



COMPARISON OF ONDANSETRON AND METOCLOPRAMIDE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANESTHESIA.

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ABSTRACT... Background: Laparoscopic cholecystectomy is a standard treatment for cholelithiasis. It is a safe and effective treatment in many cases. General anesthesia has a high incidence for PONV. But anti-emetic drugs can help in preventing PONV. **Objectives:** To compare the efficacy of ondansetron and metoclopramide in patients undergoing laparoscopic cholecystectomy under general anesthesia. **Material & Methods: Study Design:** Randomized controlled trial. **Setting:** Department of Anaesthesia, Sheikh Zayed Hospital, Lahore. **Period:** 6 months i.e. from 15-02-2017 to 15-08-2017. **Data Collection:** The patients were divided into two groups. Ondansetron was given to group A patients within 15 minutes of induction, and metoclopramide to group B patients within 15 minutes of induction. Then patients were shifted to the ward after surgery and followed-up for 24 hours for assessment of PONV. All the data was entered and analyzed on SPSS version 20. **Results:** The mean age of patients in group A was 38.40 ± 12.07 years and in group B was 42.63 ± 11.77 years. The efficacy achieved in 53 were from group A and 39 were from group B. Statistically significant difference was found between the study groups i.e. $p\text{-value} = 0.003$. **Conclusion:** Ondansetron showed significantly better efficacy than metoclopramide in preventing PONV after laparoscopic cholecystectomy under general anesthesia.

Key words: Laparoscopic Cholecystectomy, Metoclopramide, Ondansetron, PONV.

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INTRODUCTION

Post-operative nausea and vomiting (PONV) is the most common complication of surgery and anaesthesia. Along with pain, this is often listed by the patient, as their most important peri-operative concerns. The incidence of PONV in high risk groups is around 80%.^{1,2} PONV is multifactorial. Each risk factor increases the likelihood of PONV BY ~18-22%.³ Among the many factors, female gender, past history of PONV, motion sickness, use of opioids, post-operative pain, obesity, nitrous oxide and nonsmoking history are the independent predictors for PONV.^{2,4}

Prolonged PONV may lead to electrolyte imbalance, dehydration, aspiration of gastric contents, Mallory Weiss tears, esophageal rupture, wound dehiscence and hematomas.⁵ Laparoscopic surgery is associated with an appreciably high rate of PONV, because of the creation of pneumoperitoneum, during the

procedure, distension of abdomen, and irritation of diaphragm and other abdominal viscera.^{2,4}

Time to discharge was increased by 25% in patients with PONV.⁶ Emesis or vomiting is defined as 'the reflex action of ejecting the contents of the stomach through the mouth'. It is controlled by a group of closely related nuclei in the brainstem termed the 'vomiting center' that is rich in dopaminergic, histamine, 5-hydroxytryptamine, neurokinin and muscarinic cholinergic receptors.³

The traditional anti-emetics include anti-histamines, anticholinergics, and dopamine receptor antagonists. Newer class of drugs, such as serotonin receptor antagonists provides better efficacy and safety, as compared to traditional drugs.⁷ Ondansetron a prototype drug, it is the first 5HT₃ receptor antagonists to be marketed and used to control PONV. It binds to 5-hydroxytryptamine subtype 3 receptor

selectively blocking the emetogenic stimuli during anaesthesia and surgery.² Side effects of serotonin antagonists include headache, diarrhea, constipation and arrhythmias.³ Metoclopramide is a dopamine receptor antagonist and a prokinetic agent hastens the esophageal clearance, accelerates gastric emptying and shortens bowel transient time. At high doses metoclopramide associated with extrapyramidal effects such as akathisia motor restlessness etc.^{2,8}

Rationale of this study is to compare the efficacy of ondansetron and metoclopramide in patients undergoing laparoscopic cholecystectomy under general anesthesia. Many studies have compared the efficacy of ondansetron and metoclopramide, however on reviewing the literature, it was noticed that there is contradiction about the efficacy between both drugs. Some showing that ondansetron is more effective however, it was also reported that metoclopramide is more beneficial than ondansetron. So we aimed to conduct this study to resolve this dispute and implement the more efficacious and beneficial drug in future to prevent patients from post-operative complications like PONV which may lead to other severe complications like pain or delayed healing and cause longer hospital stay. There is controversy in published literature locally² and internationally.^{9,10} The drug that is more effective in this study will be used in future to prevent PONV.

OBJECTIVE

To compare the efficacy of ondansetron and metoclopramide in patients undergoing laparoscopic cholecystectomy under general anesthesia.

MATERIALS AND METHODS

Study Design

Randomized control trial.

Setting

Department of Anaesthesia, Sheikh Zayed Hospital, Lahore.

Duration

Six months i.e. 15-2-2017 to 15-8-2017.

Sample Size

The sample size of 120 cases; 60 cases in each group was estimated by using 5% level of significance, 80% power of test and expected percentage of efficacy i.e. 69%⁹ with ondansetron and 44%⁹ with metoclopramide in patients undergoing laparoscopic cholecystectomy under general anesthesia.

Sampling Technique

Non-probability, consecutive sampling.

Inclusion Criteria

Patients of age 20-60 years or either gender with diagnosis of acute cholecystitis (on medical record) with ASA-1 and 2.

Exclusion Criteria

Patients having peptic ulcer, hernia, pregnancy, having any anti-emetic drug within 24 hours of surgery, allergic to drug, having history of narcotic use or smokers or BMI > 35kg/m².

Data Collection Procedure

After approval from hospital ethical committee, 120 selected patients, fulfilling inclusion criteria, was selected. Informed consent was taken from all patients. Demographics were also noted. Then patients were randomly allocated in two groups by using random table. Patients were shifted to Operation Theater. IV access was done. Standard anesthetic regimen was given. Induction with propofol (1-2 mg/kg) and nalbuphine (0.1mg/kg). After confirmation that ventilation is normal, muscle relaxant (atrelax 0.5mg/kg), was given. Airway was secured with ETT. All patients ventilated with volume controlled ventilator, maintained by oxygen nitrous and inhalational agents. Ondansetron was given to group A patients within 15 minutes of induction, and metoclopramide to group B patients within 15 minutes of induction. At the end of procedure, inhalational agents were turned off, patient was extubated and shifted to recovery. All surgeries were performed by a single surgical team. Then patients were shifted to the ward after surgery and followed-up for 24 hours for assessment of PONV. PONV was assessed if there will be presence of nausea vomiting according to VAS* (Visual

analogue scale ≥ 5 (0-10 range) and vomiting one or more than one episode assessed at 24 hours of operation. Efficacy was labeled if there was no or mild nausea but absence of vomiting within first 24 hours after surgery All this information was recorded on proforma.

Statistical Analysis

SPSS version 20 was used to enter and analyses the data. Quantitative variables like age, weight, height, BMI and VAS score was calculated as mean and standard deviation. Qualitative variables like gender and efficacy was calculated as frequency and percentage. Both groups were compared for efficacy by using chi-square test. p-value ≤ 0.05 was taken as significant. Data was stratified for age, gender, ASA and BMI. Stratified groups were compared by using chi-square test. p-value ≤ 0.05 was taken as significant.

RESULTS

The mean age of the patients in group A was 38.40 ± 12.07 years in group B was 42.63 ± 11.77 years. In this study the male patients were 58 in which 33 were from group A and 25 were from group B, similarly the female patients were 62 in which 27 were from group A and 35 were from group B. In our study the patients with anesthesia type ASA I were 64 in which 30 were from group A and 34 were from group B, similarly the patients with anesthesia type ASA II were 56 in which 30 were from group A and 26 were from group B. The mean BMI of the group A patients was 27.14 ± 4.56 kg/m² and in group B was 25.63 ± 5.25 kg/m². Table-I

The mean VAS score of the group A patients was 1.75 ± 2.26 and in group B was 4.18 ± 2.72 . The nausea condition was found in 28 cases in which 7 were from group A and 21 were from group B (p-value=0.003). The vomiting condition was found in 17 cases in which 6 were from group A and 11 were from group B (p-value=0.191). The efficacy achieved in 92 cases in which 53 were from group A and 39 were from group B (p-value=0.003). Table-II

	Study Groups	
	Ondansetron	Metoclopramide
N	60	60
Age (years)	38.40 ± 12.07	42.63 ± 11.77
Male	33	25
Female	27	35
ASA I	30	34
ASA II	30	26
BMI (Kg/m ²)	27.14 ± 4.56	25.63 ± 5.25

Table-I. Baseline characteristics of patients

	Study Groups		P-Value
	Ondansetron	Metoclopramide	
N	60	60	
VAS	1.75 ± 2.26	4.18 ± 2.72	0.000
Nausea	7	21	0.003
Vomiting	6	11	0.191
Efficacy	53	39	0.003

Table-II. Comparison of outcome in both groups

DISCUSSION

PONV is defined as any nausea, retching, or vomiting occurring during the first 24–48 h after surgery in inpatients. PONV is one of the most common causes of patient dissatisfaction after anaesthesia, with reported incidences of 30% in all post-surgical patients and up to 80% in high-risk patients. In addition, PONV is regularly rated in preoperative surveys, as the anaesthesia outcome the patient would most like to avoid. It is therefore not surprising that patients across Europe and North America express a high willingness-to-pay (\$50–100) to avoid PONV. While suture dehiscence, aspiration of gastric contents, oesophageal rupture, and other serious complications associated with PONV are rare, nausea and vomiting is still an unpleasant and all-too-common postoperative morbidity that can delay patient discharge from the post-anaesthesia care unit and increase unanticipated hospital admissions in outpatients.⁹

PONV are unpleasant, distressing adverse effects after general anesthesia and surgery. PONV are sometimes distressing and frequent adverse events of anesthesia and surgery, with a relatively high incidence (53%-72%) after Laparoscopic Cholecystectomy. Many types of drugs are used for the treatment of nausea and vomiting.¹⁰⁻¹²

In our study the ondansetron group significantly showed better efficacy than to metoclopramide group patients in the PONV management of laparoscopic cholecystectomy under general anesthesia. In this study the efficacy achieved in 92 cases in which 53 were from group A and 39 were from group B. Some of the studies are discussed below showing the results in favour of our study and few are on contrary. Many studies reported that ondansetron is statistically superior to metoclopramide for prevention of PONV.¹³⁻¹⁵ Other published studies that evaluated the efficacy of ondansetron and metoclopramide administered intravenously have shown similar reductions in the incidence of PONV during the 24 h post recovery period.^{10,16,17}

A study has reported that efficacy (absence of PONV) with ondansetron was 88.6% while with metoclopramide was 57.6% and the results were statistically significant ($P < 0.05$).² Another study supported these results and reported that efficacy of ondansetron was 69% while with metoclopramide was 44% and the results were statistically significant ($P < 0.05$).¹⁸ In a separate survey of postoperative nausea in some studies, as well as our study, the effect of ondansetron was higher than metoclopramide.¹⁵

One study by Kulsoom Farhat et al¹⁹ presented that in comparison to metoclopramide group, the frequency of nausea and vomiting was clinically and statistically lower in ondansetron group ($p = 0.035$). They concluded that the prophylactic use of ondansetron is more effective with fewer side effects than metoclopramide in the prevention of PONV during laparoscopic cholecystectomy in adult females.

Trichak Sandhu et al¹⁴ documented that incidence of nausea was 45% for metoclopramide and 20% for ondansetron in the 24 hours postoperatively; the difference was statistically insignificant ($p = 0.05$). Postoperative nausea score did not show any significant difference between the two group in the first 2 hours ($p = 0.3$) and 4 hours ($p = 0.12$) but was significant between 4 and 24 hours ($p = 0.02$). The incidence of vomiting was 20% for metoclopramide and 2.5% for ondansetron. This

difference was statistically significant ($p = 0.02$).

Another study by Ashutosh Sayana et al²⁰ performed their study to compare the effectiveness of Granisetron, Ondansetron and Metoclopramide in the management of PONV. They revealed that in the management of PONV, Granisetron was more effective than Ondansetron which showed better results than Metoclopramide.

A study by Isazadehfar et al²¹ showed that for prevention of PONV after laparoscopic cholecystectomy, both metoclopramide and ondansetron are effective, and in preventing of nausea, ondansetron is more effective than metoclopramide, whereas there was not any significant difference between two drugs in preventing of vomiting. But a study contradict these findings and reported that efficacy of ondansetron was 92% while with metoclopramide was 80% and the results were statistically insignificant ($P > 0.05$).²²

One study supported this evidence and reported that efficacy of ondansetron was 80% while with metoclopramide was 55% and the results were statistically insignificant ($P > 0.05$).²³ But one study has found that the efficacy of ondansetron was 55% while with metoclopramide was 68% although the difference was insignificant ($P > 0.05$). This showed that metoclopramide is more efficacious than ondansetron.²⁴ One more study by Erik B Wilson et al¹⁰ demonstrated that prophylactic administration of metoclopramide or ondansetron significantly reduces the incidence of postoperative vomiting for laparoscopic cholecystectomy, but neither drug was found to be significantly more effective than the other. Metoclopramide is a more cost-effective treatment.

CONCLUSION

It has been proved in our study that the patients with ondansetron group showed significantly better efficacy than to metoclopramide group in management of patients undergoing laparoscopic cholecystectomy under general anesthesia

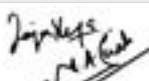
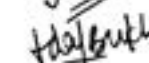
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3	Sadaf Bokhari	Concept and data collection.	