Research Article

A comparative study of prophylactic ondansetron versus palonosetron for post operative nausea and vomiting in middle ear surgeries

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Abstract

Objectives: Postoperative nausea and vomiting (PONV) is a common complication in patients undergone middle ear surgeries under general anaesthesia. The purpose of this study was to compare antiemetic efficacy of prophylactic palonosetron in comparison with ondansetron, administered intravenously in patients undergoing middle ear surgeries under general anaesthesia.

Methods: In this prospective, randomized, clinically controlled study 60 ASA grade-I & II patients of either sex, aged between 18 to 50 years, scheduled for middle ear surgery under general anaesthesia were randomly allocated to one of the two groups, group O (n=30), received Inj. ondansetron 8mg I.V., and group P (n=30), received Inj. palonosetron 0.075mg I.V. before induction of anaesthesia. Postoperatively incidences of nausea, vomiting, complete response and need for rescue antiemetics over first 24hrs after surgery were evaluated.

Results: The overall incidence of nausea, vomiting once and vomiting more than once, in first 24hrs was higher in ondansetron group than in palonosetron group i.e. 56.66%, 20%, 3.33% and 50%, 3.33%, 0% respectively, and significant statistically (p<0.05). Only 40% patients in group O while 73.3% in group P showed complete response (p=0.009). Number of patients requiring rescue antiemetic were more in group O than group P (p=0.044). Haemodynamically no any major changes were observed in either group.

Conclusion: Our study concludes that prophylactic palonosetron 0.075mg IV is more effective than ondansetron 8mg IV for prevention of post operative nausea and vomiting in patients undergoing middle ear surgeries under general anaesthesia.

Keywords: PONV; General anaesthesia; Middle ear surgeries; Ondansetron; Palanosetron

1. Introduction

Post operative nausea and vomiting (PONV) is a common and distressing complication occurring after middle ear surgeries. Nausea occurs in approximately 20% of patients in the recovery room and in 50% thereafter, with vomiting in 5% and 25% respectively. An incidence of up to 80% has been reported in literature in patients undergoing middle ear surgery under general anaesthesia.

During the past decade, there has been a general trend towards a decrease in the incidence and intensity of the problem because of the use of less emetic anaesthetic agents, improved pre and post anaesthetic medication, refinement of operative technique, and identification of patient predictive factors. 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 consequences of PONV are physical, surgical and anaesthetic complications for patients, as well as financial implications for the hospitals or institutions. Physical consequences include sweating, tachycardia, increased chances of oesophageal tear, rupture of esophagus, wound dehiscence and electrolyte imbalance, dehydration. Surgical consequences include disruption of vascular anastomoses, surgical site bleed and increased intracranial pressure. The anaesthetic consequences are aspiration pneumonitis and discomfort in recovery. In addition it also decreases the confidence level in future surgery and anaesthesia.

Risk factors related to patient characteristics, anaesthesia, and surgery have been determined. Patient-related risk factors include female sex, history of PONV or motion sickness, and non-smoking status. Anaesthesia-related risk factors include the intraoperative use of volatile anesthetics, the intraoperative and postoperative use of opioids, and the use of nitrous oxide. Surgical risk factors can involve the type and duration of surgery.

Various drugs have been used to prevent PONV namely anti-histamines, phenothiazine derivatives, anticholinergic, dopamine receptor antagonist and 5-HT3 antagonists. The 5-HT3 receptor antagonists are now a first line option because of effectiveness, more safety and favourable side-effects profile as they lack the sedative, dysphoric and extra-pyramidal side effects of other drugs.

Ondansetron was the first 5-HT3 receptor antagonist and its antiemetic efficacy is well established. It has a relatively short half life of 3-5hours. Palonosetron is the most recently introduced member of this class of drugs in India. It has unique chemical structure, the interaction pattern with the 5-HT3 receptor is different from earlier 5-HT3 receptor antagonists with additional allosteric site binding property.

Hence our study was conducted with the intention of assessing whether palonosetron conferred any advantages over ondansetron in terms of duration of prophylaxis and its effect on the incidence and severity of PONV in patients when used as the sole antiemetic agent. The endpoints were evaluated by the following parameters: episodes of nausea and emesis, rate of complete response to the drug, and need for rescue antiemetic.

2. Material and Methods

This study was conducted in Dhiraj general hospital in Department of Anaesthesiology. After obtaining approval of the institutional ethics committee and written informed consent, we studied 60 patients of Grade-I and Grade-II of American Society of Anesthesiologist’s (ASA)
classification, of either sex in the age group of 18 to 50 years, who were admitted for middle ear surgeries under general anaesthesia. Exclusion criteria: patient refusal, history of allergy to any of the two drugs, pregnant and lactating mothers, patients who were having vomiting, retching and nausea or who have taken any antiemetic drug within 24 hours before the anaesthetic procedure, history of acid peptic disease or hepatic dysfunction, history of motion sickness.

Pre-Operative Management: A thorough pre-anæsthetic evaluation was done. History of present illness, past medical or surgical history, allergic, drug sensitivity, drug intake, anaesthesia experience, smoking, alcohol consumption and other habits history were taken. Vital signs were recorded. General examination, systematic examination and airway assessment were done. Routine investigations were done. All selected patients were given tablet Alprazolam 0.25mg on night prior to the surgery and were kept nil by mouth for 8 hrs.

In the operation theatre an IV line was secured and multipara monitor was attached. Patients were allocated randomly to two equal groups, Group P (n =30) received inj. palonosetron 0.075mg i.v., Group O (n =30) received inj. Ondansetron 8mg i.v. A standard anaesthesia technique was used in all the patients. Pre-medication inj. glycopyrrolate 0.2mg; inj. tramadol 1mg/kg, inj. midazolam 0.01mg/kg IV given. Patients were preoxygenated for 3 minutes with 100% oxygen and induced with injection thiopentone sodium 2.5% (4-7mg/kg) IV, injection succinylcholine 2mg/kg to facilitate laryngoscopy and intubation. Endotracheal intubation was done with appropriate sized cuffed endotracheal tube, under direct laryngoscopy after complete relaxation of jaw. After successful intubation, bilateral air entry was checked and the tube fixed. Then the patients were connected to mechanical ventilator. Anaesthesia was maintained with N₂O 50% + O₂ 50%, isoflurane (0.2 – 1%) and inj. vecuronium 0.08mg/kg was used as a muscle relaxant as loading dose. If required the dose of vecuronium was increased. Intravenous fluid was given according to body weight and intra operative need. At the end of surgery, once the patients had attempts of spontaneous breathing they were reversed with injection neostigmine (0.05mg/kg) glycopyrrolate (0.008mg/kg). Oral suctioning was done and patients were extubated when fully awake and adequate muscle power and reflexes were gained clinically. Duration of general anaesthesia and duration of surgery were noted. All patients were shifted to recovery room and were monitored for pulse rate, blood pressure, arterial oxygen saturation for first 24hrs.

Any episode of nausea or vomiting – monitoring for PONV was done for first 24 hours postoperatively at intervals of 30 mins till first 4 hrs, then at 1 hr interval till next 8 hrs and then at 2 hrs interval till 24 hours. Incidence of the emetic episodes were compared in two groups using PONV score. PONV Score: 0 = No nausea and vomiting, 1 = Nausea only, 2 = Vomiting once, 3 = Vomiting more than once. Patients with PONV score 2 or greater were given injection metoclopramide 10mg intravenous slowly as rescue treatment. Frequency of rescue medication given were noted.

Complete response to antiemetic prophylaxis defined as the absence of nausea and vomiting and no need for rescue antiemetic during the observation period of 24 hrs. Side effects if any like Headache, constipation, diarrhoea, fatigue, abdominal pain, insomnia, dizziness were recorded.

2.1 Statistical Methods

Observation and results were evaluated and compared between the two groups using Graph Pad Prism® computer software version 6.04. Numerical variables were presented as mean & standard deviation (SD) while categorical variables were presented as percent. As regard numerical variables; unpaired student t test was done. And for categorical variables; chi-square test was done. p value < 0.05 was considered significant.

3. Results

There were no statistically significant differences between the two groups in terms of demographic characteristics namely age, sex, weight, ASA status, duration of anaesthesia and surgery, as shown in Table 1.

The hemodynamic data were noted both during the intraoperative and postoperative periods at regular intervals, no any major changes were observed in either group. (p>0.05)

The overall incidence of nausea (PONV Score 1) in 24 hrs was more in ondansetron group than palonosetron, this difference was statistically significant (p=0.037). [Table 2]

The incidence of nausea once in 24 hrs (PONV Score 2) was observed in only 1 patient in palonosetron group and in 6 patients in ondansetron group, (p=0.044), statistically significant. [Table 2]

The incidence of post operative vomiting more than once in 24 hrs (PONV Score 3) was 3.33% in patients among group O and 0% in patients of group P, not statistically significant. [p=0.313], [Table 2]

Only 40% in group O while 73.3% in group P showed complete response (no nausea vomiting) to the study drug (p=0.009), statistically significant. [Table 3]

Requirement of rescue antiemetic was in 6 (20%) patients in group O and in only 1 (3.3%) patient in group P (p=0.044), statistically significant. [Table 4]

The adverse effects were same and insignificant in both the groups.

<table>
<thead>
<tr>
<th>Table 1: Demographical profile of the patients of both the groups</th>
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<tr>
<td><strong>Groups</strong></td>
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<tr>
<td><strong>Age in years</strong>&lt;br&gt;(mean ± SD)</td>
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<tr>
<td><strong>Sex (male/female)</strong></td>
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<tr>
<td><strong>Weight in Kg</strong>&lt;br&gt;(mean ± SD)</td>
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<tr>
<td><strong>ASA grade I/I</strong></td>
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<tr>
<td><strong>Duration of surgery in mins</strong>&lt;br&gt;(mean ± SD)</td>
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</tbody>
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No statistically significant differences between the two groups in terms of demographic characteristics namely age, sex, weight, ASA status, duration of surgery (p > 0.05).

<table>
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<tr>
<th>Table 2: Comparison of incidences of postoperative nausea, vomiting once and more than once in 24 hrs in study groups</th>
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<tr>
<td><strong>Event</strong></td>
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<tr>
<td><strong>Incidence of Nausea in 24 hrs</strong>&lt;br&gt;(PONV Score 1)</td>
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<tr>
<td><strong>Incidence of Vomiting once in 24 hrs</strong>&lt;br&gt;(PONV Score 2)</td>
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<tr>
<td><strong>Incidence of Vomiting more than once in 24 hrs</strong>&lt;br&gt;(PONV Score 3)</td>
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Higher incidence of nausea as well as vomiting was observed in patients of Group Ondansetron than Palonosetron.

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Post operative nausea and vomiting (PONV) is very common sequelae of general anaesthesia and is very distressing for the patient. It is leading cause of delayed discharge, of unanticipated hospital admission after ambulatory surgical procedure, pulmonary aspiration, wound dehiscence, and dehydration. 5-HT₃ receptor antagonists in 1990s was heralded as the major advance in prophylaxis of PONV as they lack the major adverse effects which were observed commonly with traditionally used antiemetic drugs, and are routinely used now a days to prevent post operative nausea and vomiting. Currently available 5-HT₃ antagonists include ondansetron, granisetron, dolasetron, topisetron and palonosetron. FDA has approved the use of palonosetron for prophylaxis of PONV in 2008 and is now available in India.

Palonosetron is a second-generation 5-HT₃ antagonist with unique pharmacodynamic characteristics. Palonosetron is an allosteric 5-HT₃ receptor antagonist, allosteric binding creates a conformational change in the serotonin receptor so that serotonin binding is indirectly inhibited. Consequently, palonosetron has higher affinity with 5-HT₃ receptors, which ultimately leads to greater potency and longer duration of action in comparison with standard 5-HT₃ antagonists.

Present study was done to compare the efficacy of palonosetron 0.075mg and ondansetron 8mg for prevention of PONV administered 5min prior to the induction of anaesthesia in the patients undergoing middle ear surgeries under general anaesthesia.

In Pavaneti el al dosage ranging study of ondansetron they concluded that single dose ondansetron 8mg is more effective than ondansetron 4mg in the prevention of PONV. In our study, we also gave inj. ondansetron 8mg intravenously before induction of anaesthesia in group O.

In study by Kovac AL et al (2008) palonosetron in dose of 0.025mg, 0.05mg and 0.075mg were compared. The 0.075mg dose was statistically superior to placebo for all end points during the first 24 hrs, including complete remission, emesis, nausea rates and reduction in nausea severity. Also palonosetron 0.075mg was associated with significantly longer median time to first emesis and a significantly longer time to treatment failure. FDA has also approved 0.075mg as the minimum effective dose of palonosetron for PONV prophylaxis. Therefore we decided to use palonosetron 0.075mg for this study.

The demographic profile and mean duration of surgery were comparable with no statistical difference between two groups (p>0.05), and provided us the uniform platform to evenly compare the results observed. The duration of anaesthesia and surgery has a bearing on post operative nausea and vomiting as prolonged duration of surgery will increase the incidence of post operative nausea and vomiting, hence increasing the requirement of antiemetic.

No major haemodynamic changes were observed in either group. Our observations are in accordance with previous studies.

The overall incidence of post operative nausea (PONV Score 1) in 24hrs was 56.66% in patients among group O and 30% in patients of group P. The incidence is higher in group O and the difference between two groups was statistically significant (p=0.037) [Table 1].

There was a statistically significant difference in the overall incidence of vomiting once (PONV Score 2) in 24hrs, it was 20% in ondansetron group and 3.33% in palonosetron group (p=0.044). [Table 2]

And the overall incidence of vomiting more than once (PONV Score 3) in 24hrs was 3.3% in ondansetron group and 0% in palonosetron group. Though the result was statistically insignificant (p=0.313) but is more in ondansetron group. [Table 2]

Comparable to our result similar result was found in study by Moon YE Baisakhi Laha and Sarbani Swaika. All these studies confirm our finding.

Patients showing complete response (patients who had no nausea and vomiting and no need for rescue antiemetic during 24 hrs observation period) were significantly higher in group P i.e 73.3% while 40% in group O (p=0.009) [Table 3]. This is comparable with previous studies done by Nupur Chakravarty and Shadangi BK.

It has been recommended that in cases of breakthrough PONV, repeat antiemetic should be of a different class than the one used for prophylaxis. This was why metoclopramide was used as a rescue analgesic. Requirement of rescue antiemetic was 20% in group O and 3.3% in group P, which was also statistically significant (p=0.044) [Table 4]. Nupur Chakravarty study support our finding.

Both palonosetron and ondansetron are known to have non serious adverse effects like short duration headache, constipation, dizziness and prolongation of QTc interval. 2 (6.6%) patients in both groups complained of headache, and 1 (3.3%) patient in each group complained of dizziness. This difference was not significant statistically. (p=1.00). Apart from this no side effects were observed in patients of both the groups in our study.

We conclude palonosetron 0.075mg IV is more effective than ondansetron 8mg IV to prevent post operative nausea and vomiting in patients undergoing middle ear surgeries under general anaesthesia as the overall incidence of post operative nausea, vomiting, number of patients with incomplete response and requirement of rescue antiemetic were less in palonosetron group as compared to ondansetron.

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