RAMOSETRON VERSUS ONDANSETRON FOR PONV IN LAPAROSCOPIC CHOLECYSTECTOMY: A CLINICAL COMPARATIVE STUDY

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ABSTRACT

BACKGROUND AND OBJECTIVES

Postoperative Nausea and Vomiting (PONV) is one of the most unpleasant and distressing symptom associated with anaesthesia and surgery. Despite the advances in our understanding of PONV, the overall incidence of emetic sequelae after a balanced anaesthetic remains between 20% and 30% approaching 70% inpatients in certain high-risk categories The objective of the study was designed to assess the efficacy and safety of ramosetron versus ondansetron in preventing and reducing the incidence of PONV after laparoscopic cholecystectomy under general anaesthesia.

METHODOLOGY

Eighty patients of ASA grades I and II between age groups of 20-60 years posted for elective laparoscopic cholecystectomy under GA were randomly selected and allocated into two groups of 40 each. Group O received ondansetron 8 mg IV and group R received ramosetron 0.3 mg IV at the time of extubation. Anaesthetic procedure was standardised and was common to all the patients. Postoperatively, the episodes of nausea, vomiting, and the need for rescue antiemetics and side effects were assessed postoperatively for 24 hours at intervals of 0-2 hours, 2-6 hours, 6-12 hours, and 12-24 hours.

RESULTS

There was no difference in the demographic data between the two study groups. The incidence of nausea, vomiting, and use of rescue antiemetic was significantly less in ramosetron group (10%, 2.5%, 2.5%) as compared to ondansetron group (42.5%, 32.5%, 10%). Both the study groups did not have significant adverse effects reflecting that both the drugs were well tolerated.

CONCLUSION

Ramosetron 0.3 mg was more effective in preventing PONV after laparoscopic cholecystectomy as compared to ondansetron 8 mg.

KEYWORDS

PONV, Laparoscopic Cholecystectomy, Ondansetron, Ramosetron.

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INTRODUCTION: Postoperative Nausea and Vomiting (PONV) is one of the most unpleasant and distressing symptom associated with anaesthesia and surgery.[1] Despite the advances in our understanding of PONV, the overall incidence of emetic sequelae after a balanced anaesthetic remains between 20% and 30% approaching 70% in patients in certain high risk categories.[2] PONV is common with rates of more than 50% associated with strabismus surgery, tonsillectomy, adenoidectomy, orchidopexy, hernia repair, and laparoscopic cholecystectomy performed under general anaesthesia. PONV may prolong recovery and increase hospital costs. Prevention and treatment of PONV help to accelerate postoperative recovery and increase patient satisfaction.

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A number of pharmacological approaches (Antihistamines, butyrophenones, dopamine-receptor antagonists) have been investigated for the prevention and treatment of PONV, but undesirable adverse effects such as excessive sedation, hypotension, dry mouth, dysphoria, hallucinations, restlessness, changes in arterial blood pressure, and extrapyramidal symptoms have been noted.

Antiemetic drugs play an important role in therapy of PONV. Presently, there is no single PONV antiemetic medication or technique that is 100% effective for all patients.[3] and a search for better drug continues. The management of PONV has improved greatly in recent years with the introduction of 5-hydroxytryptamine ($5\text{-}HT_3$) - receptor antagonists, which are widely regarded as most efficacious antiemetics available today and are currently recommended as the agents of first choice to control nausea and vomiting in most instances.[4] Findings have demonstrated that several 5-HT3 antagonists (Ondansetron, granisetron, tropisetron, dolasetron, and ramosetron) currently available are highly efficacious for PONV.

Ramosetron, a new selective 5-HT3 receptor antagonist is more potent, has higher receptor affinity, and longer

duration of action thus having theoretical advantage over ondansetron in this setting. The present study was designed to assess the efficacy and safety of ramosetron versus ondansetron in preventing and reducing the incidence of PONV after elective laparoscopic cholecystectomy surgeries under general anaesthesia.

MATERIAL AND METHODS: After obtaining institutional ethics committee approval and patient's written informed consent, the study was conducted in 80 ASA physical status I and II hospitalised patients in the age group of 20 to 60 years who were scheduled for elective laparoscopic cholecystectomy under general anaesthesia. Patients with previous history of postoperative nausea and vomiting, motion sickness, gastroesophageal reflux disease, patient who has taken any antiemetic within 3 days of surgery, patients weighing >75 kg and pregnant females were excluded from study. Preanaesthetic review of the patients was done a day before the surgery. Preoperative investigations done include: Hb, total count, differential count, blood urea, serum creatinine, serum electrolytes, ECG >40 years. The patients were advised to be nil by mouth for 6 hours. They were administered tablet pantoprazole 40 mg in the night and two hours before shifting the patient to operation theatre with sips of water.

On arrival in the operation theatre, an intravenous line was secured and maintenance fluid started. ASA standard monitors were connected. The patient were preoxygenated for 3 minutes and induced with propofol (2 mg/kg), fentanyl (2 ug/kg), paralysed with IV succinylcholine (2 mg/kg) and the patients were intubated with appropriate size endotracheal tube. Anaesthesia was maintained with sevoflurane, nitrous oxide, and oxygen. Atracurium (0.5 mg/kg) and fentanyl (1 ug/kg) were administered when needed. The patients were mechanically ventilated to keep $EtCO_2$ between 35-40 mmHg. A nasogastric tube was inserted to empty the contents of stomach. For laparoscopic surgical procedure, peritoneal cavity was insufflated with carbon dioxide to keep intra-abdominal pressure <14 mmHg. At the end of surgical procedure, group "O" patients received ondansetron 8 mg and group "R" patients received 0.3 mg ramosetron and residual neuromuscular block was adequately reversed using intravenous glycopyrrolate (0.01 mg/kg) and neostigmine (0.05 mg/kg) and extubated.

Before tracheal extubation, the nasogastric tube was suctioned and removed. Adequate postoperative analgesia cover was given.

All patients were observed postoperatively by resident doctors who were unaware of the study drug. Patients were transferred to post-anaesthesia care unit and blood pressure, heart rate, and oxygen saturation monitored. Incidence of nausea and vomiting and the side effects was assessed postoperatively for 24 hours.

The following findings were recorded at the following intervals:

- 0-2 hours, 2- 6 hours, 6- 12 hours, and 12-24 hours in the postoperative period.
- If there were one or more episodes of PONV during first 24 hours rescue antiemetic dexamethasone 4 mg IV was given.

Postoperative Vital Score (PVS): Heart rate, noninvasive blood pressure, and respiratory rate were considered as the measures of postoperative vitals.

Scores:

2- When three parameters were within 20% of the preoperative value.

1- If any one or more of the three parameters ranged between 20-40% of the preoperative value.

0- If at least one of the three parameters was more than 40% of preoperative value.

The sample size was calculated with alpha of 0.05 and power of 0.8, which revealed 40 patients in each group. It was decided to include 40 patients in each group with total of 80 patients for this study. Demographic data, (Age, weight, height, body mass index), vascular access time are compared using one-way analysis of variance (ANOVA). Sex distribution, complications were compared by using chi-square test. P value less than 0.05 is considered significant and p <0.001 is considered highly significant.

RESULTS: A total of 80 patients were included in the study. The demographic data of the patients didn't show statistical significance between the two groups.

Time Interval	Group O	Group R
0-2 hr.	2.00	2.00
2-6 hr.	2.00	2.00
6-12 hr.	2.00	2.00
12-24 hr.	2.00	2.00

Table 1: Postoperative Mean Vital Score

There was no difference in haemodynamic changes between the two groups as compared to preoperative value, both during intraoperative and postoperative period.

	Group O				Group R				P value
	Present		Absent		Present		Absent		
	No.	%	No.	%	No.	%	No.	%	
Nausea	17	42.5	23	57.5	04	10	36	90	<0.005
Vomiting	13	32.5	27	67.5	01	2.5	39	97.5	<0.001
Rescue antiemetic	04	10	36	90	01	2.5	39	97.5	<0.005

Table 2: Overall Incidence of Postoperative Complication

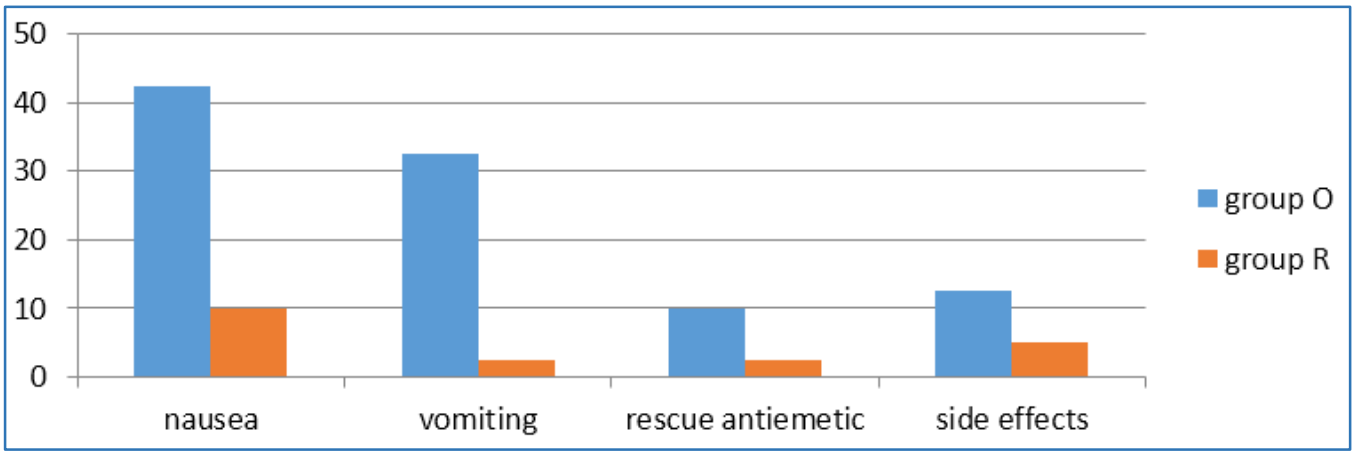

Fig. 1: Present Percentage

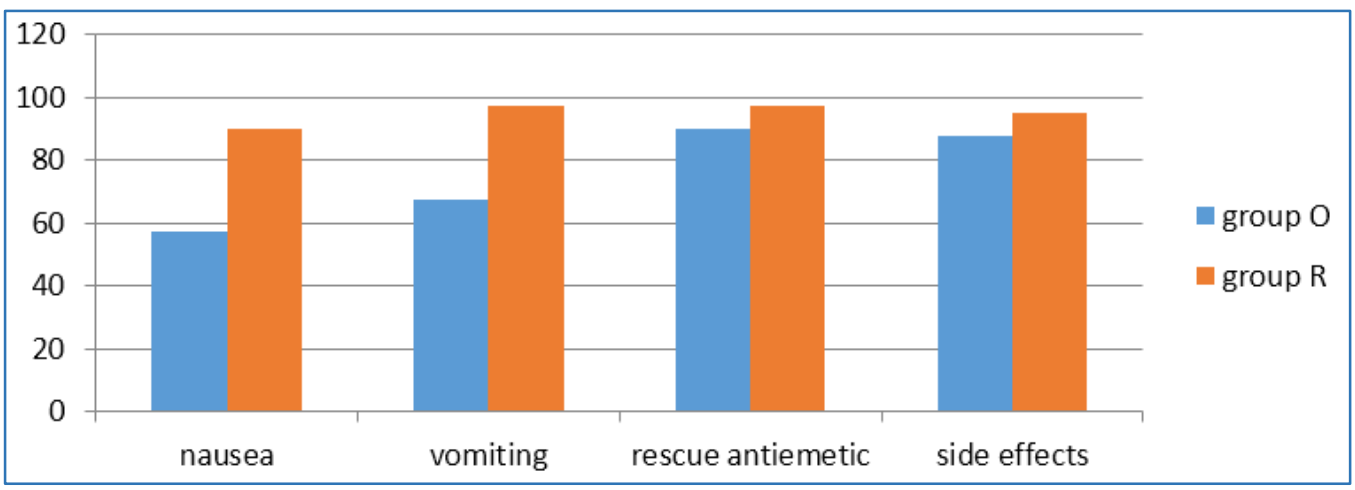

Fig. 2: Absent Percentage

In ondansetron group, nausea was 42.5% and 10% in ramosetron group. Postoperative nausea scores were lower in the ramosetron group than the ondansetron group at all the times till 24 hours, which is statistically significant (<0.005). In ramosetron group, 97.5% of patients were emesis free while in ondansetron group 67.5% patients experienced no emesis. Only 2.5% of patients in ramosetron group had vomiting compared to 32.5% of ondansetron group. It is highly significant statistically (0.001). In ondansetron group, 10% patients received rescue antiemetic and in ramosetron group 2.5% of patients received rescue antiemetic, which is statistically significant (0.005).

DISCUSSION: Postoperative nausea and vomiting is one of the most unpleasant and distressing symptom following anaesthesia and surgery.[1] Patients undergoing major laparoscopic surgery are especially prone to PONV with reported incidence of 50-75%.[4] Furthermore, severe postoperative emesis may lead to dehydration, electrolyte imbalances, venous hypertension, bleeding, haematoma formation, suture dehiscence, oesophageal rupture, aspiration pneumonitis, delayed Post-Anaesthesia Care Unit (PACU) discharge, and unanticipated hospital admission, leading to increased healthcare costs.[2]

Of the many different modes of intervention to prevent PONV, antiemetic drugs play an important role. Metoclopramide, domperidone, phenothiazines, butyrophenones, anticholinergics, and antihistamines are the commonly used drugs to prevent PONV. Even though these drugs have either alone or in combination had been proved effective to a certain extent, a search was on for newer antiemetic drugs, which led to the invention of 5-HT_3 antagonist. Studies comparing many of these drugs with ramosetron have been carried out in the recent years. It was evident that ramosetron was highly or equally effective in preventing PONV in some studies. It is reported that incidence of side effects were negligibly low or nil with ramosetron.

Where as with most of the other drugs, the incidence of side effects are significantly high like extrapyramidal symptoms (Metoclopramide, droperidol, phenothiazines), sedation (Phenothiazines, antihistamines, droperidol), hypotension (Promethazines, droperidol), dry mouth (Atropine, scopolamine, antihistamines), and dysphoria (Scopolamine, droperidol). Many factors have been thought to contribute to the PONV. These factors include age, gender, obesity, gastroparesis, anxiety, history of motion sickness, and PONV. Patients with low threshold for vomiting like gastroparesis, motion sickness, or pervious PONV and obesity were excluded from our study.

In this study, we compared the efficacy and safety of IV ramosetron and ondansetron as prophylaxis for PONV in patients undergoing laparoscopic cholecystectomy under general anaesthesia. Onset of nausea and vomiting is often associated with decreased blood flow secondary to systemic hypotension. It is proposed that hypoxaemia at the vomiting centre and vagal stimulation plays a key role in PONV. Tachycardia and hypertension are the reflection of pain, which in turn can influence the incidence of emesis in early postoperative period. In our study, scoring system was used to quantify the haemodynamic changes during surgery and in postoperative period. There was no difference in haemodynamic changes between the two groups as compared to preoperative value both during intraoperative and postoperative period. The postoperative pain scores and requirement of analgesic were essentially comparable without any significant difference between the groups.

Fujii Y et-al in 1999 compared ramosetron versus granisetron for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. In this randomised, double-blind study, 80 female patients received 3 mg granisetron and 0.3 mg ramosetron IV (n=40 of each) at the completion of surgery. The response found that the incidence of patients with no complaints PONV during the first 24 hrs. after anaesthesia was 85% with granisetron and 93% with ramosetron respectively (p=0.241); the corresponding incidence during the next 24 hours (24-48 hours) after anaesthesia was 63% and 90% (p=0.004). This study showed ramosetron was more effective than granisetron for prevention of PONV during 0-48 hours after anaesthesia for laparoscopic cholecystectomy.[5]

Ansari MM, Siddiqui OA, Haleem S, Varshney R, Akhtar S, Khan FA (2010) compared in patients who underwent laparoscopic cholecystectomy following intravenous administration of ondansetron (4 mg) or ramosetron (0.3 mg) at the end of surgery. The efficacy as well as side effects of ondansetron and ramosetron were documented and compared. Results: 130 adult females undergoing laparoscopic cholecystectomy were studied 65 patients in each of the two groups. In first 24 hours after surgery, complete response (No PONV) was observed in patients and concluded that ramosetron was found to be safe and more effective antiemetic than ondansetron in patients undergoing laparoscopic cholecystectomy.[6] Ryu J, So YM, Hwang J, Do SH (2010) compared ramosetron versus ondansetron for the prevention of postoperative nausea and vomiting in a study of 120 patients scheduled to undergo laparoscopic cholecystectomy and concluded that ramosetron 0.3 mg is more effective than ondansetron 4 mg for the prevention of PONV.[7]

In our study, 97.5% of ramosetron group patients were emesis free while in ondansetron group 67.5% patients experienced no emesis. Only 2.5% of patients in ramosetron group had vomiting, compared to 32.5% of ondansetron group, it is highly significant statistically. Severity of vomiting was also less in ramosetron group than ondansetron group.

Only one patient of group R had more than 1 emetic episode while 4 patients of group O had this, which is highly significant statistically. Sarbari Swaika, Anirban Pal, Surojit Chatterjee, Debashish Saha, Nidhi Dawar (2011) conducted a randomised, double-blinded study, 87 female patients, (ASA I and II) undergoing elective laparoscopic cholecystectomy under general anaesthesia were randomly allocated into three equal groups, the ondansetron group (8 mg IV; n=29), the ramosetron group (0.3 mg IV; n=29), and the palonosetron group (0.075 mg IV; n=29), and the treatments were given just after completion of surgery before extubation. The incidence of complete response (Patients who had no PONV and needed no other rescue antiemetic medication), over 24 hours after surgery were evaluated and concluded that ramosetron 0.3 mg IV was more effective than palonosetron 0.075 mg and ondansetron 8 mg in the early postoperative period.[8]

In our study, 'No Nausea' in ondansetron group was 40% and 66% in ramosetron group. Postoperative nausea scores were lower in the ramosetron group than the ondansetron group at all the times till 24 hours, but the scores did not achieve statistical significance. There was no significant difference in the incidence of nausea between the two groups both in early and late postoperative period. When the severity of nausea was compared between the two groups, they were found to be significantly less in ramosetron group than in ondansetron group. When major nausea episodes were considered (Score of 2 or more), significantly less number of patients in group R had 13% major nausea and 40% in group O, ($p < 0.05$). This study proved that ramosetron significantly reduced the incidence of PONV at and after 2 hour postoperatively than ondansetron.

CONCLUSION: We concluded that prophylactic therapy with ramosetron is highly efficacious and safe than ondansetron in preventing PONV in patients undergoing laparoscopic cholecystectomy with general anaesthesia.

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