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COMPARISON OF ONDANSETRON V/S RAMOSETRON FOR PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING IN LAPROSCOPIC SURGERIES (A STUDY OF 100 CASES)

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ABSTRACT

Postoperative nausea and vomiting (PONV) is one of the most common and distressing complications after anaesthesia and surgery, and may lead to serious postoperative complications. Patients undergoing laparoscopic surgery have been associated with high risk for developing PONV. This study was carried out on 100 patients of either sex from the age group 18-60 years of ASA risk I and II undergoing general anesthesia for various surgical procedure. Patients with history of motion sickness, past history of PONV, pregnancy , and who are menstruating, those who had received any anesthetic in last 24 hrs and body mass index >35 were excluded from the study. The patients were divided into 2 groups, classified as Group (O) inj ondansetron 4mg iv., Group (R) inj ramosetron 0.3mg iv.The drug was administered 5 min after induction in all the groups. Patients were monitored for emetic episodes, severity of nausea, requirement of rescue antiemetic and vital signs for immediate, 1 hour, 2-6 hour, 6-12 hour and 12-24 hour post-operative period that began when the patient responded to a vocal command after extubation. Metoclopramide 10mg/kg IV was given as a "rescue" antiemetic for vomiting or persistent nausea, if 2 or more episodes occurred within 24 hrs.Statistical analysis was performed with One-way analysis of variance (ANOVA) and Student's t-test for continuous variables with the use of EPI INFO software. Discrete variables, such as frequency of PONV and incidence of adverse effects were compared with Chi-Square test. A 'p' value <0.05 was considered significant. Ramosetron is highly effective for prophylaxis of PONV in laparoscopic surgeries and due to its longer duration of action, single dose of Ramosetron is highly effective for prevention of PONV up to 24 hrs postoperatively.

INTRODUCTION

Postoperative nausea and vomiting (PONV) is one of the most common and distressing complications after anaesthesia and surgery, and may lead to serious postoperative complications.

The overall incidence of PONV has been reported to be between 20% and 30%, but can increase up to 80% in high-risk patients. Patients undergoing laparoscopic surgery have been associated with high risk for developing PONV.

Laproscopy is a procedure allowing endoscopic access in peritoneal cavity by insufflation of gas and creating space between abdominal viscera and anterior abdominal wall. Anti-emetics are the main stay therapy for PONV .The main pharmacological classes of drugs used in the treatment are cholinergic-muscarinic, dopaminergic, histaminic or seratonergic ($5HT_3$ antagonists). Besides this dexamethasone is also considered very effective antiemetic in many situations .Combination of antiemetics as a multi

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modal therapy may sometimes be needed to control PONV successfully. Despite significant advances in the delivery of general anaesthesia, post-operative nausea and vomiting [PONV] continues to be a 'Big little problem for surgical patients.

Increase intra-abdominal pressure due to pneumoperitoneum may results in aspiration of gastric content. Anaesthetic drugs can lead to vomiting.

Many complex procedures are now a day's carried out on 'day care' basis which make PONV a significant problem. Gynaecological, middle ear, laparoscopic, and ophthalmic surgery have more risk of PONV .Morbidity related to PONV may lead to delayed discharge and increase the cost of treatment.

For PONV prevention, selective serotonin 5-hydroxytryptamine type 3 (5-HT3) receptor antagonists are considered one of the first-line therapy because of their efficacy and few side-effects compared with other antiemetics. Most research on the 5-HT3 receptor antagonists has been on ondansetron, and its antiemetic efficacy has been well established in chemotherapy-induced emesis and the prevention and treatment of PONV.

Aims and Objectives:

The present study was carried out to compare the efficacy and safety of ondansetron and ramosetron for prevention of post-operative nausea and vomiting in laparoscopic surgery with the following aims.

- To evaluate the efficacy of the Ondansetron and ramosetron in preventing post-operative nausea and vomiting in laparoscopic surgery.
- To compare the antiemetic efficacy of Ondansetron and ramosetron for prevention of post-operative nausea and vomiting following the laparoscopic surgery.
- To asses severity of nausea with both agents in different time periods up to 24 hours post operatively.
- To observe the complications of both the agents.

METHODOLOGY

This study was carried out on 100 patients of either sex from the age group 18-60 years of ASA risk I and II undergoing general anesthesia for various surgical procedure.

Patients were pre-operatively assessed a day before the surgery. Patients with history of motion sickness, past history of PONV, pregnancy , and who are menstruating, those who had received any anaesthetic in last 24 hrs and body mass index >35 were excluded from the study. Patients were weighed, physical and systemic examinations were done. Written and informed consent was taken after explaining the patients about the procedure. No pre-medication was given in the ward. Baseline pulse and BP were recorded in the pre-operative room.

The patients were divided into 2 GROUPS, classified as Group (O) inj ondansetron 4mg iv, Group (R) inj ramosetron 0.3mg iv.The drug was administred 5 min after induction in all the groups.

After taking the patient on the OT table, IV line was established. Monitoring in the form of ECG, SpO_2 and NIBP were applied and parameters were noted.

Pre medication was given intravenously in the form of inj. Glycopyrrolate (0.004 mg/kg), inj. Midazolam (0.02 mg/kg) and inj. Fentanyl (2 µg/kg). In group (0) inj. Ondensetron 4 mg i.v. and In group (R) inj. ramosetron 0.075 mg in 10 ml in 0.9% saline given.

Patients were pre-oxygenated with 100% O_2 for 3-5 min by bain's circuit. General anesthesia was administered with inj.Thiopentone Sodium 5-6mg/kg IV and intubation was facilitated using inj.Scoline 2mg/kg IV. Patients were ventilated with 100% O_2 and intubated with appropriate size oral portex cuffed endotracheal tube. Bilateral air entry was checked and tube was fixed. Nasogastric tube was inserted and stomach content suctioned. Anesthesia was maintained with 50% O_2 + 50% N_2O + Sevoflurane and Vecuronium Bromide (0.08mg/kg) IV was used as non-depolarising muscle relaxant. Intra-operative pulse, BP, SpO2, ECG and $ETCO_2$ were monitored and documented at the time of induction then every 15mins up to 1 hour then every 30mins till the end of surgery. Inj.Diclofenac Sodium (2mg/kg) IV was given as an analgesic at the end of surgery. After completion of surgery, neuromuscular blockade was reversed with inj.Glycopyrrolate (0.008mg/kg) and inj.Neostigmine (0.05mg/kg) IV. Extubation was done after adequate oropharyngeal and endotracheal suctioning was done and patients were extubated.

Patients were monitored for emetic episodes, severity of nausea, requirement of rescue antiemetic and vital signs for immediate, 1 hour, 2-6 hour, 6-12 hour and 12-24 hour post-operative period that began when the patient responded to a vocal command after extubation. Metoclopramide 10mg/kg IV was given as a "rescue" antiemetic for vomiting or persistent nausea, if 2 or more episodes occurred within 24 hrs. Adverse events (rash, headache and diarrhea) within 24 hrs of surgery were also assessed and noted and treated. Pain score and sedation score were also noted.

An emetic episode was defined as a vomiting or retching events or combination of these events that occurred in rapid succession. A patient who had no emetic episodes during the specified time period was described as emesis –free. Complete response was defined as no PONV and no administration of rescue antiemetic medication during the first 24 hours of anesthesia.

Nausea and vomiting were evaluated as:-0 - Complete response, 1- Nausea, 2-Retching, 3 -Vomiting

The efficacy of the study medication was assessed in terms of percentage of patients having complete response and mean PONV score.Statistical analysis was performed with One-way analysis of variance (ANOVA) and Student's t-test for continuous variables with the use of EPI INFO software. Discrete variables, such as frequency

of PONV and incidence of adverse effects were compared with Chi-Square test. A 'p' value <0.05 was considered significant.

RESULTS

Comparative study between use of ondansetron and ramosetron to prevent post-operative nausea and vomiting was done among 100 patients of either sex undergoing different type of laparoscopic surgeries under general anaesthesia. The following observation and results were recorded.

Demography

Table 1. Study participant demographic data

Demography Parameter	Group (O)	Group (R)	P-Value
Age (M ± SD)	36.62±14.35	36.67±12.05	0.95
Sex F/M	35/15	30/20	0.40
Weight(M±SD)	53.22±12.63	52.90±13.33	0.90
Duration of anesthesia(M±SD)	79.66±12.00	81.66±23.60	0.60

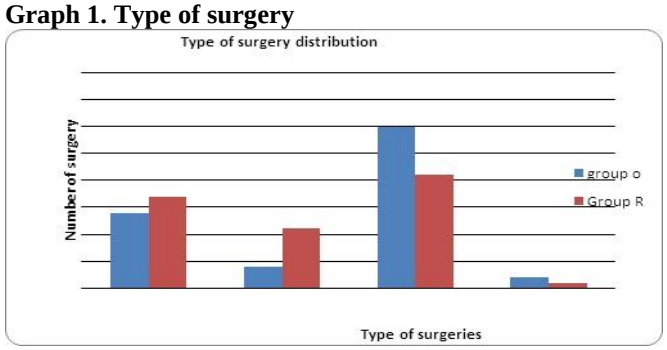
In our study, both the groups were comparable with regards to age, sex, weight and duration of anesthesia (P>0.05) (table 1).

Table 2. Rescue Antiemetic

Rescue antiemetic	Group (O) No. of patients	Group (R) No. of patients	P-Value
Immediate	1	0	0.5
1st hr	1	0	0.3
2-6 hrs	1	0	0.3
6-12 hrs	0	1	0.24
12-24 hrs	2	1	0.8

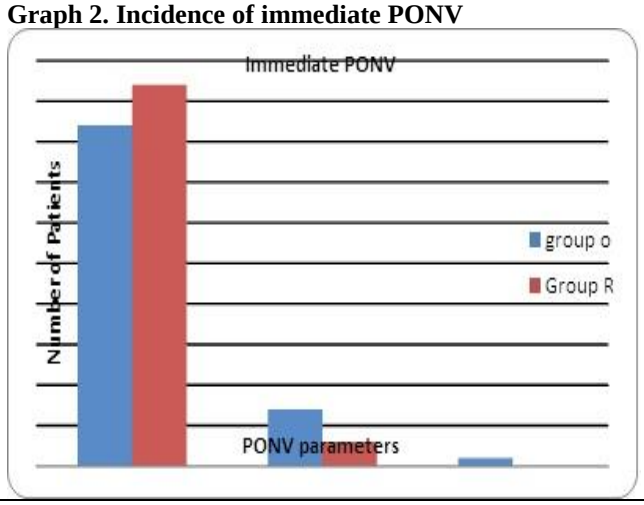
In group (O), a total of 3 patients received rescue antiemetic treatment. None of the patients in group (p) received antiemesis treatment. However, there was no statistical significant difference between two groups (P>0.05).

Graph 1. Type of surgery

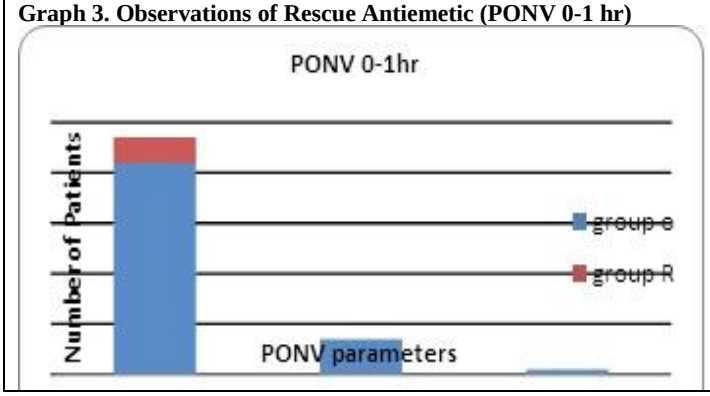


Both groups were comparable with regards to type of surgery. In group (O), Laparoscopic cholecystectomy was done in 30 patients where as 21 in group (R), and laproscopic appendicectomy was done in 14 patients in group (O) and 17 patients in group (R), so both groups are comparable(P>0.05).

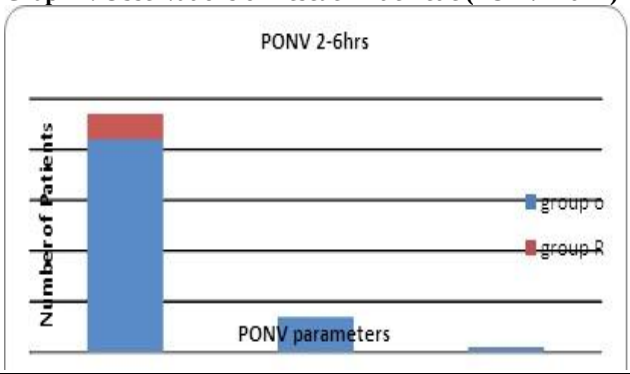
Graph 2. Incidence of immediate PONV



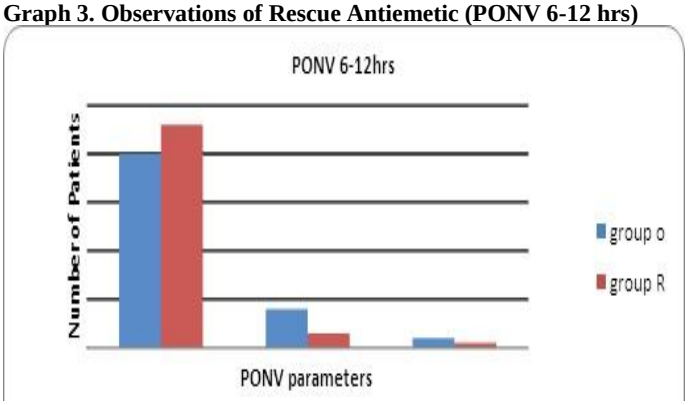
Graph 3. Observations of Rescue Antiemetic (PONV 0-1 hr)



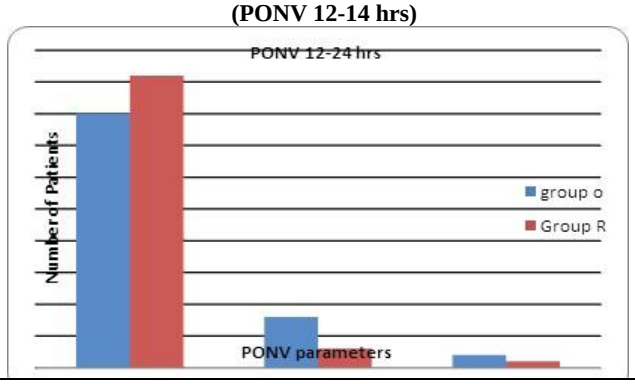
Graph 4. Observations of Rescue Antiemetic (PONV 2-6 hr)



Graph 3. Observations of Rescue Antiemetic (PONV 6-12 hrs)



Graph 3. Observations of Rescue Antiemetic (PONV 12-14 hrs)



DISCUSSION

Ramosetron is highly effective for prophylaxis of PONV in laparoscopic surgeries and due to its longer duration of action, single dose of Ramosetron is highly effective for prevention of PONV up to 24 hrs postoperatively.

In 1998, Yoshitaka Fujii concluded that prophylactic therapy with a combination of granisetron and dexamethasone was more effective than each antiemetic alone for prevention of PONV after middle ear surgery. In 1999, Yoshitaka Fujii evaluated the efficacy of two antiemetics given orally. Granisetron (40µg/kg) and perphenazine (70 µg/kg) were given for prevention of PONV in children posted for (given one hour before going for surgery) tonsillectomy. The complete response was 86% and 60% in granisetron and perphenazine group respectively for 24 hours. In 1999, Janknegt R et al concluded that granisetron and granisetron plus dexamethasone therapy was more effective than droperidol for prevention of PONV in abdominal, gynaecological and breast surgery. In 1999, Yoshitaka Fujii, compared the efficacy of granisetron and ramosetron for preventing postoperative nausea and vomiting in major gynecologic surgery. Prophylactic therapy with ramosetron was more effective than granisetron for preventing postoperative nausea and vomiting 24–48 h after anesthesia. In 2000, Yoshitaka Fujii observed the effect of granisetron 40µg/kg, droperidol 20µg/kg and metoclopramide 0.2mg/kg after experiencing PONV during first 3 hrs after recovery from anaesthesia in the patients undergoing laparoscopic cholecystectomy. Complete control was achieved in 88% patients with granisetron, 60% with droperidol and 55% with metoclopramide.It suggest that granisetron is more effective than other antiemetics. In 2002, Biswas compared granisetron plus dexamethasone to granisetron alone and concluded that the combination increases the chance of a complete response. In 2002, Noda et al concluded ramosetron 0.3mg i.v was effective in cisplastin induced vomiting. In 2003, D Bhattacharya concluded that granisetron is much more effective than ondansetron to prevent PONV following day care gynaecological laparoscope. In 2004, K Hanaoka concluded that granisetron is well tolerated and more effective than placebo in the prophylactic control of nausea and vomiting after surgery and suggested the optimal dose as 1mg. In 2005, Parhaizgar Khan et al studied the effect of granisetron ,ondansetron and propofol for prevention of emesis after gynaecological laparoscopy and concluded that prophylactic administration of iv granisetron 40µg /kg is effective and superior to ondansetron and propofol in preventing nausea and vomiting after gynaecological laparoscopic surgical procedures . In 2005, Fuji Y, Tanaka concluded 6microgram/kg dose of ramosetron is sufficient, but 3miro gram/kg is insufficient for preventing ponv during 0-48hrs after strabismus surgery, increasing dose to 12microgram/kg of ramosetron provides no additional benefit. In 2006, Paul F White found no significant difference between oral granisetron (1mg) and i.v ondansetron (4mg iv) with respect to their efficacy for preventing PONV in patients undergoing either minor or major laparoscopic procedure. Hence i.v ondansetron was a more cost effective prophylactic than oral granisetron .In 2007 Senthil Kumar S et al suggested that prophylactic antiemetic therapy with combination of granisetron 40µg/kg and dexamethasone 8mg was more effective than granisetron alone for the prevention of PONV after general anaesthesia . In 2007, indu sen et al observed that in children premedicated with clonidine both i.v granisetron and dexamethasone were efficacious in reducing incidence of ponv in strabismus surgery. In 2008, Yoshitaka fuji observed antiserotonins are more effective than traditional antiemetics, but this are not entitrely effective, combination therapy with traditional antiemetic is highly effective in prophylaxis aganist PONV. In 2009,Waleed riad et al observed prophylactic administration of either granistron, ondensetron, midazolam combined with dexamethasone decreases the incidence of PONV following strabismus surgery in paediatrics, all combination are equally effective. In 2009, SI Kim et al concluded ramosetron 0.3mg i.v. was as effective as ondanstron in decreasing incidence of ponv durin first 24hrs after gynaecological surgery. In 2011, Hala MB et al concluded prophylactic use of granisetron is effective in preventing post-operative retching and vomiting in strabismus repair in children as compared to dexamethasone. In 2011, Won Oak Kim et al, concluded

prophyctic effect of 0.3mg ramosetron is effective and safe in children and adults in terms of prevention of ponv. In 2011, Dong Chul Lee et al, found ramostron to be effective at reducing incidence of ponv in women underwent total thyroidectomy with propofol based TIVA. In 2012, So Young Yang et al concluded combination of ramosetron and dexamethasone significantly reduced incidence of vomiting compared to ramosetron alone after surgery.

In conclusion Ramosetron is highly effective for prophylaxis of PONV in laparoscopic surgeries and due to its longer duration of action,single dose of Ramosetron is highly effective for prevention of PONV up to 24 hrs postoperatively.

Though ramosetron is expensive than ondansetron but it appears to be more cost effective than ondansetron due to its longer duration and decrease need for observation for PONV.

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