



STUDY OF INTRAVENOUS ONDANSETRAN VERSUS INTRAVENOUS GRANISETRAN FOR PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN MIDDLE EAR SURGERY AFTER GENERAL ANAESTHESIA

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ABSTRACT

BACKGROUND: Postoperative nausea and vomiting (PONV) is one of the complex and significant problems in anaesthesia practice. Various drugs such as neurokinin-1 receptor antagonist (aprepitant) are used along with serotonin (5-hydroxytryptamine subtype 3) receptor antagonists, corticosteroids, anticholinergics, antihistaminic, and butyrophenones for PONV prophylaxis. Present study was aimed to evaluate the efficacy of intravenous Ondansetron & Granisetron in preventing PONV in middle ear surgery patients under general anaesthesia at a tertiary hospital. **MATERIAL AND METHODS:** Present study was single-center, prospective, comparative study, conducted in patients of age 18-60 years of both genders undergoing middle ear surgery under general anaesthesia, patient belonging to ASA 1 & 2. Just before surgery patients were randomly divided into two groups of 50 each into Group O (Ondansetron group) & Group G (Granisetron group). **RESULTS:** Total 100 patients were included in the study. Patient population were comparable across the two groups with respect to Age, sex, weight, ASA grade, type of procedure, vitals (Systolic BP, Diastolic BP, Heart rate). All parameters were comparable in both groups & difference was statistically insignificant ($p > 0.05$). The incidence of nausea & vomiting was maximum during the first four hours and it was more in the group O. In present study, need for rescue antiemetic is more in group O compared to group G which was statistically significant. (P value > 0.05). PONV score was favorable in group G as compared to Group O & difference was statistically significant. Also number of patients who suffered side effects were more in Ondansetron group. **CONCLUSION:** In present study incidence of nausea, vomiting, use of rescue antiemetic, simplified PONV scale scoring & side effect occurrence was more common in Ondansetron as compared to Granisetron. Finally we conclude that Granisetron is better alternative to Ondansetron in preventing post-operative nausea and vomiting and has less side effects in patients undergoing middle ear surgeries under general anaesthesia.

KEYWORDS : PONV, Ondansetron, Granisetron, middle ear surgeries, general anaesthesia.

INTRODUCTION

Postoperative nausea and vomiting (PONV) is one of the complex and significant problems in anaesthesia practice. Despite continuing advances in anaesthetic and surgical techniques, both the incidence and severity of post-operative nausea and vomiting have remained relatively unchanged. It can cause serious complications such as wound dehiscence or surgical site bleeding due to frequent retching, dehydration, electrolyte imbalance, & increased pain.¹

The introduction of 5HT-3 receptor antagonists was a major advancement in control of post-operative nausea & vomiting because of less adverse effects than commonly used conventional antiemetics. Certain procedures such as middle ear surgeries, strabismus surgeries, laparoscopic surgeries, Gynecological surgeries are associated with a higher incidence of PONV.²

Various drugs such as neurokinin-1 receptor antagonist (aprepitant) are used along with serotonin (5-hydroxytryptamine subtype 3) receptor antagonists, corticosteroids, anticholinergics, antihistaminic, and butyrophenones for PONV prophylaxis.

Combination of drugs from different classes with different mechanisms of action are administered for optimized efficacy in adult with moderate risk for PONV.^{3,4,5} Present study was aimed to evaluate the efficacy of intravenous Ondansetron 4mg(2ml) & Granisetron 2mg(2ml) in preventing PONV in middle ear surgery patients under general anaesthesia at a tertiary hospital.

MATERIAL AND METHODS

Present study was single-center, prospective, comparative study, conducted in department of anaesthesiology, at XXX medical college & hospital, XXX, India. Study duration was of 2 years (July 2018 to June 2019). Study was approved by institutional ethical committee.

INCLUSION CRITERIA

- All patient of age 18-60 years of both genders undergoing middle ear surgery under general anaesthesia, patient belonging to ASA 1 & 2.

EXCLUSION CRITERIA

- Patients unwilling for giving their consent
- Patient aged < 18 or > 60 years.
- Patient giving history of drug allergy to above drugs.
- Patient having renal & liver disorders.
- Pregnant & lactating women, patient underlying comorbid condition.
- Patient belonging to ASA 3 & 4.

Study was explained to patients & a written informed consent was taken from patients. They were premedicated with 0.2mg/kg Inj. diazepam orally 12 hr. before giving general anesthesia (to allay anxiety and apprehension) Patients were kept NPO for 12 hours before surgery. Just before surgery patients were randomly divided into two groups of 50.

- Group – „O – Ondansetron group (n = 50)
- Group – „G – Granisetron. group (n = 50)

In the preoperative room, iv line was secured. In the operation theatre routine monitoring devices pulse oximetry, NIBP, ECG monitors were attached, and baseline blood pressure, heart rate and O₂ saturation values were recorded. Later capnography was attached after the intubation.

The anaesthetic regimen and surgical procedures were standardized for all patients. Anaesthesia was induced with inj. Glycopyrrolate 5 μ gkg⁻¹ intravenous inj. Propofol 2mg/kg. For intubation inj. scholine 2mg/kg is used. Anaesthesia was maintained with N₂O 66%, O₂ 33%, halothane 0.5-2% ,and intermittent doses of inj. Vecuronium Bromide and inj. Fentanyl 1.5 μ g/kg was used for analgesia.

Ventilation was controlled mechanically and adjusted so as to keep the end tidal carbon dioxide 35-40 mm of Hg. During surgery the patients were placed in supine position. At the end of the surgery Group O patients received 4mg Inj ondansetron and Group G patients received 2mg Inj. granisetron administered slow iv over period of 30 seconds. Residual neuromuscular block was routinely reversed with inj. glycopyrrolate 0.005mgkg⁻¹ and inj. neostigmine 0.05mgkg⁻¹

and patient were extubated. In post anaesthesia care unit Blood pressure and Heart rate is recorded every 5 min for 30 min. Episodes of nausea and vomiting experienced by each patient was recorded by direct questioning. The number of patients who suffered nausea/vomiting was noted during the periods 0-4hrs, 4-12hrs, 12-24hrs. Rescue Antiemetic (inj. Metaclopramide 10mg) was used if patient had vomiting.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

Total 100 patients were included in the study. Patient population were comparable across the two groups with respect to Age, sex, weight, ASA grade, type of procedure, vitals (Systolic BP, Diastolic BP, Heart rate). All parameters were comparable in both groups & difference was statistically insignificant (p>0.05).

Table: 1 Baseline characteristic

Baseline characteristic	Group G	Group O	P value
Age (in years)			
19-30	25(50%)	28 (56%)	P=0.374
31-40	7(14%)	12 (24%)	
41-50	11(22%)	5 (10%)	
51-60	7(14%)	5(10%)	
Mean ±SD	35.21±13.03	32.81±11.11	
Sex			0.159
Male	19(38%)	27 (54%)	
Female	31 (62%)	23 (46%)	
Weight (in kgs)			0.10
40-55	12 (67%)	19 (77%)	
56-70	38 (33%)	31(23%)	
Mean weight ±SD	59.63±7.05	57.1±7.92	
ASA Grade			0.72
I	31 (62%)	32 (64%)	
II	19 (38%)	18(36%)	
Type of Procedure			0.56
Endoscopic T plasty	11 (22%)	12 (24%)	
Endoscopic MRM	4 (8%)	1 (2%)	
Exploratory Tympanotomy	1 (2%)	1 (2%)	
MRM	17 (34%)	21 (42 %)	
T Plasty	17 (34%)	15 (30%)	
Vitals			
MEAN PULSE	83.14±5.8	84.96±5.64	0.46
Mean SBP	130.14±5.54	130.44±5.46	0.69
Mean DBP	81.71±5.86	83.18±4.12	0.159

In present study, Occurrence of nausea in group O and group G showed that incidence of nausea in 0-2 hours were 7 cases (14%) in group O as compared to 4 cases (8%) in group G (P<0.01). Incidence of nausea in 2-3 hours were 4 cases (8%) in group O as compared to 1 case (4%) in group G (P<0.05).Incidence of nausea in 3-6 hours was only 3 case (6%) in group O as compared to 2 cases (4%) in group G. Incidence of nausea in 6-12 hours was only 3 case (6%) in group O as compared to 1 case (2%) in group G. The incidence of nausea was maximum during the first four hours and it was more in the group O.

In present study, incidence of vomiting episodes in group O were 9 cases (18%) as compared to 4 cases (7%) in group G in 0-2 hours (P<0.01). In 2-3 hours group O had 13 cases (26%) of incidence of vomiting as compared to 6 case (12%) in group G

(P<0.05). Again, the incidence of vomiting was maximum during first four hours and 1 patient had vomiting from 12 hours onwards in group O.

Table 2: Incidence of nausea & vomiting

Duration	Group O	Group G	P value
Incidence of Nausea			
0-2hr	**7(14%)	**4 (8%)	0.0002
2-3hr	*4(8%)	*2 (4%)	0.031
3-6hr	3(6%)	2(4%)	0.62
6-12hr	*3(6%)	*1(2%)	0.04
12-24hr	1(2%)	0	-
Incidence of Vomiting			
0-2hr	**9(18%)	**4 (8%)	0.0001
2-3hr	**13 (26%)	**6 (12%)	0.0001
3-6hr	2(4%)	3(6%)	0.09
6-12hr	2(4%)	1(2%)	0.5
12-24hr	1(2%)	0	-

In present study, need for rescue antiemetic is more in group O compared to group G which was statistically significant. (P value >0.05). PONV score was calculated by simplified PONV impact scale^{5,4}. A PONV impact scale 5 defines clinically important PONV. In present study, Grade 0 was obtained in 56% in group G as compared to 26% in group O. Grade 1 was obtained in 42% in group G as compared to 52 % in Group O. Grade 2 was obtained in 0% of group G as compared to 20% in Group O. The following data has P value of 0.004 which is statistically significant.

In present study, Occurrence of side effects like headache, Diarrhea and sedation in Ondansetron group are 7(14%), 7(14%),2(4%) respectively compared to 5 (10%), 4(8%),2 (4 %) in Granisetron group. The number of patients who suffered side effects were more in Ondansetron group.

Table 3: Post-operative characteristics

Anesthetic Sequelae	Group O	Group G	P Value
Rescue antiemetic	7 (23 %)	3 (10 %)	
PONV score			0.004
0	13(26%)	28(56%)	
I	26 (52%)	22(42%)	
II	10 (20%)	00(00%)	
Side effects			
Headache	*5(10%)	*7 (14 %)	0.036
Diarrhea	*4(8%)	*7 (14 %)	0.028
Sedation	2 (4%)	2 (4 %)	0.84

DISCUSSION

Post-operative nausea and vomiting is a common disturbing complication of anaesthesia and surgery. PONV is the second common complaint with pain being the most common, both of which are an important perioperative concern which lead to increased cost related to hospital stay.⁴ PONV is multifactorial; it is influenced by multiple factors which are related to the patient, surgery, and pre-, intra-, and post-operative anaesthesia factors. Past history of PONV, motion sickness, female gender, use of opioids are some of the predictors of PONV.⁵

It is well appreciated that a number of things (e.g., various insults, chemotherapeutic agents, radiation) may lead to the release of serotonin from the enterochromaffin of the gastrointestinal tract. Released serotonin may then bind to certain 5-HT3 receptors and promote nausea/vomiting. 5HT3 receptor antagonists may ameliorate nausea/vomiting in a number of circumstances and have been utilized as important antiemetics for multiple conditions such as chemotherapy-induced nausea/vomiting (CINV), radiation induced emesis (RIS), and postoperative nausea/vomiting (PONV).⁶

Postoperative nausea and vomiting (PONV) are of multifactorial

origin. The incidence of PONV after anaesthesia, despite the advances in antiemetic therapy in the last decades is still found to be relatively high. Gold et al noted that the three most common causes for admission following day care surgery are pain, bleeding and intractable vomiting.¹

Our study shows no statistically significant difference in the baseline values of hemodynamic variables between the two groups before, during or after giving drug. Study conducted by Dev et al.,⁷ also shows the same results. There was no hemodynamic alteration seen in PR, SBP and DBP during study period. According to Gigilla et al.,⁸ they noticed hemodynamic variation in SBP, DBP and HR. Ondansetron mediated bradycardia and hypotension was reported in their study group.

Study done by Pueyo et al.,⁹ observed that nausea and vomiting was more common in first 6 hours post operatively. Same results were seen in the study done by Fujii⁴. According to Raphael et al.,¹⁰ optimal dose of Ondansetron for preventing post-operative nausea vomiting was 4 mg and half-life was 3 hours. While optimal dose of Granisetron was 2 mg and half-life are 8-9 hours. So, it was observed that after 6 hours Granisetron was more effective than Ondansetron for preventing PONV.

Updated guidelines for managing postoperative nausea and vomiting were recently announced at the Annual Meeting of American Society of Anaesthesiologists in Chicago, Illinois, USA.¹¹ Evaluating the current medical literature, they recommended the use of antiemetics, with an emphasis on the use of the 5HT₃ receptor antagonists. The guidelines also suggest a potential benefit of combination prophylaxis. Overall, the panel recommended, "prophylactic therapy with combination, three or more interventions, in patients at high risk for PONV."¹¹

In present study, the use of rescue antiemetic in ondansetron group which was about 7(23%) whereas in Granisetron group about 3(10%) of the patients received rescue antiemetic. Stewart et al.,¹² in his study also observed same results. In present study, there was a significant decrease in simplified PONV scale scoring in granisetron group compared to ondansetron group shows statistically significant. Shirin Salajegheh et al.,¹³ in his study also observed same result.

In present study, incidence of side effects was significant in our study groups. Incidence of headache was 20% in Ondansetron group while it was 12% in Granisetron group shows statistically significant difference (P < 0.05). Similarly, findings were noted in other studies.^{5,6}

Limitations of present study were small sample size, single center based, in patients undergoing middle ear surgeries only. Larger, multicentric studies are required to confirm findings of present study.

CONCLUSION

In present study incidence of nausea, vomiting, use of rescue antiemetic, simplified PONV scale scoring & side effect occurrence was more common in Ondansetron as compared to Granisetron. Finally we conclude that Granisetron is better alternative to Ondansetron in preventing post-operative nausea and vomiting and has less side effects in patients undergoing middle ear surgeries under general anaesthesia.

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