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## RESEARCH ARTICLE

### A COMPARATIVE STUDY OF PALONOSETRON VERSUS ONDANSETRON FOR PREVENTION OF POST- OPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDER GOING ENT SURGERIES

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#### ABSTRACT

With the change in the emphasis from an inpatient to outpatient, hospital and office-based medical/surgical enhancement, there has been increased interest in the 'big little problem' of PONV, one of the main complaints in patients undergoing surgery under general anaesthesia. It is one of the most important factors that determine the length of hospital stay after ambulatory anaesthesia, can delay discharge and result in unplanned overnight hospital admission. This high incidence may justify the use of prophylactic antiemetic therapy and among them, the 5-HT<sub>3</sub> antagonists are very effective in preventing post-operative nausea and vomiting and do not produce any significant side effects. This randomized, open study compares the efficacy of Ondansetron and Palonosetron in the prevention of post-operative nausea and vomiting. The incidence of PONV was significantly less in the Palonosetron group (5.55%) as compared to the Ondansetron group (43.33%), with a lesser need for rescue antiemetic in the Palonosetron group (10% vs. 53%). Though the side effects of Ondansetron and Palonosetron are comparable, Palonosetron is one of the most effective anti-emetic drug used for prevention of PONV in ENT surgeries.

#### INTRODUCTION

Nausea and vomiting have been associated for many years with the use of general anaesthetics and subarachnoid block for surgical procedures. With the change in the emphasis from an inpatient to outpatient, hospital and office-based medical/surgical enhancement, there has been increased interest in the 'big little problem of PONV. There has been a general trend towards a decrease in the incidence and intensity of the problem because of the following

- Use of anaesthetic agents with less emetic effects..
- Improved pre-and post anaesthetic medication (e.g. analgesics)
- Refinement of operative as well as anaesthetic techniques and
- Identification of patient predictive factors.(risk factors of PONV)

However, in spite of these advances, nausea and vomiting still occur with unacceptable frequency in association with surgery and anaesthesia and the description of it as "the big little problem" encapsulates much of the general perception.

#### The various detrimental effects of PONV are

**Physical:** Retching and vomiting are fairly violent acts and may place considerable stress upon certain structures leading

to oesophageal tears, resulting in haemorrhage (Mallory – Weiss syndrome) and rupture of the oesophagus (Boerhaave syndrome), rib fracture, gastric herniation, muscular strain and fatigue. Vomiting may cause wound dehiscence, intraocular bleeding and bleeding from skin flaps in the upper body after plastic surgery. The major problem associated with vomiting in the postoperative period is aspiration of vomitus, respiratory obstruction and aspiration pneumonia.

**Metabolic:** The metabolic effects include anorexia, dehydration and alkalosis with hypokalemia.

**Psychological:** Nausea is a very aversive stimulus and if induced by operative experience, may cause life-long aversion to surgery (Gan, 2003). Over the years, numerous approaches have been used in the management of PONV. The traditional antiemetics include anticholinergics (scopolamine); dopamine receptor antagonists which include the phenothiazines (promethazine), benzamides (metoclopramide) and butyrophenones (droperidol) and benzodiazepines (midazolam and lorazepam). The non-traditional antiemetics include ephedrine, propofol and corticosteroids. The newest class of antiemetics used for prevention and treatment of PONV are serotonin (5-HT<sub>3</sub>) receptor antagonists—ondansetron, granisetron, tropisetron palonosetron and dolasetron. These antiemetics do not have adverse effects of older traditional antiemetics (Apfel, 2003).

The annual cost of treatment of PONV in the United States is thought to approach a billion dollars. Thus, costs can be lowered and drug side-effects prevented when given as prophylaxis, lowering the economic burden imposed due to complications and increased medical care resulting from PONV. Palonosetron is a "second generation" 5HT<sub>3</sub>-RA newly approved for the prevention of PONV since March 2008. Unlike the representatives of the first generation with competitive inhibition of the 5-HT<sub>3</sub> receptor, palonosetron seems to exhibit allosteric binding and positive cooperativity leading to effects persisting beyond the mere receptor binding time

**In the present study**, intravenous ondansetron and palonosetron are being compared in the prevention of postoperative nausea and vomiting in Otorhinolaryngeal (ENT) surgeries.

**Aim of the Study:** To compare the intravenous Palonosetron with intravenous Ondansetron for prevention of nausea and vomiting during postoperative period in patients undergoing ENT Surgeries under General Anaesthesia.

## MATERIALS AND METHODS

After obtaining approval from institutes ethical committee and informed consent, a randomized double blind clinical study was conducted on 60 ASA Grade I&II patients scheduled for ENT Surgeries under General Anaesthesia. They were randomly divided into two groups, Group I and Group II, each consisting of 30 patients.

**Group I** received 4 mg of Ondansetron I.V and

**Group II** received 1.5 mcg/kg of Palonosetron I.V, 30 minutes before the induction of anaesthesia.

### Selection of patients

#### Inclusion criteria

- Patients of ASA Grades I, and II
- Patients between the age group of 20 to 55 years who are to undergo ENT surgeries.

#### Exclusion criteria

- Patients belonging to ASA Grade IV and V.
- Patients below the age of 20 years.
- Patients above the age of 55 years.
- History of gastro-esophageal reflux.
- Patient scheduled to undergo emergency surgery.
- Patient scheduled to receive propofol during the maintenance phase of anaesthesia.
- Patient with vomiting from any organic cause.
- Any drug with a potential anti-emetic effect within 24 hours prior to the administration of anaesthesia.

### Methods

Preoperative visit was conducted on the previous day of surgery and a detailed history and present complaints were noted. General and systemic examinations of cardiovascular, respiratory and central nervous system were done.

Routine laboratory investigations like complete haemogram, routine urine, blood urea, serum creatinine, and blood sugar, ECG, serum electrolytes, bleeding time and clotting time were done. All patients received Tab. Alprazolam 0.5 mg and Tab. Ranitidine 150 mg on the previous night and 6 AM on the morning of surgery. Patients were instructed to remain nil orally after 10PM on the previous night of surgery.

General anaesthesia with controlled ventilation was used in all patients. Preoperative pulse rate, blood pressure and peripheral oxygen saturation were recorded in the operation theatre after connecting the following monitors:

- Continuous electrocardiogram
- NIBP
- Pulse oximeter
- Capnography

Peripheral venous access was established and intravenous fluid was started with 5 % dextrose normal saline.

**Pre-medication** with Inj. Midazolam 1 mg IV and Glycopyrrolate 0.2 mg IV were given.

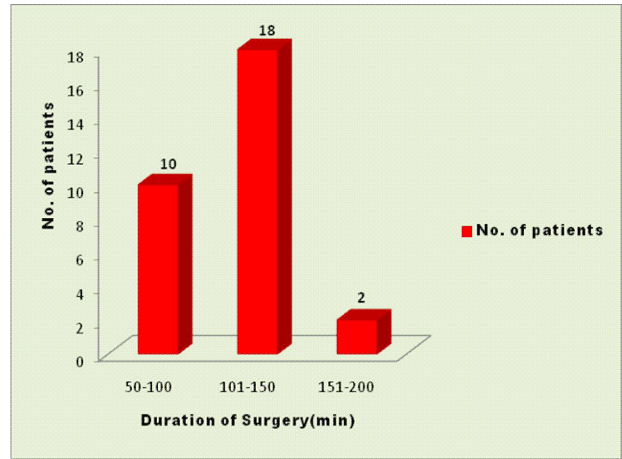
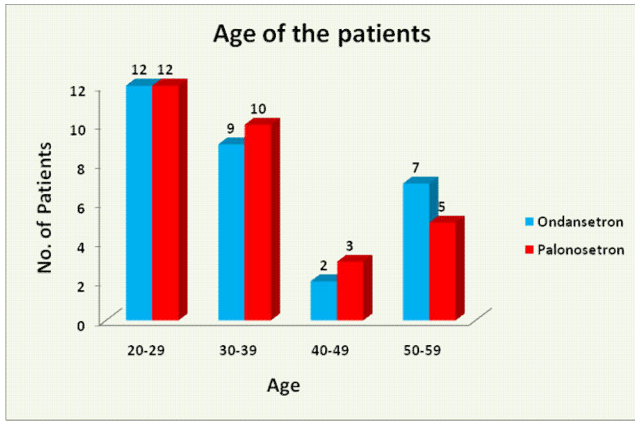
The study medications were administered intravenously just before induction as patients were preoxygenated for 5 minutes before induction of anaesthesia with Inj. Thiopentone sodium 4-5 mg/kg IV. Inj. Succinylcholine 1.5 –2.0mg/kg IV was given and Endotracheal intubation with appropriate size cuffed tube was done. Inj. Fentanyl 1-2 µg/kg IV was used for analgesia and Inj. Atracurium 0.5 mg/kg i.v or Inj. Vecuronium 0.08 mg/kg i.v were used to provide muscle relaxation during surgery depending on the type and duration of the procedure. Maintenance of anaesthesia was with nitrous oxide (50%) and oxygen (50%) with sevoflurane (0.2-0.8%) using controlled ventilation with Bain's circuit. Patients were monitored during anaesthesia using continuous ECG, heart rate, blood pressure, pulse oximetry and capnography. On completion of surgery, the residual paralysis was reversed with Inj. Neostigmine 0.05 mg/kg IV and glycopyrrolate 0.008 mg/kg IV. Patients were transported to the recovery room and later to the ward after confirming an adequate level of consciousness and intact reflexes. The incidences of PONV were recorded with in the first 72 hours after surgery at intervals of:

- 0-12 hours.
- 12-24 hours and
- 24-72 hours.

Episodes of PONV were identified by spontaneous complaints by the patients, by direct questioning and by Nausea Scale (Visual Analogue Scale) 0 -10. "Complete response" was defined as the absence of nausea, retching or vomiting and no need for rescue antiemetic during the 24-hour observation period. Rescue antiemetic was provided with Inj. Ondansetron 4mg i.v in the event of 1 or more episodes of vomiting depending on the observer's discretion. Observation and results were evaluated and compared between the two groups:

## RESULTS

The following were the observations and results of the variables among the Ondansetron group in comparison with the Palonosetron group:



Mean age of patients Ondansetron – 36.6±11.57

Mean age of patients Palonosetron – 35.28±11.68

Sex distribution in Ondansetron male : female :: 17:13

Sex distribution in Palonosetron male : female :: 14:16

Mean weight of patients Ondansetron – 60.13±6.23

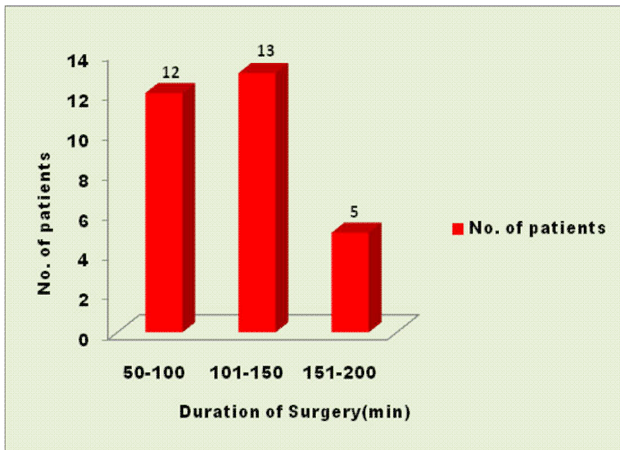
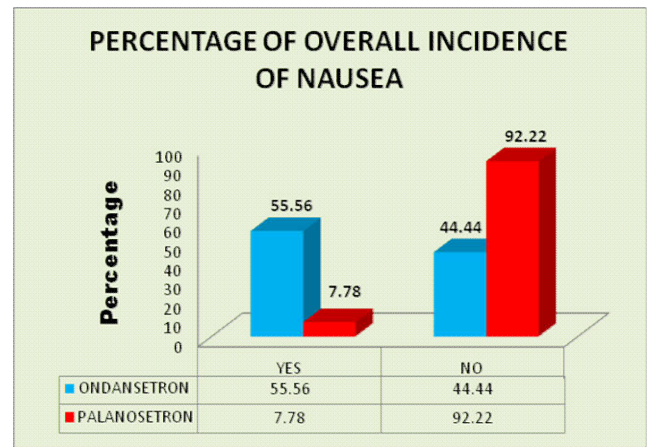
Mean weight of patients Palonosetron – 58.97±7.46

It is observed that the variations in the Age Group, Sex Distribution and Weight of the patients among the Ondansetron group compared with the Palonosetron group was significantly less.

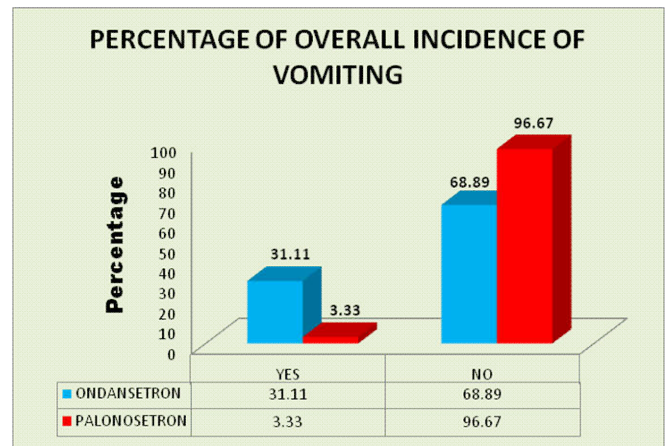
**Duration of the surgery (ondansetron)**

Duration ( mins )	No. of patients
50 – 100	12
101 – 150	13
151 - 200	05

**Overall incidence of Nausea**



**Overall incidence of Vomiting**



**Table 6. Duration of the surgery ( palonosetron)**

Duration ( mins )	No. of patients
50 – 100	10
101 – 150	18
151 - 200	02

The duration of Surgery is prolonged (>60 minutes) in both the study groups. Hence this prolonged duration of surgery is considered as a risk factor for PONV among these groups of patients. In all the post-operative duration of 72 hours (comprising 3 periods), the incidence of nausea was more in the Ondansetron group as compared to the Palonosetron group. incidence of vomiting was significantly less with Palonosetron group as compared with Ondansetron group in all the 3 periods of 72 hours post operative duration.

Though there was no statistical significance in the incidence of head ache, there was a moderate incidence of 57 % and 40% among the Ondansetron and Palonosetron groups respectively in the post operative period and this was caused by the prolonged duration, involvement of the vestibular system and parasympathetic nerve supply to the inner ear. There was no statistically significant difference in the incidence of the other side effects such as dizziness, abdominal discomfort and rash. From the above values the overall incidence of nausea is 55.56% in Ondansetron and 7.78% in Palonosetron group while the overall incidence of vomiting is 31.11% in Ondansetron and 3.33% in Palonosetron group. Thus, the risk of getting nausea and vomiting is highest in Ondansetron and least in Palonosetron group.

Only 10 % of patients in the Palonosetron group needed rescue antiemetics, where as nearly 53% in the Ondansetron group required rescue drug.

## DISCUSSION

PONV is one of the main complaints in patients undergoing surgery under general anaesthesia and the incidence of its occurrence is 20-40%. It is one of the most important factors that determine the length of hospital stay after ambulatory anaesthesia. This can delay discharge and result in unplanned overnight hospital admission. In fact, its contribution to patient dissatisfaction is such that over 70% of patients have considered avoidance of PONV to be very important. This high incidence of PONV after general anaesthesia may justify the use of prophylactic antiemetic therapy. Various factors can affect PONV, such as age, gender, obesity, history of motion sickness and / or PONV, use of opioids, anaesthetic technique, duration and type of the surgical procedure and postoperative pain. Numerous drugs have been used in the past in the prevention of post – operative nausea and vomiting, but they also have been associated with undesirable side effects. The 5-HT<sub>3</sub> antagonists are very effective in preventing post-operative nausea and vomiting and do not produce any significant side effects. This study compares the efficacy of Ondansetron and Palonosetron in the prevention of post – operative nausea and vomiting. In the present study, majority of these factors (age, gender, weight, duration and type of the procedure) were not statistically significant between both the groups. The anaesthetic technique was standardized (general anaesthesia with controlled ventilation) in all patients. The incidence of PONV was significantly less in the palonosetron group (5.55%) as compared to the ondansetron group (43.33%), with a lesser need for rescue antiemetic in the palonosetron group (10% vs. 53%). Both the study groups did not have significant adverse effects reflecting that both the drugs were well-tolerated.

## Conclusion

PONV is one of the most distressing side-effects of anaesthesia and surgery with a high incidence following general anaesthesia. The quest for more effective antiemetic drugs without the potential for sedative or extrapyramidal side-effects has led to the development of a relatively new class of drugs, 5-HT<sub>3</sub> antagonists of which ondansetron is a prototype. The need for drugs with improved performance within this group arose on account of relatively less potency and shorter duration of action, besides detectable binding to other 5-HT receptors by ondansetron. Palonosetron is a potent and highly selective 5-HT<sub>3</sub> receptor antagonist that has little or no affinity for other 5-HT receptors. In our study, we have compared the efficacy of ondansetron 4 mg i.v and Palonosetron 1.5mcg/kg i.v given prophylactically just before induction of anaesthesia in adult patients undergoing elective surgeries under general anaesthesia.

Palonosetron is superior to the established first generation 5-HT<sub>3</sub>-Receptor Antagonists in respect of pharmacokinetic data such as a high receptor binding affinity (pK<sub>i</sub> 10.45) and a prolonged mean elimination half life (40 hours) after intravenous administration. In clinical trials Palonosetron 0.075 mg is statistically superior to Ondansetron in preventing PONV. Efficacy in the delayed period of 24–72 hours

postoperatively is as overwhelming as expected. In conclusion, we have found that Palonosetron at a dose of 1.5mcg/Kg IV is safe and well-tolerated and proved more effective than Ondansetron 4 mg IV in the prevention of PONV. Though the side effects of Ondansetron and Palonosetron are comparable, till the further newer and better antiemetic drugs to be clinically evaluated, Palonosetron is one of the most effective anti-emetic drug used for prevention of PONV in ENT surgeries.

**Conflict of Interest statement:** Nil

**Funding statement:** Nil

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