Research Paper

Comparison of Intravenous Ramosetron and Ondansetron as Prophylaxis for Postoperative Nausea and Vomiting following General Anesthesia

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Abstract

Objective: To compare the efficacy and side effects of $5HT_3$ antagonists, ramosetron, and ondansetron as prophylaxis for postoperative nausea and vomiting (PONV) following general anesthesia. **Materials and Methods:** One hundred and ten patients of the American Society of Anesthesiology Grade I–II, between the age group of 18 to 60 years weighing 40 to 70 kg, undergoing general anesthesia were studied. Group 1 received ramosetron 0.3 mg intravenous (IV) and Group 2 received ondansetron 8 mg IV 15 min before the end of surgery. The incidence of PONV, need for rescue antiemetic, and side effects were evaluated in both the groups. QTc interval prolongation was also evaluated in both the groups by taking electrocardiograms at regular intervals. **Results:** This study showed that there was no statistically significant difference in the incidence of PONV between the ondansetron group and the ramosetron group during the first 24 h after surgery. For PONV score of ≥2 during the first 6 h, the incidence was 3.59% and 1.81% for ramosetron and ondansetron, respectively, and during 6–24 h, the incidence was 1.81% for both the drugs. **Conclusion:** IV ramosetron 0.3 mg is as effective as IV ondansetron 8 mg in preventing PONV in patients undergoing general anesthesia.

Keywords: 5 HT3, drugs, efficacy, rescue antiemetic

Introduction

PONV referred to as the "big little problem" or "the little big problem" after surgery/anesthesia is common, causing delay in discharge from post anesthesia care units and hospital and delay in resuming daily activities.[1] Patients not only experience discomfort but vomiting also increases intracranial pressure with detrimental effects on cerebral perfusion. It may also lead to dehydration and electrolyte imbalance and affect acid–base homeostasis. It has an additional risk of aspiration in patients with impaired reflexes.[2]

Risk factors for postoperative nausea and vomiting (PONV) include female gender, obesity, long duration of surgery, use of nitrous oxide, and inhalational agents to mention a few. In 1997, Koivuranta *et al*. identified five risk factors and came up with a risk score based on these factors[3] and in the year 1999, Apfel *et al*. identified four risk factors and devised the Apfel simplified risk score.[4] Patients having <2 risk factors have a low risk of developing PONV.[5]

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$5HT_3$ antagonists, metoclopramide, promethazine, and dexamethasone are few drugs which have been evaluated for prophylaxis of PONV with regard to dose, timing of administration, and adverse effect.[6] Of the various drugs, $5\text{-}HT_3$ antagonists are the most commonly used antiemetic for PONV. Ramosetron has higher potency and longer duration compared to other $5HT_3$ receptor antagonists.[7,8]

This study was conducted to compare the efficacy of ramosetron 0.3 mg i.v. with ondansetron 8 mg i.v. for prophylaxis of PONV and to compare the side effects of these two drugs. The primary outcome measure of this study was the incidence of nausea and vomiting during the first 24 h after operation, and the secondary

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outcome measures were the need for rescue medication and presence of any side effects.

Materials and Methods

A randomized controlled study was conducted after obtaining institutional ethical committee permission (Number – 25115) in the Department of Anesthesia in Goa Medical College from September 2015 to August 2017. One hundred and ten American society of Anesthesiologists Grade I–II patients aged 18–60 years weighing 40 to 70 kg undergoing general anesthesia with intraoperative opioids and duration of surgery more than 60 min were included in the study [Figure 1]. Exclusion criteria were history of preoperative nausea, vomiting or use of antiemetic 24 h prior, requirement of nasogastric tube postoperatively, known hypersensitivity to study drugs, cardiac disease, patients with electrocardiogram (ECG) showing bradycardia and prolonged QT interval preoperatively, patients of cardiac and neurosurgery, and pregnant patients.

Written informed consent was obtained from all patients after explaining the procedure. Patients were divided by computer-generated random number table into two groups**:** Group 1 received ramosetron 0.3mg intravenous (IV) and Group 2 received ondansetron 8 mg IV 15 min before the end of surgery by double-blind method. The person giving the drug and the one doing the study were not aware of the drug administered.

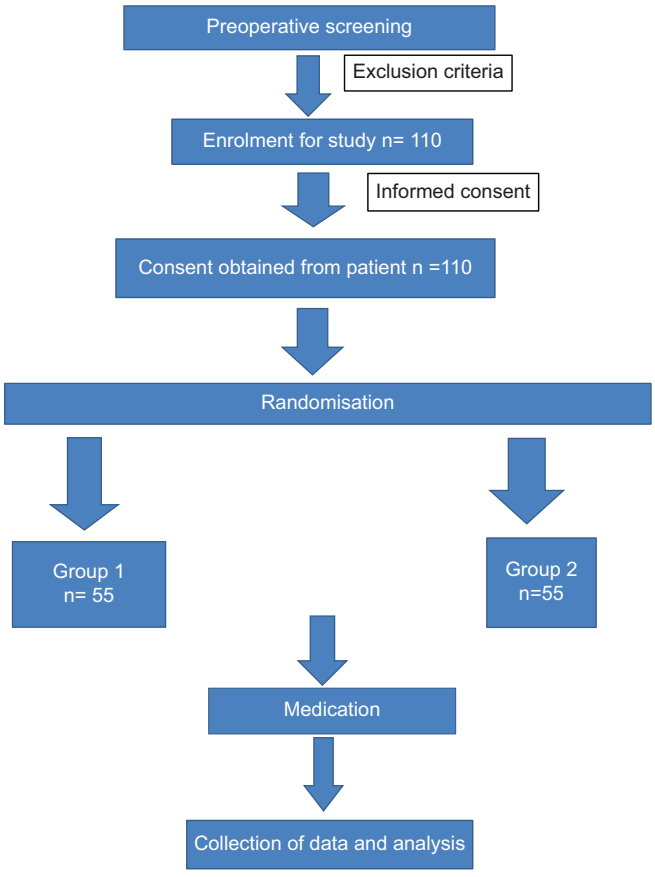

Figure 1: Consort flowchart

Continuous ECG, blood pressure monitoring, oxygen saturation, and end-tidal carbon dioxide were recorded. Patients were premedicated with IV glycopyrrolate 0.2 mg, IV midazolam 1 mg, and IV fentanyl 2 μg/kg. Patients were induced with injection thiopentone sodium (3–5 mg/kg). IV vecuronium 0.1 mg/kg was given to facilitate intubation. Anesthesia was maintained with nitrous oxide: 66%, oxygen: 33%, 2% sevoflurane, and fentanyl: 1 μg/kg/hr and vecuronium. Ringer lactate was used as maintenance IV fluid. ECG was taken preoperatively, 10 min before the end of surgery, and 1 h after the end of surgery. The study drug was given 15 min before end of surgery drawn up to 4 ml volume each, by anesthesiologist who was not part of the study. Patients were reversed with injection neostigmine 0.05 mg/kg and injection glycopyrrolate 0.01 mg/kg at the end of surgery and extubated.

PONV was rated with the help of PONV score (0 – no nausea/vomiting; 1 – nausea/retching; 2 – vomiting once; and 3 – vomiting 2 or more times in 30 min).[9] The PONV score was noted in all patients in both the groups every 15 min for the 1st h postoperatively, every two hourly for the next 6 h and at 24 h. If the events of vomiting or retching were separated by more than 1 min, they were considered as separate episodes.[9] Rescue antiemetic was administered when the PONV score was 2 or 3 and timing was noted. IV metoclopramide 10 mg was used as the rescue antiemetic. Patients were also monitored for adverse effects such as rashes, headache, constipation, and QT prolongation. The QTc interval was calculated using the Bazett's formula.[10] Using this formula, the accepted upper limit of normal for the duration of repolarization is 440 ms.[11]

The sample size was predetermined using a power analysis to achieve an 80% chance of detecting a 40% reduction in PONV from a basal incidence of 70% with a level of significance $\alpha = 0.04$. A calculated minimum sample size was 49 patients in each group. However, we took a sample size of 55 patients in each group keeping in mind possible dropouts. Chi-square test and ANOVA test were used to analyze the data statistically. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software version 16 (IBM Corp., Armonk, NY, USA) for Windows. $P < 0.05$ was considered statistically significant. Data were presented as mean (standard deviation), numbers, or percentages.

Results

The patients were comparable for age, weight, and sex distribution. The difference was found to be statistically insignificant ($P > 0.05$) [Table 1]. The incidence of patients having no PONV (PONV score: 0) in the first 6 h and 6–24 h was not significant ($P = 1.00$ and $P = 0.65$, respectively) [Table 2]. The incidence of nausea (PONV score: 1) in the first 6 h and in the late postoperative period (6–24 h) was not significant when the groups were compared together ($P = 0.133$ and $P = 0.563$, respectively). The incidence of PONV in the first

6 h and PONV in 6–24 h was not significant ($P = 0.58$ and $P = 1.00$, respectively) [Table 2].

Comparison of QTc 1 h after giving the drug shows that there is no statistically significant increase in QT interval for ramosetron as $P = 0.41$. However, in the ondansetron group, increase in QT interval was statistically significant with $P = 0.0005$, but it is not prolonged more than normal limits. P value of comparison is not significant (0.09) [Table 3]. The side effects were compared in both the groups. It was seen that it was more in the ondansetron group compared to the ramosetron group. It was found to be statistically significant ($P < 0.05$) [Table 4]. We used metoclopramide in our study as a rescue antiemetic which was used in five patients, two from ondansetron group and three from ramosetron group with PONV score ≥2.

Discussion

Nausea and vomiting are among the most common complaints in the postoperative period which occur after general as well as regional anaesthesia.[12] Selective $5HT_3$ receptor antagonists are preferred as the first-line drugs in the prevention of PONV as they have acceptable side effects.[13,14] Hence we conducted a study to compare the efficacy of ramosetron and ondansetron for PONV.

In the present study there was no statistical difference in the effectiveness of IV ramosetron 0.3 mg and IV ondansetron 8 mg in prevention of PONV in both the early (0–6 h) and late (6–24 h) periods following general anaesthesia. For PONV score of ≥2 during the first 6 h the incidence was 3.59% and 1.81% for ramosetron and ondansetron respectively. And during 6–24 h, the incidence was 1.81% for both the drugs.

This is similar to the study by Kim *et al*.[15] The purpose of this study was to evaluate the efficacy of ramosetron for the prevention of PONV with that of ondansetron or placebo in high-risk patients undergoing gynaecological surgery. Here they found ramosetron, 0.3 mg to be as effective as 8 mg ondansetron. Ansari *et al*.[16] also showed that there was no difference in the incidence of PONV between the ondansetron group and the ramosetron group during the first 24 h after surgery following laparoscopic cholecystectomy. This is also similar to the study conducted by Ryu *et al*.[17] who found that ramosetron 0.3 mg was as effective as ondansetron 8 mg for prophylaxis of nausea and vomiting after laparoscopic cholecystectomy.

In our study, we found that QTc was not prolonged beyond normal limits with 8 mg ondansetron and 0.3 mg ramosetron. This is similar to the study by Lee *et al*.[18] which showed that QTc interval increased after giving ondansetron but it was not more than 440 ms. The mean QTc at preinduction period was 413.8 ms. The mean Sevo alone and Sevo+Ondansetron QTc was 432.5 ms and 439.2 ms, and the differences in the increase in QTc between stages were all significant ($P < 0.01$).

In our study, ondansetron had more incidence of headache, sedation, and dizziness which was significant compared to ramosetron. In a study by Yokoi *et al*., they showed that the incidence of dizziness may be lower in patients receiving ramosetron than in patients receiving ondansetron.[19]

Metoclopramide was used in our study as a rescue antiemetic which was used in five patients, two from ondansetron and three from ramosetron group with vomiting. This is in accordance with consensus guidelines which states that the antiemetic to be given should be from a pharmacologic class that is different from the prophylactic drug initially given.[5] Ramosetron is more expensive than ondansetron and is almost double the price of ondansetron. Considering that there was no statistically significant difference in the outcome on PONV between the two drugs, using ramosetron would only double the cost of treatment.

Conclusion

IV ramosetron 0.3 mg is as effective as IV ondansetron 8 mg in preventing PONV in patients undergoing general anesthesia. Ondansetron is associated with side effects such as headache

Table 1: Demographics

Patient characteristics	Ramosetron	Ondansetron	*P*
Age (years)	38.05±12.86	42.61±15.86	0.1
Weight (kg)	55.54±7.85	58.03±7.46	0.091
Sex (male/female)	28/27	23/32	0.339

Table 2: Incidence of postoperative nausea and vomiting in percentage

PONV score (h)	Ramosetron	Ondansetron	*P*
0			
0-6	83.63	83.63	1
6-24	94.54	96.36	0.65
1			
0-6	5.45	14.54	0.133
6-24	3.63	1.81	0.563
≥2			
0-6	3.59	1.81	0.58
6-24	1.81	1.81	1

PONV=Postoperative nausea and vomiting

Table 3: QTc_1 h after surgery

Group	*n*	Mean Qtc (ms)	*P*	*P* value of comparison
Ramosetron	55	402.37	0.41	0.09
Ondansetron	55	426.54	0.0005	

Table 4: Comparison of side effects in both the groups

Drug	Constipation	Headache	Sedation	Dizziness	*P*
Ramosetron	3	1	0	1	0.012
Ondansetron	0	5	3	4	

and dizziness compared to ramosetron. Further, both the drugs do not cause prolongation of QTc interval beyond normal limits.

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Conflicts of interest

There are no conflicts of interest

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