

## Original Article

# Comparison of Ondansetron Used Alone and in Combination with Dexamethasone as a Prophylaxis for Postoperative Nausea and Vomiting Following Laparoscopic Cholecystectomy

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### Abstract :

Postoperative nausea and vomiting (PONV) is common after anaesthesia and surgery. In patients undergoing laparoscopic cholecystectomy (LC) without antiemetic prophylaxis, the incidence can be as high as 76% which would cause unexpected delay in hospital discharge. This study was designed to compare the efficacy of the ondansetron alone with combination of ondansetron and dexamethasone the given as prophylaxis for PONV in patients undergoing laparoscopic cholecystectomy. One hundred patients undergoing elective laparoscopic cholecystectomy were selected and randomly divided into 2 groups of 50 each. Group I received 4mg of ondansetron intravenously (iv), whereas Group II received ondansetron 4mg and dexamethasone 4mg just before induction of anaesthesia. Postoperatively, the patients were assessed for episodes of nausea, vomiting and need for rescue antiemetic. Complete response defined as no nausea and vomiting during first 24 hours, was noted in 76% of patients in Group I and in 92% of patients in Group II. Rescue anti emetic requirement was less in Group II (4%) than Group I (20%). So it can be concluded that the combination of ondansetron and dexamethasone is more effective in preventing PONV in patients undergoing laparoscopic cholecystectomy than ondansetron alone.

**Key words :** Ondansetron, Dexamethasone, Laparoscopic Cholecystectomy, Postoperative nausea vomiting (PONV).

### Introduction :

Nausea is a subjective phenomenon of unpleasant wave like sensation experienced in the back of throat and/or epigastrium that may or may not culminate into vomiting. Vomiting is forceful expulsion of contents of stomach, duodenum or jejunum through the oral cavity. Postoperative nausea and vomiting (PNOV) are two most common and unpleasant side effects following anaesthesia and surgery. In the absence of antiemetic treatment, the incidence of PONV varies from 20% to 30% for all surgical intervention under anaesthesia<sup>1,2</sup>. However, the incidence of PONV after laparoscopic cholecystectomy (LC) is higher than that after other type of surgery<sup>3,4</sup>. A rate of 46% to 75% has been reported for patients who did not receive antiemetic treatment after LC<sup>3-5</sup>.

Increased patient discomfort due to PONV remains a cause of concern for the surgeons as well as anaesthesiologist and has some definite implications on recovery. This often leads to a delay in the discharge of these patients with increased burden on hospital.

PONV has a multifactorial etiology involving anaesthetic, surgical and individual risk factors<sup>6</sup>. Many different anti emetic drugs are available for treatment of PONV. 5-HT<sub>3</sub> receptor antagonists, e.g., ondansetron, granisetron, and tropisetron are by far the best studied drugs and have used extensively either alone or in combination with other anti emetics like metoclopramide, dexamethasone, dropridrol. In spite of plenty of antiemetic drugs are available, no single agent is 100% effective against PONV<sup>4</sup>. Recent interest has focused on the use of a combination antiemetics acting at different receptors and the adoption of a multimodal approach to tackle this problem. Ondansetron in combination with dexamethasone has been used successfully to treat PONV refractory to ondansetron alone<sup>7</sup>.

The present study was undertaken to compare the efficacy of ondansetron alone and in combination with dexamethasone for prevention of PONV in patient undergoing laparoscopic cholecystectomy.

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**Materials and Methods :**

This randomized prospective clinical study was carried out in Faridpur Central Hospital, Faridpur during period of January 2013 to December 2013. In this study 100 patients of both sexes scheduled for elective laparoscopic cholecystectomy were selected.

**Inclusion criteria**

- 1) Patients between 18 and 60 years of age.
- 2) American Society of Anaesthesiologists (ASA) Grade I and II

**Exclusion criteria**

- 1) Patients belonging to ASA grade III and IV
- 2) Patients with a history of PONV and motion sickness
- 3) Patients who had received opioids, nonsteroidal anti-inflammatory drugs, steroids, and antiemetic agents during previous 24 hour
- 4) Patients with history of hypersensitivity to study drug, impaired liver function test
- 5) Female patients who are pregnant and lactating.

They were randomly divided into Group I and Group II with 50 patients in each group. Group I received 4mg of ondansetron intravenously (iv), whereas Group II received ondansetron 4mg and dexamethasone 4mg IV just before the induction of anaesthesia.

A day prior to surgery, preoperative evaluation of patients was done. All the patients received Tab. Diazepam 10 mg at night before day of surgery. In the operating room, after establishing an IV line, the study medication was administered one minute prior to induction of anaesthesia. Standard general anaesthesia was given to all the patients. After preoxygenation for 3-5 minutes with 100% oxygen, induction of anaesthesia was done with inj. Fentanyl (1mg/kg body weight) and inj. Thiopentone sodium (5mg/kg body weight) and endotracheal intubation was done after giving inj. Suxamethonium (1.5mg/kg body weight). Maintenance of anaesthesia with N<sub>2</sub>O 70%, O<sub>2</sub> 30% and halothane 0.5-1% with long acting nondepolarizing neuromuscular blocking agent Vecuronium (0.1 mg/body weight). Intraoperative fluid was maintained with Hartmann's solution or Normal saline. All operations were performed using four port standard laparoscopic technique. Time of surgery was within 1.5 hours. After completion of operation residual effect of neuromuscular blocking agent was reversed by inj. Neostigmine (0.04mg/kg body weight) and inj. Atropine (0.02mg/kg body weight) and tracheal extubation performed.

Patients were then transported to recovery room and later to the ward after confirming that there was adequate level of consciousness and intact reflexes. Incidence of PONV was recorded every 6 hourly for a period of 24 hours. Episodes of PONV were identified by spontaneous complaints by the patients or by direct questioning. Nausea and vomiting was evaluated on a three point scale :

0 = Complete response (defined as the absence of any nausea or vomiting and no need for rescue antiemetic during the whole observation period).

- 1= Nausea
- 2= Vomiting

Rescue antiemetic was provided with inj. Ondansetron 4mg iv in case of patient complaining of nausea or had vomiting.

**Results :**

Demographic data, duration of anaesthesia, duration of surgery among the groups are demonstrated in table I.

**Table I:** Comparison of demographic data and other characteristic in two groups

Characteristic	Group I	Group II
Age (Years), mean ± SD	34.65 ± 7.95	34.05 ± 6.78
Male/ Female	7/43	11/39
Weight (Kgs), mean ± SD	47.36 ± 8.92	46.97 ± 8.37
Duration of anaesthesia in minutes, mean ± SD	50.46 ± 19.95	53.78 ± 17.42
Duration of surgery in minutes, mean ± SD	52.12 ± 17.40	51.46 ± 18.65

PONV was present in 12 of 50 patients in Group I, whereas 4 of 50 patients had PONV in Group II. This is shown in table II. It was found to be statistically significant (p<0.029).

**Table II:** Comparison of incidence of PNOV during 0-24 hours between 2 groups

Groups	PONV		p value	Remarks
	Yes (%)	No (%)		
Group I (n=50)	12 (24%)	38 (76%)	0.029	Significant
Group II (n=50)	4 (8%)	46 (92%)		

Table III shows PONV scores. Of 12 patients who complained of PONV in Group I, 7 had nausea and 5 had vomiting. This can be compared to Group II in which out of 4 patients who complained of PONV, only 3 had nausea and 1 had vomiting.

**Table III:** PONV score in Group I and II

PONV score	Group I	Group II
0 (No nausea/vomiting)	38	46
1 (Nausea)	7	3
2 (Vomiting)	5	1

In this study, ondansetron 4 mg was used as rescue anti emetic in both the groups. In Group I, of the 12 patients who complained of PONV, 10 patients received rescue anti emetic, whereas 2 patients who had mild nausea did not need rescue antiemetic. In Group II, all of the 4 patients who complained of PONV received rescue anti emetic.

**Table IV:** Distribution of the patients by groups and administration of rescue antiemetic

Groups	PONV No (%)	Administration of Rescue anti emetic No (%)
Group I (n=50)	12 (24%)	10 (20%)
Group II (n=50)	4 (8%)	4 (8%)

### Discussion :

Postoperative nausea and vomiting is one of the most commonly reported adverse effects of postoperative period. These are frequently the cause of great distress to patients that may increase medical costs and delay discharge and recovery. Though PONV are observed with all types of surgery, its prevalence in LC is very high, ranging from 46 to 75%<sup>3-5</sup>. The aetiology of PONV is complex and multifactorial and it includes patient factors, anaesthetic factors and postoperative care<sup>8</sup>. In fact, laparoscopic surgery itself is a main risk factor for PONV. In laparoscopic cholecystectomy, PONV may be associated with stretching of peritoneum due to CO<sub>2</sub> pneumoperitoneum and the gallbladder surgery itself<sup>9</sup>.

Pharmacological therapy consists of anticholinergics (e.g. scopolamine), butyrophenones (e.g. doperidol), benzamides (e.g. metoclopramide) and anti serotonin (e.g. ondansetron, granisetron, ramosetron). Nontraditional anti emetics e.g., propofol, dexamethasone, tandospirone and midazolam, have also been used in the prophylaxis of PONV. However, anti emetics in the group of anticholinergics, antihistaminics, butyrophenones, and benzamides are associated with a significant incidence of undesirable side effects like sedation, hypotension, dry mouth, dysphoria, restlessness and extrapyramidal symptoms. Anti serotonin produces no sedation, no extrapyramidal symptoms and adverse effects on vital signs. Serotonin receptor (5 HT<sub>3</sub>) antagonists affect the chemoreceptor trigger zone and act at vagal afferents in the gastrointestinal tract. Anti serotonin (5 HT<sub>3</sub> receptor antagonists) are one of the most effective treatment options available for control of PONV after surgery under general anaesthesia including laparoscopic cholecystectomy<sup>10</sup>. Ondansetron, the most commonly used anti serotonin (5 HT<sub>3</sub> receptor antagonists), has been shown to be effective in the prevention and treatment of PONV in many studies.

Dexamethasone was reported as effective anti emetic in patients receiving cancer chemotherapy in 1981<sup>11</sup>. The mechanism of action of dexamethasone is unknown; however there have been some suggestions, such as central/ peripheral inhibition of production of 5 HT, central inhibition of synthesis of prostaglandins, or changes in permeability of the blood brain barrier to serum protein<sup>7,12</sup>. The major concern regarding use of dexamethasone is infection, delayed wound healing and other side effect. But various studies in literature have shown that a single dose of dexamethasone does not increase complications<sup>5,7,13</sup>.

In recent years interest has been focused on combination therapy because no single agent is effective against PONV. This may be because it is multifactorial in origin and there is no single stimulus for PONV. The idea of combination therapy for prevention and treatment of PONV came from various studies where ondansetron plus dexamethasone have been used successfully to treat emesis refractory to ondansetron alone.

In our study, a complete response (no nausea and vomiting) was observed in 92% patients in Group II (Ondansetron plus dexamethasone) as compared to 76% in Group I (Ondansetron only), the difference was statistically highly significant ( $p < 0.029$ ). This is comparable to the study conducted by Bhattarai et al<sup>12</sup> and Panda et al<sup>14</sup>. Lopez-Olando et al<sup>15</sup> concluded that prophylactic administration of a combination of dexamethasone and ondansetron is effective in

preventing PONV in patients undergoing gynaecological surgery with fewer patients requiring rescue anti emetic compared to other regimen of placebo, ondansetron and dexamethasone. Biswas et al<sup>16</sup> also found that combination of dexamethasone and ondansetron provide adequate control of PONV in patients undergoing laparoscopic tubal ligation with overall complete response in 78% of patients. Gautam et al<sup>17</sup> compared efficacy of ondansetron-dexamethasone combination with each drug alone as a prophylaxis against PONV in patients after elective laparoscopic cholecystectomy. They concluded that the combination of ondansetron and dexamethasone was better than each drug alone in preventing PONV.

In our study, 12 cases in Group I had complaints of PONV of which 10 cases (20%) needed rescue antiemetic. This can be compared with 4 cases (8%) in Group II who had complaints of PONV and all of them needed rescue anti emetic. The need for rescue antiemetic more in group I (20%) than in group II (4%) which is comparable to a study conducted by Elhakim et al<sup>18</sup>.

### Conclusion :

PONV has been identified as an essential component in achieving patient satisfaction and can be more distressing than pain, which is even higher after laparoscopic surgeries. None of the available anti emetic drugs is entirely effective for preventing PONV. This has led to a number of studies investigating the efficacy of combination of various anti emetic with an assumption that using a combination anti emetic acting on different receptors can further reduce the incidence of PONV, as there are different major receptor systems involved in aetiology of PONV.

In our study we have compared the efficacy of ondansetron 4mg alone with the combination of ondansetron 4mg and dexamethasone 4mg iv given just before induction of anaesthesia in preventing PONV following laparoscopic cholecystectomy. It has been concluded from this study that the combination of ondansetron with dexamethasone is more effective than ondansetron alone in preventing PONV. Further studies on prophylactic combinations of drugs should be done to make PONV a rare occurrence.

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