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POST-OPERATIVE NAUSEA VOMITING IN LAPAROSCOPIC CHOLECYSTECTOMY: A PROSPECTIVE, RANDOMIZED, DOUBLE BLIND COMPARATIVE STUDY OF RAMOSETRON AND ONDANSETRON

Anaesthesiology

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ABSTRACT

Introduction: Postoperative nausea and vomiting(PONV) is a distressing complication after anaesthesia, which should be prevented to accelerates postoperative recovery and patient satisfaction. Therefore this study was conducted to compare the efficacy and safety of ramosetron and ondansetron in patients undergoing standard laparoscopic cholecystectomy

Methodology: This prospective, randomized, double blinded comparative study was carried out at department of Anaesthesiology, Medanta Abdur Razzaque Ansari Memorial Weavers' Hospital, Ranchi. Total of 168 patients undergoing laparoscopic cholecystectomy under general anaesthesia were randomized into group O and group R based on a computer generated random table to receive Ondansetron 4 mg IV and ramosetron 0.3 mg IV respectively. Patients were closely monitored for first 24 hour post-surgery for post-operative nausea and vomiting.

Results: It is concluded that, prophylactic administration of single dose of ramosetron 0.3 mg iv has better efficacy and is more potent than single dose ondansetron 4 mg iv in reducing post-operative nausea and vomiting in patients undergoing laparoscopic cholecystectomy.

KEYWORDS

Ramosetron, Ondansetron, PONV, Laparoscopic Cholecystectomy

Introduction:

Postoperative nausea and vomiting (PONV) is one of the most common and distressing adverse events experienced by patients after anaesthesia.[1] Around 30% patients undergoing surgery experience PONV;10% with zero known risk factors and 61%-79% in patients with multiple risk factors[2] Increased patient discomfort due to PONV, prolonged recovery, delay patient discharge and increase hospitalization costs remains a concern for patients, surgeons and anaesthesiologists.[3-4] Thus preventing and treating PONV accelerates postoperative recovery and patient satisfaction.[5] Laparoscopic cholecystectomy(LC) is a commonly performed surgery and the incidence of PONV in these patients is reported to be 53%-72%.[6,7] LC requires carbon dioxide insufflation resulting in peritoneal distension, increasing peritoneal pressure which is a very important risk factor causing nausea and vomiting.[8]

Selective serotonin [5 Hydroxytryptamine Type-3 (5 Ht3)] receptor antagonists like ondansetron, granisetron and newer drug such as ramosetron are devoid of undesirable side effects with proven efficacy, making them first line drugs in preventing PONV.[1,9-11]Recently, studies showed ondensetron to have less anti-nausea and more anti-vomiting efficacy[12] with concerns in cardiac safety[13] whereas ramosetron has higher potency and prolonged activity with better safety.[14–16]There are only few studies[3,17–19] which have directly compared efficacy of ramosetron and ondansetron in post-operative period and revealed conflicting results. Therefore this study was conducted to compare the efficacy and safety of ramosetron and ondansetron for prevention of PONV in patients undergoing LC.

Methodology:

After obtaining Ethical Committee approval, study was conducted at Department of Anaesthesiology, Medanta Abdur Razzaque Anasari Memorial Weavers` Hospital, Ranchi, Jharkhand, which is a super specialty, tertiary care centre. The sample size for this study was calculated for assessing the difference between two means at power-90% and confidence interval-95% (alpha 0.05) with ratio of sample in each group to be 1:1, using the mean values of PONV at 6 hours post-operation as found in study conducted by Banerjee D etal[17]. Thus sample size in each group was 84. Thus study included 168 subjects of 18 - 60 years of both sexes undergoing LC under general anaesthesia with American Society of Anaesthesiologist (ASA) class 1 and 2. Patients not willing to take part in study, those with history of motion sickness, gastro-oesophageal reflux disease, diabetes mellitus, cardiovascular disease, on chronic steroid therapy or receiving antiemetic within 24 hour before surgery were excluded from the study.

The selected patients were randomly divided into group O and group R based on a computer generated random table. Patient and anesthesiologist were blinded to the drug. Ondansetron 4 mg IV was given to the patient belonging to group O and ramosetron 0.3 mg IV was given to the patient belonging to group R. Medications were prepared by a paramedic who was not involved in study in identical 5ml syringes and was administered by the blinded anesthesiologist according to the randomization list and was given just before the induction of surgery.

All the study patients were subjected to routine pre-anaesthetic evaluation in the evening before surgery and overnight fasting was maintained. The procedure was explained to the patients and informed consents were obtained. A well-defined anaesthesia regimen was used in all the patients, induced with inj. Propofol 2 mg/kg and inj. fentanyl 12µg/kg. Intubation was facilitated by using inj. Atracurium 0.5mg/kg. A nasogastric tube was inserted after securing the endotracheal tube in place. Anaesthesia was maintained with nitrous oxide (66%) and isoflurane (12%) in oxygen. Intraoperative muscle relaxation was maintained with inj. Atracurium. At the end of the surgery, inj. Diclofenac 75 mg IV was given before the reversal of neuromuscular blockade to prevent the postoperative pain. Muscle relaxation was reversed with inj. neostigmine (0.04 mg/ kg) and inj. Glycopyrrolate (0.01 mg/kg). Nasogastric suction was done to remove any residual gastric contents. All port sites was infiltrated with inj. Bupivacaine (0.25%).

All subjects were closely monitored for first 24 hour post-surgery for study variables by blinded investigator. The incidence and severity of post-operative nausea, vomiting and retching, need for rescue drug and need for rescue antiemetic were recorded over the next 24 hours and was divided into two intervals early as 0 – 6 hours and late as 6 – 24 hours.[18] Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit. Vomiting was defined as the forceful expulsion of gastric contents from the mouth; and retching as the laboured spasmodic, rhythmic contraction of the abdominal muscles without expulsion of gastric contents.[1] Rescue antiemetic consisting of Inj. metoclopramide 0.15mg/kg was administered as an additional rescue antiemetic in patients with two or more than two episodes of vomiting and/or significant nausea at any time within 24 hour post-operation.

Statistical Analysis: Data was entered into MS Excel and analysed using Epi Info version7.1 and Open Epi Online Calculator Version3.03a. Following calculation of descriptive statistics, comparison of both groups for normally distributed continuous

variables was done using mean values by applying z test; and for nominal categorical data using proportions by applying Chi-Square test. P value <0.05 was considered as level of significance.

Results:

The characteristics of study subjects are shown in table 1. The demographic characteristics of the study subjects in both the groups were comparable. There was no statistically significant difference between both groups in MPS, ASA grading, duration of anaesthesia and surgery.

Table 1: Characteristics of study subjects

Patient Characteristics	Group R	Group O	P value
Age (in years)	44.8 (±7.59)	45.9 (±6.37)	0.31
Gender			0.87
Male	49(58.33%)	48(57.14%)	
Female	35(41.67%)	36(42.86%)	
Weight (in kg)	67.27(±9.40)	66.86 (±9.17)	0.82
ASA			0.09
I	62(73.81%)	52(61.9%)	
II	22(26.19%)	32(38.1%)	
Mallampmati score(MPS)			0.69
1	55(65.48%)	51(60.71%)	
2	26(30.95%)	28(33.33%)	
3	03(03.57%)	05 (05.96%)	
Duration of Anaesthesia	104.46(±12.82)	101.36(±16.10)	0.16
Duration of Surgery	83.15(±12.43)	79.16(±14.86)	0.06

Data is represented as Mean (±standard deviation), or Number (Percent)

Table 2 shows the comparison of incidence of PONV and retching in both groups. The incidence of nausea, vomiting and retching was consistently lower in Group R in comparison with Group O in both early and late phase and this difference was statistically significant except for retching in late phase.

Table 2: Comparison of incidence of nausea, vomiting and retching.

Incidence	Group R	Group O	P value
Nausea	08(09.52%)	20(23.8%)	0.01*
Early (0-6hr)	09(10.71%)	18(21.43%)	0.05*
Post (6-24hr)			
Vomiting	07(08.33%)	16(09.05%)	0.04*
Early (0-6hr)	06(07.15%)	15(17.85%)	0.03*
Post (6-24hr)			
Retching	07(08.33%)	18(21.43%)	0.01*
Early (0-6hr)	08(09.52%)	16(19.05%)	0.07
Post (6-24hr)			
Need of rescue drug	03(03.57%)	06(07.14%)	0.30

* Significant

Table 3 shows that incidence of adverse side effects was low in both the group with no serious effects.

Table 3: Comparison of adverse side effect.

Adverse side effects	Group R	Group O
None	80(95.24%)	78(92.86%)
Headache	03(03.57%)	04(04.76%)
Diarrhoea	01(01.19%)	01(01.19%)
Dizziness	00(00.00%)	01(01.19%)
P value	0.51	

Discussion:

In the present study, both groups were comparable with no statistically difference with regards to mean age, gender, weight, MPS and ASA grading. Also duration of anaesthesia and surgery was comparable, signifying that both groups had similar baseline characteristics. This finding was supported by many other authors too.[3,17,20-23]

There was statistically significant difference between incidence of both early and late onset nausea in group R and group O with p value 0.01 and 0.05 respectively. Thus it was seen that ramosetron was more effective in preventing both early and late onset nausea in comparison to ondansetron. Authors like Banerjee D *etal*[17], Chauhan D *etal*[20] Kaja S *etal*[22], Fujii *etal*[23], Pandharpukar S *etal*[24], Das A *etal*[25] and Swaika S *etal*[26]. On the contrary to our study, some authors[18,27] could not establish a statistically significant difference between the drugs for preventing nausea.

The incidence of vomiting was higher in subjects given ondansetron when compared against ramosetron. This was supported by statistically significant difference of p value 0.04 and 0.03 for 0–6 hour and 6–24 hour respectively. This findings of our study was in concordance with the studies conducted by Chauhan D *et al*[20], Fujii Y *et al*[23], Pandharpukar S *et al*[24], Das A *et al*[25] and Bansal S R *et al*[28].

Comparatively higher number of subjects from group O needed rescue drug, but this difference was not statistically significant with p value 0.30, because rescue drug was administered in this study only after >2 episodes of vomiting. Similar finding were noted by many other studies,[3,18,20,26] whereas some others reported contradictory to our study.[22,24,26,28] There was no significant difference between both the drugs regarding adverse effects, p value 0.51, signifying comparable safety profile of ramosetron and ondansetron. This finding was in concordance with majority of other studies.[3,21,22,28]

From our results we could note that incidence of PONV was lower in group R, which could be due to high plasma concentration of ramosetron. Ramosetron was more effective even in preventing late onset PONV, because it has longer receptor antagonizing effect compared with older 5-HT3 receptors antagonists[29] with longer elimination half-life; ramosetron-9hr and ondansetron-3.5hr.[14,30] Due to these pharmacological properties, ramosetron, is more potent with a longer duration of action in comparison to ondansetron.[14,27,31]

Conclusion:

Prophylactic administration of single dose of ramosetron 0.3 mg iv has better efficacy and is more potent than single dose ondansetron 4 mg iv in reducing the incidence of PONV over the first 0 – 6 hour and also in subsequent 6 – 24 hour, in patients undergoing laparoscopic cholecystectomy under general anaesthesia; with comparable safety profile.

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