studies mentioned above were collated, therefore in the present study, ondansetron 8 mg was infused as a bolus and palonosetron 0.075 mg was infused as a bolus.

Recently, there have been studies comparing the effects of palonosetron and other 5-$HT_3$ receptor antagonists on PONV prevention.[22-24] Park and Cho studied the use of ondansetron 8 mg and palonosetron 0.075 mg before anesthesia induction on patients with two or more risk factors.[22] Palonosetron (42.2%) was far better than ondansetron (66.7%) in PONV prevention up to 24 hrs. The effects of ondansetron and palonosetron was compared in PONV prevention in high-risk patients with three or more risk factors.[23] Similar to the present study, ondansetron was added to IV-PCA. As a result, palonosetron was far more effective than ondansetron in PONV prevention for 2-24 hrs (42% vs 62%). However, in the present study the PONV incidence rates were lesser in the palonosetron group (16.7%) and the ondansetron group (43.3%). Palonosetron, as a 5-$HT_3$ receptor antagonist, also has side-effects such as headache, dizziness, and drowsiness. In the present study the two groups showed no difference in the incidence of side-effects.

For ethical reasons, this study did not include a control group using placebos for high-risk patients for PONV. Thus the present study is limited in the sense that it could not define the base incidence rate for PONV in this particular procedure. Another limitation of the present study is that optimal doses were used for comparisons instead equipotent doses of the two drugs. For further study, these limitations need to be addressed and many other methods should be used with a large number of patients.

In conclusion, bolus of palonosetron 0.075 mg had preventive effects on PONV better than ondansetron after laparoscopic cholecystectomy.

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