

Comparative Study of Ondansetron versus Metoclopramide for Prevention of Post Operative Nausea and Vomiting after General Anaesthesia

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Abstract—

Background: Patients who undergo laparoscopic cholecystectomy under general anaesthesia may be at risk of experiencing post-operative nausea and vomiting (PONV). Commonly used traditional antiemetics for PONV include the anticholinergics (Scopolamine), Phenothiazines (Promethazine), Antihistamines (diphenhydramine), butyrophenones (Droperidol) and benzamides (Metoclopramide). These antiemetics have adverse effects such as dry mouth, sedation, hypotension, extrapyramidal symptoms, dystonic effects and restlessness. The newest class of antiemetics used for the prevention and treatment of PONV are serotonin receptor antagonist (Ondansetron, Granisetron). These antiemetics do not have the adverse effects of the older antiemetics except headache and dizziness. This study compared the prophylactic intravenous use of Metoclopramide and Ondansetron for the prevention of nausea and vomiting in patients who underwent laparoscopic cholecystectomy under general anaesthesia in Nepalese population.

Material and Methods: In this hospital based prospective cross sectional study 80 ASA I or II patients undergoing laparoscopic cholecystectomy under general anaesthesia were included. The anesthetic technique drugs, monitoring and care were standardized in all patients during peri-operative period. The patients were divided into 2 groups: Group O (n=40) received Ondansetron 4 mg while Group M (n=40) received Metoclopramide 10 mg just before induction of anaesthesia. Patients were observed for the initial 24 hours after anaesthesia. The presence or absence of nausea and vomiting was assessed by direct questionnaire method. Complete response is defined as no nausea and no vomiting.

Result: Out of 40 patients in Metoclopramide group, 13 patients had nausea, 10 patients had vomiting and complete response occurred in 17 patients. In Ondansetron group, 10 patients had nausea, 8 patients had vomiting and complete response occurred in 22 patients.

Conclusion:

This study showed that prophylactic use of Ondansetron is more effective than Metoclopramide in the prevention of PONV during laparoscopic cholecystectomy.

Keywords— Antiemetic prophylaxis; Laparoscopic Cholecystectomy; Metoclopramide; Ondansetron; Post-operative nausea and vomiting (PONV).

I. INTRODUCTION

Nausea and vomiting are the most common postoperative complaints. They can occur after general, regional or local anaesthesia [1]. The aetiology of post-operative nausea and vomiting (PONV) is multi-factorial and includes factors like patients characteristic, type of surgery, anaesthetic techniques and post-operative care [2].

Post-operative nausea and vomiting usually defined as nausea, retching or vomiting within 24 hours of surgery and affects 20-30% of patients [3]. The term nausea refers to a subjective feeling of the urge to vomit. The nauseated patient does not necessarily vomit or retch. This may be brief or prolonged, often occurring in waves and may precede vomiting or occurs in isolation. Vomiting usually alleviates the sensation of nausea. Vomiting or emesis is the actual oral expulsion of gastrointestinal contents resulting from the contractions of the gut and the thoraco-abdominal wall musculature. Retching is the term used to describe the muscular events of vomiting without expulsion of gastric contents [4].

PONV is an important problem and can lead to potentially serious outcomes and an increase healthcare expenditure [5]. Post-operative nausea and vomiting increases recovery room time, requiring expanded levels of nursing care and delays mobilization following surgery as movement often exacerbates PONV [6]. As a result, the early discharge of ambulatory surgery patients is frequently delayed with around 1% requiring overnight admission [7]. Persistent vomiting can result in dehydration, electrolyte imbalance and metabolic alkalosis [8]. The oral administration of drugs, nutrition and fluids may also be delayed and the level of post-operative analgesia that can be obtained may be limited if effective dose of opiate cannot be administered orally [9]. Vomiting also increases the risk of esophageal perforation, bleeding and pulmonary aspiration whilst the increased abdominal pressure during emesis may cause tension on suture lines resulting in incisional hernias [6]. An equally important issue surrounding PONV is the high level of patient dissatisfaction and discomfort [5]. Research has shown that nausea and vomiting are feared far more in comparison to post-operative pain, and PONV is ranked as a major concern by the most surgical patients [8].

There are several factors that increase the likelihood of PONV.

These factors can generally be separated into patient factors, Surgical factors and pharmacological factors.

PATIENT FACTORS INCREASING THE RISK OF POST OPERATIVE NAUSEA AND VOMITING [6,10]

- Female gender (especially menstruating or pregnant)
- Previous history of PONV
- Previous history of motion sickness
- Non-smoking status

SURGICAL FACTORS INCREASING THE RISK OF POST OPERATIVE NAUSEA AND VOMITING:

Surgeries associated with increased risk of PONV:

- Laparoscopy
- Laparotomy
- ENT surgery
- Neurological surgery
- Breast surgery
- Gynaecological surgery
- Duration of surgery (the risk of PONV increases with the length of the surgical procedure)[10]

PHARMACOLOGICAL FACTORS INCREASING THE RISK OF POST OPERATIVE NAUSEA AND VOMITING:

Anaesthetic techniques associated with increased risk of PONV:

- General anaesthesia (increases the risk of PONV 11-fold compared to regional anaesthesia)[10]
- Use of volatile anaesthetic agents
- Use of nitrous oxide
- Use of reversal agents e.g. Neostigmine
- Use of opioids either intra or post-operatively[8]

OTHER FACTORS INCREASING THE RISK OF POST OPERATIVE NAUSEA AND VOMITING:

• Inexperienced anaesthetic technique [11] e.g. Poor bag and mask ventilation may cause gastric distension and subsequent nausea.

- Poor hydration during or immediately following surgery
- Intra-operative hypotension [10]
- Patient stress / anxiety [9]

Laparoscopic surgery provides benefits to patients, including tremendous faster recovery, shorter hospital stay and prompt return to normal activities. It has decreased the morbidity associated with cholecystectomy and has become a routine procedure for symptomatic cholelithiasis. Despite the minimally invasive nature of laparoscopy, high incidence of PONV remains a major cause for morbidity. PONV can result in morbidity like wound dehiscence, bleeding, pulmonary aspiration of gastric contents, fluid and electrolyte disturbance, delayed hospital discharge, unexpected hospital admission and decreased patient satisfaction.

Despite extensive research and the introduction of newer classes of antiemetic drugs with better efficacy and safety profiles, there seems to be little progress in reducing the incidence of PONV.

Considering the above mentioned facts, the present study has been designed to compare the efficacy of Metoclopramide with Ondansetron for controlling PONV after laparoscopic cholecystectomy.

II. MATERIALS AND METHODS

This was a hospital based retrospective study of 80 patients of cholelithiasis undergoing laparoscopic cholecystectomy surgery under general anaesthesia to compare the efficacy of Metoclopramide and Ondansetron for the prevention of post-operative nausea and vomiting. The study was conducted at Nepalgunj Medical College Teaching Hospital Kohalpur for 12 months (Sept 2013 to August 2014) after the approval of proposal by Institutional Review Committee.

An informed and written consent was obtained from all the patients.

The study was carried out in 2 groups consisting of randomly selected 40 patients in each group.

Pethidine in the dose of 1mg/kg body weight I.V was given for analgesia 5 minutes before induction. The study drugs Metoclopramide 10mg and Ondansetron 4mg were administered intravenously (i.v) just before induction of anaesthesia by the Anaesthetist. Then these patients were divided in 2 groups. Those receiving Metoclopramide 10 mg i.v were categorized as Group M and those receiving Ondansetron 4mg i.v categorized as Group O. Anaesthesia was induced with intravenous administration of Propofol 2.5 mg/kg. Induction was confirmed by loss of eyelash reflex, followed by administration of Succinylcholine in the dose of 1.5mg/kg to facilitate tracheal intubation and ventilated with oxygen through Bain circuit. After administration of Succinylcholine, laryngoscopy was performed with a standard Macintosh laryngoscope blade and trachea intubated with an appropriate size cuffed endotracheal tube and ventilated with oxygen (33%), nitrous oxide (66%) and halothane (0.75%) using a Bain circuit. After the surgery, patient was reversed with Neostigmine (0.05mg/kg) and Atropine (0.02mg/kg). Postoperatively, all episodes of nausea and vomiting experienced by the patient during the first 24 hours after anaesthesia, was recorded by direct questioning. All the data was recorded on a pre-designed proforma. Statistical analysis was done with SPSS for windows. Categorical data was presented in percentages and proportions.

Inclusion Criteria:

- i. In patients of either sex aged (16-65) years who will undergo surgery under General Anesthesia and will be hospitalized for at least 24 hours after recovery.
- ii. Patients belonging to American Society of Anesthesiologists (ASA) Grade I and Grade II.
- iii. Patients giving written consent after explanation about the study.

Exclusion Criteria:

- i. Patients with Renal impairment, Hepatic disease, Neurological and Endocrinal abnormality.
- ii. Patient hypersensitive to any of the study drugs.
- iii. Patients belonging to ASA grade III, IV and V.
- iv. Patient receiving antiemetic drug during the 24 hours before anaesthesia.

- v. Patients who are pregnant or menstruating.
- vi. Patient undergoing emergency surgery.

III. RESULTS

Out of 80 patients of cholelithiasis undergoing laparoscopic cholecystectomy, 70 patients (87.5%) were female whereas 10 patients (12.5%) were male.

a. Metoclopramide Group:

Out of 40 patients, 35 patients (87.5 %) were female whereas 5 patients (12.5 %) were male.

b. Ondansetron Group:

The male patients in the study were 5 (12.5 %) out of 40 patients whereas 35 patients (87.5 %) were female.

i. Distribution of nausea and vomiting:

While the patients were in the post postoperative ward, occurrence of PONV was recorded by direct questioning. Out of 40 patients belonging to Metoclopramide group, 27 patients (67.5%) had no nausea and 13 patients (32.5%) had nausea whereas 30 patients (75%) had no vomiting and 10 patients (25%) had vomiting. Out of 40 patients belonging to Ondansetron group, 30 patients (75 %) had no nausea and 10 (25 %) patients had nausea whereas 32 patients (80 %) had no vomiting and 8 patients (20 %) had vomiting. (Table 1 and Fig i)

TABLE 1: Distribution of Nausea and Vomiting (n=40)

Groups	Nausea		Vomiting	
	Number	Percentage (%)	Number	Percentage (%)
Metoclopramidee	13	32.5	10	25
Ondansetron	10	25	8	20

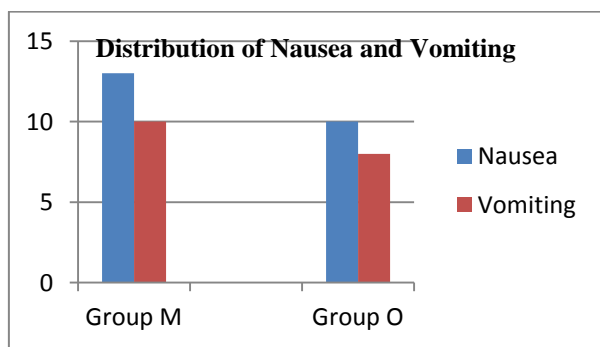


Fig. i: Distribution of Nausea and Vomiting

The number of patients showing Complete response (Neither nausea nor vomiting), Nausea only, vomiting (nausea followed by vomiting) and PONV (nausea only + nausea followed by vomiting) in both groups along with their respective percentage has been summarized in Table 2 and Fig ii. Statistical analysis of data among the 2 different groups was performed by one-way analysis of variation (one way ANOVA). A p value of less than 0.05 was considered significant.

Out of 40 patients, complete response (no nausea and no vomiting) occurred in 17 patients (42.5%) in Group M whereas it was in 22 patients (55%) in Group O. The reduction in incidence of nausea and vomiting (complete response) by Ondansetron compared to Metoclopramide was found to be statistically significant (p=0.017).

13 patients (32.5%) experienced nausea in Group M whereas in Group O only 10 patients (25%) experienced nausea. The reduction in episodes of nausea only by Ondansetron compared to Metoclopramide was found to be statistically insignificant (p=0.06).

The incidence of vomiting was slightly higher in Group M as compared to Group O. 10 patients (25%) had vomiting in Group M whereas it was only in 8 patients (20%) in Group O.

The reduction in incidence of vomiting by Ondansetron compared to Metoclopramide was found to be statistically significant (p=0.042).

The overall incidence of post-operative nausea and vomiting was in 23 patients (57.5%) in Group M compared to 18 patients (45%) in Group O. The reduction in incidence of nausea and vomiting by Ondansetron compared to Metoclopramide was found to be statistically significant (p=0.02).

TABLE 2: Comparison of nausea only, vomiting, complete response, overall PONV and need for rescue antiemetic in Group M and Group O (n=40 in each).

Parameters	Group M		Group O		P* Value
	Number	Percentage (%)	Number	Percentage (%)	
Nausea Only	13	32.5	10	25	p> 0.05
Vomiting	10	25	8	20	p< 0.05
Complete Response	17	42.5	22	55	p< 0.05
Overall PONV	23	57.5	18	45	p< 0.05

p* = probability of no significance

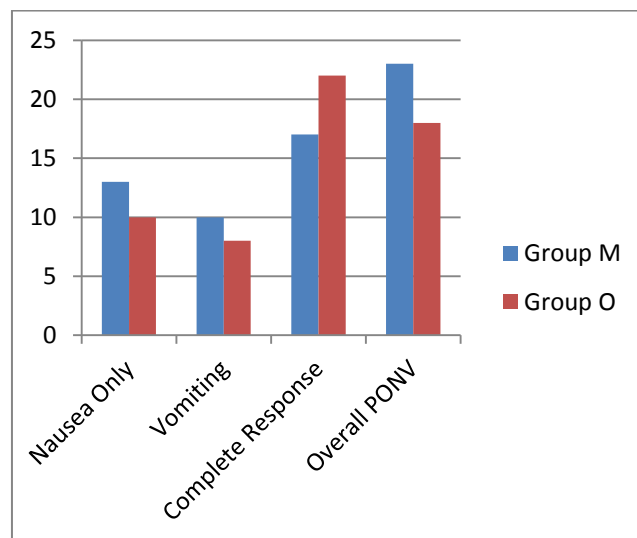


Fig. ii: Comparison of nausea only, vomiting, complete response and overall PONV in Group M and Group O.

IV. DISCUSSION

This study showed the reduction in incidence of nausea and vomiting by Ondansetron compared to Metoclopramide was found to be statistically significant ($p=0.02$) which was similar to the study done by Dabbous A et al. in the year 1998 in Lebanon [12]. In the study, subjects received intravenously either 4 mg Ondansetron or 10 mg Metoclopramide after induction of general anesthesia. The incidence of emesis in female group was lower ($p<0.05$) in Ondansetron group than Metoclopramide group.

The result of our study is dissimilar to study done by Kaki AM et al at Saudi Arabia [13]. In the study, they included 75 patients scheduled for laparoscopic cholecystectomy to receive either Metoclopramide 10 mg ($n=25$), Ondansetron 4 mg ($n=25$) or placebo ($n=25$) at the end of surgery. They found frequency of Post operative nausea and vomiting were equal for 2 groups, i.e, 7 patients from each Metoclopramide and placebo group and lower among Ondansetron group, i.e, 5 patients ($p>0.05$).

Sandhu T et al. in the year 2008 compared effectiveness of Ondansetron versus Metoclopramide in prophylaxis of nausea and vomiting for laparoscopic cholecystectomy in Thailand [14]. The incidence of nausea was 45% for Metoclopramide and 20% for Ondansetron in 24 hours postoperatively; the difference was statistically insignificant ($p>0.05$) which is similar to the result of our study. The incidence of vomiting was 20% for Metoclopramide and 2.5% for Ondansetron which is statistically significant ($p=0.02$) which is again similar to result of our study.

A prospective, randomized double blind study for comparison of Ondansetron and Metoclopramide for PONV prophylaxis in laparoscopic cholecystectomy was done by Farhat K et al in 2013 [15]. They found the frequency of nausea and vomiting was lower in Ondansetron group as compared to Metoclopramide group and the results were statistically significant ($p=0.032$) which was similar to the result of our study.

Comparison between Ondansetron and a combination of low-dose Dexamethasone and Metoclopramide in the prevention of nausea and vomiting after laparoscopic cholecystectomy was done by Hassan MA et al in the year 2013 [16]. 120 patients were divided into 3 groups with 40 patients in each group who received Ondansetron, Dexamethasone- Metoclopramide and Placebo. All patients underwent similar standardized anaesthetic and surgical techniques. Nausea and vomiting were assessed during the first 24h after surgery. The total incidence of PONV during the first 24h after surgery was 30% in Dexamethasone and Metoclopramide group (GDM) compared with 35% in group Ondansetron(GO) and 72.5% in placebo group(GP). There was no significant difference between GO or GDM in the incidence of PONV ($P=0.811$) whereas it was statistically significant between GDM and GP. They concluded that the

combination of low-dose Dexamethasone (2.5mg) and Metoclopramide (10mg) was as effective as Ondansetron (4mg) in the prevention of PONV after laparoscopic cholecystectomy without significant side effects.

V. CONCLUSION

This study showed that the reduction in incidence of nausea and vomiting (complete response), vomiting and PONV by Ondansetron compared to Metoclopramide was found to be statistically significant whereas reduction in incidence of nausea only by Ondansetron compared to Metoclopramide was found to be statistically insignificant.

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