Research Article

iMedPub Journals
www.imedpub.com

Journal of Anaesthesiology and Critical Care

2018
Vol.1 No.2:8

Intravenous Ondansetron versus Palonosetron for Prevention of Post-Operative Nausea-Vomiting in Middle Ear Surgery under General Anaesthesia

Pratibha Jain Shah, Rashmi Thakur and Hemendra Kumar Sahu*

Pt. Jawahar Lal Nehru Memorial Medical College, Raipur, Chhattisgarh, India

***Corresponding author:**
Hemendra Kumar Sahu

hsahu122@gmail.com

Pt. Jawahar Lal Nehru Memorial Medical College, Raipur, Chhattisgarh, India.

Tel: +919589911103

Citation: Shah PJ, Thakur R, Sahu HK (2018) Intravenous Ondansetron versus Palonosetron for Prevention of Post-Operative Nausea-Vomiting in Middle Ear Surgery under General Anaesthesia. J Anaesthesiol Crit Care Vol.1 No.2:8

Abstract

Introduction: Postoperative nausea and vomiting (PONV) is the most common (25-30%) unpleasant and exhausting complication that causes delayed recovery, prolonged hospital admission and increased treatment cost. The incidence of PONV is up to 80% in middle ear surgeries under general anesthesia. The aim of this study was to evaluate the efficacy of intravenous Ondansetron and Palonosetron in the prevention of PONV in middle ear surgeries under general anesthesia.

Method: Total 100 young patients who underwent middle ear surgery under general anesthesia who received *i.v.* either Ondansetron 8.0 mg or Palonosetron 0.075 mg before induction were taken and divided into two groups (n=40) Group O & Group P, respectively. Data of 80 patients were analysed Incidence of complete response to the drug, post-operative nausea, and vomiting, mean PONV score, use of rescue medication and adverse effects were assessed at the intervals of first 4 h, 4-12 h, 12-24 h and 24-72 h postoperatively. Intravenous metoclopramide was used as the rescue antiemetic.

Results: In initial 4 h, complete response to the drugs, incidences of nausea, vomiting, use of rescue medication and adverse events were found insignificant ($p>0.05$). These parameters were found higher in group O in later time intervals.

Conclusion: Ondansetron and Palonosetron both are equally effective in the prevention of PONV in initial period but Palonosetron has added effectiveness in the late postoperative period.

Keywords: Ondansetron; Palonosetron; General anaesthesia; Middle ear surgery; PONV

Received: April 11, 2018; **Accepted:** April 27, 2018; **Published:** May 09, 2018

Introduction

Postoperative nausea and vomiting (PONV) is the most common unpleasant complication that may occur after surgery. The incidence of PONV is estimated as 25% to 30% in patients undergoing surgeries that further increases up to 80% in middle ear surgeries. PONV can lead to physical complications like sweating, tachycardia, oesophageal rupture, wound dehiscence & electrolyte imbalance, surgical complications like disruption of vascular anastomosis, surgical site bleed and increased intracranial pressure and anaesthetic complications like aspiration pneumonitis and discomfort in recovery. There are various risk factors for PONV such as patient related (female, history of motion sickness and acid peptic disease and non-smoking status), anesthesia-related (use of volatile anaesthetics, opioids, Nitrous oxide) and surgery related (type and duration of surgery). So, there has been a constant quest for the agent which reduces PONV with minimal side effects [1].

Selective 5-hydroxytryptamine type 3 (5-HT3) receptor antagonists are first-line drugs for the prevention of PONV because of better efficacy with favourable side effects as

compared to previously used anti-emetics like butyrophenone, antihistaminic and dopamine receptor antagonist. Ondansetron, the first-generation serotonin antagonist is more effective and devoid of extrapyramidal symptoms or sedation. Palonosetron, the second-generation serotonin antagonist shows a unique mechanism of allosterically binding to its receptor, was initially approved for prophylaxis of chemotherapy-induced nausea and vomiting. It is more potent with persistent effects up to 40 h [2,3].

This study was conducted to assess the efficacy of intravenous Palonosetron and Ondansetron in terms of incidence and severity of PONV. The endpoints for evaluations were the rate of complete response to the drug, episodes of nausea and vomiting and need for rescue medication.

Materials and Method

This prospective observational study was conducted from January 2016 to July 2017 after approval from the Institutional Ethics Committee. Total 100 patients aged 18-50 years of ASA grade I-II, who underwent middle ear surgery under general anaesthesia and received either Ondansetron 8.0 mg or Palonosetron 0.075 mg intravenously at the time of induction were included in the study, out of which 80 patients were divided into two groups during data analysis into Group O (received *i.v.* Ondansetron 8.0 mg) and Group P (received *i.v.* Palonosetron 0.075 mg) with 40 patients in each group. Patients with the acid peptic disease, hepatic dysfunction, motion sickness, allergy, who used any antiemetic drug within 24 h before surgery, pregnant and lactating mothers, smokers, patients with prolonged QT interval syndrome and taking antiarrhythmic drugs treatment were excluded from the study.

After thorough pre-anaesthetic check-up and written informed consent, patients were shifted to operation theatre and baseline vitals (ECG, non-invasive blood pressure, heart rate and SpO_2) were recorded using Philips MP30 multipara monitor. Intravenous line was established and Ringer lactate was started. All the patients were premedicated with Ranitidine 50 mg, Glycopyrrolate 0.2 mg, Pentazocine 0.5 mg/kg and Midazolam 1.0 mg along with either Ondansetron 8.0 mg or Palonosetron 0.075 mg (diluted up to 4 ml with normal saline) intravenously 30 s prior to induction. After preoxygenation with 100% for 3 min induction of general anaesthesia was done using *i.v.* Thiopentone 5-7 mg/kg, Succinylcholine 1.5 mg/kg was injected to facilitate endotracheal intubation. Intubation was done with proper sized cuffed oral endotracheal tube (8.0-8.5 mm ID for adult male and 7.0-7.5 mm ID for adult female) and adequate depth of anaesthesia was maintained with N_2O:O_2 (2:1), Isoflurane (0.4-1.5%), *i.v.* Atracurium (0.25 mg/kg bolus followed by 0.1 mg/kg in incremental doses) along with controlled ventilation (tidal volume of 8.0 ml/kg, respiratory rate 12/min to maintain end-tidal carbon dioxide ($EtCO_2$) to 35-45 mm Hg). Heart rate and mean arterial blood pressure were maintained within 20% of baseline parameters. At the end of surgery, the residual effect of neuromuscular blocking agent was reversed with *i.v.* Neostigmine 0.05 mg/kg, *i.v.* Glycopyrrolate 0.01 mg/kg and patient extubated following thorough oral suction in fully awake condition. Intraoperatively all the hemodynamic parameters (PR, SBP, DBP, MAP and SpO_2) were monitored at every 5 min intervals up to 30 min followed by every 15 min till the end of procedure and every hour till 4 h and then at the intervals of 12 h, 24 h and 72 h postoperatively. The evaluation of nausea and vomiting was done as per the PONV score as 0=no nausea or vomiting, no rescue medication; 1=nausea; 2=vomiting once; 3=vomiting more than once [1]. Any adverse effects (headache, drowsiness, dizziness, constipation) were recorded every hour till 4 h and then at the intervals of 12 h, 24 h and 72 h. IM Diclofenac 75 mg, 8 hourly was used for postoperative analgesia. Metoclopramide was used intravenously as rescue antiemetic drug for PONV score ≥ 2 or on patient demands. All the patients were kept nil oral for up to 6 h after surgery and liquid diet was allowed for next 24 h thereafter. Meanwhile, Ringer lactate was used as maintenance fluid.

Complete response to the drug (no complaint of any nausea or vomiting) was the primary outcome of the study. Secondary outcomes were the incidence of nausea and vomiting, PONV score, use of rescue medication and side effects.

Statistical analysis

For the purpose of power analysis, we used the study of Singh et al. [1]. The Sample size was calculated by using the mean values from the above-mentioned study and using the formula:

$$n=(Z_{\alpha/2}+Z_{\beta})2*(p1(1-p1)+p2(1-p2))/(p1-p2)2$$

where $Z_{\alpha/2}$ is the critical value of the Normal distribution at α/2 (e.g. for a confidence level of 90%, α is 0.05 and the critical value is 1.65), Z_{β} is the critical value of the Normal distribution at β (e.g. for a power of 80%, β is 0.2 and the critical value is 0.84) and p1 and p2 are the expected sample proportions of the two groups. From the formula above we have calculated the sample size to be 40 samples in each group with a total of 80 patients.

Statistical analysis was conducted with SPSS version 13.0 for Windows statistical package using unpaired student's t-test. A p-value <0.05 was considered as statistically significant and <0.001 was considered as highly significant.

Results

Both the groups were statistically comparable demographically, i.e., mean age of patients, sex distribution, the weight of patients and for the mean duration of surgery **(Table 1)**.

Complete response to drugs was statistically comparable during initial 4 h (p=0.128) in both the groups, but significantly higher in group P during the 4-12 h interval (p=0.00095), 12-24 h interval (p=0.00124) and 24-72 h interval (p=0.0035) as compared to group O **(Table 2)**.

The incidence of nausea, mean PONV score and need for rescue medication were comparable during initial 4 h (p>0.05) while the incidence of vomiting was comparable during initial 4 h (p=0.555) as well as during 4 h-12 h interval (p=0.1645) between both the groups. All the outcomes were found significantly higher in Group O as compared to Group P **(Table 3)**.

Headache & dizziness were reported in both the groups, constipation, and drowsiness were reported only in Group O and were statistically comparable (p>0.05). All the side effects reported were of mild severity and required no special treatment **(Table 4)**.

Discussion

Post-operative nausea and vomiting (PONV) are second most common and disastrous complication following surgery after post-operative pain but usually not paid attention properly. PONV may prolong hospital stay and lead to many serious physical, surgical and anaesthetic complications, such as aspiration of gastric contents, suture dehiscence, oesophageal rupture, subcutaneous emphysema or pneumothorax.

There were many confounding factors in for PONV such as female gender, non-smoker status, history of PONV or motion sickness, use of perioperative opioids, use of volatile anaesthetics, duration of surgery, duration of anaesthesia and type of surgery that would affect the outcome. In our study, demographic profile of the patients including age, sex distribution, mean weight of patients and mean duration of surgery were comparable in both the groups **(Table 1)**.

Various 5-HT3 antagonists have been used to prevent PONV. Ondansetron inhibits emetic symptoms by binding with the 5-HT3 receptor located in the central chemoreceptor trigger zone and the gastrointestinal tracts and it is constantly in use for prevention and treatment of PONV. Paventi et al. [4] found that single dose Ondansetron 8mg is more effective than 4.0 mg in the prevention of PONV. 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. Kovac et al. [5] compared different doses of Palonosetron 0.025 mg, 0.05 mg and 0.075 mg and found that 0.075 mg dose was statistically during the first 24 h for prophylaxis of PONV. Palonosetron 0.075 mg was also approved by FDA. So, Intravenous Ondansetron 8.0 mg & Palonosetron 0.075 mg was used in our study.

Complete response, the primary outcome of our study was comparable during the initial 4 h period (p>0.05) but after that patients in Palonosetron group showed significantly higher rates of complete response (p<0.05). The incidence of postoperative nausea, mean PONV score and need for rescue antiemetic were comparable between both the groups during initial 4 h (p>0.05) but the incidence of vomiting was comparable during initial 4 h as well as during 4-12 h. The incidence of postoperative nausea was significantly higher in Ondansetron group after 4 h up to 72 h as compared to Palonosetron group (p<0.05). The incidence of vomiting was higher in Ondansetron group during 12-24 h and 24-72 h interval. Mean PONV score was significantly higher in Ondansetron group after initial 4 h up to 72 h. Need for rescue antiemetic was significantly higher in Ondansetron group after initial 4hr up to 24 h but it was again comparable during the 24 h-72 h interval. This could be due to shorter half-life of Ondansetron ($t_{1/2}$=3.5 h) as compared to Palonosetron ($t_{1/2}$=40 h) and earlier weaning of antiemetic effect of *i.v.* Ondansetron which lasts for 4-8 h. We reported adverse effects like headache, constipation, drowsiness and dizziness in our study but these adverse effects were non-significant between both the groups, mild and required no any special treatment. Results of our study are comparable with the results found in the studies of Singh et al. [1], Chakravarty and Raghuwanshi [6], Shadangi et al. [7], Abd El-Hamid et al. [8] and Bhalla et al. [9]. Park and Cho [10] found a higher incidence of postoperative nausea in Ondansetron group and slightly higher incidence of vomiting in Palonosetron group during the initial 4 h postoperative period. They explained that Ondansetron has a more antiemetic effect than anti-nausea

Table 1 Demographic profile of patients.

	Group O	Group P	p value
Age (years) (mean ± SD)	41 ± 11.3	43 ± 11.2	0.4005
Sex (M:F)	21:19	23:17	-
Weight (kg) (mean ± SD)	52.45 ± 7.75	53.1 ± 8.11	0.715
Duration of surgery (min) (mean ± SD)	100.75 ± 15.0	102.25 ± 13.81	0.643

Table 2 Complete response to drugs.

Time interval (h)	Group O n (%)	Group P n (%)	p Value
0-4	31 (77.5%)	36 (90%)	0.128
4-12	23 (57.5%)	36 (90%)	0.00095
12-24	18 (45%)	32 (80%)	0.00124
24-72	16 (40%)	32 (80%)	0.0035

Table 3 Incidence of PONV, mean PONV score, need for rescue antiemetic and adverse effects.

Time	Group O	Group P	p value
0-4 h			
Nausea	17.50%	7.50%	0.177
Vomiting	5%	2.50%	0.555
Mean PONV	0.275 ± 0.547	0.125 ± 0.399	0.165
Rescue antiemetic	15%	5%	0.136
4-12 h			
Nausea	32.50%	7.50%	0.005
Vomiting	10%	2.50%	0.164
Mean PONV	0.55 ± 0.669	0.125 ± 0.399	0.0009
Rescue antiemetic	20%	0%	0.022
12-24 h			
Nausea	40%	17.50%	0.026
Vomiting	15%	2.50%	0.047
Mean PONV	0.775 ± 0.697	0.225 ± 0.480	0.001
Rescue antiemetic	20%	5%	0.042
24-72 h			
Nausea	50%	20%	0.0049
Vomiting	12.50%	0%	0.021
Mean PONV	0.775 ± 0.679	0.325 ± 0.6	0.0066
Rescue antiemetic	5%	0%	0.152

Table 4 Adverse effects.

Adverse effects	Group O	Group P	p value
Headache	20%	7.50%	0.105
Dizziness	20%	5%	0.395
Constipation	5%	0%	0.152
Drowsiness	5%	0%	0.152

effect and use of IV Fentanyl for post-operative pain might be the cause for a higher incidence of PONV. Gupta et al. [11] and Laha et al. [12] reported higher incidence of postoperative nausea and high mean PONV score in Ondansetron group that could be because they had used a lower dosage of Ondansetron 4.0 mg. Moon et al. [13] found a higher incidence of postoperative vomiting in Ondansetron group as compared to Palonosetron group during an early postoperative period that could be due to the inclusion of only females only in their study and used iv opioids for postoperative analgesia. Kim et al. [14] used IV PCA including fentanyl for postoperative pain in their study for both the groups but they added additional Ondansetron 8mg in IV PCA in Ondansetron group and found the comparable incidence of nausea and no significant differences in the requirement of rescue antiemetic drug in both the groups during all intervals up to 72 h.

There were several limitations to our study. The efficacy of Palonosetron and Ondansetron were compared based on the known optimal doses. Some degree of subjective error is inevitable in the assessment of symptoms. The postoperative antibiotic and analgesic regime were kept uniform in all cases but were not exactly identical in all cases. The baseline incidence of PONV was not evaluated by the inclusion of placebo group because it would be inhumane and unethical to withhold prophylactic antiemetic drugs in all patients especially those who are at high risk for PONV.

From the present study, we concluded that both Ondansetron and Palonosetron are equally effective for initial four hours thereafter Palonosetron is more effective than Ondansetron up to 72 h for prevention of PONV following middle ear surgery under general anesthesia.

Conclusion

We concluded that Ondansetron and Palonosetron both are equally effective for initial postoperative period but Palonosetron is more effective for the late postoperative period in prevention of PONV following middle ear surgery under general anesthesia.

References

1 Singh T, Shah N, Patel C, Upadhyay RM (2014) A comparative study of prophylactic ondansetron versus palonosetron for post-operative nausea and vomiting in middle ear surgeries. International J Biomed Adv Res 5: 619-622.

2 Rao JS, Geetha C, Naik RP (2017) Comparision of palonosetron with ondansetron for prevention of nausea and vomiting during postoperative period in patients undergoing ENT surgeries. Int J Contemp Med Res 4: 1486-1489.

3 Elahl MI, Badea M (2013) Palonosetron in preventing postoperative nausea and vomiting in middle ear surgery: A randomized-controlled study. Egypt J Otolaryngol 29: 156-158.

4 Paventi S, Santevecchi A, Ranieri R (2001) Efficacy of a single-dose ondansetron for preventing post operative nausea and vomiting after laparoscopic cholecystectomy with sevoflurane and remifentanil infusion anaesthesia. Eur Rev Med Pharmacol Sci 5: 59-63.

5 Kovac AL, Eberhart L, Kotarski J, Clerici G, Apfel C, et al. (2008) A randomized, double-blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo in preventing postoperative nausea and vomiting over a 72 h period. Anesth Analg 107: 439-444.

6 Chakravarty N, Raghuwanshi SK (2013) Comparison between efficacy of palonosetron and ondansetron in postoperative nausea and vomiting in middle ear surgery: A randomized double-blind study. Int J Pharm Bio Sci 4: 67-74.

7 Shadangi BK, Agrawal J, Pandey R, Kumar A, Jain S (2013) A prospective, randomized, double-blind, comparative study of the efficacy of intravenous ondansetron and palonosetron for prevention of postoperative nausea and vomiting. Anaesth Pain Intensive Care 17: 55-58.

8 Abd El-Hamid AM, Afifi E, Othman MSK, Afifi EE (2014) Palonosetron versus ondansetron for prevention of postoperative nausea and vomiting during middle ear surgery: A double-blind, randomized, comparative trial. Ains Shams J Anaesth 7: 309-313.

9 Bhalla J, Baduni N, Bansal P (2015) Comparison of palanosetron with ondansetron for postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia. J Minim Access Surg 11: 193-197.

10 Park SK, Cho EJ (2011) A randomized, double-blind trial of palonosetron compared with ondansetron in preventing postoperative nausea and vomiting after gynaecological laparoscopic surgery. J Int Med Res 39: 399-407.

11 Gupta K, Singh I, Gupta PK, Chauhan H, Jain M, et al. (2014) Palonosetron, ondansetron and granisetron for antiemetic prophylaxis of postoperative nausea and vomiting: A comparative evaluation. Anesth Essays Res 8: 197-201.

12 Laha B, Hazra A, Mallick S (2013) Evaluation of antiemetic effect of intravenous palonosetron versus intravenous ondansetron in laparoscopic cholecystectomy: A randomized controlled trial. Indian J Pharmacol 45: 24-29.

13 Moon YE, Joo J, Kim JE, Lee Y (2012) Anti-emetic effect of ondansetron and palonosetron in thyroidectomy: A prospective, randomized, double-blind study. Br J Anaesth 108: 417-422.

14 Kim Y, Moon SY, Song DU, Lee KH, Song JW, et al. (2013) Comparison of palonosetron with ondansetron in prevention of postoperative nausea and vomiting in patients receiving intravenous patient-controlled analgesia after gynecological laparoscopic surgery. Korean J Anesthesiol 64: 122-126.