

# Attenuation of Post-operative Nausea and Vomiting with Granisetron and Ramosetron after General Anesthesia

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## Abstract

**Background:** Nausea and vomiting are one of the most common complications after general anesthesia.

**Objective:** The aim of present study was to prevent nausea and vomiting after general anesthesia with granisetron and ramosetron.

**Materials and Methods:** Total 90 patients undergoing general anesthesia were randomly divided into three groups of 30 patients like Group 1 - Granisetron 10 mcg/kg intravenous (IV), Group 2 - Ramosetron 0.3 mg/kg IV and Group 3 - Normal saline 2 ml IV.

**Results:** In our study, out of both the 5HT<sub>3</sub> receptor antagonist, granisetron was found to be more effective in controlling nausea and vomiting after general anesthesia.

**Conclusion:** Both the drugs prevent nausea and vomiting after general anesthesia, but granisetron is more effective.

**Key words:** Granisetron, nausea, ramosetron and vomiting

## INTRODUCTION

There are various complications of general anesthesia like hypoxia, post-operative nausea and vomiting (PONV), hypoventilation, hypotension, hypertension, Out of these, PONV is one of the most distressing and frequent adverse effect occurring after general anaesthesia.<sup>1</sup>

The present study was undertaken to compare the antiemetic effects of granisetron and ramosetron in preventing PONV after general anesthesia.

## Course of PONV

The mechanisms of PONV are multifactorial and include:<sup>2</sup>

### Pre-operative factors

- Food
- Anxiety and stress
- Premedication.

### Intraoperative factors

- Anesthetics
- Surgery.

### Post-operative factors

- Residual effects of drugs
- Pain.

## Mechanism of Action of Antiemetic Agents

Four neurotransmitter systems play important roles in mediating the emetic response:<sup>3</sup>

- Dopaminergic (D<sub>2</sub>)
- Histaminergic (H<sub>1</sub>)

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3. Cholinergic muscarinic
4. Serotonin (5HT<sub>3</sub>).

### Pharmacology

#### Granisetron

Granisetron is a potent and highly selective 5-HT<sub>3</sub> receptor antagonist.<sup>4</sup> It is rapidly and completely absorbed the following oral administration; although oral bioavailability is reduced to about 60% as a result of first-pass metabolism that ranges from 34% to 59%. Granisetron metabolism involves N-demethylation and aromatic ring oxidation followed by conjugation.<sup>5</sup>

Doses:<sup>6</sup>

1. Oral: 20-40 µg/kg
2. Intramuscular: 10-20 µg/kg
3. Intravenous (IV): 15-25 µg/kg

#### Ramosetron

Ramosetron is a selective 5-HT<sub>3</sub> receptor antagonist.<sup>7</sup> After oral administration of ramosetron hydrochloride, the plasma concentration of the unchanged drug exhibits its C<sub>max</sub> at approximately 2 h after administration, and the half-life is about 5 h.<sup>8</sup> The effective bioavailability for oral dose is 50% or a higher based on the plasma concentration. About 13% of the drug is excreted unchanged in the urine.<sup>9</sup>

Doses:<sup>9</sup>

1. Oral: 1-2 µg/kg
2. IV: 0.2-0.3 µg/kg

## MATERIALS AND METHODS

The study was approved by Institutional Ethical Committee and written informed consent was obtained from each patient. A total of 90 patients, belonging to ASA Grade I and II, 20-60 years age group undergoing surgical procedures under general anesthesia, were enrolled.

Group 1 (*n* = 30): Received injection granisetron 10 mcg/kg IV.

Group 2 (*n* = 30): Received injection ramosetron 0.3 mg IV.

Group 3 (*n* = 30): Received injection normal saline (0.9%) 2 ml IV.

### Anesthetic Procedure

Patients were pre-oxygenated with 100% O<sub>2</sub> for 3 min. Then patients were pre-medicated with injection glycopyrrolate 0.005 mg/kg, injection midazolam 0.02 mg/kg and injection fentanyl 2 mcg/kg. Injection granisetron, injection ramosetron or injection normal saline was administered IV 3 min before induction according to the respective study group. Then, the patient was induced with injection thiopentone sodium 3-5 mg/kg body weight and endotracheal intubation was facilitated with injection succinylcholine 1.5 mg/kg.

Maintenance of anesthesia was done with nitrous oxide (60%) and oxygen (40%) and isoflurane and injection vecuronium.

The patient was monitored during anesthesia using continuous electrocardiogram, heart rate, blood pressure and pulse oximetry. On completion of surgery, the neuromuscular block was reversed with injection neostigmine 0.05 mg/kg and injection glycopyrrolate 0.008 mg/kg. Injection diclofenac 1 mg/kg i.m. was given for post-operative analgesia.

### Score Table (Wadaskar *et al.*, 2009)

- “0”: No nausea
- “1”: Mild nausea
- “2”: Severe nausea
- “3”: Mild vomiting
- “4”: Severe vomiting

## RESULTS

Table 1 represents the mean and standard deviation of age and duration of anesthesia in all the three groups and the comparison of *P* values among all the three groups. No significant difference in the three groups with respect to age and duration of anesthesia was found (*P* > 0.05).

Table 2 represents number and percentage of patients with mild nausea not requiring rescue antiemetic in 24 h. The least incidence of nausea not requiring rescue antiemetic was found in Group 1 (*P* < 0.035).

Table 3 represents number and percentage of patients with severe nausea or vomiting requiring rescue antiemetic in 24 h. The incidence of severe nausea or vomiting requiring rescue antiemetic was least in Group 1 followed by Group 2, and then Group 3.

Table 4 represents number and percentage of patients with no nausea or vomiting for 24 h postoperatively. The incidence of no nausea or vomiting for 24 h postoperatively was maximum in Group 1 followed by Group 2, and then Group 3.

Table 5 represents the mean and standard deviation of all types of PONV scores in all three groups. It is clear that PONV score for all types was least in Group 1 followed by Group 2 and Group 3, respectively.

## DISCUSSION

### Base Line Comparison of Groups

#### Age

The study included the patients of age group between 20 and 60 years of age. In present study the age (mean ± standard

**Table 1: Comparison of age and duration of anesthesia**

Variables	Group 1	Group 2	Group 3	P value (independent t-test)		
				1 versus 2	1 versus 3	2 versus 3
Age (years)	35.36±8.37	35.53±7.32	34.5±6.41	0.9349	0.6670	0.5761
Duration of anesthesia (min)	111.00±26.30	112.00±28.33	109.00±29.98	0.8878	0.7846	0.6919

**Table 2: Number (percentage) of patients with mild nausea (PONV 1) not requiring rescue anti-emetic (in 24 h)**

Percentage of Patients	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	P value (ANOVA)
Number of patients	2	6	5	0.035
Percentage of patients	6.6	20	16.6	

PONV: Post-operative nausea and vomiting

**Table 3: Number and percentage of patients with severe nausea or vomiting (PONV 2, 3 and 4) requiring rescue anti-emetic (in 24 h)**

Percentage of Patients	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	P value (ANOVA)
Number of patients	5	8	19	0.028
Percentage of patients	16.6	26.6	63.3	

PONV: Post-operative nausea and vomiting

**Table 4: Number and percentage of patients with no nausea or vomiting (PONV 0) for 24 h**

Percentage of Patients	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	P value (ANOVA)
Number of patients	23	16	6	0.018
Percentage of patients	76.6	53.3	20	

PONV: Post-operative nausea and vomiting

**Table 5: Comparison of mean PONV score in the three groups**

Percentage of Patients	Group 1	Group 2	Group 3	P value (ANOVA)		
				1 versus 2	1 versus 3	2 versus 3
PONV (mean±SD)	0.15±0.5747	0.325±0.6412	0.6917±1.0516	0.0341	0.0000	0.0000

PONV: Post-operative nausea and vomiting, SD: Standard deviation

deviation [SD]) in Group 1 was  $35.36 \pm 8.37$ , in Group 2 was  $35.53 \pm 7.32$  and in Group 3 was  $34.5 \pm 6.41$ . The age is comparable in all the three groups. This is shown in Table 1.

#### *Duration of anesthesia*

In our study, the duration of anesthesia in minutes (mean  $\pm$  SD) in Group 1 was  $111.00 \pm 26.30$ , in Group 2 was  $112.00 \pm 28.33$  and in Group 3 was  $109.00 \pm 29.98$ . The duration of anesthesia in minutes (mean  $\pm$  SD) in patients of all the three groups was comparable. This is shown in Table 1.

#### **Comparison of PONV Score among All Groups in 24 h**

##### *PONV 1 (mild nausea not requiring rescue antiemetic)*

In our study, the number (percentage) of patients with mild nausea (PONV 1) not requiring rescue anti-emetic in Group 1 was 2 (6.6%), Group 2 was 6 (20%), and

Group 3 was 5 (16.6%) (Table 2). Thus, the incidence of mild nausea not requiring rescue anti-emetic was least in granisetron group.

##### *PONV 2, 3 and 4 (severe nausea or vomiting requiring rescue antiemetic)*

In our study, the number (percentage) of patients with severe nausea or vomiting (PONV 2, 3, 4) requiring rescue anti-emetic in Group 1 was 5 (16.6%), Group 2 was 8 (26.6%), and Group 3 was 19 (63.3%) (Table 3). Thus, the incidence of severe nausea or vomiting requiring rescue anti-emetic was least in granisetron group.

##### *PONV 0 (No nausea or vomiting)*

In our study, the number (percentage) of patients with no nausea or vomiting (PONV 0) in Group 1 was 23 (76.6%), Group 2 was 16 (53.3%), and Group 3 was 6

(20%) (Table 4). Thus, the number (percentage) of nausea and vomiting free patients was least in granisetron group.

## CONCLUSION

Hence, it can be concluded that granisetron is a more effective drug than ramosetron for controlling PONV with less incidence of side effects. We observed minimal emetic and nausea episodes in the post-operative period in patients who had received IV granisetron in comparison to IV ramosetron.

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