

# A COMPARATIVE STUDY OF ONDANSETRON, GRANISETRON AND PALONOSETRON IN PREVENTION OF NAUSEA AND VOMITING IN ELECTIVE ABDOMINAL SURGERIES UNDER GENERAL ANAESTHESIA

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## ABSTRACT

### BACKGROUND

Post-operative nausea and vomiting are the common complaints in patients undergoing surgery under general anaesthesia. This is one of the factors that determine the length of hospital stay after anaesthesia. The concept of day care surgery requires good, enhanced, quick post-operative recovery, for early discharge from the hospital. This requires a better antiemetic without any adverse effects. We wanted to compare efficacy of Ondansetron, Granisetron, and Palonosetron in patients undergoing abdominal surgeries, under general anaesthesia, in prevention of post-operative nausea and vomiting.

### METHODS

A prospective randomized control study was carried out, from June, 2016 to December, 2018 in the Department of Anaesthesia, Sri Venkateswara Medical College. Patients undergoing abdominal surgeries, under general anaesthesia were included in the study after fulfilling the inclusion and exclusion criteria. They were divided into 3 groups and antiemetics were given. Presence nausea, vomiting, requirement of rescue antiemetic and adverse effects of drugs were measured.

### RESULTS

Incidence of postoperative nausea and vomiting were noted for 24 hours postoperatively. We could not find any major adverse drug reactions in the study.

### CONCLUSIONS

Palonosetron was found to be effective in preventing post-operative nausea and vomiting, without any adverse reaction in the study in comparison with other drugs.

### KEYWORDS

Post-Operative Nausea and Vomiting (PONV), Ondansetron, Granisetron, Palonosetron, General Anaesthesia, Abdominal Surgeries

**HOW TO CITE THIS ARTICLE:** Jeevan Babu A, Vijayakumari Y, Sudheer K. A comparative study of ondansetron, granisetron and palonosetron in prevention of nausea and vomiting in elective abdominal surgeries under general anaesthesia. J. Evid. Based Med. Healthc. 2019; 6(34), 2335-2338. DOI: 10.18410/jebmh/2019/477

### BACKGROUND

The incidence of postoperative nausea and vomiting in patients undergoing surgery, under general anaesthesia is around 20-40%.<sup>1</sup>

It not only increases patient discomfort, it is even more distressing than post-operative pain and lead to mild complication like dehydration, electrolyte imbalance and can lead to rare but serious complications such as aspiration of

gastric contents, post-operative dehiscence, oesophageal rupture, subcutaneous emphysema or pneumothorax. These adverse consequences may lead to delay in patients discharge from post anaesthesia care unit (PACU), unexpected extended hospital stay adds the hospital expenditure and delayed return to work. Pain, bleeding and post-operative nausea and vomiting are the three common causes for the unplanned hospital admission of the patients in day care surgery.<sup>2</sup> PONV is one of the important contributions of patient dissatisfaction (around 70%) postoperatively.<sup>3</sup> These were the indications which led to use of prophylactic anti-emetics during anaesthesia to prevent. Earlier drugs used are antihistamines, phenothiazine derivatives, anticholinergics and dopamine receptors antagonists. But these drugs had certain side effects like delayed recovery, sedation and extra-pyramidal symptoms. Hence the requirement of ideal antiemetic drugs necessitated further research resulted in discovery of 5HT<sub>3</sub>

*Financial or Other, Competing Interest: None.*  
*Submission 13-07-2019, Peer Review 18-07-2019,*  
*Acceptance 01-08-2019, Published 26-08-2019.*

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*DOI: 10.18410/jebmh/2019/477*



antagonists. These drugs have immediate action, easily metabolized by liver, no drug interactions during the period of anaesthesia, no adverse effects, and quick recovery. These drugs act on receptors which are present in vomiting inducing sites such as nucleus tractus solitaries, area postrema and vagal afferents.<sup>4</sup> There is insufficient literature about the best antiemetic agent to be used in avoiding PONV. We thought of starting a study to compare the effects of Ondansetron, Granisetron and Palonosetron and their role in prevention of PONV in abdominal surgeries done under general anaesthesia.

**METHODS**

A prospective, computer generated open randomized controlled trial study was carried out in Department of anaesthesia, Sri Venkateswara Ram Narayan Ruia Government General Hospital, Sri Venkateswara Medical College, Tirupati. Ethical committee approval was taken. Informed written consent from the patients was taken. Patients posted for the abdominal surgeries, under general anaesthesia were included in the study. Patients were randomly divided into three groups of 30 patients each according to computer generated random allocation, on fulfilling inclusion and exclusion criteria. Group O- Ondansetron, Group G- Granisetron, Group P- Palonosetron.

**Inclusion Criteria**

1. Patients aged between 20-60 years.
2. Patients belonging to ASA grade I and II.
3. Patients posted for elective abdominal surgeries under general anaesthesia.

**Exclusion Criteria**

1. Patients who refused for the consent were excluded from the study.
2. Patients with co-morbidities and unfit for the surgery.
3. Pregnant and lactating mothers.
4. History of motion sickness.
5. Patients on antiemetic drugs within 24 hours prior surgery.
6. History of drug allergy towards these medications.

Pre-operative check-up, a day before surgery for general and systemic examination was carried out. Routine Haemogram, renal and hepatic function tests were carried out. ECG, cardiology and general medicine check-up before surgery were taken up. Fitness from other departments was taken in case of necessity and requirement. All the patients received Tablet Alprazolam 0.5 mg on previous night of surgery and were instructed to remain nil orally after 10 PM midnight. Peripheral venous access was established, and intravenous fluid were started before induction of anaesthesia.

The study medications were administered intravenously as follows-

1. Inj. Glycopyrrolate 0.2 mg
2. Inj. Pantoprazole 40 mg
3. Inj. Fentanyl 1-2 mg/Kg body weight.
4. Antiemetic for that particular group were administered.

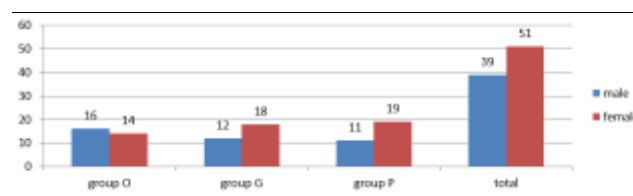
After preoxygenation for 3-5 minutes, General anaesthesia procedure was started and patients maintained under it, till end of surgical procedure. On the completion of surgery patients were reversed of anaesthesia. They transported into recovery room and later to the ward after confirming an adequate level of consciousness and intact reflexes. The incidence of PONV was recorded with in first 24 hours after the surgery at intervals of 0-4 hours, 4-12 hours and 12-24 hours. Episodes of PONV were identified by spontaneous complaints by the patients or by direct questioning. Rescue antiemetic was provided with inj. Ondansetron 4 mg IV in the event of episodes of vomiting. Post-operative pain relief was maintained with Inj. Diclofenac 75-150 mg IM given instead of Inj. Tramadol to prevent false positive PONV. Complete response was defined as the absence of nausea retching or vomiting and no need for rescue antiemetic during the 24-hour observation period.

**Statistical Analysis**

Observations and results were tabulated. Statistical evaluation was done with Chi-square test.

**RESULTS**

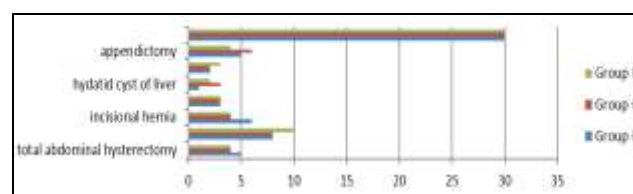
Total 90 patients were included in the study. Each group was openly randomized with 30 patients. Patients were disturbed equally in all groups in terms of gender, age and other factors to prevent bias in the findings. There were 39 male and 51 female patients.



**Figure 1. Sex Distribution of Patients in Each Group**  
(ChiSquare test value- 1.9005 df -2 p value- 0.3866 p<0.05)

Age (in Years)	Groups						Total
	Group O (Ondansetron)		Group G (Granisetron)		Group P (Palonosetron)		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
20-29	5	16.67%	3	10.01%	7	23.33%	15 (16.66%)
30-39	8	26.67%	10	33.33%	6	20.01%	24 (26.66%)
40-49	13	43.33%	10	33.33%	10	33.33%	33 (36.66%)
50-60	4	13.33%	7	23.33%	7	23.33%	18 (20.02%)
Total	30	100%	30	100%	30	100%	90 (100%)

**Table 1. Age Distribution of Patients in Various Groups**



**Figure 2. Type and Number of Surgeries in Each Group**

Post-operative data suggests that incidence of postoperative nausea and vomiting, is more in group Ondansetron and Granisetron groups on comparison with Palonosetron group. Complete response is better in group Palonosetron with no requirement of rescue dose of antiemetic medication thereafter. We had minor symptoms of headache and dizziness in our study, but no noticeable drug interactions like rashes and allergic reactions.

Groups	Post-Operative Nausea and Vomiting			
	Present		Absent	
	No. of Cases	Percentage	No. of Cases	Percentage
Group O	21	70%	9	30%
Group G	14	46.6%	16	53.33%
Group P	4	13.4%	26	86.6%
Total	39	43.34%	51	56.66%

**Table 2. Incidence and Percentage of PONV in Various Groups**  
(Chi square test -19.819 p value -0.00005 p<0.05)

Groups	Complete Response		Rescue Antiemetic Required with Symptoms of PONV		Symptoms of PONV but No Rescue Antiemetic Required	
	No. of Cases	%	No. of Cases	%	No. of Cases	%
Group G	16	53.3%	9	30%	5	16.7%
Group P	26	86.66%	3	10%	1	3.34%
Total	51	56.67%	29	32.2%	10	11.1%

**Table 3. Complete Response and Requirement of Rescue Antiemetic Cases in Various Groups**  
(Chi square test value- 21.3951, p value- 0.000264 p<0.05)

**DISCUSSION**

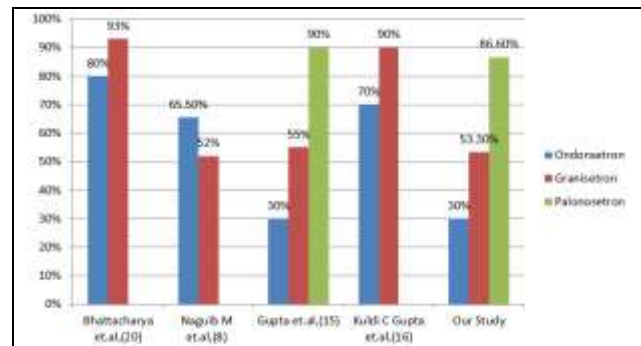
The high incidence of PONV after general anaesthesia may justify the use of prophylactic antiemetic therapy. We do infer and believe it be ethical to avoid placebo group in our study. Numerous factors can affect PONV, such as age, gender, obesity, history of motion sickness and PONV, opioids use as a part of postoperative analgesic, N<sub>2</sub>O, technique of anaesthesia, duration and type of surgical procedure, and post-operative pain. Female patients have higher incidence of PONV on comparison with male patients.<sup>2,5</sup> But we could not find any significant statistical difference in between these populations in our study (Figure 1). Guidelines for managing postoperative nausea and vomiting were announced in 2014 annual meeting of American Society of Anesthesiologists in Chicago, USA after evaluation of medical literature. They recommended the use of antiemetic, mostly use of 5HT<sub>3</sub> receptor antagonists.<sup>6</sup> Selectiveness of 5HT<sub>3</sub> receptor, affinity, and longer half-life of compounds varies with drugs. Palonosetron is the best, followed by Granisetron<sup>7</sup> and Ondansetron, in terms of receptor affinity, longer half-life, little and no affinity to other serotonin receptors.

The drug doses in study were given 5 minutes before intubation of general anaesthesia. The incidence of nausea and vomiting in our study in various groups was Palonosetron (13.4%), Granisetron (46.6%) and Ondansetron (70%). This stands comparable with other studies like Gupta et.al,<sup>15</sup> Ondansetron (50%), Palonosetron

(7.5%) and Granisetron (12,5%), and Kuldip C Gupta et.al,<sup>16</sup> Ondansetron (13.3%). Granisetron (10%).

Ondansetron Dose	Granisetron Dose	Palonosetron Dose
Naguib M et al, <sup>8</sup> - 4 mg Rajeeva V et al, <sup>9</sup> - 4 mg Argiriadou H et al, <sup>10</sup> - 4 mg Yukse MS et al, <sup>11</sup> - 4 mg	Wilson J et al, <sup>12</sup> - 1 mg Mikawa K et al, <sup>13</sup> - >5 mcg/Kg body weight Raphael et al, <sup>14</sup> - 2 mcg Kumkum Gupta et al, <sup>15</sup> - 2 mg Kuldip C Gupta et al, <sup>16</sup> - 40 mcg/ Kg body weight	Candiotti KA et al, <sup>17</sup> - 0.075 mg White PF et al, <sup>18</sup> - 0.05 mg Kovac AL et al, <sup>19</sup> - 0.025 mg, 0.05 mg and 0.075 mg Kumkum Gupta et al, <sup>15</sup> - 0.075 mg
Our Study - 4mg	Our Study- 1 mg	Our Study - 0.075 mg

**Table 4. Drug Doses Used in Various Studies in Comparison with Our Study**



**Figure 3. Comparison of Complete Drug Response in Various Studies with Our Study**

A “complete Response” to the prevention of PONV is defined as the absence of nausea, retching or vomiting and no need for rescue antiemetic during the 24 hours observation period post-operatively. We had this highest in Group P with 26 patients (86.6%) followed by 16(53.3%) and 9(30%) patients (53.3%) in G and O groups respectively. Figure 3 data shows varied “complete response” in various studies. Palonosetron is better antiemetic than others in terms of efficacy. We used injection Ondansetron 4 mg intravenously as a rescue antiemetic in our study. The number of patients required rescue antiemetic in group P was 3 when compared to 9 and 17 in groups G and O respectively. Requirement of rescue antiemetic is significantly lower in Palonosetron group.

Studies show good safety record of 5HT<sub>3</sub> antagonist with mild and transient side effects like headache, constipation and dizziness.<sup>21</sup> in our study we had transient headache and dizziness with no other recordable adverse drug reactions. Based upon our study findings we infer Palonosetron as best antiemetic with quick onset of action, good half-life, extended period of action, easily metabolized by liver (cytochrome P450). Palonosetron can used in all patients posted for abdominal surgeries (open and laparoscopic) done under general anaesthesia.

**CONCLUSIONS**

Palonosetron is the best in the prevention of post-operative nausea and vomiting when compared with Ondansetron and Granisetron. The requirement of rescue antiemetic was comparatively less in Palonosetron. All the three drugs do not have significant adverse effects and are well tolerated.

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