Original Research Article

A Comparative study of Ramosetron Versus Ondansetron for Prevention of Postoperative Nausea and Vomiting in patients undergoing laproscopic surgeries under general anaesthesia

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Abstract

Background: Nausea and vomiting are distressing symptoms after laparoscopic surgeries. Number of drugs is used but none is devoid of side effects. Introduction of 5-HT3 receptors antagonists heralded the major advance in the treatment of postoperative nausea and vomiting. Hence search for ideal new 5-HT3 receptors antagonists goes on. **Aim:** The aim of the present study was to compare the efficacy of intravenous ramosetron and ondansetron for prevention of postoperative nausea and vomiting in patients undergoing elective laparoscopic surgeries under general anaesthesia. **Subjects andMethods:** 144 patients of ASA physical status I and II, posted for elective laparoscopic surgeries under general anaesthesia were included inthis prospective randomized study. Patients were randomly allocated into two groups to receive either injection Ramosetron 0.3 mg or injection Ondansetron 4 mg intravenously. Incidence of nausea, vomiting or both, need of rescue antiemetic and complete response were recorded for 24 hrs. Data was analyzed statistically. **Results:** Overall incidence of PONV was observed in 15.27% patients in group R and 36.11% in group O. Rescue antiemetic was used in 5.55% patients in group R compared to 22.22% in group O. Complete response was found in 84.74% patients of group R and 63.88% of group O. **Conclusion:** Intravenous Ramosetron with dose of 0.3 mg appears to be a promising drug for prevention of postoperative nausea and vomiting in laparoscopic surgery under general anaesthesia.

Keywords: Postoperative nausea and vomiting (PONV), Ramosetron, Ondansetron.

Introduction

Nausea and vomiting are the most common distressing symptoms in postoperative period. Its incidence is found to be more than 30% after surgeries under anaesthesia[1]. The consequences of PONV are harmful from physical, surgical and anaesthesia point of view. Physical effects include tachycardia, sweating, discomfort, electrolyte imbalance, etc. Disruption of anastomoses and wound dehiscence are surgical problems associated with PONV. From anaesthesia point of view, aspiration is possible consequence of PONV. It increases hospital stay of patient therefore increasing patients and hospital expenses.

The risk of PONV depends on factors related to patients, surgeries and type of anaesthesia. Patient related factors include age, female gender, history of motion sickness and PONV in previous surgeries[2-4]. Anaesthesia factors include use of opioids inhalational anaesthetic agents like halothane and nitrous oxide[5-7]. There are more incidences of PONV if Patients undergo gastrointestinal tract, middle ear, squint and laparoscopic surgeries.

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Patients of laparoscopic surgeries are prone for PONV due to pneumoperitoneum, hypercarbia and positions. Numbers of drugs like antihistaminic, phenothiazine, dopamine receptors antagonists etc. are used for prophylaxis of PONV but side effects such as sedation, dysphoria and extrapyramidal symptoms are observed[8]. Introduction of serotonin (5-HT3) antagonist was a milestone in the treatment of PONV due to absence of adverse effects observed with conventional antiemetic drugs. The entire 5HT3 receptor antagonists have favorable drug profile. Ondansetron is commonly used drug throughout the world[9].

There is ongoing research to find out better antiemetic drugs. Some studies reported that ramosetron exhibited more potent and sustained antagonistic activities against 5HT3 receptors than existing drugs in this group.

Therefore, this study was conducted with the intention of assessing whether ramosetron conferred any advantages over ondansetron in terms of prophylaxis on the incidence and severity of PONV as a sole antiemetic in patients of laparoscopic surgeries under general anaesthesia.

Materials and Methods

This prospective randomized study was conducted at Department of Anesthesia and Critical Care, at Patna Medical College and Hospital, Patna. The study was approved by the institutional research and ethical committee. The study was conducted between September 2020 and March 2021. An informed and written consent was taken from the participating subjects prior to the commencement of the study.

This study was carried out including 144 patients of ASA I and II physical status. Patients were randomly allocated into either group

O (patients receiving intravenous ondansetron 4 mg, n=72) or group R (patients receiving intravenous ramosetron 0.3mg, n=72). Randomization was done by computer generated random number table. Patients who had risk factors for PONV i.e. migraine, Meniere's disease etc. were excluded from the study. Patients with known allergy to 5HT3 receptor antagonist and who received antiemetic, steroids and psychoactive medications were also excluded from the study.

Preanaesthetic evaluation comprised of history, general examination, systemic examination and investigations like blood grouping, complete blood count, blood sugar, blood urea, serum creatinine, liver function test, ECG and chest X- ray. Day before surgery, details of study were explained to patients and relatives. In operation theatre multipara monitor used to monitor spo2, noninvasive blood pressure, electrocardiogram and end tidal co2 after intubation. Intravenous line was secured. Both the groups received injection ranitidine 1 mg/kg, glycopyrrolate 4mcg/kg, fentanyl 1 mcg/kg and injection midazolam 0.03mg/kg intravenously. Then 5 minutes before induction patients randomly received either injection ondansetron 4 mg or injection ramosetron 0.3 mg intravenously. After preoxygenation, patients in both groups were induced with intravenous injection of thiopentone sodium 5 mg/kg followed by injection suxamethonium 2mg/kg. After laryngoscopy, intubation was achieved with appropriate size cuffed endotracheal tube and loading dose of injection vecuronium 0.1mg/kg was given as muscle relaxant. Anaesthesia was maintained with oxygen, nitrous oxide, sevoflurane and injection vecuronium 0.02mg/kg. Patient's ventilation was controlled on closed circuit with circle absorber. Intraoperative heart rate, blood pressure, ECG, Spo2 and Etco2 were monitored. At the end of surgery, neuromuscular block was reversed with injection neostigmine 0.05mg/kg and injection glycopyrrolate 0.01 mg/kg intravenously and subsequently the patients were extubated after thorough oropharyngeal suction.

Patients were monitored for 2 hours in the recovery room. Any instances of nausea, retching, vomiting and its frequency were noted. Nausea was graded by simplified postoperative verbal rating scale10. No nausea-0, mild nausea-1, moderate nausea-2, severe nausea-3. After 2 hours patients were shifted to ward for 24 hours observation. Rescue medication, injection metoclopramide 10 mg intravenously was given to patients with severe nausea and vomiting. Absence of nausea, retching and vomiting in postoperative period was considered as complete response.

Statistical analysis: continuous variables were presented as Mean ± SD. Categorical variables were expressed in frequency and percentages. Age, duration of surgery, vital parameters between two groups were compared by performing independent t-test. Categorical variables between two groups were compared by performing Pearson's chi- square test. For small numbers, Fisher exact test was used wherever applicable. $P<0.05$ was considered significant.Statistical software STATA version 14.0 was used for data analysis.

Results

Total 144 patients were included in the study. Demographic parameters like age, sex and ASA grades were comparable in both the groups. For both the groups no significant statistical difference was found in preoperative, intraoperative and postoperative haemodynamic parameters like pulse rate, systolic blood pressure, diastolic blood pressure and spo2. Mean duration of surgery was 95.0±20.67 minutes in groupR and 99.72±29.11 minutes in group O which was statistically non-significant.

Table 1: Demographics

Patients characteristics	Group R	Group O	P value
Age	29.94±10.80	31.36±12.05	0.458
Sex(M:F)	25:47	33:39	0.2505
Duration of surgery	95.0±20.67	99.72±29.11	0.2637
ASA(I:II)	60:12	59:13	1.00

Table 2: Incidence of nausea, vomiting, nausea and vomiting, rescue antiemetic and complete responder

Nausea	Group R	Group O	P value
0 – 2 hrs	1(1.38)	8(11.11)	0.0335
2 – 6 hrs	4(5.55)	13(18.05)	0.0395
6 – 12 hrs	7(9.72)	7(9.72)	1.00
Nausea score			
Mild	2(2.72)	6(8.30)	0.275
Moderate	5(6.94)	4(5.55)	1.00
Severe	4(5.55)	14(19.44)	0.021
Vomiting			
0 – 2 hrs	0	0	
2 – 6 hrs	0	2(2.78)	0.497
6 – 12 hrs	0	0	
Nausea and vomiting			
0 – 2 hrs	0	2(2.77)	0.497
2 – 6 hrs	2(2.77)	3(4.17)	1.00
6 – 12 hrs	0	2(2.77)	0.002
Overall PONV	11	24	0.004
Rescue antiemetic	4(5.55)	16(22.22)	0.002
Complete response	61(84.72)	46(63.88)	0.0076

After surgery in 0-2 hours, one patient in group R and eight patients in group O had nausea. This difference was statistically significant. In 2-6 hours, nausea was found in 4 patients of group R against 13 patients of group O. This difference for nausea was statistically significant. Finally in 6-12 hours, 7 patients of each group had nausea which was statistically not significant. When severity of nausea noted by nausea score, grade 3 (severe nausea) was found in 4 patients of group R and 14 patients of group O. This difference in numbers of patients was statistically significant. No statistical significance found for grade 1 and 2. Isolated vomiting noted only in 2 patients of group O in 2-6 hrs. No patients in group R experienced isolated vomiting from 0 to 4 hrs. Both nausea and vomiting was noted only in 2 patients of group R. In group O both nausea and vomitingwere found in 2, 3 and 2 patients at 0-2, 2-6 and 6-12 hours respectively. The incidence of nausea and vomiting in boththe groups together were statistically not significant.

4 patients in group R and 16 patients in group O received rescue medication, the difference was statistically significant. No specific side effects related to 5HT3 antagonists were observed but side effects like headache was noted in one patient of group R and 2 patients of group O. Dizziness was found in one patient of group O. These side effects were statistically non-significant. There were no other side effects like allergic reaction, ECG changes etc. in both the groups.

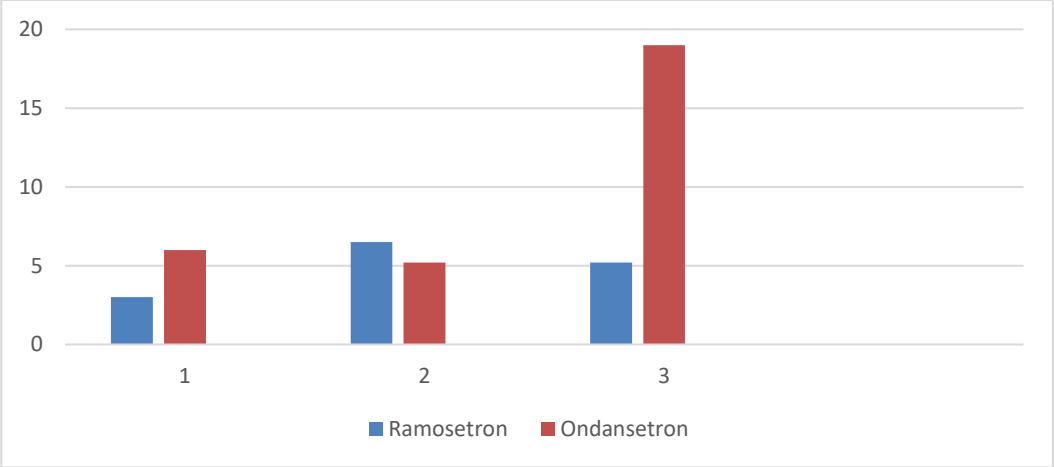

Fig 1:Severity of nausea

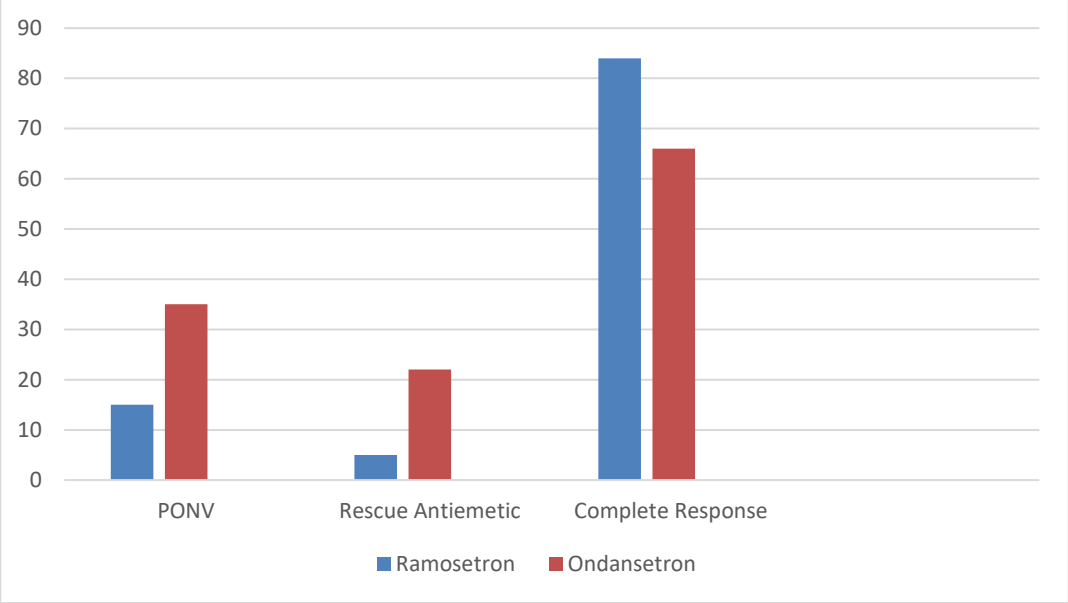

Fig 2:Incidence of PONV,Requirement of rescue antiemetic and complete response

Discussion

Postoperative nausea and vomiting (PONV) has always been concern for anaesthesiologists and surgeons due to its deleterious effects on patients. Laparoscopic surgeries are associated with high incidence of PONV. Various drugs are used to prevent PONV and there has been always quest to find better drugs to prevent PONV.Ondansetron is known 5HT3 blocker drug to prevent PONV. Various literatures reported efficient action of Ramosetron to prevent PONV. Therefore, present study was done.Patients in both the groups were comparable with respect to demographic parameters. Duration of anaesthesia and surgery were comparable. Ramosetron and ondansetron were given before induction of anaesthesia as it takes 5- 10 minutes to reach peak plasma level and hence antiemetic action effectively established before surgical incision. We used Ramosetron in dose of 0.3 mg as Fujii et al found 0.3 mg dose effective in prevention of PONV11. In most of the studies effective dose of ondansetron was 4 mg12.

In immediate postoperative period, for 2 hours of observation 1 patient of group R and 8 patients of group O reported nausea. This difference was statistically significant. Our observations correlate with study of Joo, et al in which incidence of nausea was less in Ramosetron group (9.4%) than ondansetron group (34.6%)[13]. Again statistically significant difference was found in incidence of nausea between 2 to 6 hrs. After 6 hours, no statistical difference noted for nausea in two groups. None of the patient from either group reported nausea after 12 hrs. In our study, nausea score was noted. No statistically significant difference found for mild and moderate nausea in two groups. But severe nausea was recorded in 5.55% patients of group R and 19.20% of group O which was statistically significant. Results of Ansari et al are comparable with

our study[14]. In their study they found severe nausea in 3.1% patients of group R and 9.2% in group O.

Isolated vomiting (without nausea) was noted only in 2 patients of group O at 2-6 hrs. None of the patient in group R suffered from vomiting. Nausea, retching and vomiting may be present together in an individual patient. In our study although retching was not encountered, in some patients nausea and vomiting were present together. In group R only 2.77% patients had nausea and vomiting compared to 9.72% in group O. The difference was not significant when statistical test applied. Results of Kim et al study are comparable with the results of our study[15].

An attempt was made to analyze if PONV is affected by gender of patients. We found that the frequency of PONV was higher in female patients irrespective of the antiemetic drug they received. Overall incidence of PONV was observed in 11 patients (15.27%) in group R as compared to 26 patients (36.11%) in group O. In the study by Sandip Agarkar et al incidence of PONV was lower in Ramosetron compared to Ondansetron group[16].

Some of the patients in our study suffered from PONV, in spite of administration of antiemetic drugs Ramosetron or Ondansetron. Patients who had severe nausea or vomiting or both received rescue antiemetic drug. Patients requesting antiemetic for persistent nausea received rescue drug. We used injection Metoclopramide 10 mg intravenously as rescue antiemetic drug. In our study statistically significant difference was found in number of patients receiving rescue drug in group R (5.55%) and group O (22.22%). Results are comparable with study of Joo et al.In present study prophylactic administration of intravenous injection of Ramosetron 0.3 mg and injection Ondansetron 4 mg for PONV was finally assessed. Those patients who did not suffer from PONV were labeled as complete response. Ramosetron group had 61 (84.74%) patients with complete response compared to 46 (63.88%) patients in Ondansetron group with significant statistical difference. Ryu J et al intheir study found higher complete response for Ramosetron than Ondansetron which correlates with our study[17].

Study of any drug is incomplete without mentioning the side effects. In this study known side effects of 5HT3 antagonists were searched. No known significant side effects like allergic reaction and QTc interval prolongation were observed in our study.

Conclusion

From our study we conclude that injection Ramosetron is more effective than injection Ondansetron for prevention of PONV in laparoscopic surgeries.

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