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# Palonosetron plus Dexamethasone versus Palonosetron Alone for Prevention of Nausea and Vomiting in Patients Undergoing Laparoscopic Cholecystectomy under General Anesthesia

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**Abstract: Background:** One of the most prevalent issues with anesthesia is postoperative nausea and vomiting (PONV) in patients having laparoscopic cholecystectomy while under general anesthesia. Since Palonosetron is a 5-HT3 receptor antagonist of the second generation, it may be more effective than other 5-HT3 antagonists when used alone to prevent PONV.

**Aim:** comparing the efficacy of palonosetron + dexamethasone in preventing postoperative nausea and vomiting (PONV) in patients having general anesthesia for laparoscopic cholecystectomy compared to palonosetron alone in the first twenty-four hours after surgery.

**Patients and Methods:** Taking place from January to October 2023, this prospective randomized trial was carried out at Badr University Hospital, which is part of Helwan University. Ninety individuals who were about to have laparoscopic cholecystectomy while under general anesthesia were part of the research. Group PD consisted of 45 patients given palonosetron 0.075 mg in addition to 8 mg of dexamethasone, while Group P consisted of 45 patients given palonosetron alone. Within the first six hours (early PONV) and between six and twenty-four hours (late PONV), patients were polled using a questionnaire to assess postoperative nausea and vomiting (PONV) based on the Rhodes index.

**Results:** Late nausea occurred 20% of patients in group P compared to 4.4% in group PD, with statistically significant difference ($p < 0.05$). The percentage of patients who needed rescue antiemetic throughout the first 6 hours in group P (8.9%) were comparable with those in the group PD (6.7%). The percentage of patients who needed rescue antiemetic throughout the >6–24 hours in the group P (11.16%) were higher than those in the group PD (4.4%), with no statistically significant difference ($p > 0.05$). When comparing the two groups' median Rhodes scores for vomiting frequency, there was a statistically significant difference between the P group and the PD group at 0-6 hours (two against one), but no difference between the two groups at 6-24 hours. At both the 0-6 and 6-24 hour marks, there was a statistically significant difference in the median ratings of vomiting distress between the two groups, with 2 in the P group and 1 in the PD group, respectively. This difference persisted throughout the whole duration of the study. The median scores of the two groups differed significantly in terms of vomiting amount only at ر6-24 hours (1 in the P group versus 0 in the PD group). At 0-6 hours, there was a statistically significant difference in the median Rhodes scores of retching frequency between the two groups. One patient in the P group and zero in the PD group were involved in this study.

**Conclusion:** Combining palonosetron with dexamethasone was more effective than palonosetron alone in lowering the incidence of postoperative nausea and vomiting (PONV) in patients receiving laparoscopic cholecystectomy within the first 24 hours after surgery.

**Keywords:** *Dexamethasone, Palonosetron, Vomiting, Laparoscopic Cholecystectomy, General Anesthesia*

**Introduction**

Up to 70% of patients undergoing general anesthesia for laparoscopic cholecystectomy have postoperative nausea and vomiting (PONV), making it one of the most prevalent complications of anesthesia ***(1).*** PONV is a stressful event that can lead to a great deal of unhappiness for the patient. Additionally, postoperative nausea and vomiting (PONV) is linked to lengthier time in the post-anesthesia care unit (PACU), more expensive medical treatment, and unplanned hospitalizations. ***(2).***

Several studies have shown that anti-emetic drugs called 5-HT3 antagonists can prevent postoperative nausea and vomiting (PONV). This is why these medications have found such widespread use. Ondansetron, ramosetron, tropisetron, and granisetron are the most often used 5-HT3 antagonists at the moment ***(3).*** One synthetic glucocorticoid that has been used for a long time to lessen the occurrence of postoperative nausea and vomiting (PONV) after many procedures, including laparoscopic surgeries, is dexamethasone ***(4).***

Another 5-HT3 receptor antagonist of the second generation is palonosetron. With a terminal half-life of 40 hours—ten times longer than ondansetron—and an affinity for the 5-HT3 receptor that is one hundred times higher, palonosetron is clearly the superior drug. For the prevention of PONV, palonosetron monotherapy outperforms other 5-HT3 antagonists such as ramosetron, ondansetron, and granisetron. The high price tag of palonosetron was probably a limiting factor in its utilization. The Food and Drug Administration has authorized generic versions of palonosetron for use since 2018. Because of this, palonosetron will probably be less expensive ***(5).***

Patients who have at least one risk factor for PONV should be treated with multimodal prophylaxis, according to the current guidelines and literature (3). Although dexamethasone and 5-HT3 antagonists form a common multimodal prophylactic regimen, the effectiveness of palonosetron in combination with dexamethasone remains unknown ***(6).***

For patients having laparoscopic cholecystectomy under general anesthesia, we intended to see how well palonosetron + dexamethasone worked compared to palonosetron alone in preventing postoperative nausea and vomiting on the first day after surgery.

**Patients and Methods**

This study was carried out at Badr University Hospital at Helwan University and was prospectively randomized with single-blind control. Participants were patients having general anesthesia for laparoscopic cholecystectomy who had previously been approved by the Institutional Review Board (IRB) and who had provided written informed consent.

**Inclusion criteria:**

Participants' ages ranged from eighteen to sixty-five. Physical status levels I and II as defined by the American Society of Anesthesiologists (ASA) **(7).**

**Exclusion criteria:**

Pregnant or menstruating, History of motion sickness, Known smokers, Coexisting gastrointestinal pathology e.g., gastritis, peptic ulcer, hiatus hernia, GERD, patients On chronic antiemetic medications, Previously on opiates within 48 h before surgery, History of allergy to palonosetron or dexamethasone.

Eligible patients were randomized (as per computer-generated random numbers) into two groups:

- Palonosetron-dexamethasone group (Group PD, n = 45): received palonosetron 0.075 mg plus dexamethasone 8 mg.
- Palonosetron group (Group P, n = 45): received palonosetron 0.075 mg.

**Perioperative management**

The patients underwent routine preoperative assessments, including a complete blood count, coagulation profile, and electrocardiogram. A capnogram, noninvasive blood pressure, electrocardiography, and oxygen saturation were used to monitor the patients.

Before anesthesia was induced, the two medications were diluted in 5 ml of normal saline and slowly given intravenously over 30 seconds. Each patient in the two groups underwent a standardized balanced anesthesia procedure, which included the following: fentanyl at 1-2 µg/kg, propofol at 1.5-2.5 mg/kg, atracurium at 0.5 mg/kg, and isoflurane at 1 MAC in FiO2 1 every 20 minutes thereafter. Patients were also given paracetamol (1 mg) and ketolac (30 mg) intravenously prior to cutaneous insertion.

Every 20 minutes, the baseline data were recorded, which included noninvasive blood pressure, peripheral oxygen saturation, end-tidal CO2, and heart rate. The volatile anesthetic was halted when the skin was closed during the operation, and neostigmine 0.05 mg/kg with atropine 0.02 mg/kg was injected to counteract neuromuscular blockage. Following oropharyngeal suction and satisfactory post-GA recovery (i.e., spontaneous breathing, sufficient tidal volume (4 ml/kg), and localization), extubation was performed. In the first twenty-four hours following surgery, patients were transferred to the post-anesthesia care unit (PACU) to receive intramuscular injections of diclofenac sodium (1.5 mg/kg) for pain relief, and their noninvasive blood pressure and oxygen saturation levels were closely monitored.

**Assessments**

One measure of PONV was the Rhodes index of nausea, vomiting, and retching (RINVR) (8). The primary objective of this study was to compare the two groups' incidence and Rhodes score of positive occurrences of nausea, vomiting, or retching within the first 24 hours. Early PONV was defined as a positive event of PONV occurring within 6 hours of surgery, while late PONV was defined as a positive event occurring between 6 and 24 hours following surgery. When you feel like throwing up but can't bring yourself to physically puke, you're said to be nauseated. The term "vomiting" refers to the actual ejection of gastrointestinal contents from the mouth, whereas "retching" refers to the act of trying to vomit without actually vomiting.

A questionnaire in Arabic was developed based on the RINVR claims. After 6 and 24 hours following surgery, patients were asked to fill out this survey. Questions on nausea (how often, how painful, and for how long), vomiting (how often, how painful, and how much) and retching (how often, how painful, and how long) were also part of the survey.

Intravenous metoclopramide was used as a rescue medication at a dose of 10 mg given whenever required for PONV.

**Statistical analysis**

The data was analyzed using SPSS-22, a statistical tool for the social sciences developed by IBM and located in Chicago, USA. The means ± standard deviations (SD) or medians [interquartile range] of continuous variables were used for comparisons with Student's t test or the Mann-Whitney U test, respectively. We used Chi-square and Fisher's exact tests, respectively, to compare dichotomous variables, which were reported as the number of patients (%). A statistically significant result was defined as $P < 0.05$. Using PASS 11, a confidence level of 95% and a margin of error of 0.15 were entered into the sample size calculation.

**Results**

During the period from January to October 2023, a grand total of 90 patients who met the inclusion criteria were enrolled, 45 in each of the two groups. All of the patients who were enrolled were included in the research. See Table 1 for a breakdown of the two groups' patient demographics. In terms of demographic variables including age, gender, height, weight, ASA class, and controlled concomitant conditions, there was no statistically significant difference between the two research groups. No statistically significant difference was seen in the duration of surgery, volume of fluid administration, or anesthetic between the two study groups. (Table 2).

There was no statistically significant difference between the two groups when looking at the incidence of PONV using the Apfel risk score; the majority of patients in both groups had score 2, with 37 patients (82.2%) in group P and 39 patients (86.7%) in group PD having this score (Table 3).

**Table (1):** Patient characteristics of the two study groups (n = 90).

| **Parameters** | | **Group P n = 45** | **Group PD n = 45** | **Test Value** | **P-value** | **Sig.** |
|---|---|---|---|---|---|---|
| Age (years) | Mean ± SD.<br>Range | 42.49 ± 8.59<br>25-63 | 40.64 ± 6.61<br>25-55 | 1.141 | 0.257 | NS |
| Gender | | | | | | |
| Male | n (%) | 8 (17.8) | 6 (13.3) | 0.338* | 0.561 | NS |
| Female | n (%) | 37 (82.2) | 39 (86.7) | | | |
| Hight (cm) | Mean ± SD.<br>Range | 162.71 ± 5.14<br>150-174 | 164.04 ± 4.70<br>155-175 | 1.284 | 0.203 | NS |
| Wight (kg) | Mean ± SD.<br>Range | 77.58 ± 9.29<br>61-109 | 77.82 ± 8.83<br>62-106 | 0.128 | 0.898 | NS |
| ASA class | | | | | | |
| I | n (%) | 31 (68.9) | 32 (71.1) | 0.053* | 0.818 | NS |
| II | n (%) | 14 (31.1) | 13 (28.9) | | | |
| Comorbid Dis. | | | | | | |
| Hypertension | n (%) | 10 (22.2) | 10 (22.2) | 0.000* | 1.000 | NS |
| Diabetes | n (%) | 7 (15.6) | 6 (13.3) | 0.090* | 0.764 | NS |

**Table (2):** Surgical procedure characteristics of the two study groups (n = 90).

| **Parameters** | | **Group P n = 45** | **Group PD n = 45** | **Test value** | **P-value** | **Sig.** |
|---|---|---|---|---|---|---|
| Operation time (min) | Mean ± SD. | 80.11 ± 8.56 | 79.44 ± 7.70 | 0.388 | 0.699 | NS |
| | Range | 75 – 105 | 75 – 100 | | | |
| Anesthesia time (min) | Mean ± SD. | 104.89 ± 6.61 | 104.22 ± 5.83 | 0.507 | 0.613 | NS |
| | Range | 100 – 120 | 100 – 120 | | | |
| Fluid admin (ml) | Mean ± SD. | 585.33 ± 40.65 | 581.33 ± 37.94 | 0.483 | 0.631 | NS |
| | Range | 540 – 690 | 530 – 690 | | | |

**Table (3):** Apfel risk score in the two study groups (n = 90).

| **Score** | | **Group P n = 45** | **Group PD n = 45** | **Test value** | **P-value** | **Sig.** |
|---|---|---|---|---|---|---|
| 1 | n (%) | 08 (17.8) | 06 (13.3) | 0.338* | 0.561 | NS |
| 2 | n (%) | 37 (82.2) | 39 (86.7) | | | |

The frequency of early PONV in both groups is displayed in Table 4. Twelve patients (26.7% of the total) in group P experienced nausea attacks within the first six hours after surgery, whereas eleven patients (24.4% of the total) in group PD did not. There was no statistically significant difference here. Four patients (8.9%) in group P experienced vomiting episodes within the first six hours after surgery, compared to two patients (4.4%) in group PD. There was no statistically significant difference here. Within the first six hours following surgery, two patients (4.4%) in group P and one patient (2.2%) in group PD experienced retching episodes; nevertheless, there was no statistically significant difference between the two groups. None of the groups showed a statistically significant difference in the total incidence of early PONV; however, group PD had a rate of 31.1% and group P had a rate of 40.0% (Figure 1).

**Table (4):** Incidence of early PONV in the two study groups (n = 90).

| **Event(s)** | | **Group P n = 45** | **Group PD n = 45** | **Test value** | **P-value** | **Sig.** |
|---|---|---|---|---|---|---|
| Nausea | n (%) | 12 (26.7) | 11 (24.4) | 0.498* | 0.480 | NS |
| Vomiting | n (%) | 04 (08.9) | 02 (04.4) | 0.155* | 0.694 | NS |
| Retching | n (%) | 02 (04.4) | 01 (02.2) | | | |
| Overall | n (%) | 18 (40.0) | 14 (31.1) | 0.776* | 0.378 | NS |

The frequency of late PONV in the two research groups is displayed in Table 5. In the first six to twenty-four hours after surgery, nine patients (20%) in group P experienced nausea attacks, while just two patients (4.4%) in group PD did so. A statistical analysis confirmed this disparity. Five patients (11.1%) in group P experienced vomiting episodes between six and twenty-four hours after surgery, compared to two patients (4.4%) in group PD. There was no statistically significant difference here. Each group had one patient who experienced a retching attack. Group P had a greater overall incidence of late PONV (33.3%) compared to group PD (11.11%). The disparity was found to be statistically significant. (Figure 2).

***Table (5):** Incidence of late PONV in the two study groups (n = 90).

| **Event(s)** | | **Group P n = 45** | **Group PD n = 45** | **Test value** | **P-value** | **Sig.** |
|---|---|---|---|---|---|---|
| Nausea | n (%) | 09 (20.0) | 02 (04.4) | 4.406 | 0.036 | S |
| Vomiting | n (%) | 05 (11.1) | 02 (04.4) | 1.394 | 0.238 | NS |
| Retching | n (%) | 01 (02.2) | 01 (02.2) | | | |
| Overall | n (%) | 15 (33.3) | 05 (11.1) | 6.429 | 0.011 | S |

Table 6 displays the number of patients in both groups who required rescue antiemetic medicine. In the first six hours following surgery, 8.9% of patients in group P and 6.7% of patients in group PD required rescue antiemetic; there was no statistically significant difference between the two groups. Patients in group P were more likely to require rescue antiemetic during the first six to twenty-four hours after surgery (11.16% vs. 4.4%), however this difference was not statistically significant (Figure 3).

**Table (6):** Use of rescue antiemetic in the two study groups (n = 90).

| **Time (hours)** | | **Group P n = 45** | **Group PD n = 45** | **Test value** | **P-value** | **Sig.** |
|---|---|---|---|---|---|---|
| 0-6 | n (%) | 4 (8.9) | 3 (6.7) | 0.155* | 0.694 | NS |
| >6-24 | n (%) | 5 (11.1) | 2 (04.4) | 1.394* | 0.238 | NS |
| Overall | n (%) | 9 (20.0) | 5 (11.1) | 1.353 | 0.245 | NS |

In terms of frequency, pain, and length, Table 7 compares the two groups' Rhodes ratings for nausea at 0-6 hours and 6-24 hours postoperatively. There was no statistically significant difference in the median scores of frequency and distress between the two groups at either 0-6 hours or 6-24 hours postoperatively. Statistical analysis revealed that there were significant differences in the median scores of the two groups when it came to the duration of nausea at 0-6 hours (2 in the P group vs 1 in the PD group) and at ˜6-24 hours (1 in the P group versus 0 in the PD group).

**Table (7):** Comparing Rhodes scores of nausea at 0-6 hours and >6-24 hours postoperatively for the two study groups.

| **Nausea** | | **Group P** | **Group PD** | **Test value** | **P-value** | **Sig.** |
|---|---|---|---|---|---|---|
| | | **No. = 45** | **No. = 45** | | | |
| **Frequency** | | | | | | |
| 0 to 6 hours | Median (IQR) | 1(1 – 2) | 1(1 – 1) | -1.479≠ | 0.139 | NS |
| | Range | 0 – 2 | 1 – 1 | | | |
| **>** 6 to 24 hours | Median (IQR) | 1(0 – 1) | 0(0 – 0) | -1.902≠ | 0.057 | NS |
| | Range | 0 – 1 | 0 – 1 | | | |
| **Distress** | | | | | | |
| 0 to 6 hours | Median (IQR) | 2(1 – 2) | 1(1 – 1) | -1.925≠ | 0.054 | NS |
| | Range | 0 – 2 | 1 – 2 | | | |
| **>** 6 to 24 hours | Median (IQR) | 1(0 – 1) | 0(0 – 0) | -1.625≠ | 0.104 | NS |
| | Range | 0 – 1 | 0 – 1 | | | |
| **Duration** | | | | | | |
| 0 to 6 hours | Median (IQR) | 2(2 – 2) | 1(1 – 1) | -2.524≠ | 0.012 | S |
| | Range | 1 – 2 | 1 – 2 | | | |
| **>** 6 to 24 hours | Median (IQR) | 1(1 – 1) | 0(0 – 0) | -2.524≠ | 0.012 | S |
| | Range | 0 – 1 | 0 – 1 | | | |

≠: Mann-Whitney test

In terms of frequency, distress, and volume, Table 8 compares the two groups' Rhodes ratings for vomiting at 0-6 hours and 6-24 hours postoperatively. after 0-6 hours, there was a statistically significant difference in the median frequency scores between the two groups (2 in the P group against 1 in the PD group), but after ˜6-24 hours, the difference was not statistically significant. At both 0-6 hours and 6-24 hours, there was a statistically significant difference in the median scores of distress between the two groups. In the P group, this difference was 2 vs 1 in the PD group. The only time there was a significant difference in the median scores between the two groups for the amount of vomiting—1 in the P group and 0 in the PD group—was at ˛6-24 hours.

**Table (8):** Comparing Rhodes scores of vomiting at 0-6 hours and >6-24 hours postoperatively for the two study groups.

| **Vomiting** | | **Group P** | **Group PD** | **Test value** | **P-value** | **Sig.** |
|---|---|---|---|---|---|---|
| | | **No. = 45** | **No. = 45** | | | |
| **Frequency** | | | | | | |
| 0 to 6 hours | Median (IQR) | 2(1 – 2) | 1(0 – 1) | -2.053≠ | 0.040 | S |
| | Range | 0 – 3 | 0 – 2 | | | |
| **>** 6 to 24 hours | Median (IQR) | 1(0 – 1) | 0(0 – 1) | -0.669≠ | 0.503 | NS |
| | Range | 0 – 1 | 0 – 1 | | | |
| **Distress** | | | | | | |
| 0 to 6 hours | Median (IQR) | 2(2 – 2) | 1(0 – 1) | -2.846≠ | 0.004 | HS |
| | Range | 0 – 3 | 0 – 1 | | | |
| **>** 6 to 24 hours | Median (IQR) | 1(0 – 1) | 0(0 – 0) | -2.094≠ | 0.036 | S |
| | Range | 0 – 1 | 0 – 0 | | | |
| **Amount** | | | | | | |
| 0 to 6 hours | Median (IQR) | 2(1 – 2) | 1(0 – 1) | -1.956≠ | 0.050 | NS |
| | Range | 0 – 2 | 0 – 1 | | | |
| | Median (IQR) | 1(0 – 1) | 0(0 – 0) | -2.094≠ | 0.036 | S |

| | | | | | | |
|---|---|---|---|---|---|---|
| > 6 to 24 hours | Range | 0 – 1 | 0 – 0 | | | |

≠: Mann-Whitney test

Table 9 shows the comparison of Rhodes scores of retching at 0–6 hours and >6–24 hours postoperatively in terms of frequency and distress for the two study groups. The only time a statistical difference in median frequency scores occurred between the two groups was between 0 and 6 hours, with 1 in the P group and 0 in the PD group. When comparing the two groups' median distress scores between 0 and 6 hours, there was no statistically significant difference.

**Table (9):** Comparing Rhodes scores of retching at 0-6 hours and >6-24 hours postoperatively for the two study groups.

| **Retching** | | **Group P** | **Group PD** | **Test value** | **P-value** | **Sig.** |
|---|---|---|---|---|---|---|
| | | **No. = 45** | **No. = 45** | | | |
| **Frequency** | | | | | | |
| 0 to 6 hours | Median (IQR) | 1(1 – 1) | 0(0 – 1) | -2.274≠ | 0.023 | S |
| | Range | 0 – 2 | 0 – 1 | | | |
| > 6 to 24 hours | Median (IQR) | 0(0 – 0) | 1(0 – 1) | -1.245≠ | 0.213 | NS |
| | Range | 0 – 1 | 0 – 1 | | | |
| **Distress** | | | | | | |
| 0 to 6 hours | Median (IQR) | 1(1 – 1) | 0(0 – 1) | -1.895≠ | 0.058 | NS |
| | Range | 0 – 1 | 0 – 1 | | | |
| > 6 to 24 hours | Median (IQR) | 0(0 – 0) | 1(0 – 1) | -1.648≠ | 0.099 | NS |
| | Range | 0 – 1 | 0 – 1 | | | |

≠: Mann-Whitney test

**Discussion**

Without the use of a prophylactic antiemetic, the rate of postoperative nausea and vomiting (PONV) during laparoscopic cholecystectomy ranges from 50 to 75 percent ***(9; 10).***

This study set out to compare the efficacy of two different groups of patients following laparoscopic cholecystectomy under general anesthesia in preventing postoperative nausea and vomiting (PONV): those given palonosetron alone (group P) and those given palonosetron plus dexamethasone (group PD). Experiencing nausea or vomiting within the initial six hours following surgery was referred to as early postoperative nausea and vomiting (PONV), whilst symptoms occurring between six and twenty-four hours postoperatively were marked as late PONV.

Poison oak needle (PONV) is more common in women, those with a history of PONV or motion sickness, those who don't smoke, those who are overweight, the kind and length of the surgery, the anesthetic used, the dosage, and the use of analgesics to manage pain after the treatment. ***(11).***

In the present study, the two study groups were comparable, with no statistically significant difference in terms of age, gender, height, weight, ASA class, or controlled comorbid diseases, as well as duration of surgery, anesthesia, or volume of fluid administration ($p > 0.05$). Most patients in this study had Apfel score 2, accounting for 37 patients (82.2%%) in group P and 39 patients (86.7%) in group PD, with no statistically significant difference ($p > 0.05$). Thus, it is proposed that any difference in PONV between the two study groups could be attributed to the additive or synergistic effect of adding dexamethasone to palonosetron.

Patients at moderate to high risk for PONV should be treated with combination antiemetic treatments targeting multiple receptors, according to current PONV guidelines ***(1).***

Previous research has shown that the incidence of PONV can be reduced by combining dexamethasone with a 5-HT3 receptor antagonist, as opposed to using a 5-HT3 receptor antagonist alone **(12).** Leading ideas suggest that prostaglandin antagonism and endorphin release are involved in dexamethasone's antiemetic action,

although the exact mechanism is yet unknown **(13).** In addition, dexamethasone's anti-inflammatory effects may block the activation of 5-HT receptors in the gastrointestinal tract, or it may deplete tryptophan, a precursor to 5-HT, which in turn inhibits 5-HT production and release **(14).**

With its 40-hour elimination half-life and allosteric interactions that cause receptor internalization, palonosetron has the highest receptor affinity of any 5-HT3 antagonist currently available ***(15; 16).***

Based on prior research suggesting that 75 mcg of palonosetron is more efficacious than 25 or 50 mcg for PONV in laparoscopic procedures, a single intravenous dose of 0.075 mg was administered before induction anesthesia in the current trial ***(17; 18). Nathalia Ferreira et al. (19)*** performed a prospective, randomized study involving 80 female patients undergoing breast surgery. Patients received an intravenous body weight-adjusted dose of palonosetron (1 μg kg) or a fixed dose of palonosetron (75 μg). All patients received dexamethasone (4 mg). They concluded that a body weight-adjusted dose of palonosetron was as effective as 75 μg for preventing PONV for 48 hours in obese female patients who underwent breast surgery.

Several studies including meta-analysis showed that palonosetron provided better prophylaxis for early (0–6 h) and late (6–24 h) postoperative nausea, as well as late (6–24 h) postoperative vomiting, compared with ondansetron ***(20; 21; 22; 23).*** In another meta-analysis, palonosetron was more effective in preventing postoperative vomiting than ramosetron during the delayed period (24–48 h) and in females and after laparoscopic surgery ***(24).***

In the present study, the combination of palonosetron with dexamethasone was more effective in reducing incidence of early and late PONV compared to monotherapy with palonosetron in patients undergoing laparoscopic cholecystectomy under general anesthesia. The incidence of early nausea in the palonosetron group was 26.7.1% versus 24.4% in the palonosetron-dexamethasone group ($p < 0.05$). The incidence of early vomiting in the palonosetron group was 8.9% versus 4.4% in the palonosetron-dexamethasone group ($p < 0.05$). The incidence of early retching in the palonosetron group was 4.4% versus 2.2% in the palonosetron-dexamethasone group ($p < 0.05$). In addition, the incidence of late nausea in the palonosetron group was 20.0% versus 4.4% in the palonosetron-dexamethasone group ($p > 0.05$). The incidence of late vomiting in the palonosetron group was 11.1% versus 4.4% in the palonosetron-dexamethasone group (< 0.05). The incidence of late retching was identical in the two study groups.

This finding corroborated previous research showing that palonosetron and dexamethasone reduced postoperative nausea and vomiting (PONV) more than palonosetron alone following laparoscopic cholecystectom. ***(25; 26).***

In the study by ***Bala et al. (25),*** 84 patients undergoing laparoscopic cholecystectomy were randomized to receive palonosetron 0.075 mg or palonosetron 0.075 mg plus dexamethasone 8 mg. The incidence of early PONV in the palonosetron group was 40.4% and 11.9%, versus 14.2% and 4.8% in the palonosetron-dexamethasone group, respectively. The incidence of late PONV in the palonosetron group was 35.7% and 23.8%, versus 14.3% and 7.1% in the palonosetron-dexamethasone group, respectively ***(25).*** The higher incidence of early and late PONV in ***Bala et al., (25)*** may be attributed to using nitrous oxide with isoflurane during maintenance anesthesia and using postoperative tramadol as a second rescue analgesic. The current trial, on the other hand, maintained general anesthesia with a mixture of isoflurane and oxygen/air.

During the first 48 hours after surgery, the incidence of postoperative nausea and vomiting (PONV) was considerably lower in the palonosetron-dexamethasone group (61.5% vs. 77.1%), according to the study by **Cho et al. (26).** Possible differences in surgical procedures and postoperative pain medication might explain why **Cho et al. (26)** reported a higher incidence of postoperative nausea and vomiting (PONV) than the current study. Although **Cho et al. (26)** looked at opioid use as a postoperative analgesic for patients having upper limb surgeries, the current study focused on patients having laparoscopic cholecystectomy and used Diclofenac sodium.

Opioid dosage for postoperative pain control is significantly associated with the occurrence of postoperative nausea and vomiting (PONV). Therefore, it is important to carefully adjust the dosage of opioids given so as to have a minimal impact on the efficacy of antiemetic medications ***(27,28).***

In contrast, the results of the present study disagreed with other studies reporting that the effect of palonosetron alone was comparable to that of combined palonosetron with dexamethasone ***(29; 30).***

The incidence of PONV 24 hours was 23.4% in the palonosetron-dexamethasone group and 27.2% in the palonosetron group, according to **Chatterjee et al. (29).** While patients in the trial by Chatterjee et al. (29) were given antiemetic premedications like ranitidine with alprazolam or midazolam with fentanyl and thiopentone before induction anesthesia, no such medication was administered in the current investigation.

In patients having breast surgery and getting intravenous opioid pain medication, the use of palonosetron and midazolam together did not reduce the occurrence of postoperative nausea and vomiting (PONV) any more than either drug alone did ***(31).*** However, among patients having laparoscopic cholecystectomy and using ketorolac for pain after the procedure, the combination of midazolam and palonosetron, given during the induction of anesthesia, was better than palonosetron alone ***(32).***

In a study including one hundred patients who were going to undergo gynecological laparoscopic surgery, Aya et al. (30) evaluated four groups: one that received 5 ml of saline as a control, one that received 0.075 mg of palonosetron, one that received 8 mg of dexamethasone, and a fourth that received 0.075 mg of palonosetron and 8 mg of dexamethasone combined. According to their findings, the rate of PONV in the first 24 hours after starting palonosetron (21.7% for the combination drug) was similar to or higher than that of dexamethasone (46%), the control group (63%), and palonosetron alone (17.4%). The controversy between the present study finding and the ***Aya et al. (30)*** finding may be attributed to the different types of surgery and patents gender. ***Aya et al. (30)*** performed their study on female patients undergoing gynecological laparoscopic surgery.

In the ***Park et al. (33)*** study, Comparing the incidence of PONV over 24 hours between palonosetron monotherapy (14% against 9.8%) and palonosetron with dexamethasone (14% versus 9.8%), no significant reduction was seen. Possible explanations for the discrepancy between the results of the current study and those of **Park et al. (33)** include variations in surgical procedures and gender. The research conducted by **Park et al. (33)** involved female patients who were scheduled to have thyroidectomy, mastoidectomy with tympanoplasty, or laparoscopic gynecologic surgery. This study also utilized a dose of dexamethasone that was not ideal, specifically 4 mg. The lowest effective dose of dexamethasone for PONV prevention is 2.5–5 mg, while some sources say that 8 mg is the sweet spot **(12; 34).** For female patients undergoing laparoscopic cholecystectomy, a recent study by **Khan et al. (35)** shown that palonosetron (0.075 mg) is just as effective as dexamethasone (4 mg) as a preventive antiemetic.

***Sahni et al. (36)*** evaluated the efficacy of two different doses of palonosetron (0.075 mg) and a combination of the two drugs (0.075 mg plus 8 mg) in preventing postoperative nausea and vomiting (PONV) in ninety patients having general anesthesia for middle ear surgery. The palonosetron group had a nausea incidence of 15.5% and the palonosetron plus dexamethasone group of 8.8% ($p = 0.522$), while the vomiting incidence was 6.7% and 2.2% ($p = 0.610$) in the two groups, respectively. Possible explanations for the discrepancy between the two sets of findings include the use of different patient demographics and surgical procedures in the two studies.

The 72-hour incidence of postoperative nausea and vomiting (PONV) was 31% in the palonosetron + dexamethasone 8 mg group and 32% in the palonosetron monotherapy group in a study of 118 patients having outpatient laparoscopic gastric banding surgery ***(37).***

Because of its delayed onset of effect, palonosetron is typically given during the induction of anesthesia ***(1).*** The two antiemetics used in this trial were diluted in 5 ml of normal saline and administered intravenously over the course of 30 seconds prior to induction anesthesia. On the other hand, whether antiemetics should be given before surgery instead of after could lessen postoperative nausea and vomiting (PONV), and there is no set policy for when these medications should be given. ***(26; 33).*** Therefore, even though palonosetron is given at the same time in both groups, the timing of its administration may influence the incidence of postoperative nausea and vomiting (PONV) in the palonosetron group in the 0-6 h postoperative period. Nonetheless, prior research has demonstrated that palonosetron effectively decreases PONV irrespective of the timing of administration. ***(38).*** Furthermore, one trial found no significant effect of timing palonosetron delivery on

prevention of PONV ***(39).*** Thus, to find out when to provide palonosetron for PONV prophylaxis, more studies are needed.

In the present study, the incidence of early postoperative nausea was higher than late postoperative nausea in both groups: 26.7% versus 20.0% in the palonosetron group and 24.4% versus 4.4% in the palonosetron-dexamethasone group. Similar findings were demonstrated by ***Nale et al. (40),*** the incidence of postoperative nausea with palonosetron was higher during the early postoperative period (0–4 hours) than during the late postoperative period (4–24 hours), 27.8% versus 2.3%, respectively, in patients undergoing laparoscopic cholecystectomy, which was contradictory to the results in the present study. This could be because all patients enrolled in the ***Nale et al. (40)*** study were female, received Midazolam during induction anesthesia, and postoperatively were given an intravenous infusion of fentanyl for pain relief.

Palonosetron was also compared with more recent NK-1 receptor antagonists. ***Braga et al. (41)*** found that the incidence of PONV in the first 48 hours after surgery for fosaprepitant (an NK-1 receptor inhibitor) in comparison with palonosetron was comparable (13.6 and 18.2%, respectively) in women undergoing laparoscopic cholecystectomy.

In the present study, RINVR, which depends on the patients' perception, was used to measure PONV ***(8).*** Although the severity of positive events was mild to moderate, the overall Rhodes scores were higher in group P patients compared with group PD patients, suggesting a greater severity of PONV in this group.

Several grading and scoring tools exist to measure one or more of the components of nausea, vomiting, and retching, such as the Functional Living Index- Emesis **,** Visual Analog Scales ***(26; 40),*** or Morrow Assessment of Nausea and Emesis***.*** Still, others have studied PONV with dichotomous measures (yes or no answers) or severity levels (score 0-no nausea, score 1- nausea only, score 2-nausea with retching, score 3-nausea) ***(30).***

Objective tools for measuring PONV are still challenging to come by, and there is a lot of variability in how they are measured. This is despite the fact that clinical tools that help patients become more involved, improve communication between providers and patients, and encourage shared decision-making can reduce symptom intensity and distress ***(30).***

Patients experiencing PONV were given injections of 10 mg of metoclopramide as a rescue antiemetic in this trial. Metoclopramide is a popular antiemetic medicine at our institute, and its side effects profile is tolerable, so we choose to use it even if it isn't as effective as 5-HT3 blockers pharmacologically. Distinct from the antiemetics under study is its mode of action, which involves blocking D2 receptors. The current study found that the palonosetron group (20.0%) needed rescue antiemetic more often than the palonosetron-dexamethasone group (11.1%). According to **Chatterjee et al. (29),** similar outcomes were demonstrated. On the other hand, the **Aya et al. (30)** study found that both the palonosetron group and the palonosetron-dexamethasone group had similar rates of patients requiring rescue antiemetics in the first day after surgery (21.7% and 17.4%, respectively).

The idea of a family history of PONV, which was discovered to be a substantial risk factor in pediatric patients, first provided support for the idea that an individual's genetic predisposition to PONV plays a role. ***(42),*** not to mention the contentious possible role of ethnicity. ***(43).*** Postoperative, chemotherapy-induced (CINV), and pregnancy-related nausea and vomiting have all been the subject of efforts to identify genetic factors influencing these symptoms using candidate gene approaches and genome-wide association (GWAS) methods. ***(44).***

Gloor et al. (45) genotyped 601 patients within the first 24 hours for PONV without antiemetic treatment in an effort to better characterize specific genetic risk factors for the condition and identify people at risk. In order to determine the frequency and persistence of PONV, they looked at the effect of six cytochrome P450 family enzymes on drug metabolism in the liver and a few specific single nucleotide polymorphisms (SNPs) in thirteen genes. Their findings supported the significance of type 3B serotonin receptor genetic variants in PONV occurrence and suggested that individuals at risk of PONV could be better targeted with antiemetic therapy if the rs3782025 genotype was included in preoperative risk assessments.

In a different study conducted not long ago, **Angela Ribeiro et al. (46)** examined 82 women who underwent laparoscopic cholecystectomy and looked at how CYP2D6 isoenzyme and ABCB1 gene polymorphisms affected the incidence of PONV when ondansetron or palonosetron was used. Saliva was used to obtain DNA. A real-time polymerase chain reaction was used to analyze genetic polymorphisms. Here are the polymorphisms that were examined: rs3892097 C/T, rs1128503 A/G, rs16947 A/G, rs1065852 A/G, rs1045642 A/G, rs2032582 C/A, and rs20325821 C/A. In total, 57.5% of patients experienced severe nausea, while 22.5% experienced vomiting. Those in the palonosetron group who had the GG genotype (rs16947 A/G) reported significantly worse nausea ($p = 0.043$). The ondansetron group showed a correlation between mild nausea ($p = 0.034$) and increased vomiting ($p = 0.034$) in patients with the AA genotype (rs1065852 A/G), as well as rs16947 A/G in patients with the same genotype. In laparoscopic cholecystectomy, they determined that ondansetron had a poor antiemetic response when administered with the AA genotype (rs16947 A/G) and the AA genotype (rs1065852 A/G), and palonosetron had a poor therapeutic response when administered with the GG genotype (rs16947 A/G).

The present study has several limitations. To begin, in order to determine the exact risk decrease of PONV, a placebo group is necessary; however, this trial did not contain one. Furthermore, the majority of patients were released the next day, limiting the duration of observation to just one day following surgery, in this particular study. Finally, patient satisfaction was not measured in this study, but it is a surrogate end point that can be difficult to assess.

**Conclusion**

Combining palonosetron with dexamethasone was more effective than palonosetron alone in lowering the incidence of postoperative nausea and vomiting (PONV) in patients receiving laparoscopic cholecystectomy within the first 24 hours after surgery.

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