

STUDY TO COMPARE THE EFFICACY OF GRANISETRON WITH RAMOSETRON AS PROPHYLACTIC ANTIEMETIC IN GENERAL ANAESTHESIA

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Abstract

Background: Post-operative nausea and vomiting (PONV) is one of the most distressing and frequent adverse event occurring after general anaesthesia. **Objectives:** To compare the efficacy of Granisetron with Ramosetron in preventing post-operative nausea and vomiting (PONV) after general anaesthesia. **Study Design:** The study was conducted over a period of 1 year in the Department of Anaesthesiology in MVASMC, Basti, on patients undergoing elective surgeries under general anaesthesia. **Materials and Methods:** 60 patients of American Society of Anaesthesiologists (ASA) status I and II were randomly divided into two groups. Group 1(n=30) Granisetron 10mcg/kg and Group 2(n=30) Ramosetron 0.3mg i.v. Incidence of nausea and vomiting was observed upto 24 hours post operatively after extubation. The efficacy was assessed in terms of number (percentage) of patients with mild nausea not requiring rescue antiemetic, number (percentage) of patients with severe nausea or vomiting requiring rescue antiemetic and number (percentage) of patients with no nausea or vomiting for 24 hours post operatively. **Statistical Analysis:** Data presented as number and percentages. Analysis done using ANOVA followed by Chi square, unpaired 't-test'. **Results:** The number (percentage) of patients with mild nausea not requiring rescue antiemetic in group 1 was 2(6.6%) and in group 2 was 6(20%). The number (percentage) of patients with severe nausea or vomiting requiring rescue antiemetic in group 1 was 5(16.6%) and in group 2 was 8(26.6%). The number (percentage) of patients with no nausea or vomiting in group 1 was 23(76.6%) and in group 2 was 16(53.3%). **Conclusions:** Granisetron is the better drug for prevention of postoperative nausea and vomiting than Ramosetron.

INTRODUCTION

General Anaesthesia is defined as reversible, intentional, temporary, controlled, drug induced loss of consciousness. There are various complications of general anaesthesia out of which, post-operative nausea and vomiting (PONV) is one of the most distressing and frequent adverse event.^[1] General anaesthesia using volatile anesthetic agents is associated with an average incidence of PONV ranging between 60% and 30%. Incidence of PONV has decreased from 60% when ether and cyclopropane were used, to approximately 30% nowadays. Descriptions of these side effects

induced by ether and chloroform were included in the earliest textbooks of pharmacology and therapeutics.^[2] During the past decade, anaesthesiologists have been modifying their anaesthetic techniques to ensure a more rapid and smooth recovery. There has been a general trend towards decrease in the incidence of the problem of post-operative nausea and vomiting because of the use of lesser emetogenic anaesthetic agents, improved pre-operative and postoperative medications, refinement of operative technique and identification of patient predictive factors.^[3,4] However in spite of these advances, nausea and vomiting still occur with unacceptable frequency in

association with surgery and anaesthesia, the description of it as “the big little problem”³ encapsulates much of the general perception. Though several traditional antiemetic agents viz, metoclopramide, prochlorperazine, droperidol are available in the anaesthetic armamentarium, they are not in much use for the prophylaxis because of their relative ineffectiveness and higher incidence of serious side effects.

There are a number of drugs that are used to manage postoperative nausea vomiting (PONV). These drugs are generally antihistaminics, phenothiazine derivatives, anticholinergics and dopamine receptor antagonist with unwanted side effects like sedation, dysphoria, extrapyramidal symptoms, dry mouth, restlessness and tachycardia.^[5,6] Recently introduced selective serotonin 5-hydroxytryptamine type 3 (5HT₃) receptor antagonists (5HT₃ RA) are devoid of such side effects and are highly effective and thus the first line therapies in prevention of PONV.^[7,8] These drugs include ondansetron, granisetron, dolasetron and tropisetron. Currently introduced 5HT₃ RA include ramosetron and palanosetron.

Most research on the 5HT₃ RA has been on ondansetron and its antiemetic efficacy has been well established in the prevention and treatment of PONV.^[7,8] Granisetron is also effective in the prevention of post-operative nausea and vomiting after gynaecological surgeries.^[9,10] and laparoscopies.^[9,11,12]

The present study was undertaken to compare the antiemetic efficacies of granisetron and ramosetron in preventing post-operative nausea and vomiting after general anaesthesia in terms of number (percentage) of patients with mild nausea not requiring rescue antiemetic, number (percentage) of patients with severe nausea or vomiting requiring rescue antiemetic and number (percentage) of patients with no nausea or vomiting for 24 hours post operatively.

MATERIALS AND METHODS

The study was conducted over a period of 1 year from October 2021 to October 2022 in the Department of Anaesthesiology in Maharshi Vashistha Autonomous State Medical College, Basti on patients undergoing elective surgeries under general anaesthesia. After obtaining approval from institutional ethical committee (IEC) and informed written consent of patients, 60 patients of ASA grade I and II, aged between 12 to 58 years, both male and female sex undergoing various surgical procedures under general anaesthesia were selected for the study. Patients who had received antiemetic drug within the preceding 24 hours, with history of alcohol or drug abuse within last 3 months, allergic

to any of the study medications, posted for ENT and obstetric surgeries, known case of GIT diseases like hiatus hernia, GERD, peptic ulcer disease, with history of motion sickness, with history of PONV in previous surgery were excluded from the study. All patients were subjected to thorough pre-anaesthetic evaluation and all other relevant laboratory investigations as per institution protocol. A standard anaesthetic protocol was used in both the groups of patients.

60 patients were divided randomly into two groups by computer generated random number list with 30 patients in each group. GROUP 1: patients in this group received inj granisetron 10mcg/kg i.v. three minutes before induction. GROUP 2: patients in this group received inj ramosetron 0.3mg i.v. three minutes before induction.

The incidence of nausea and vomiting was observed up to 24 hours post operatively after extubation. The episodes of post-operative nausea and vomiting were identified by spontaneous complaints by the patients.

Score Table (Wadaskar Et Al, 2009):

0. No nausea.

1. Mild nausea.

2. Severe nausea.

3. Mild vomiting.

4. Severe vomiting.

“Complete response” was defined as the absence of nausea, retching or vomiting and no need for rescue antiemetic during the observation period. Rescue antiemetic was provided with Inj. Metoclopramide 0.3mg/kg iv for vomiting or persistent nausea.

Statistical Considerations

Data are presented as number and percentages. The statistical analysis was pre-formed using SPSS version 20. Analysis of demographic data was done by Chi-square test. Unpaired or independent ‘t- test’ and ANOVA (Analysis of variance) was used to compare intergroup differences. A ‘p’ value of less than 0.05 was considered statistically significant.

RESULTS

The study was conducted in 60 patients undergoing elective surgery under general anaesthesia. The patients were randomly divided into two groups with 30 patients each.

The mean age of patients in group 1 (Granisetron) was 35.36 ± 8.37 years and in group 2 (Ramosetron) was 35.53 ± 7.32 years. (Table 1)

The duration of anaesthesia in group 1 was 111.00 ± 26.30 minutes and in group 2 was 112.00 ± 28.33 minutes. No significant difference was found in both groups with respect to age and duration of anaesthesia (p > 0.05) (Table 1)

Table 1: Demographics, Age and Duration of Anaesthesia

VARIABLES	GROUP 1	GROUP 2	p value (independent 't' test)
			1 Vs 2
AGE(IN YRS.)	35.36 ± 8.37	35.53 ± 7.32	0.9349
DURATION OF ANAESTHESIA (IN MINUTES)	111.00 ± 26.30	112.00 ± 28.33	0.8878

The number (percentage) of patients with mild nausea (PONV 1) not requiring rescue antiemetic in group 1 was 2(6.6%) and in group 2 were 6(20%). So, it was observed that mild nausea not requiring rescue antiemetic was significantly less (p=0.035) in granisetron group than ramosetron group [Table 2].

Table 2: No. Of Patients with Mild Nausea (Ponv 1) Not Requiring Rescue Antiemetic (In 24 Hours)

	GROUP 1 (n=30)	GROUP 2 (n=30)	p value (ANOVA)
NO. OF PATIENTS	2	6	0.035
PERCENTAGE OF PATIENTS	6.6%	20%	

The number (percentage) of patients with severe nausea or vomiting requiring rescue antiemetic in group 1 was 5 (16.6%) and in group 2 was 8(26.6%). So, it was observed that severe nausea or vomiting requiring rescue antiemetic was significantly less (p=0.028) in granisetron group than ramosetron group [Table 3].

Table 3: No. Of Patients with Severe Nausea Or Vomiting (Ponv 2, 3 & 4) Not Requiring Rescue Antiemetic (In 24 Hours)

	GROUP 1 (n=30)	GROUP 2 (n=30)	p value (ANOVA)
NO. OF PATIENTS	5	8	0.028
PERCENTAGE OF PATIENTS	16.6%	26.6%	

The number (percentage) of patients with no nausea or vomiting for 24 hours postoperatively in group 1 was 23(76.6%) and in group 2 was 16(53.3%). So, it was observed that number (percentage) of patients with no nausea or vomiting was significantly more (p=0.018) in granisetron group than ramosetron group [Table 4].

Table 4: No. Of Patients with No Nausea or Vomiting (Ponv 0) For 24 Hours

	GROUP 1 (n=30)	GROUP 2 (n=30)	p value (ANOVA)
NO. OF PATIENTS	23	16	0.018
PERCENTAGE OF PATIENTS	76.6%	53.3%	

Out of 30 cases in Group 1, 4(13.33%) had headache and 2(6.67%) had dizziness. As compared with group 2 only 1(3.33%) had dizziness and 3(10%) had headache. The difference between the incidence of headache and dizziness between the 2 groups was statistically not significant (p>0.05). (Table 5)

Table 5: Comparison of Side Effects in Study Groups

Side effects	GROUP 1 (n=30)	GROUP 2 (n=30)	p value
Dizziness	2(6.67%)	1(3.3%)	>0.05
Headache	4(13.33%)	3(10%)	>0.05

DISCUSSION

Postoperative nausea and vomiting (PONV) are common sequelae of general anaesthesia and a leading cause of delayed discharge of unanticipated hospital admission after ambulatory surgical procedure.^[13] This is very frequent in abdominal surgeries leading to recommendation of routine prophylactic administration of antiemetics. The etiology of nausea and vomiting after abdominal surgeries under general anaesthesia are multifactorial in origin. Age, type of surgery, anaesthetic procedure and duration of surgery may influence PONV.^[14]

The introduction of 5-HT₃ receptor antagonist in 1990 was heralded as a major advance of the treatment of PONV, because of absence of adverse effects that were observed with commonly used

traditional antiemetics. The 5-HT₃ receptor antagonists produced no sedation, extrapyramidal reactions, adverse effects on vital signs or laboratory tests or drug interactions with other anaesthetic medications.

Updated guidelines for managing postoperative nausea and vomiting were recently announced at the 2006 annual meeting of the American Society of Anaesthesiologists in Chicago, Illinois, USA. Evaluating the current medical literature, they recommended the use of antiemetics, with an emphasis on the use of the 5HT₃ receptor antagonists.^[15]

Newstar Syiemiong, Lairenlakpam Deban Singh et al.^[16] compared the efficacy of ramosetron and granisetron in prevention of postoperative nausea and vomiting (PONV) after laparoscopic cholecystectomy. The mean age (Mean ± SD) of

patients in group G (granisetron) was 43.95 ± 12.85 and in group R (ramosetron) was 43.43 ± 13.34 . There was no statistically significant difference between the two groups with respect to age. This is comparable with our study.

Sarbari Swaika, Anirban Pal et al.^[17] studied the antiemetic efficacy of intravenous ondansetron 8mg, ramosetron 0.3mg and palonosetron 0.075 mg for prophylaxis of PONV in high risk patients undergoing laparoscopic cholecystectomy. The mean age (Mean \pm SD) of patients in ramosetron group was $41.5 \pm (14.52)$, in palonosetron group was $38.9 (13.09)$ and in ondansetron group was $45.9 (16.07)$. There was no statistically significant difference between the three groups with respect to age. This is comparable with our study.

Newstar Syiemiong et al.^[16] compared the efficacy of ramosetron and granisetron in prevention of postoperative nausea and vomiting (PONV) after laparoscopic cholecystectomy. The duration of anaesthesia (Mean \pm SD) in group G (granisetron) was 62.0 ± 19.0 minutes and in group R (ramosetron) was 63.38 ± 2.058 minutes. There were no statistically significant difference between the two groups. This is comparable with our study.

Yoshitaka fuji et al.^[18] compared granisetron with droperidol for reducing the incidence and severity of PONV after laparoscopic cholecystectomy. The duration of anaesthesia (Mean \pm SD) in granisetron group was 96.6 ± 25.0 minutes and in droperidol group was 94.0 ± 30.6 minutes. There were no statistically significant difference between the two groups. This is comparable with our study.

Yoshitaka fuji et al.^[19] compared the antiemetic effects of granisetron and droperidol for preventing postoperative nausea and vomiting in patients undergoing general anaesthesia for major gynaecological surgery. The duration of anaesthesia (Mean \pm SD) in granisetron group was 106.1 ± 35.7 minutes and in droperidol group was 109.1 ± 32.3 minutes. There were no statistically significant difference between the two groups. This is comparable with our study.

Wilson AJ et al.^[20] compared three doses (0.1 mg, 1.0 mg and 3.0 mg) of the 5-HT₃ receptor antagonist, granisetron as prophylactic therapy for the prevention of postoperative nausea and vomiting and found that the two higher doses of granisetron (1.0 mg and 3.0 mg) provided effective prophylaxis against vomiting, with 78 % and 77 % of patients, respectively, being free from vomiting in the first 6 h after surgery, and 63 % and 62 % in the first 24 h. This compares with 50 % and 34 % at 0.6 h and 0.24 h, respectively, in the placebo group. Granisetron proved effective in the prevention of PONV and was well tolerated in the optimum dose of 1.0 mg.

In our study, the incidence of severe nausea or vomiting requiring rescue antiemetic (PONV 2, 3, 4) was less in granisetron group compared to that in ramosetron group. This observation is supported by various studies conducted in the past.

Shobhana Gupta et al.^[21] 74 compared efficacy of granisetron with that of ondansetron as prophylactic antiemetic in 90 patients undergoing laparoscopic surgeries. The patients were divided into three groups of 30 patients each. In group- G, patients received granisetron 40 mcg/kg intravenously 3 min before induction. Group-O patients received ondansetron 80 mcg/kg intravenously 3 min prior to induction while group-C patients received 3 ml of 0.9% normal saline as control. All the patients were observed up to 12 hours postoperatively. In group G, only 3(10%) patients experienced nausea as compared to group O in which 9(30%) patients experienced nausea and in group C 12(40%) patients experienced nausea. So, in group G patients, incidence of nausea was comparatively less than group O patients. The statistical analysis showed that granisetron is significantly efficient for prevention of post-operative nausea and vomiting (PONV) ($p < 0.05$) in comparison to ondansetron and is highly significant ($p < 0.01$) in comparison to control group. This is comparable with our study.

Newstar Syiemiong et al.^[16] 80 compared the efficacy of ramosetron and granisetron in prevention of postoperative nausea and vomiting (PONV) after laparoscopic cholecystectomy. In a randomized, double-blind study, 80 patients of ASA I and II were enrolled and received either 3 mg granisetron iv. or 0.3 mg ramosetron i.v. (n = 40 each) ten minutes before induction of anaesthesia. The incidence of nausea from 0-24 hours after anaesthesia in patients who received granisetron was 15(37.5%) and in patients who received ramosetron was 9(22.5%). This is not comparable with our study.

CONCLUSION

It can be concluded that granisetron is more effective drug than ramosetron for controlling postoperative nausea and vomiting with less incidence of side effects. We observed minimal emetic and nausea episodes in the postoperative period in patients who had received intravenous granisetron in comparison to intravenous ramosetron.

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