

# Post-operative Nausea and Vomiting: Comparison of the Role of Ramosetron and Ondansetron

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## Abstract

**Background:** Post-operative nausea and vomiting (PONV) is the most common symptom having incidence of 53-72% in laparoscopic surgeries. Ondansetron is the most popular drug used for controlling nausea and vomiting postoperatively. Both ondansetron and ramosetron are selective 5HT<sub>3</sub> receptor antagonists. A prospective, randomized, double-blind controlled study was done in patients undergoing laparoscopic cholecystectomy, comparing the efficacy of ondansetron and ramosetron.

**Materials and Methods:** About 150 patients admitted in Teerthanker Mahaveer Medical College for elective laparoscopic cholecystectomy were divided into two groups. These patients were divided into two equal groups ( $n = 75$ ) by computer-generated randomization. The control group was given ondansetron and the experimental group was given ramosetron for preventing PONV.

**Result:** In the early phase (<24 h) of post-operative period, 53.33% in control group and 50.66% in experimental group experienced PONV and retching. However, this was statistically insignificant. Whereas in the late phase (>24 h), the percentages were 28% and 13.33% in control and experimental groups, respectively, which were statistically significant ( $P < 0.05$ ). Besides, this severity of nausea, vomiting, and retching was more in the control group as compared to other.

**Conclusion:** The present study concludes that ramosetron plays a better role in controlling PONV, both in early and late phase as compared to ondansetron in laparoscopic surgeries. The severity of symptoms was also less in patients taking ramosetron.

**Key words:** Laparoscopic cholecystectomy, Ondansetron, Post-operative nausea and vomiting, Ramosetron

## INTRODUCTION

The common symptom which commonly appears after any surgical intervention is post-operative nausea and vomiting (PONV), with the high incidence of 30-40%. The etiology of this symptom can be surgical or drugs of anesthesia. Few individuals have more risk for developing the PONV, the reason for which is not known. It is believed that laparoscopic surgeries have a high incidence of PONV. Laparoscopic cholecystectomy has 53-72% chances of incidence of PONV.<sup>1</sup>

Sometimes, PONV becomes a main cause of delay in discharge of the patient, and thus, the burden on the

hospital increases. It also causes patient uneasiness, thus remains a cause of concern for the anesthesiologists. The drugs such as ondansetron and granisetron are used to control PONV. In severe cases, these drugs are used in combination with other antiemetics such as droperidol and metoclopramide.<sup>2</sup> Recently, a new drug named ramosetron has been introduced which is also a 5HT<sub>3</sub> receptor antagonist. Some studies recommend this drug to be more potent and selective than ondansetron.<sup>1-3</sup> The literature related to studies on the randomized controlled trials or case-controlled studies on the use of ramosetron is lacking.

In 1990, ondansetron was first used for controlling PONV. It is the most popular drug used for controlling nausea and vomiting post-operatively, after radiotherapy and chemotherapy. The drug can be administered orally, intramuscularly, and intravenously. The serious adverse effects of this drug are allergic reactions and ECG abnormalities such as prolonged QT interval.<sup>4</sup>

Both ondansetron and ramosetron are selective 5HT<sub>3</sub> receptor antagonists. These receptors are commonly

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present in vomiting inducing sites such as nucleus tractus solitarius, area postrema, and vagal afferents. These drugs act by inhibiting the binding of serotonin to the 5HT<sub>3</sub> receptors and thus control PONV. These drugs are not only highly selective but also show little affinity for some other receptors such as histamine, dopamine, and acetylcholine (muscarinic) receptors.<sup>5</sup>

These drugs are metabolized in the liver by isoenzymes of cytochrome P450 and do not have any major drug interactions. Thus, these are safe to administer. The only important side effect of the drug is asymptomatic alterations in electrocardiogram, mostly elongation of PT and QTc interval.<sup>6,7</sup>

Since the literature comparing the efficacy of ondansetron and ramosetron is lacking, so we have designed a prospective, randomized, double-blind controlled study in patients undergoing laparoscopic cholecystectomy.

## MATERIALS AND METHODS

The 150 patients aged between 25 and 55 years admitted in Teerthanker Mahaveer Medical College for elective laparoscopic cholecystectomy were divided into two groups. Ethical approval was taken from the Institutional Committee. Patients were informed about the study, and the written consent was taken. About 150 patients were divided into two equal groups ( $n = 75$ ) by computer-generated randomization. The control group was given ondansetron, and the experimental group was given ramosetron for preventing PONV.

In the present study, the dose of the ramosetron and ondansetron used were 0.3 mg and 4 mg, respectively. Patient was pre-medicated with lorazepam (0.5 mg) orally one night before, and the patient was advised to remain nil per orally after midnight. Injection propofol 2 mg/kg and injection fentanyl 1-2 µg/kg were used to sedate the patient. During surgery, anesthesia was maintained with nitrous oxide (66%) and sevoflurane (1-2%) in oxygen. Injection vecuronium 0.1 mg/kg was given which assisted in smooth intubation. After the completion of surgery, injection diclofenac 75 mg IM was administered and later post-operative analgesia was provided by injection tramadol 2 mg/kg IM. Injection neostigmine (0.04 mg/kg) and injection glycopyrrolate (0.01 mg/kg) were given for the reversal of muscle relaxation. Before shifting the patient to post-operative room, ondansetron (4 mg) or ramosetron (0.3 mg) was administered according to the group.

With the help of an autonomous observer who was unaware or blinded of the study was used to monitor the patient for 48 h and record any complaint of nausea,

vomiting, and retching. The patients who experienced significant nausea or >2 episodes of vomiting, injection metoclopramide (10 mg intravenous) was given.

Nausea is defined as a subjectively disagreeable sensation related with consciousness of the desire to vomit. Retching is defined as the irregular, rhythmic contraction of the abdominal muscles without expulsion of gastric contents. Vomiting is defined as the vigorous expulsion of gastric contents from the oral cavity.<sup>8</sup>

Nausea was calculated with the help of visual analog scale which ranges from 0 = No nausea to 10 = Nausea as worst as can be:

- Score > 5 (Severe)
- Score = 5 (Moderate)
- Score < 5 (Mild).

Retching episodes of:

- >2 (Severe)
- =2 (Moderate)
- <2 (Mild).

All the statistical tests were two-tailed. All the values were expressed as a mean  $\pm$  standard deviation. The data were recorded on standardized case report forms and analyzed in SPSS, version 17 (SPSS Inc., USA). A  $P < 0.05$  was considered statistically significant.

## RESULT

In the present study, 150 patients who were divided into two groups underwent elective laparoscopic cholecystectomy in duration of 1 year. The difference in the mean age, height, and weight of these patients was non-significant ( $P > 0.05$ ). The control and experimental groups were also comparable with respect to the duration of surgery, duration of anesthesia, and duration of CO<sub>2</sub> insufflation (Table 1).

In the early phase (<24 h) of post-operative period, 53.33% in control group and 50.66% in experimental

**Table 1: Comparison of demographic data of patients and details of surgery in two groups**

Characteristics	Control group	Experimental group	Significance
Age of patient	40.42±3.69	40.18±2.99	NS
Height of patient	160.25±2.59	159.99±2.71	NS
Weight of patient	55.18±3.63	54.98±3.44	NS
Duration of surgery (min)	60.61±2.74	59.27±3.01	NS
Duration of anesthesia	68.11±3.42	67.82±3.33	NS
Duration of CO <sub>2</sub> insufflation	62.68±1.73	61.15±2.01	NS

NS: Non significant ( $P > 0.05$ ), PONV: Post-operative nausea, vomiting

group experienced PONV and retching. However, this was statistically insignificant. Whereas in the late phase (>24 h), the percentages were 28% and 13.33% in control and experimental groups, respectively, which were statistically significant ( $P < 0.05$ ) (Table 2 and Figure 1).

Severity ratings of nausea, vomiting, and retching observed in patients of the two groups are detailed in Tables 3 and 4; Figure 2.

## DISCUSSION

Any surgical intervention can be followed by PONV, but it is found in more than 50% of the patients undergoing laparoscopic surgery. The most important pathway for PONV is the signals received from cerebrum, receptors of viscera, and chemoreceptor trigger zone (CTZ). Besides, this in laparoscopic surgeries, the CO<sub>2</sub> insufflation also causes peritoneal distension which irritates the neurogenic pathway resulting in PONV.<sup>9</sup>

Various drugs such as anticholinergics, antiserotonins, benzamides, and dexamethasone have been used as prophylaxis or treatment of PONV. However, these drugs are associated with adverse effects such as low blood pressure, dryness in oral cavity, dizziness, and extrapyramidal symptoms. 5HT<sub>3</sub> receptor antagonists are considered as drug of choice for PONV, and they

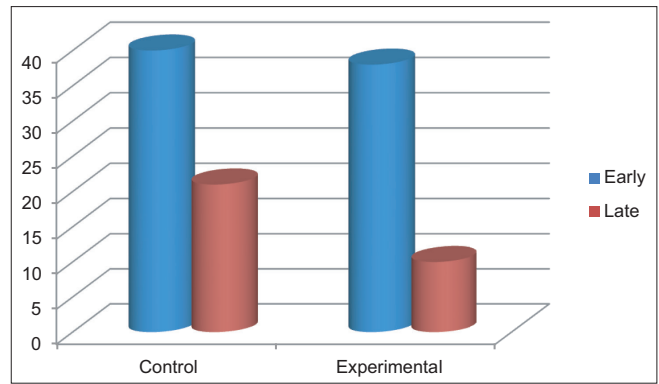


Figure 1: Presence of post-operative nausea and vomiting in early and late phase in both the groups

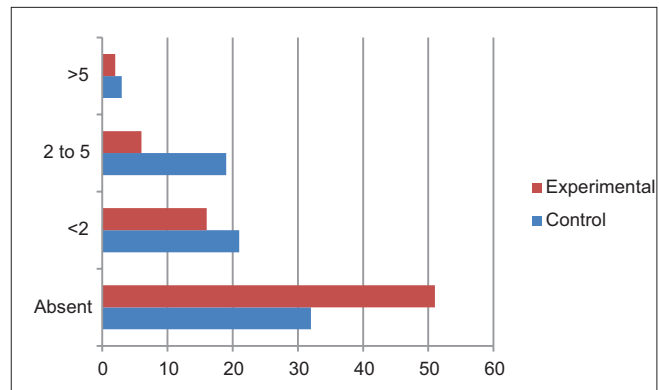


Figure 2: Comparison of number of episodes of vomiting in two groups

Table 2: Comparison of the incidence of PONV and retching in two groups

PONV and retching	Early phase (<24 h)			Late phase (>24 h)		
	Control	Experimental	P value	Control	Experimental	P value
Present	40	38	>0.05	21	10	<0.05
Absent	35	37	>0.05	54	65	<0.05

$P < 0.05$  - significant, PONV: Post-operative nausea, vomiting

Table 3: Comparison of severity of nausea in two groups

Post-operative nausea	Early phase (<24 h)			Late phase (>24 h)		
	Control	Experimental	P value	Control	Experimental	P value
Absent	35	37	>0.05	54	65	<0.05
Mild	11	19	<0.05	10	7	>0.05
Moderate	19	13	<0.05	6	2	<0.05
Severe	10	6	>0.05	5	1	<0.05

$P < 0.05$  - significant

Table 4: Comparison of severity of retching in two groups

Post-operative retching	Early phase (<24 h)			Late phase (>24 h)		
	Control	Experimental	P value	Control	Experimental	P value
Absent	32	41	<0.05	39	53	<0.05
Mild	13	12	>0.05	17	10	<0.05
Moderate	18	10	<0.05	11	7	<0.05
Severe	12	12	>0.05	8	5	>0.05

**Table 5: The comparison of adverse effects of the drugs in two groups**

Side effect	Control group (%)	Experimental group (%)	P value
Sedation	5 (6.6)	2 (2.6)	NS
Headache	3 (4)	1 (1.3)	NS
Weakness	2 (2.6)	1 (1.3)	NS
Dyspepsia	3 (4)	1 (1.3)	NS
Dryness in oral cavity	0 (0)	0 (0)	-

NS: Nonsignificant

act by inhibiting CTZ and the vagal afferents in the gastrointestinal tract.<sup>7,10</sup>

Keeping the demographic profile of the patients and conditions of surgery similar, the comparative study was done to observe the effect of ondansetron and ramosetron on PONV. Besides this, the side effects of these drugs were also studied and compared.

In the early phase of the post-operative period, no statistically significant difference was found in efficacy and side effects of the drugs (Tables 2-5). However, in the late phase of post-operative period, the statistically significant difference was seen in the efficacy of the two drugs. Similar findings were present in the study of Rajeeva *et al.*,<sup>11</sup> who also stated significantly lower frequency of PONV in the ramosetron group when compared to the ondansetron group in the patients after laparoscopic cholecystectomy.

In this study, we also noted the incidence of adverse drug effects in both the groups. These effects were mild and momentary in nature and were statistically insignificant in between ramosetron and ondansetron groups. These findings are supported by Fujii *et al.*<sup>12</sup> in his study.

Some researchers<sup>9-13</sup> believe that use of nitrous oxide during surgery also plays an emetogenic role. Ignoring nitrous oxide and using a continuous infusion of a short-acting opioid might have been a better choice, so the use of nitrous oxide is now controversial. Certain studies<sup>14-16</sup> advocate the use of a combination of drugs in controlling PONV, especially in the patients who are more prone to develop it. Besides this, addition of dexamethasone to the newer 5HT<sub>3</sub> receptor antagonists has been reported more efficacious in patients undergoing laparoscopic cholecystectomy.

The only limitation of our study was that we did not include a placebo group, as this is unethical to expose the patient to distressing symptoms of post-operative period.

## CONCLUSION

The present study concludes that ramosetron plays a better role in controlling PONV, both in early and late phase as compared to ondansetron in laparoscopic surgeries. The severity of symptoms was also less in patients taking ramosetron. Besides this, both the drugs cause lesser side effects.

## REFERENCES

- Taylor E, Feinstein R, White PF, Soper N. Anesthesia for laparoscopic cholecystectomy. Is nitrous oxide contraindicated? *Anesthesiology* 1992;76:541-3.
- Macario A, Weinger M, Carney S, Kim A. Which clinical anesthesia outcomes are important to avoid? The perspective of patients. *Anesth Analg* 1999;89:652-8.
- Habib AS, Gan TJ. Evidence-based management of postoperative nausea and vomiting: A review. *Can J Anaesth* 2004;51:326-41.
- Naguib M, el Bakry AK, Khoshim MH, Channa AB, el Gammal M, el Gammal K, *et al.* Prophylactic antiemetic therapy with ondansetron, tropisetron, granisetron and metoclopramide in patients undergoing laparoscopic cholecystectomy: A randomized, double-blind comparison with placebo. *Can J Anaesth* 1996;43:226-31.
- Rabasseda X. Ramosetron, a 5-HT<sub>3</sub> receptor antagonist for the control of nausea and vomiting. *Drugs Today (Barc)* 2002;38:75-89.
- Cohen MM, Duncan PG, DeBoer DP, Tweed WA. The postoperative interview: Assessing risk factors for nausea and vomiting. *Anesth Analg* 1994;78:7-16.
- Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? *Anesthesiology* 1999;91:109-18.
- Camu F, Lauwers MH, Verbessem D. Incidence and aetiology of postoperative nausea and vomiting. *Eur J Anaesthesiol Suppl* 1992;6:25-31.
- Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: Conclusions from cross-validations between two centers. *Anesthesiology* 1999;91:693-700.
- Tang J, Wang B, White PF, Watcha MF, Qi J, Wender RH. The effect of timing of ondansetron administration on its efficacy, cost-effectiveness, and cost-benefit as a prophylactic antiemetic in the ambulatory setting. *Anesth Analg* 1998;86:274-82.
- Rajeeva V, Bhardwaj N, Batra YK, Dhaliwal LK. Comparison of ondansetron with ondansetron and dexamethasone in prevention of PONV in diagnostic laparoscopy. *Can J Anaesth* 1999;46:40-4.
- Fujii Y, Uemura A, Tanaka H. Prophylaxis of nausea and vomiting after laparoscopic cholecystectomy with ramosetron: Randomised controlled trial. *Eur J Surg* 2002;168:583-6.
- Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. *Anesthesiology* 1992;77:162-84.
- McCracken G, Houston P, Lefebvre G; Society of Obstetricians and Gynecologists of Canada. Guideline for the management of postoperative nausea and vomiting. *J Obstet Gynaecol Can* 2008;30:600-16.
- Ryu J, So YM, Hwang J, Do SH. Ramosetron versus ondansetron for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. *Surg Endosc* 2010;24:812-7.
- Kawabata Y, Sakiyama H, Muto S. Clinical evaluation and pharmacokinetics of ramosetron against the nausea and vomiting induced by anticancer drugs. *Nishinohon J Urol* 1994;56:1445-56.

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