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**Original Research Article**

# A Comparative Study between Palonosetron hydrochloride and Granisetron hydrochloride to Prevent Postoperative Nausea and Vomiting after Gynaecological Surgery

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## Abstract

**Aim:** Our aim of this randomized & prospective clinical study was to investigate and compare the efficacy of palonosetron HCl and granisetron HCl to prevent postoperative nausea and vomiting after gynaecological surgery.

**Method:** Fifty female patients of ASA grade I and II in between 18-60 years of age posted for elective gynaecological surgery were randomly divided into two groups containing 25 patients each.
Before induction of anaesthesia group P received bolus dose of palonosetron 75 mcg and group G received bolus dose of granisetron 2.5 mg intravenously slowly over a period of 30 seconds.

**Result:** In the postoperative period (0-3 hrs), the incidence of complete response (no postoperative nausea & vomiting, no rescue medication) was 88% with palonosetron and 76% with granisetron (p value-0.46) .During 3-24 hrs postoperatively the incidence was 92% with palonosetron and 80% with granisetron (p value-0.417). During 24-48 hrs postoperatively the incidence was 92 % with palonosetron and 60 % with granisetron (p value-0.018). During 48-72 hrs incidence was statistically insignificant (p value-0.1284). Insignificant incidence of side effects between the groups was found.

**Conclusion:** Palonosetron is more potent and long acting than granisetron for the prevention of post operative nausea & vomiting after gynaecological surgery.

**Keywords:** Gynaecological Surgery, Palonosetron, Granisetron, Postoperative nausea and vomiting.

## 1. Introduction

One of the most common and distressing symptoms after anaesthesia and surgery is postoperative nausea and vomiting (PONV). It is considered by some patients to be even worse than postoperative pain. Vomiting may cause wound dehiscence, bleeding, dehydration, electrolyte imbalance, pulmonary aspiration of gastric contents, and delayed hospital discharge.[1] For the prevention of PONV several antiemetics of different pharmacological classes are available. A number of pharmacological agents (antihistamines, butyro-phenones, and dopamine receptor antagonists) have been tried for the prevention and treatment of PONV but undesirable adverse effects such as excessive sedation, hypertension, dry mouth, dysphoria, hallucinations and extra pyramidal symptoms have been noted.[1]

Four predictors for PONV are female gender, history of motion sickness (MS) or PONV, non-smoking, and the use of postoperative opioids. For patients with at least two out of these four identified predictors, a prophylactic antiemetic strategy should be considered.[2]

Currently, selective 5-hydroxytryptamine type 3 (5-$HT_3$) receptor antagonists are frequently used for the prevention of PONV because of their efficacy and fewer side-effects as compared with other antiemetics. [3,4] Granisetron produces irreversible block of the 5-$HT_3$ receptors with half life of 5 to 8 hours.[5,6] Palonosetron is a 5-$HT_3$ receptor

antagonist used for preventing chemotherapy induced nausea and vomiting. It has a greater receptor binding affinity and longer half-life than older 5-$HT_3$ antagonists. Recent studies mention that palonosetron is further differentiated from other 5-$HT_3$ antagonist by interacting with 5-$HT_3$ receptors in an allosteric, positively cooperative manner at sites different from those that bind with ondansetron and granisetron.[7] This sort of receptor interaction may be associated with long lasting effects on receptor ligand binding and functional responses to serotonin.[8]

We designed this prospective randomized study to assess and compare the antiemetic efficacy of palonosetron and granisetron to prevent PONV for 72 hours postoperatively in patients undergoing gynaecological procedures requiring general anaesthesia.

## 2. Method

After obtaining the institutional ethical committee approval and informed consent from every patient, fifty ASA I & II patients, aged 18-60 years, undergoing elective gynaecological surgery were randomly assigned to one of the two groups, containing twenty five patients each. Patients who had gastrointestinal disease, had history of motion sickness and/ or PONV and those who had vomiting, retching, nausea in the 24 hours preceding the administration of anaesthesia, taken antiemetic medication within last 24 hours were excluded from the study.

Patients were randomly allocated into two groups (n=25each) to receive one of the following regimens: palonosetron 75µg in 2.5 ml [group P] or granisetron 2.5 mg in 2.5 ml [group G] (0.9% saline was added to make the desired volume).The study drugs were administered immediately before the induction of anaesthesia.

All patients were kept nil by mouth after midnight and received tablet Lorazepam 1 mg orally at night and tablet diazepam 5mg in the morning three hours before surgery as premedication. On the operation table, routine monitors (ECG, pulse oximetry, NIBP) were applied and baseline vital parameters like heart rate (HR), blood pressure (systolic, diastolic and mean) and oxygen saturation ($SpO_2$) were recorded. An intravenous line was secured.

Patients were preoxygenated for 3 minutes. Induction of anaesthesia was done by fentanyl 2µg /kg and thiopentone 5mg/kg. Intubation with appropriate size endotracheal tube was done with vecuronium bromide in a dose of 0.08mg/kg. Anaesthesia was maintained with oxygen in nitrous oxide (40:60%) and sevoflurane 2%. Muscle relaxation was maintained by intermittent bolus doses of vecuronium bromide. The patients were mechanically ventilated to keep $EtCO_2$ between 35-40 mm Hg. A nasogastric tube was inserted to make the stomach empty of air and other contents. Residual neuromuscular block was adequately reversed using intravenous glycopyrrolate and neostigmine at the end of surgical procedure and extubation was done. Patients were transferred to postanaesthesia care unit and blood pressure, heart rate and oxygen saturation were monitored. All episodes of PONV (nausea, retching and vomiting) were recorded for 0-3 hours, 3-24 hours, 24-48 hours and from 48-72 hours in postoperative ward.

Complete response (free from emesis) was defined as no PONV and no need for any rescue medication. If there were two or more episodes of PONV during 72 hours, rescue antiemetic (metoclopramide10 mg i.v.) was given.

Data were analyzed using computer statistical software system Graph Pad. Comparisons between groups were performed by using student t test and Fisher's exact t test as appropriate. The results were expressed in mean±SD and number (%).

## 3. Results

The groups were comparable with respect to age, weight, ASA grade and duration of surgery [Table 1]. The incidence of a complete response (no PONV, no rescue medication) during 0-3 hours in the postoperative period was 88% with palonosetron and 76% with granisetron. The incidence during 3-24 hours postoperatively was 92% with palonosetron and 80 % with granisetron. During 24-48 hours, the incidence was 92% and 60% respectively. During 48-72 hours, the incidence was 80% and 56% respectively[Table 2].Thus a complete response during 24-48 hour in the postoperative period was significantly more in patients who had received palonosetron than in those who had received granisetron (p value -0.0181) [Table 2, Figure-1].

The commonly observed adverse effects were headache, dizziness and constipation but those were statistically insignificant between the groups. [Table 3].

**Table1: Patients characteristics (Mean± SD)**

| | **Group P (n=25)** | **Group G ( n=25)** |
|---|---|---|
| Age ( years ) | 45.3 ± 5.23 | 46.1 ± 4.82 |
| Weight ( kg ) | 50.14 ± 6.32 | 52.23 ± 5.61 |
| Duration of Surgery (min) | 126.32 ± 22.41 | 124.58 ± 21.62 |

**Table 2: Incidence of Complete Response, nausea, vomiting, retching and rescue drug**

| Time interval | Patients with | Palonosetron | Granisetron | P value |
|---|---|---|---|---|
| 0-3 hrs | Complete response | 22 (88%) | 19(76%) | 0.4635 |
| | Nausea | 2 (8%) | 3(12%) | 1 |
| | Retching | 1(4%) | 1(4%) | 1 |
| | Vomiting | 0 | 2(8%) | 0.4898 |
| | Rescue drug | 0 | 2(8%) | 0.4898 |
| 3-24 hrs | Complete response | 23(92%) | 20(80%) | 0.4174 |
| | Nausea | 2(8%) | 2(8%) | 1 |
| | Retching | 0 | 1(4%) | 1 |
| | Vomiting | 0 | 2(8%) | 0.4898 |
| | Rescue drug | 0 | 2(8%) | 0.4898 |
| 24-48 hrs | Complete response | 23(92%) | 15(60%) | 0.0181 |
| | Nausea | 1(4%) | 4(16%) | 0.3487 |
| | Retching | 1(4%) | 2(8%) | 1 |
| | Vomiting | 0 | 4(16%) | 0.1099 |
| | Rescue drug | 0 | 4(16%) | 0.1099 |
| 48-72 hrs | Complete response | 20(80%) | 14(56%) | 0.1284 |
| | Nausea | 3(12%) | 5(20%) | 0.7019 |
| | Retching | 1(4%) | 3(12%) | 0.6092 |
| | Vomiting | 1(4%) | 3(12%) | 0.6092 |
| | Rescue drug | 2(8%) | 4(16%) | 0.6671 |

**Figure 1: Postoperative period**

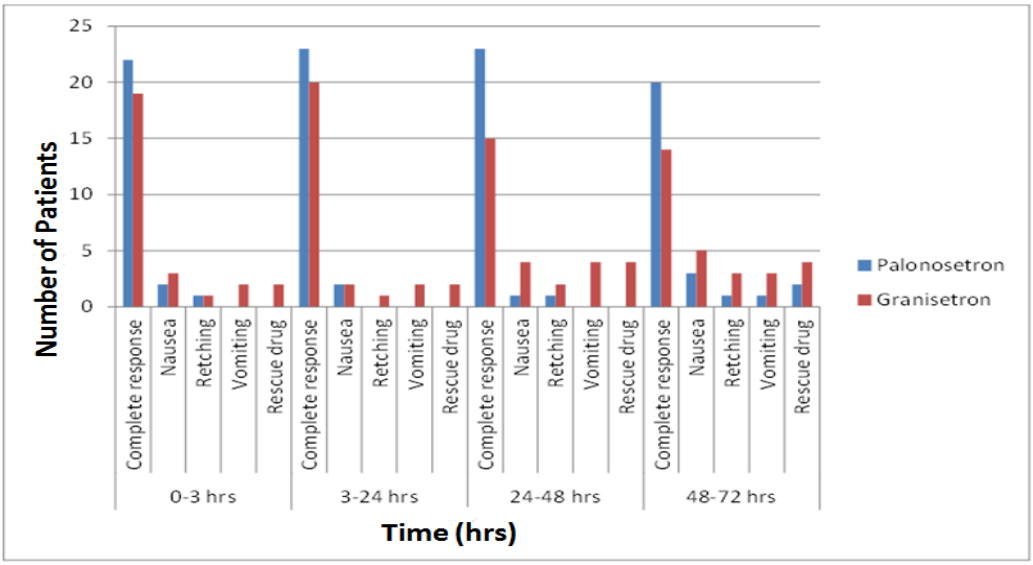


**Table 3: Side Effects**

| Side Effects | Group-P (n=25) | Group-G ( n=25) | P value |
|---|---|---|---|
| Headache | 4 (16%) | 5 (20%) | 1 |
| Dizziness | 2(8%) | 2(8%) | 1 |
| Constipation | 3(12%) | 3(12%) | 1 |

## 4. Discussion

PONV lowers patient satisfaction but is treatable. The effective, evidence-based measures of preventing and treating it should be implemented in routine practice.

Although the precise etiology of PONV is unknown, various risk factors have been identified for PONV which include female gender, non-smoker status, and history of PONV or motion sickness, use of perioperative opioids.[1] The incidence of postoperative nausea and vomiting (PONV) after general anaesthesia increases up to 30% when inhalational anaesthetics are used with no prophylaxis. This results in PONV, one of the most common complaints following surgery under general anaesthesia.[9]

In this study, however, both the groups were comparable with respect to patient demographics, duration of surgery and anaesthesia and analgesics used postoperatively. Therefore the difference in a

complete response (no PONV, no rescue medication) between the groups can be attributed to the study.

Granisetron is effective for the treatment of cancer chemotherapy induced emesis.[10] The precise mechanism of granisetron for the prevention of PONV has been suggested that it may act on sites containing 5-$HT_3$ receptors with demonstrated antiemetic effects.[11] Granisetron can be used in the dose of 40-80µg/kg for the treatment of cancer chemotherapy induced emesis .[12] The dose of granisetron 2.5 mg (approximately 45µg /kg) selected for this study was within its effective dose range (40-80µg /kg).

The exact mechanism of palonosetron in the prevention of PONV is unknown but palonosetron may act on the area postrema which contain a number of 5-$HT_3$ receptors.[8]

Rojas *et al* have described the unique pharmacology of palonosetron compared with the other 5$HT_3$ receptor antagonists including differences in half life and receptor internalization that may provide a longer duration of action. Its efficacy in preventing chemotherapy induced nausea and vomiting has been demonstrated in various studies.[15,16]

Kovac *et al* have concluded that a single 0.075mg intravenous dose of palonosetron significantly reduced emesis, intensity of nausea and the use of rescue anti-emetics in addition to delaying emesis and treatment failure. They demonstrated that palonosetron 75µg is the more effective dose for the prevention of PONV after major gynaecological and laparoscopic surgery than 25µg and 50µg.[13] Lower doses were not effective.

Chun *et al* also confirmed that 0.075mg of palonosetron was effective antiemetic dose in out patients.[14] So in our study we used this dose as it was found to have best treatment effect.

Bhattacharjee and Dawn[17] concluded that prophylactic therapy with palonosetron is more effective than granisetron for the long term prevention of PONV after laparoscopic surgery In our study the antiemetic efficacy of palonosetron is similar to that of granisetron for preventing PONV during the first 24 hours (0-3 and 3-24 hours) after gynaecologic surgery and palonosetron is more effective than granisetron for getting a complete response (no PONV, no rescue medication) for 24-48 hours. The reason may be related to the half lives (granistron 8-9 hrs versus palonosetron 40 hrs) and/or the binding affinities of 5-$HT_3$ receptor antagonists (palonosetron interacts with 5-$HT_3$ receptors in an allosteric, positive cooperative manner at sites different from that bind with granisetron)[7,8]. This suggests that palonosetron has longer lasting antiemetic effect than granisetron. The antiemetic efficacy of palonosetron is similar to that of granisetron for preventing PONV during 48-72hours.

Adverse effects with a single bolus dose of Palonosetron and Granisetron were not clinically serious and there was no significant difference in incidence of headache, dizziness and constipation between two groups. Thus both were devoid of clinically important side effects.

## 5. Conclusion

Prophylactic therapy with IV palonosetron is more effective than IV granisetron for the long term prevention of PONV after gynaecological surgery under general anaesthesia.

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