

**Original article:**

## **Effect of palonosetron versus granisetron to prevent postoperative nausea and vomiting after laparoscopic surgery : a case study**

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### **Abstract:**

**Background:** Postoperative nausea and vomiting ( PNOV) is noted to be the most common complications of inpatient and day case surgical procedures. Postoperative nausea and vomiting accounts for equal or more debilitation than surgery itself and may cause patients to lose wages due to absence from work. Reducing the incidence of nausea and vomiting and its associated problems may therefore provide opportunities to improve patient care, decrease the size of waiting lists and improve utilisation of scarce healthcare resources. Selective 5-hydroxytryptamine type 3 (5-HT<sub>3</sub>) receptor antagonists are reported to have potent antiemetic effects for postoperative nausea and vomiting (PONV). The purpose of this study was to prospectively evaluate the efficacy of palonosetron and granisetron for the prevention of PONV in patients undergoing laparoscopic surgery.

**Methods :** In this prospective, randomized observational study, 100 patients of ASA status I and II scheduled for laparoscopic surgery under general anaesthesia were enrolled. Patients were randomly allocated into two groups one group received 0.075 mg Palonosetron (Group p) and other group received 1mg Granisetron (Group g). The severity of nausea and vomiting was measured by 4-point verbal descriptive scale in postoperative period for 72 hrs. Any side effects in postoperative were also analysed.

**Result:** The incidence of PONV was significantly lower in group p than in group g with p value less than 0.05 (0.03) during the first 72 hrs, incidence of complete response was 86% in group p and 58% in group g.

**Conclusion:** Palonosetron was comparatively more effective than Granisetron for prevention of PONV after laparoscopic surgery under general anaesthesia.

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

### **INTRODUCTION :**

Laparoscopic surgeries are rapidly emerging as preferred surgical procedures these days. These have considerably decreased the surgical mortality . However, advantages of Laparoscopic surgery may be counteracted by a high incidence of distressing side effects such as postoperative nausea and vomiting (PONV). PONV is defined as nausea and/or vomiting occurring within 24 h after surgery. PONV accounts for one of the most common cause of patient dissatisfaction after anesthesia, in all post-surgical patients reported incidences is 30% and a relatively high incidence (60–80%) after ear, nose and throat (ENT) surgery.<sup>(1)</sup> ENT surgeries have a high incidence of postoperative emesis when no prophylaxis is done.<sup>(2)</sup>

Despite the advances made in anaesthesia, postoperative nausea and vomiting (PONV) is one of the most common postoperative complications. Several factors may be associated which influence PONV, such as the patient's gender, weight, age, presurgical anxiety state, as well as the surgical procedure, type and duration of anaesthesia. To prevent and treat PONV numerous antiemetics like anticholinergics and benzamide have been studied.<sup>(3-5)</sup> However, these agents can cause undesirable side effects such as sedation, dry mouth and hypotension. Selective 5-hydroxytryptamine 3 (5-HT<sub>3</sub>) are the primary therapy for PONV prevention due to their efficacy and fewer side effects such as sedation or extrapyramidal symptoms as compared to other antiemetics.<sup>(6)</sup> Most 5-HT<sub>3</sub> receptor antagonist research has focused on ondansetron, and the antiemetic efficacy of these compounds has been well established for the prevention and treatment of chemotherapy-induced emesis, as well as for PONV.<sup>(6,7)</sup>

Granisetron is a highly selective first generation potent 5-HT<sub>3</sub> receptor antagonist. Granisetron selectively blocks the 5-HT<sub>3</sub> receptor with half-life of 4 to 9 hrs.<sup>(8)</sup> Palonosetron is a second-generation 5-HT<sub>3</sub> receptor antagonist. It can be distinguished from other 5-HT<sub>3</sub> receptor antagonists by its allosteric inhibition, greater binding affinity and longer half-life of 40 hrs.<sup>(9)</sup>

So we designed this prospective randomized double blind study to assess and compare Granisetron and Palonosetron for management of PONV following laparoscopic surgeries under general anaesthesia.

#### **MATERIAL & METHOD:**

This study was approved by the institutional ethics committee and informed written consent were taken from all the patients included in the study. Randomly selected 100 adult patients, divided into 2 groups of 50 patients each with age ranging between 15 to 65yrs of both sexes (ASA grade I and II) who were scheduled for laparoscopic surgery under general anaesthesia were included in study. Patient in group G were given Granisetron 1 mg and Palonosetron 0.075 mg intravenously in group P. Exclusion criteria include history of allergy to any 5-HT<sub>3</sub> antagonist, motion sickness, administration of an antiemetic medication or steroids within 48 hours before surgery, major cardiovascular, respiratory, endocrine, gastrointestinal, liver, renal disease.

After shifting the patient to operation theatre, consent for study was checked again. In the operating room, the vital signs of the patient were continuously monitored using electrocardiogram, pulse oximetry, and measurement of noninvasive arterial pressure. After performing peripheral intravenous cannulation (18G), 25 minutes before induction of anaesthesia study drug was given to patient. The printout of lead II ECG data was taken out on a paper at interval of 0 min, 5 min, 10 min, 15 min, 20 min and 25 min after administration of drug. The QT and RR intervals on the ECG trace were measured manually. The QTc (Corrected QT) was calculated with the help of Bazett's formula.

Opioid (Fentanyl 2µg/kg), midazolam 1mg intravenously was given 5 minutes before induction of anaesthesia. Following 3 minutes of preoxygenation with 100% oxygen, a priming dose 0.01mg/kg of Vecuronium was given 2 min before induction. Induction was done with Propofol (2.5mg/kg) followed with 0.1mg/kg of Vecuronium. After 90 sec. of induction direct laryngoscopy and endotracheal intubation with appropriate size tube was done. Confirmation of endotracheal tube was done by auscultation and with ETCO<sub>2</sub>. Anaesthesia was maintained with mixture of Oxygen, Nitrous oxide (30%;70%), Isoflurane & Vecuronium was used for skeletal muscle relaxation intraoperatively. At the end of surgery, the residual neuromuscular blockade was antagonized with appropriate doses of inj. neostigmine and inj. Glycopyrrolate.

In postoperative period, following parameters was analyzed for 72 hrs.

Complete response : No nausea/vomiting episode, Partial response: any episode of nausea/vomiting and Treatment failure: 2 or more episode of nausea/vomiting or the receipt of a rescue anti emetic.

4-point VDS score was used to evaluate the severity of Postoperative nausea; 0=no nausea, 1=mild, 2=moderate and 3=severe. Any side effects like headache, dizziness, myalgia, constipation in postoperative period were also analyzed.

The study was conducted on 100 patients for their postoperative assessment of PONV. All the two groups were comparable for their demographic profiles with respect to age, sex, BMI and duration of surgery and anesthesia.

**Statistics**

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The comparison between two groups was made with student t test and chi square test as appropriate. Results were expressed as Mean±SD and number (%). For the study minimum sample size was 50 with  $\alpha$  error 5% and confidence level 95%.

**RESULT :**

	<b>Group P (Mean±SD)</b>	<b>Group G (Mean±SD)</b>	<b>p-value</b>
Age (yrs.)	25±9.0	25±10.1	0.787
Sex (M/F)	26/24	29/21	0.546
BMI	21±2.4	20±2.2	0.897
Duration of surgery (mins)	79±37.6	75±36.8	0.556
Duration of anesthesia (mins)	105±39.0	102±39.3	0.684
<i>Demographic profile of patients</i>			

(BMI- body mass index.)

We observed QTc of patients for 25 mins after administration of drug before induction of anesthesia. There was no QTc prolongation in any patient and no arrhythmia was present in any patient.

<b>Time interval</b>	<b>Group P(Mean±SD)</b>	<b>Group G(Mean±SD)</b>	<b>t value</b>	<b>p value</b>
0 min	407±21.8	410±20.2	0.779	0.437
5 min	403±20.7	403±15.3	0.081	0.934
10 min	410±20.3	407±18.3	0.907	0.366
15 min	416±25.8	414±21.9	0.566	0.572
20 min	417±27.6	413±24.9	0.734	0.464
25 min	419±21.5	412±19.2	1.810	0.073
<i>QTc interval</i>				

	<b>Complete response (%)</b>	<b>Partial response (%)</b>	<b>Treatment failure (%)</b>
Group P	41(82)	6(12)	3(6)
Group G	29(58)	14(28)	7(14)
Total	70	20	10
<b>Response</b>			

The  $\chi^2$  is 6.857. The p value is 0.032. The result is significant if p value is <0.05. The incidence of nausea was recorded for up to 72 hrs in the postoperative period.

	<b>Nausea (%)</b>	<b>No nausea (%)</b>
Group P	7(14)	43(86)
Group G	19(38)	31(62)
<b>Incidence of Nausea</b>		

The  $\chi^2$  value is 7.484. The p value for this is 0.006. The result is significant if p value is <0.05. 86% patients reported no nausea in group P while 62% patient reported in group G. The incidence of postoperative nausea was significantly reduced in Palonosetron group.

The severity of nausea was recorded by visual descriptive scale (VDS). Nausea was graded as 0=no; 1=mild; 2=moderate; 3=severe.

Score	<b>Group P (n=50)</b>		<b>Group G (n=50)</b>	
	N	percentage	N	Percentage
0(none)	43	86	31	62
1(mild)	2	4	6	12
2(moderate)	5	10	11	22
3(severe)	0	0	2	4
<b>VDS score</b>				

$\chi^2$  value is 8.196. p value is 0.0421. p value <0.05 is significant.

	Rescue drug received (%)	No rescue drug received (%)
Group P	3(6)	47(94)
Group G	10(20)	40(80)
<b>Rescue antiemetic</b>		

The  $\chi^2$  value is 4.332. The p value is .037. The result is significant if p value is  $<0.05$ .

This shows that there is significant reduction in requirement of rescue antiemetics in group P as compared to group G.

Symptoms	Group P		Group G		$\chi^2$	P- value
	No.	%	No.	%		
Headache	13	26	14	28	0.050	0.822
Constipation	9	18	9	18	0	1.0
Myalgia	6	12	8	16	0.322	0.564
Dizziness	7	14	6	12	0.088	0.766
<b>Adverse effects in two groups</b>						

## DISCUSSION:

Postoperative nausea and vomiting (PONV) is a common and distressing complication of surgery under general anesthesia. PONV are frequent and unpleasant symptoms following general anaesthesia. Postoperative nausea and vomiting (PONV) is defined as any nausea, retching, or vomiting occurring during the first 24–48 hrs after surgery in patients. PONV may take place in single or multiple episodes, which may last minutes, hours, or even days. Persistent PONV can cause tension on suture line, venous hypertension, increase bleeding under skin flaps, esophageal rupture and even expose patient to increase risk of pulmonary aspiration of vomitus if airway reflexes are depressed due to residual anaesthetic dosage in body.<sup>(10)</sup>

In spite of so much advancement in the management of postoperative nausea and vomiting like invention of new drugs, multi modal approaches of management like administering multiple different antiemetic medications, less emetogenic anaesthetic techniques, adequate intravenous hydration, adequate pain control etc., the incidence of PONV remains still high.

In our study 41(82%) patient showed complete response i.e. no nausea or vomiting with Palonosetron while with Granisetron 29(58%) patients showed complete response during the first 72 hrs. The severity of nausea was recorded by VDS scale. It was more severe in Granisetron group than in Palonosetron group.

The rescue antiemetic was given to refractory or treatment failure patients. 20% patients in Granisetron group received rescue antiemetic while 6% received rescue antiemetic in Palonosetron group. They shows a statistically significant difference in both the groups.

We did not include a control group receiving placebo in our study. Aspinall and Goodman have suggested that if active drugs are available, placebo controlled trials may be unethical because PONV are very much distressing after laparoscopic surgery<sup>(11)</sup>.

Adverse effects with a single therapeutic dose of granisetron or palonosetron were not clinically serious and there were no significant differences in the incidence of headache, dizziness and drowsiness between the groups. Thus both palonosetron and granisetron are devoid of clinically important side effects. The adverse effects of drugs in both the groups were similar. Headache was the most common side effect found in 26% cases of Palonosetron group and 28% in Granisetron group.

#### **Conclusion:**

In conclusion prophylactic therapy with palonosetron is more effective than prophylactic therapy with granisetron for the long term prevention of PONV after laparoscopic surgery.

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