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Palonosetron – A Promising New Prophylactic for PONV

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Abstract

Aim and Objective: The aim of the study was to evaluate the efficacy of palonosetron 0.075 mg for prevention of postoperative nausea and vomiting (PONV) in patients undergoing middle ear surgeries in comparison with ondansetron.
Methods: In this prospective observational study, 70 healthy patients who were undergoing elective middle ear surgeries were divided into 2 groups: Group P (palonosetron 0.075 mg i.v., n = 35) and group C (ondansetron 8 mg i.v., n = 35). The drugs were given 5 minutes before induction of anaesthesia. The incidence of nausea, vomiting, retching, severity of nausea, use of recue antiemetic and incidence of complete response were evaluated.
Results: The incidence of nausea, vomiting and severity of nausea was lower in palonosetron group as compared to ondansetron group but this difference was not statistically different. The incidence of use of rescue antiemetic (5.71% vs 23.53%) was significantly lower in palonosetron group. The incidence of complete response was higher in palonosetron group (88.87% vs 68.57%) but the difference was not statistically significant.
Conclusion: The prophylactic intravenous administration of single dose of palonosetron 0.075 mg is not more effective in controlling postoperative nausea and vomiting as compared to ondansetron 8 mg in middle ear surgery.
Keywords: PONV, palonosetron, ondansetron, antiemetic, nausea, vomiting.

1. Introduction

Postoperative nausea and vomiting is most common and distressing complication after surgery especially after middle ear surgery with high incidence rate (upto 80%) thereby increasing hospital expenses. In middle ear surgeries one of the causes of PONV is physical stimulus caused by otologist drilling and irrigating bone adjacent to the inner ear. Also vestibular stimulus increases PONV caused by opioids [1]. Postoperative nausea and vomiting not only decreases patient satisfaction but also relates to rare but severe adverse consequences, including sweating, tachycardia, dehydration, wound dehiscence, aspiration pnuemonitis, surgical site bleeding, etc. [2].

Postoperative Nausea and Vomiting (PONV) continues to be the most frequent complication of anesthesia and surgery in spite of availability of so many antiemetic drugs and regimens for prevention. Many class of drugs have been tried till now like phenothiazines, antihistaminics, dopaminergic receptor antagonist, 5 HT3 receptor antagonist, etc. [2]. The 5-hydroxytryptamine -3 receptor antagonists (5-HT3RAs) are the most popular pharmacologic class of antiemetics for PONV. The first generation 5-HT3RAs (ondansetron) have been shown to have similar efficacy and safety for PONV prophylaxis during the first 24 hr after surgery. Compared with the first-generation 5-HT3RAs, studies have shown that palonosetron has greater receptor binding affinity to 5-HT3R and a longer plasma half-life [3,4].

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

The study was approved by the IEC of Indira Gandhi Government Medical College, Nagpur (Ref.: IEC/366-70/14) before study commencement and registered with DGCI (ECR/485/Inst/MH/2013). After receiving written informed consent, 70 healthy patients with ASA physical status I-II, aged 18 – 50 years, who were undergoing elective middle ear surgeries, were enrolled in this prospective observational study. The study period was from Nov. 2013 to October 2015. Exclusion criteria were ASA III-IV, history of nausea, vomiting or retching within 24 hours prior to operation, pregnancy, obese patients, patients with history of any coronary artery disease or arrhymias, liver, respiratory, kidney and endocrine diseases, history of asthma, allergy or hypersensitivity to 5HT3 antagonists, patients on any psychiatric medications and patients with seizures or raised ICP.

A thorough preanaesthetic evaluation was conducted and all necessary investigations like CBC, KFT, blood sugars were done and wherever necessary others investigations like ECG, chest X-ray, USG, etc. were done. In operation theatre IV line was secured and multipara monitor was attached. All patients were premedicated with Raniditine 50 mg IV, Glycopyrrolate 4 mcg/kg IV, Dexmedetomidine 0.5 mcg/kg IV (over 10 minutes), Midazolam 0.03 mg/kg IV and fentany 1-2 mcg/kg IV. Then patients were administered to one of the 2 drug: Palonosetron 0.075 mg IV (Group P) or Ondansetron 8 mg IV (Group C) over 10 seconds 5 minutes before induction. Later patients were preoxygenated with 100% oxygen for 3 – 5 minutes. Anaesthesia was induced with thiopentone 4 – 5 mg/kg IV. Tracheal intubation was facilitated with suxamethonium 1.5 mg/kg IV. Anaesthesia was maintained with oxygen (40%), nitrous oxide (60%) and sevoflurane (1-3%). Muscle relaxation was maintained with intermittent boluses of vecuronium. Ventilation was controlled and adjusted to maintain end tidal partial pressure of CO2 between 30-40 mmHg. Intraoperatively, pulse rate, mean arterial pressure, ECG, SPO2 and etCO2 were monitored throughout. At the end of surgery neuromuscular block was reversed with glycopyrrolate 8 mcg/kg IV and neostigmine 0.05 mg/kg IV and subsequently patients were extubated. Postoperative pain relief was provided by Diclofenac 75 mg IM or paracetmol 1 gm IV. No opioids were administered postoperatively for pain relief.

After surgery patients were monitored for 2 hours in recovery room. The primary aim of our study was to measure the incidence of nausea, vomiting and retching. Secondary aim was to measure incidence of severity of nausea, use of rescue anti-emetics and complete response. They were evaluated at following intervals 0-2, 2-6, 6-12, 12-24, 24-48 and 48-72 hours. The severity of nausea was assessed using verbal rating scale (0 – no nausea, 1 – mild nausea, 2 – moderate nausea and 3 – severe nausea). Nausea was defined as sensation of unease or discomfort in stomach with an urge to vomit, whereas retching was defined as labored, spasmodic, rhythmic contraction of the respiratory muscles without expulsion of gastric contents from mouth and vomiting was defined as the forceful expulsion of gastric contents from mouth & nose. Metoclopramide 10 mg IV was given as rescue anti-emetic for the patients with severe nausea and for patients who had an episode of vomiting. A complete response was defined as no postoperative nausea and vomiting and no need of rescue anti-emetics. Any incidences of adverse effects like headache, dizziness, constipation, etc. were noted.

Sample size was calculated by using statistical software STATA – 13 (α error = 5% and $1 - \beta = 80\%$) and it came to be 32 in each group but for our convenience we took it as 35 in each group (2). Numerical variables were compared between groups by Student's t - test. And categorical variables were compared using Chi square and Fisher's exact test. P value < 0.05 was considered as significant.

3. Results

As seen in Table 1, there was no significant difference between 2 groups in terms of patient's demography and operative data. The hemodynamic data were also comparable during intraoperative and postoperative period.

Table 1: Patient characteristics and operative data

Parameter	Group P (Palonosetron)	Group C (Ondansetron)
No. of patients	35	35
Age (years)	28.22 ± 10.19	29.79 ± 10.9
Male: Female	18 : 17	15 : 20
ASA status (I : II)	32 : 3	32 : 3
Duration of surgery (mins)	166 ± 12.88	169.71 ± 13.39

Table 2: Incidence of Postoperative nausea and vomiting (PONV), incidence according to severity of nausea, need of rescue antiemetics, incidence of complete response and incidence of adverse effects

Events in postoperative period	Palonosetron group No. of patients (%)	Ondansetron group No. of patients (%)
0 – 2 hours		
Nausea	2 (5.71%)	5 (14.29%)
Vomiting	1 (2.86%)	4 (11.43%)
Nausea + Vomiting	1 (2.86%)	3 (8.57%)
2 – 6 hours		
Nausea	2 (5.71%)	5 (14.29%)
Vomiting	0	1 (2.86%)
Nausea + Vomiting	0	0
6 – 12 hours		
Nausea	0	3 (8.57%)
Vomiting	1 (2.86%)	1 (2.86%)
Nausea + Vomiting	0	1 (2.86%)
Severity of nausea		
Mild nausea	1 (2.86%)	1 (2.86%)
Moderate nausea	1 (2.86%)	0
Severe nausea	2 (5.71%)	8 (22.86%)
Rescue antiemetics	2 (5.71%)*	10 (23.53%)*
Complete response	31 (88.87%)	24 (68.57%)
Adverse effects		
Dizziness	0	1 (2.86%)
Headache	1 (2.86%)	0
Constipation	0	0

Data represented as n (%) of patients. *$p < 0.05$ for palonosetron group compared to ondansetron group; Chi square test and Fisher's exact test.

As seen in Table – 2, the incidences of nausea (including mild, moderate & severe nausea), incidence of vomiting and incidence of nausea + vomiting were lower in palonosetron group but were not statistically significant. No patients had nausea or vomiting during 12 – 72 hours postoperatively. Incidence of use of rescue antiemetics was significantly lower in palonosetron group (5.71%) as compared to ondansetron group (23.53%). Incidence of complete response was higher in palonosetron group but was not statistically significant. Adverse effects were infrequent in both the groups.

4. Discussion

Despite continuing advances in anaesthetic technique and surgical skills, PONV still remains one of the major complications amongst patient during postoperative period. Middle ear surgery is associated with high incidence of PONV. Risk factors for nausea and vomiting include female gender, non smoking status, history of motion sickness, postoperative opioids, types of surgeries like laparoscopic surgery, middle ear surgery, ophthalmic surgery, duration of surgery, etc. [3]. In this present study all these risk factors were well balanced in between both the groups.

5-HT3 receptor antagonist group of drugs have action in both central and periphery resulting in blocking the trigger of the vomiting reflex by emetogenic stimuli [5]. Ondansetron and palonosetron are both 5-HT3 receptor antagonists, later being latest to this group. Palonosetron has unique chemical structure, greater binding affinity and considerable long half life [6].

Palonosetron 0.075 mg was chosen in the study based on previous study result of Candiotti et al [7] in 2008 showed that the minimum effective dose of palonosetron is 0.075 mg IV and this has been also approved by FDA. They found that palonosetron 0.075 mg significantly reduced the incidence of PONV in first 24 hour after anaesthesia as compared to placebo. Ondansetron dose was selected as 8 mg in our study on the basis of study conducted by Paventi et al, [8] (2001) in which they concluded that single dose of ondansetron 8 mg IV is more effective than ondansetron 4 mg IV for prevention of PONV.

In our study, incidence of nausea during 0 -2, 2 – 6, and 6 – 12 hour time interval was less in the palonosetron group than ondansetron group but this difference was not statistically significant. Similar results were observed in his study by Ahmed and his colleagues (2014) [9] where they studied the incidence of PONV in patients who were given either palonosetron or ondansetron for prophylaxis of postoperative nausea and vomiting in middle ear surgery. In this study the incidence of vomiting was also lower in palonosetron group but was not significantly different between the two groups. Results similar to this were again observed by Ahmed et al [9] in his comparative trial of palonosetron vs ondansetron in middle ear surgery.

In our study, we studied the incidence of nausea and vomiting together. We observed that the incidence was low in palonosetron group as compared to ondansetron group but it was not statistically different. Retching was not observed in our study in both the groups. We also compared incidence of nausea according to its severity and found that incidence was lower in palonosetron group but it was not statistically different in ondansetron group.

In present study, nausea, vomiting and the two together as a complication as well as retching were not seen beyond 12 hours of postoperative period. This was true for the groups, palonosetron as well as ondansetron. This may be partly attributed to the disappearing/ diminishing effects of residual anaesthetic agents and adjuvant as the time passes. Also an important additional factor was avoidance of narcotics agents for providing pain relief in the postoperative period in all of our patients.

Rescue antiemetic used in our study was Inj. Metoclopramide 10 mg i.v. Rescue antiemetic was provided

to the patients whenever patients complained of severe nausea or vomiting or in mild/ moderate nausea if patient demanded. In our study 2 (5.71%) patients in palonosetron group and 10 (23.53%) patients in ondansetron group had to be given rescue antiemetic and this difference was statistically significant. This observation of ours was also true in the study conducted by Singh et al (2014) [2] where they compared palonosetron and ondansetron for prophylaxis of postoperative nausea and vomiting in patients undergoing middle ear surgery.

Complete response was defined as patients having no nausea, no vomiting and no retching in postoperative period. 31 (88.87%) patients in palonosetron group and 24 (68.57%) patients in ondansetron group had complete response. This difference was not statistically significant. Similar results were obtained by Laha et al (2013) [5] where they conducted comparative trial in patients undergoing laparoscopic cholecystectomy. They compared palonosetron with ondansetron in this study for prophylaxis postoperative nausea and vomiting.

One patient in palonosetron group complained of headache and one patient in ondansetron group complained of dizziness. Their incidence was very low in both the groups. Similar results were observed by Ahmed et al [9]. We did not encounter any other adverse effects like constipation, pruritis, allergic reaction, arrhythmias, etc. The adverse effects were minimal and did not require any intervention.

There were several limitations to our study: the efficacies of palonosetron and ondansetron were compared based on the known optimal doses without knowledge of equipotent doses; the baseline incidence of PONV was not evaluated by the inclusion of a placebo group because it would unethical that we do not administer prophylactic antiemetic drugs in patients who are at high risk for postoperative nausea and vomiting.

Thus from our observation and analyzed data we have come to the conclusion that prophylactic intravenous administration of single dose of palonosetron 0.075 mg is not more effective in controlling postoperative nausea and vomiting as compared to ondansetron 8 mg in patients undergoing middle ear surgery. The incidence of use of rescue antiemetic was also significantly less in patients using palonosetron for prophylaxis of postoperative nausea and vomiting as compared to patients using ondansetron. Incidence of complete response was higher in palonosetron group than ondansetron group but this incidence was not significantly different between the two groups. The study also showed that incidence of adverse effects was infrequent in both the groups. Thus we can say that palonosetron can be used as an alternative to ondansetron for control of postoperative nausea and vomiting.

5. Conclusion

The present study concluded that the prophylactic intravenous administration of single dose of palonosetron 0.075 mg is not more effective in controlling postoperative nausea and vomiting as compared to ondansetron 8 mg in middle ear surgery.

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