Original Research Article

A Comparative Study of Prophylactic Ondansetron Versus Palonosetron for Post Operative Nausea and Vomiting in Patients Undergoing Major Surgeries under General Anaesthesia

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ABSTRACT

Background
Postoperative nausea and vomiting (PONV) a typical side effect of major operations, can unexpectedly postpone hospital discharge. The present study was done to compare prophylactic Inj Ondansetron 4 mg IV versus Inj. Palonosetron 0.075mg IV for post operative nausea and vomiting in major surgery.

Methods
The present study was done in department of Anaesthesia at Terna Hospital and Research Centre. After approval from ethical committee 60 patients undergoing major surgeries under GA were studied during the period of one year. Patients were allocated into two groups with 30 patients in each group. The statistical program SPSS 25.0 was used to analyse the data statistically.

Results
The mean age of patients in both groups was between 40 to 50 years. Female patients (13/17) were higher in group P and male patients (17/13) were higher in group O**.** The results were significant for comparison at 24 to 48 hours for PONV and VAS. Group O there was no need of rescue antiemetic where as in group P it was done between 0 to 6 hrs. for 1 patient and 6 to 24 hrs. for 1 patient.

Conclusion
When compared to Palonosetron, Ondansetron has a superior antiemetic, anti-nausea effect, and a lower incidence of PONV in the patients undergoing major procedures.

Keywords: Postoperative nausea and vomiting, Ondansetron, Palonosteron, General anaesthesia.

INTRODUCTION

Any nausea, vomiting or retching that happens in the first 24 to 48 hours following surgery is referred to as postoperative nausea and vomiting.[1] After surgery, nausea and vomiting affect 20% to 30% of patients and ranks second in terms of most common complaints, with pain ranking first.[2] It prevents ambulatory surgical patients from being discharged early and increases the risk of an unplanned hospital stay.[3]

Following Watcha and White's 1992 analysis, postoperative nausea and vomiting emerged as the most widely used clinical phase.[4] PONV resulted in a slower rate of recovery, more nursing care and a possible prolonged hospital stay, all of which raised the overall expenses of health care. Additionally linked to PONV is a high degree of patient discomfort. Patients frequently rate postoperative nausea and vomiting (PONV) as worse than postoperative pain[5], and hence preventing PONV is more important.

Consequently, a lot of research has been done on medications and strategies to stop PONV. Because it has fewer side effects and is more effective than other antiemetics in the prevention and treatment of PONV, the 5-Hydroxytryptamine (5-HT3) receptor antagonist is frequently used [6]. Granisetron and Ramosetron are also used as 5-HT3 receptor antagonists, although Ondansetron is the most commonly used medication. Palonosetron has recently been reported to be useful in preventing PONV[7,8] especially with patients on chemotherapy drugs.[9,10]

A recently created antagonist of the 5-HT3 receptor is called Palonosetron. Compared to other antagonists, it has a stronger receptor affinity. It is also known to be more effective than Ondansetron at preventing nausea and vomiting in patients taking anticancer medications [8]. Its plasma half-life is very long.[11,12] There are, however few studies contradicting Palonosetron's ability to prevent PONV with that of other 5-HT3 receptor antagonists.

Hence the present study was done to compare prophylactic Inj Ondansetron 4 mg IV versus Inj Palonosetron 0.075mg IV for post operative nausea and vomiting in patient undergoing major surgeries under GA.

MATERIAL AND METHODS

The present study was done in department of Anesthesia at Terna Hospital and Research Centre amongst patients undergoing major surgeries under GA during the study period of one year. Ethical approval was taken from institutional ethical committee before the commencement of study. Written informed consent was taken from each patient before starting the procedure.

Total 60 patients were selected through consecutive sampling with odd or even distribution on the basis of following criteria.

Inclusion criteria

1. Patients with age 18 to 60 years.
2. Patients with ASA grade I and II.
3. Patients undergoing major surgery under general anaesthesia

Exclusion criteria

1. Patients with allergy to experimental drugs.
2. Patients with ASA grade III, IV and V.
3. Patients with Opioid dependence.
4. Patients with history of PONV and motion sickness.
5. Patients with use of antiemetics 24 hr. prior to surgery.

After applying multipara monitors baseline HR, NIBP, ECG, SPO2 were recorded. Patients were allocated into two groups with 30 patients in each group on odd or even basis. Patients were premedicated with inj. Glycopyrrolate 4mcg/kg i.v + inj.Fentanyl 2 mcg/kg i.v. 5 min before induction of anaesthesia Inj. Ondansetron 4 mg i.v for group O and inj. Palanosetron 0.075 mg i.v was given to group P. Induction was done with Inj Propofol 2-3 mg/kg i.v. + Inj Atracurium 0.5mg/kg i.v. Patients were intubated. Anaesthesia was maintained with 50 % oxygen + 50% nitrous oxide with Isoflurane and Inj Atracurium 0.1mg/kg i,v. Patients were ventilated in VCV mode. At the end of the surgery patients were reversed with Inj Neostigmine 80ug/kg+ Inj Glycopyrolate 8ug/kg i.v. Patients were extubated following extubation protocols. Every patient was monitored for nausea and vomiting for first 48 hrs. after surgery. PONV score was compared between the two groups. Patients with PONV score >2 were given Inj Metoclopromide 10mg i.v. for rescue medication and frequency of administration of rescue medication was also studied.

The statistical programme SPSS 25.0 was used to analyse the data statistically. The baseline characteristics were described using descriptive statistics. Whereas the qualitative factors were shown as numerical percentages, the quantitative variables were represented by the mean and standard deviation. The One Way ANOVA test was used to compare continuous numerical variables. Fisher's exact test was used to compare dichotomous variables. A P value of less than 0.05 was deemed significant.

RESULT

The mean age of patients in both groups was between 40 to 50 years. Female patients (13/17) were higher in group P and male patients (17/13) were higher in group O. Number of patients in ASA I category were higher. Average duration of surgery and anaesthesia time was also calculated as shown in table 1.

Table 1 Subject and anaesthetic characteristics. Values are number, mean (SD), or number (%). PONV, postoperative nausea and vomiting

Variable	Group P (n=30)	Group O (n=30)
Mean Age	44.4±13.6	45.9±17.5
Male /Female	13/17	17/13
ASA I/II	24/6	23/7
Duration of surgery (min)	147.6±56.9	130.3±52.8
Anaesthesia time (min)	162.5±59.4	143.8±54.7

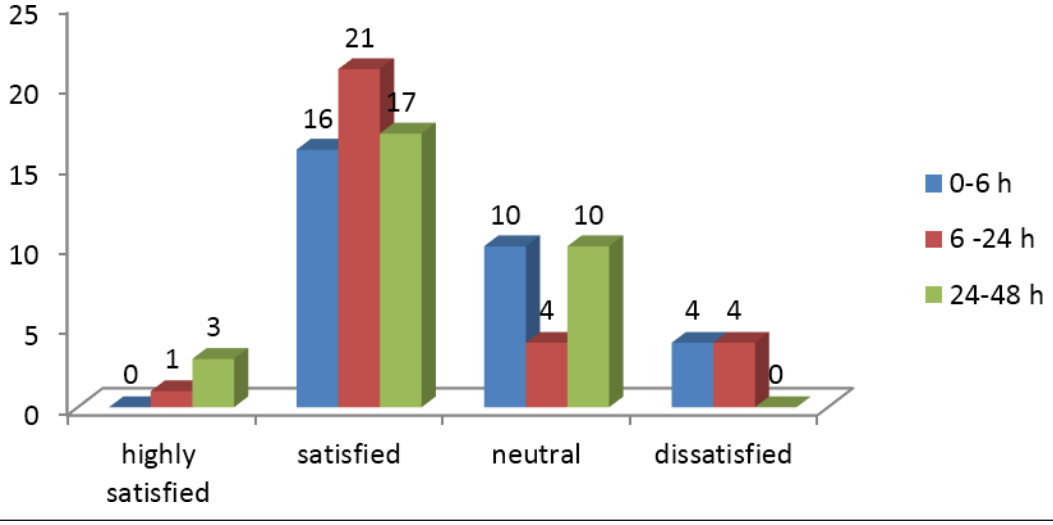
Comparison of two groups on the basis of post operative nausea and vomiting symptoms at 6 hrs., 6 to 24 hrs. and 24 to 48 hrs. was calculated. It was found that in group O the mean values were lower than group P. The results were significant for comparison at 24 to 48 hrs. as shown in table 2.

Table 2 Comparison of two groups on the basis of post operative nausea and vomiting symptoms

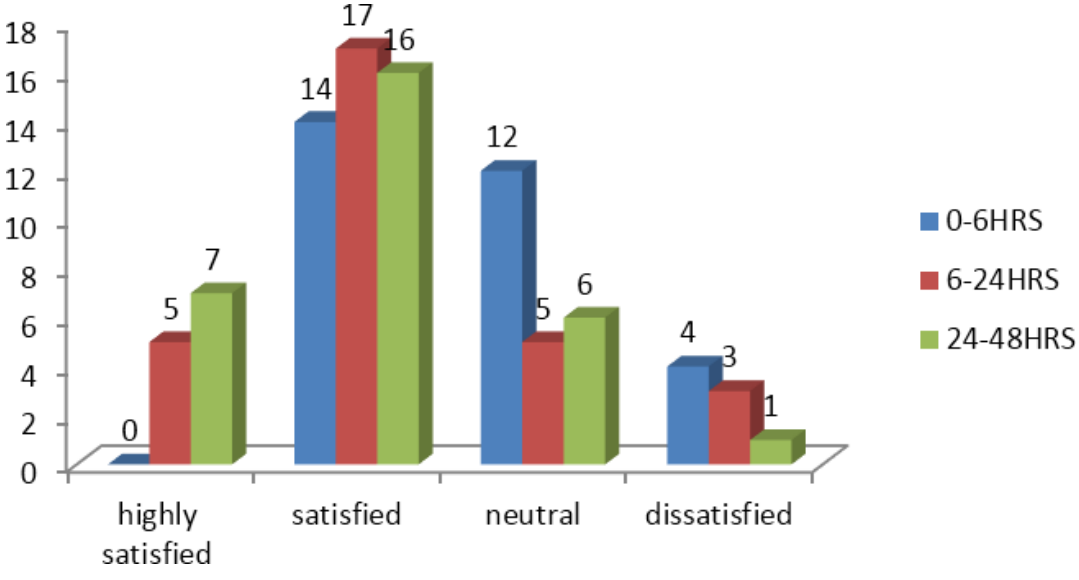
Groups	Nausea		
	0-6 hrs.	**6-24 hrs.**	**24-48 hrs.**
Group P	0.33±0.4	0.2±0.4	0.03±0.1
Group O	0.33±0.4	0.13±0.3	0.03±0.18
P value	0.323	0.218	0.001
	Vomiting		
Group P	0.03±0.1	0.03±0.1	0
Group O	0	0	0
P value	-	-	-
	VAS		
Group P	3.16±1.1	2.6±1.3	2.13±0.9
Group O	2.6±0.8	2±0.7	1.6±0.6
P value	0.213	0.221	0.000
	PONV		
Group P	0.36±0.5	0.23±0.5	0.03±0.18
Group O	0.3±0.4	0.13±0.3	0.06±0.2
P value	0.125	0.210	0.000

Comparison of two groups on Likert scale was done having options as highly satisfied, satisfied, neutral and dissatisfied and are represented in graph 1 (a) and (b).

Graph 1 (a) and (b) comparison of two groups on the basis of Likert scale



(a) Group P



(b) Group O

Comparison of two groups on the basis of rescue hours was done and it was found in group O there was no need of rescue where as in group P it was done between 0 to 6 hrs and 6 to 24 hrs as shown in table 3.

Table 3 Comparison of two groups on the basis of rescue hours

Groups	Rescue hours		
	0-6 hrs.	**6-24 hrs.**	**24-48 hrs.**
Group P	0.03±0.18	0.03±0.18	0
Group O	0	0	0

DISCUSSION

Patients who have undergone surgery may experience discomfort and dissatisfaction due to a condition called PONV. There are numerous approaches to treating and preventing it. Nonetheless than 20–30% of PONV cases occur and are influenced by the patient factors, anaesthesia techniques and surgical factors.[13] According to Apfel et al.[14], the most significant risk factors for PONV among patients receiving inhaled anaesthesia were female gender, a history of PONV or motion sickness, non-smoker and postoperative opioid use. For every additional risk factor, the incidence rate of PONV increased to 21, 39, 61, and 79% respectively.

The emetic centre, which is located in the lateral reticular formation near the Tractus Solitarius in the brain stem regulates the complex act of vomiting, which involves the coordination of the muscles of the respiratory system, gastrointestinal tract and abdomen. The emetic centre may be impacted by stimuli from regions of the central nervous system.[15]

These comprise afferents from the mediastinum, throat and gastrointestinal tract in addition to those from the upper cortical centre and the postrema chemoreceptor trigger zone. The brain's postrema region is abundant in 5-HT3, opioid and dopamine receptors.

Major neurotransmitter systems including dopaminergic, muscarinic, histaminic (H1), and 5-HT3, are involved in mediating the emetic reflex. Thus, all four of these receptors should be able

to be blocked by the perfect antiemetic drug. However, the majority of the effect of current antiemetic drugs is limited to one or two receptors.[16]

Many therapeutic strategies have been investigated to prevent nausea and vomiting. Acupuncture, electroacupuncture, transcutaneous electrical nerve stimulation, acupoint stimulation, and acupressure are examples of non-pharmacological techniques. Pharmacological methods include dopamine receptor antagonists (Phenothiazines, Butyrophenones and Benzamides), histamine receptor antagonists (dimenhydrinate), muscarinic receptor antagonists (Scopolamine), and serotonin receptor antagonists (ondansetron).[17]

Other medications such as Ephedrine, Propofol, Clonidine, and Dexamethasone are also tested to prevent nausea and vomiting. These medications have variable degrees of success in lowering PONV but comes with unfavourable side effects.[18]

Since 5-HT3 receptor antagonists do not have the significant side effects associated with antiemetic medications, their debut in the 1990s was regarded as a significant advancement in the prevention and treatment of PONV. There were no sedative effects, extrapyramidal reactions, negative effects on vital signs, negative laboratory test results, or medication interactions from these 5-HT3 receptor antagonists. These days, 5-HT3 receptor antagonists are frequently used to help patients having abdominal procedures under general anaesthesia to avoid experiencing nausea and vomiting after the procedure. The 5-HT3 antagonists Ondansetron, Granisetron, Dolasetron, Tropisetron, and Palonosetron are now on the market.[19,20]

Palonosetron was licenced by the FDA in 2008 for the prevention of PONV and is currently accessible for usage in India. The fundamental double nitrogen ring backbone of all 5-HT3 receptor antagonists makes up their molecular structure. This could be where the 5-HT3 receptor antagonists' therapeutic influence on serotonin occurs.

Ondansetron's half-life is 3.5 to 5.5 hours, while Palonosetron's half-life is 40 hours. This means that Palonosetron has a longer half-life of action and requires fewer doses than Ondansetron. The binding affinity of Palonosetron to 5- HT3 receptor is 100 times that of Ondansetron which makes it unlikely that Palonosetron will produce undesirable effects at the other receptor sites.

A rescue drug was employed, as it is advised that patients be given an antiemetic medication for rescue purposes that is entirely distinct from the antiemetic medication used for prophylaxis.[21] In our study the rescue drug Inj Metoclopromide 10mg iv was given in group P. However it was not needed in group O.

Additionally, we observed that in individuals who had received Ondansetron, the incidence of vomiting was lower than the incidence of nausea. This finding is consistent with other researches that found Ondansetron to have a stronger antiemetic impact than an antinauseous effect.[22] Palonosetron also exhibits a higher anti-nausea than anti-emetic impact.[23] In prior studies, there hasn't been much evidence to compare the effectiveness of Palonosetron with Ondansetron; instead, placebo has been employed primarily in clinical trials.[24] Our results, however, are not consistent with the few recent trials that have compared Palonosetron and Ondansetron where improved efficacy of Palonosetron was noted. This might be due to female predominance along with longer duration of surgery and anaesthesia exposure in the group of patients who received Palonosetron.

Moon et al,[25] found Palonosetron to be more efficacious than Ondansetron for high risk patients receiving fentanyl based patient controlled analgesia after thyroidectomy in the 2-24 h interval after surgery. A single pre-induction intravenous dosage of Palonosetron (75 mcg) was found to be more effective than an 8 mg dose of Ondansetron in a randomised controlled trial

involving day care surgery. This was evident in the number of individuals who experienced a PONV episode and the amount of rescue antiemetic that was needed.[26]

Withholding prophylactic antiemetic medication from all patients, especially those who are at high risk for PONV, would be inhumane and unethical, so the baseline incidence of PONV was not assessed by including a placebo group which serve as limitation to this study.

CONCLUSION

In summary, the current study's results unmistakably show that Ondansetron has a superior antiemetic and anti-nausea effect, a lower overall incidence of PONV, than Palonosetron in patients undergoing major surgery. As a result, patients can expect a smoother recovery period with less PONV.

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