

## Comparison of metoclopramide–dexamethasone combination and metoclopramide alone for prophylaxis of postoperative nausea vomiting in laparoscopic cholecystectomy

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### ABSTRACT

**BACKGROUND & OBJECTIVE:** Postoperative nausea and vomiting (PONV) is an important concern in laparoscopic surgeries. Aim of this study is to identify the role of metoclopramide dexamethasone combination for prophylactic management of post laparoscopic cholecystectomy nausea and vomiting in comparison to metoclopramide alone.

**METHODOLOGY:** The study group comprised 150 patients. These were the patients with symptomatic gallstones for whom elective laparoscopic cholecystectomy was planned. Study was conducted from 15-04-2018 to 15-07-2019. Non-probability consecutive sampling technique was used. Two groups were generated by a simple random method. Group M was given injection metoclopramide only, whereas patients in Group D+M were injected with both dexamethasone and metoclopramide intravenously before induction of anesthesia. Parameters observed for 24 hours during the postoperative period included; nausea, episodes of vomiting, the requirement for rescue antiemetic drugs, and the total duration of hospital stay after the surgical procedure.

**RESULTS:** In Group D+M (dexamethasone+metoclopramide), out of total 75 patients, 6(8%) developed nausea while, 5(5.33%) had both nausea along with emesis. While in group M (metoclopramide), 12(16%) out of the total 75 patients had nausea only but 14(18.7%) patients had complaints of nausea and emesis with p-value=0.002 shows significant association in both groups. Three patients out of 75, that is (4%) from group (D+M) had extended duration of hospital admission (>24 hours), while in group M, this percentage was 13.33% that is 10 patients.

**CONCLUSION:** A combination of metoclopramide with dexamethasone for prophylaxis against PONV in laparoscopic cholecystectomy patients is preferred to metoclopramide alone.

**KEYWORDS:** PONV, Metoclopramide, Dexamethasone, Laparoscopic cholecystectomy.

### INTRODUCTION

Over the years, there has been a continuous evolution in surgical techniques. Minimally invasive techniques like laparoscopic cholecystectomy are now employed for various surgical conditions. It has become increasingly popular in practice since 1987 [1]. It offers certain advantages over the standard open surgical procedure in terms of less tissue trauma, less postoperative pain, and an advantage of being performed as day case procedures. However, the patient's physical status and an uneventful procedure determine the

outcome [2].

Insufflation of carbon dioxide gas into the abdominal cavity is the mainstay of laparoscopic cholecystectomy, as it provides room for tissue dissection and excision [3]. However, this gas may produce significant hemodynamic and ventilatory consequences in the human body [4]. One of the important concerns of this particular laparoscopic procedure is nausea and vomiting in postoperative period. The incidence is high, it approximates 40-70% and is related to peritoneal insufflation with carbon dioxide gas. The pathway is the activation or stimulation of the chemoreceptor trigger zone

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through the activation of serotonin receptors in the gut [5]. There are certain known risk factors related to PONV, such as a history of motion sickness, stress type personalities, young females, non-smokers, and general anesthesia [6,7].

Our study aims to compare the effect of injection metoclopramide when administered alone and a combination with dexamethasone, as an antiemetic, in laparoscopic cholecystectomy patients. Our hypothesis supports that combination drug therapy prophylaxis will be better as compared to a single antiemetic therapy.

## METHODOLOGY

Approval for this observational study was granted by the ethical review committee of the institute. A total of 150 patients participated in the study. These patients were admitted for an elective laparoscopic cholecystectomy at Aziz Fatimah teaching Hospital, Faisalabad from 15-04-2018 to 15-07-2019. Patients were distributed among two groups (group M and Group D+M) 75 in each, using non-probability consecutive sampling.

Group M patients received injection metoclopramide 10mg, and patients in Group D+M were given metoclopramide 10mg + dexamethasone 8mg intravenously. Administration of study drugs and collection of data were assigned to separate individuals; moreover, patients and anesthetists involved in data collection were unaware of the type of antiemetic that was administered.

Patients enrolled into the study were ASA I and ASA II patients, those who fall in the age group of 18 to 60 years, having chronic cholecystitis and with well controlled comorbid states. Patients with poorly controlled diabetes mellitus, hypertension or any other co-morbidity, presentation of acute disease, history of motion sickness, and those unwilling to take part in the study were not included. Informed consent was taken from the patients who were part of the study.

Once in the operating room, baseline vitals were recorded, and the monitor was attached for continuous monitoring throughout the surgical procedure. Study drugs were injected before induction of general anesthesia to the patients according to the assigned group. Antisialogogues and analgesic were administered. Induction of general anesthesia was achieved with the injection propofol and the endotracheal tube passed once adequate muscle relaxation was achieved. Oxygen, nitrous oxide, isoflurane, and a bolus of muscle relaxant were given during the maintenance phase of anesthesia. Continuous vitals monitoring was done. After the procedure, patients stayed in the recovery room and were shifted with a modified Aldrete score of 9/10.

The primary outcome variables; nausea, nausea with vomiting, were recorded for 24 hours postoperatively. Other variables recorded were the need for antiemetic drugs and extended stay in the hospital longer than 24 hours because of nausea and vomiting. A structured proforma was used for keeping a record of data.

The scoring system used was:

- (a) Score 0 = no nausea.
- (b) Score 1 = nausea only.
- (c) Score 2 = nausea with vomiting.

SPSS version 18 was used for data entry and analysis. Quantitative variable (age) analysis was done using mean and standard deviation. For the qualitative variable (gender), frequency and percentages were derived. Stratification was applied to control confounding factors.  $p \leq 0.05$  was taken as significant by application of the chi-square test and Fisher exact test.

## RESULTS

Analysis of the data showed that the mean age of patients in Group(D+M) was  $46.49 \pm 12.550$  and in Group(M) was  $48.63 \pm 12.023$ . Gender distribution was comparable for the two groups,  $p = 0.60$  excluded gender as a potential risk in our study (table-I).

In Group D+M, 65(86.7%) of patients did not have symptoms of retching or emesis, 6(8%) had nausea while 4(5.33%) had nausea and vomiting. Whereas in Group M, 49(65.3%) of patients had no complaint of nausea or vomiting, while 12(16%) patients had nausea and 18.7% had nausea and emesis with  $p$ -value = 0.002 shows a significant association between both groups (table-II).

A 20(26.7%) patients from Group M needed antiemetic drugs as compared to 7(9.33%) patients from Group D+M (table-III). 3(4%) from Group D+M had longer than expected 24 hours stay as compared to 10(13.33%) patients from Group M; the Fisher exact test  $p$ -value = 0.0783 shows non-significant association (Table-IV).

**Table-I: Association among the gender and groups.**

	Female	Male	Total (n)	p-value
Group D+M	26 (34.7%)	49 (65.3%)	75	<b>0.60</b>
Group M	23 (30.7%)	52 (69.3%)	75	

**Table-II: Association among nausea, vomiting, and groups.**

Groups	No Nausea & Vomiting (%)	Nausea & Vomiting (%)	Total(n)	p-value
Group D+M	65(86.66%)	10 (13.33%)	75	<b>0.002</b>
Group M	49(65.33%)	26 (34.66%)	75	

**Table-III: Association among the rescue antiemetic requirements and groups.**

Groups	Antiemetic given	No antiemetic	Total(n)	p-value
Group D+M	7 (9.33%)	68 (90.7%)	75	<b>0.006</b>
Group M	20 (26.7%)	55 (73.3%)	75	

**Table-IV: Association among the hospital stay time and group.**

Groups	24 hr stay	>24 hr stay	Total(n)	Fisher exact test
Group D+M	72 (96%)	3 (4%)	75	<b>0.078</b>
Group M	65 (86.7%)	10 (13.3%)	75	

## DISCUSSION

Laparoscopic cholecystectomies are now increasingly being performed. Shorter hospital stay is the advantage of this procedure, but PONV may lengthen stay in the hospital and increases the treatment cost [8]. Moreover, postoperative nausea and vomiting is a distressful state and has certain adverse effects, including fluid and electrolyte disturbances and pain [4]. Vomiting is a reflex action and is mediated by multiple receptors; thus, it allows multiple drugs to provide an antiemetic effect via action at various sites. So, it has been found to be beneficial to use multiple drugs to manage nausea and vomiting rather than using a single pharmacologic agent. More research is required to establish which agents have more efficacy and low cost for PONV prophylaxis [9].

Metoclopramide is an antiemetic used in routine practice, and it exerts an antagonistic effect on centrally and peripherally located dopaminergic receptors. Moreover, it is a prokinetic for the gastrointestinal system. Once dose is given intravenously, the peak effect is reached within 15 minutes [10]. Another pharmacologic agent which reduces inflammation and pain is Glucocorticoids. Various studies show that they have been used as a monotherapy for PONV prophylaxis [11]. Dexamethasone acts as an antiemetic via central inhibition of the synthesis of prostaglandin as well as by a reduction in brain levels of serotonin [12]. When a dose of 8mg is administered preoperatively in laparoscopic cholecystectomy patients, it results in lesser pain scores, minimal fatigue, less nausea, and a short hospital stay [13]. A meta-analysis reached the conclusion that a combination of dexamethasone with another antiemetic agent offers improved prophylaxis against PONV following laparoscopic cholecystectomy rather than when one agent was used, but further work in this context is required [14].

In Group D+M, 6 patients had complaint of nausea while only 4 had a score of 02, that is, PONV. Whereas in Group M, out of 75 patients, 12 patients had 01 score and 14 had PONV and were given 02 scores. p-value for these statistics was  $p=0.006$ . These statistics show similarity with another study according to which combination therapy provides better antiemetic prophylaxis as compared to monotherapy. This study also showed that fewer patients from the group receiving combination therapy required antiemetics postoperatively. Our study also showed comparable results, in which antiemetic drugs were administered to 7 patients from a group (D+M) and 20 patients from a group (M) ( $p<0.001$ ) [15].

Another study by Alkaissi et al. showed that 16.7% and 33.3% of patients from combination therapy and metoclopramide groups had nausea, and the antiemetic requirement was

for 20% and 43.3% of patients, respectively. This shows a significant difference and thus shows that dexamethasone or its combination with metoclopramide is preferred over metoclopramide alone. The study showed that combination drugs show better patient satisfaction and less morbidity in postoperative time [16].

According to another study, 16% of patients from the combination group and 28% from the monotherapy (metoclopramide only) group showed a requirement for antiemetic therapy after surgery. In terms of hospital stay beyond 24 hours, 6% of patients receiving combined drug therapy and 26% in metoclopramide drug group had to stay longer, with  $p=0.012$ . It shows dissimilarity to our results, that is, 4% ( $n=03$ ) in a group (D+M) while 13.33% ( $n=10$ ) patient in Group M stayed in the hospital longer than 24 hours (fisher test= $0.0783$ , not significant at  $p\leq 0.001$ ) [17].

Amer MU et al. conducted a study where 62% of patients from the metoclopramide group compared to 26% from the metoclopramide-dexamethasone group presented with PONV [18]. A meta-analysis, showed that antiemetic drugs when combined with dexamethasone lead to a significant reduction in incidence of PONV [19]. Another study observed that compared to metoclopramide and normal saline dexamethasone is a more suitable choice for the prevention of PONV [20]. These studies support our results of using combination therapy with dexamethasone-metoclopramide.

We made a conclusion that by adding dexamethasone to the routine antiemetic prophylaxis with metoclopramide, greater benefit is offered in terms of reduction of PONV incidence. Moreover, dexamethasone is a cheaper drug, and its addition produces satisfactory results by reducing patients' stress and anxiety with a very low need for the administration of postoperative antiemetics. Our study could not establish the benefit of shorter hospital stay owing to the use of combination antiemetic.

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**Author's Contribution:**

**Humaira Ahmad:** Conception, design, and acquisition of data.

**Sarwat Bibi:** Data compilation and manuscript drafting.

**Samina Aslam:** Statistical analysis and interpretation of data.

**Asif Sagheer:** Manuscript drafting and final approval of the version.

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