



Comparison of Post Operative Nausea and Vomiting in Metoclopramide alone and Combination of Metoclopramide with Dexamethasone in Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Background: Postoperative nausea and vomiting is a common complication after anesthesia and surgery especially in patients undergoing laparoscopic cholecystectomy. It causes discomfort, delays oral intake, increases hospital stay and reduces patient satisfaction. Single drug antiemetic therapy may not always provide adequate control in high risk surgeries. **Objective:** To compare the frequency of postoperative nausea and vomiting in patients receiving metoclopramide alone and those receiving a combination of metoclopramide with dexamethasone after laparoscopic cholecystectomy. **Methodology:** This randomized controlled trial was conducted in the Department of Anesthesiology Lady Reading Hospital Peshawar from January 2024 to July 2024. A total of 98 patients aged 20 to 70 years undergoing laparoscopic cholecystectomy were included. Group A received metoclopramide alone while Group B received metoclopramide with dexamethasone intravenously before anesthesia induction. Postoperative nausea and vomiting was assessed within 24 hours after surgery. Data were analyzed using chi square test and Fischer exact test with statistical significance set at $p < 0.05$. **Results:** Postoperative nausea and vomiting occurred in 30.6% patients in the metoclopramide alone group and 14.3% patients in the combination group. In patients with body mass index greater than 25 kg per meter square, postoperative nausea and vomiting was significantly lower in the combination group compared to monotherapy ($p = 0.007$). **Conclusion:** Combination of metoclopramide with dexamethasone is more effective than metoclopramide alone in reducing postoperative nausea and vomiting.

INTRODUCTION

Postoperative nausea and vomiting (PONV) is a common and distressing complication occurring after anesthetic and surgical procedures.¹ Moreover, it has a remarkable incidence among patients who have undergone laparoscopic cholecystectomy. PONV usually occurs within the first 24 hours following surgical procedures and can lead to several adverse sequelae by causing discomfort, a delay in oral intake, a prolonged postoperative hospital stay, and a decrease in patient satisfaction.² The pathogenesis of PONV has a multifactorial etiology and involves factors related to general anesthetic administration, opioid analgesia use, surgical stimulation during surgical procedures, pneumoperitoneum used during laparoscopic procedures, and patient-related variables like female gender and a previous history of motion sickness.³ While usually not a potentially lethal complication of PONV, it can lead to serious clinical sequelae like dehydration and electrolyte disturbances in the event of significant fluid and fluid content loss.⁴ In addition, it can also lead to wound

dehiscence and the possible aspiration of vomited material.

Metoclopramide is a common antiemetic for the prevention and treatment of PONV.⁵ Its mechanism of action is primarily antagonistic to dopamine D2 receptors in the chemoreceptor trigger zone, in addition to its prokinetic action, which enhances gastric emptying and gastrointestinal motility.⁶ In this manner, it has contributed to an overall decrease in PONV.⁶ The medication is easily accessed and cost-effective, making it a commonly used anesthetic agent. However, when it is used in monotherapy for the prevention of PONV, it may pose certain limitations in more risk-some surgeries, including laparoscopic cholecystectomy.⁷ In addition, it can cause certain side effects, including somnolence, agitation, and extrapyramidal reaction, but this is less common when it is given in usual dosages.⁸ The combination of metoclopramide and dexamethasone has also been studied for the augmentation of antiemetic prophylaxis in the prevention of postoperative nausea and vomiting.⁹ The mechanism of action of dexamethasone has been suggested to involve anti-inflammation and the

prevention of the release of proemetic mediators.¹⁰ In combination with metoclopramide, the additive effect of the antiemetics in the prevention of postsurgical vomiting is potentiated.¹¹ The combination of the two agents has been found to produce superior results in the prevention of nausea and vomiting, in addition to having very few additional adverse reactions when given in combination with metoclopramide, making it a viable consideration for the treatment of laparoscopic cholecystectomy procedures, in which the risk of PONV is very high.¹² A study observed the frequency of post-operative nausea and vomiting in patients undergoing laparoscopic cholecystectomy and reported a significantly higher incidence with metoclopramide alone compared to the combination of metoclopramide and dexamethasone (36% vs 12%).¹³

This study is necessary in the province of Peshawar because the high prevalence and occurrence of postoperative nausea and vomiting remain uncontrolled after laparoscopic cholecystectomy. Additionally, there is a lack of information from the region. It is important to consider the fact that the patients treated in hospitals in Peshawar may respond to anesthesia and the availability of antiemetics in varying ways to patients treated in other parts of the world. A significant number of patients remain dissatisfied because their nausea and vomiting remain uncontrolled. Through this study, the primary intention is to generate more credible information beneficial in the choice of the antiemetic to administer to patients.

METHODOLOGY

This randomized controlled trial was carried out in the Department of Anesthesiology at Lady Reading Hospital Peshawar over a period from 10 January 2024 to 10 July 2024. Approval for the study was obtained from the Ethical Committee of the hospital as well as from the research department of CPSP Karachi before initiation of data collection. Confidentiality of patient information was ensured throughout the study period and all procedures were conducted according to institutional ethical standards. The sample size was calculated using the WHO sample size calculator for comparative studies. The calculation was based on a confidence level of 95% and a power of 80%. The expected frequency of post-operative nausea and vomiting was taken as 36% in patients receiving metoclopramide alone and 12% in patients receiving the combination of metoclopramide and dexamethasone.¹³ Based on these assumptions a total sample size of 98 patients was achieved with 49 patients allocated to each group. Patients of both genders aged between 20 and 70 years, who were scheduled for laparoscopic cholecystectomy were included in the study. Patients with chronic kidney disease and those having a documented history of allergy to metoclopramide or dexamethasone were excluded from the study. Written informed consent was obtained from all enrolled patients prior to data collection. Demographic variables including age, gender, body mass index, diabetes and hypertension were recorded for each participant.

Eligible patients undergoing laparoscopic cholecystectomy were randomly divided into two equal groups using blocked randomization. Patients in Group A

received metoclopramide alone, administered intravenously as 10 mg in a 3 ml coded syringe, 30 minutes prior to induction of anesthesia. Patients in Group B received a combination of metoclopramide 5 mg and dexamethasone 4 mg, administered intravenously through a 3 ml coded syringe, 30 minutes prior to induction of anesthesia. Post-operative nausea and vomiting was assessed after completion of the procedure and during the first 24 hours following administration of the study medications in both groups. This variable was treated as a single categorical outcome. Post-operative nausea and vomiting referred to the presence of an unpleasant sensation associated with an urge to vomit or the forceful expulsion of gastric contents from the mouth within 24 hours after surgery.

Data were entered and analyzed using SPSS version 25. Numerical variables such as age, weight, height and body mass index were expressed as mean and standard deviation. Categorical variables including gender and post-operative nausea and vomiting were presented as frequencies and percentages. Comparison of post-operative nausea and vomiting between the two groups was performed using chi-square test and a p-value less than 0.05 was considered statistically significant. Effect modifiers such as age, gender, body mass index, diabetes and hypertension were controlled through stratification and post-stratification chi-square test was applied with a significance level of p-value less than 0.05.

RESULTS

The mean age was 37.37 ± 8.13 years in metoclopramide alone group while it was 38.37 ± 8.13 years in combination group. The average weight of patients were 71.92 ± 9.52 kg and 71.25 ± 9.11 kg in group A and group B respectively. Height measurements revealed 1.64 ± 0.06 m in both treatment arms. Body mass index was recorded as 26.71 ± 2.44 kg/m² for metoclopramide alone group and 26.46 ± 2.28 kg/m² for combination therapy group. Gender distribution was identical in both groups with 17 (34.7%) males and 32 (65.3%) females in each group. Regarding comorbidities, diabetes was present in 9 (18.4%) patients in group A and 10 (20.4%) patients in group B, while hypertension was observed in 4 (8.2%) and 5 (10.2%) patients in respective groups (as shown in Table 1).

Table 1
Patient Demographics in Both Groups

Variables	Metoclopramide Alone	Metoclopramide + Dexamethasone
	n=49 Mean ± SD	n=49 Mean ± SD
Age (years)	37.37 ± 8.13	38.37 ± 8.13
Weight (kg)	71.92 ± 9.52	71.25 ± 9.11
Height (m)	1.64 ± 0.06	1.64 ± 0.06
BMI (kg/m ²)	26.71 ± 2.44	26.46 ± 2.28
Gender	n (%)	n (%)
Male	17 (34.7%)	17 (34.7%)
Female	32 (65.3%)	32 (65.3%)
Diabetes		
Yes	9 (18.4%)	10 (20.4%)
No	40 (81.6%)	39 (79.6%)
Hypertension		
Yes	4 (8.2%)	5 (10.2%)
No	45 (91.8%)	44 (89.8%)

The comparison of postoperative nausea and vomiting between two groups demonstrated that PONV occurred in

15 (30.6%) patients who received metoclopramide alone compared to 7 (14.3%) patients in combination therapy group. The remaining 34 (69.4%) patients in group A and 42 (85.7%) patients in group B did not experienced PONV. The p-value for this comparison was 0.053, which approaching but not reaching statistical significance (as shown in Table 2).

Table 2
Comparison of Post-Operative Nausea and Vomiting Between the Two Groups (n=98)

PONV (Metoclopramide Alone)	Group A	Group B (Metoclopramide + Dexamethasone)	P value
	n=49 n (%)	n=49 n (%)	
Yes	15 (30.6%)	7 (14.3%)	0.053
No	34 (69.4%)	42 (85.7%)	
Total	49 (100%)	49 (100%)	

For age stratification, among patients ≤45 years, PONV was present in 15 (46.9%) patients in group A versus 7 (23.3%) in group B, with p-value of 0.073. In patients >45 years, no PONV cases was observed in either group, yielding p-value of 1.000. Gender-based analysis showed that among males, 5 (29.4%) in group A and 3 (17.6%) in group B experienced PONV (p=0.749), while in females, the rates were 10 (31.3%) and 4 (12.5%) respectively, with p-value of 0.074. BMI stratification revealed that for patients with BMI ≤25 kg/m², PONV occurred in 7 (50.0%) of group A patients and 7 (43.8%) of group B patients (p=0.736). However, among patients with BMI >25 kg/m², 8 (22.9%) in group A experienced PONV while none of the patients in group B had PONV, demonstrating statistically significant difference with p-value of 0.007. Diabetes status showed no PONV cases among diabetic patients in either groups (p=1.000), whereas among non-diabetics, PONV rates were 15 (37.5%) in group A and 7 (17.9%) in group B (p=0.055). Similarly, hypertensive patients showed no PONV in both groups (p=1.000), while among non-hypertensive patients, the rates were 15 (33.3%) in group A and 7 (15.9%) in group B, with p-value of 0.088 (as shown in Table 3).

Table 3
Association of Post-Operative Nausea and Vomiting with Demographic Variables

Demographics Variables	Group	PONV		P-value
		Yes (n, %)	No (n, %)	
Age (years)	≤45	A	15 (46.9%)	0.073
		B	7 (23.3%)	
	>45	A	0 (0%)	1.000*
		B	0 (0%)	
Gender	Male	A	5 (29.4%)	0.749*
		B	3 (17.6%)	
	Female	A	10 (31.3%)	0.074
		B	4 (12.5%)	
BMI (kg/m ²)	≤25	A	7 (50.0%)	0.736
		B	7 (43.8%)	
	>25	A	8 (22.9%)	0.007*
		B	0 (0%)	
Diabetes	Yes	A	0 (0%)	1.000*
		B	0 (0%)	
	No	A	15 (37.5%)	0.055
		B	7 (17.9%)	
Hypertension	Yes	A	0 (0%)	1.000*
		B	0 (0%)	
	No	A	15 (33.3%)	0.088
		B	7 (15.9%)	

*Fischer Exact Test

DISCUSSION

The incidence of PONV was lower in combination group 7 (14.3%) compared to metoclopramide alone group 15 (30.6%), though the difference was not reached statistical significance (p=0.053). This trend toward reduced PONV with combination therapy can be explained by synergistic mechanism of action of both drugs. Metoclopramide acts as dopamine antagonist at chemoreceptor trigger zone and also enhance gastric emptying, while dexamethasone exerts antiemetic effect through multiple pathway including inhibition of prostaglandin synthesis and release of endorphins. The combination of these two different mechanism provides more comprehensive coverage against various pathway involved in PONV. The most significant finding was observed in patients with BMI >25 kg/m² where combination therapy completely prevented PONV occurrence 0 (0%) compared to 8 (22.9%) in metoclopramide alone group (p=0.007). This is of great clinical importance since obesity is known to be a risk factor for postoperative nausea and vomiting (PONV) because of the increased intra-abdominal pressure, the longer surgery time, and the different pharmacokinetic properties of the drugs used. Moreover, the anti-inflammatory properties of dexamethasone may play an important role in this respect since obesity is known to be associated with inflammation. In the remaining non-diabetic patients, the incidence of PONV was found to be less in the combination group (7 patients, 17.9%) compared to the monotherapy group (15 patients, 37.5%), but there was only borderline significance (p = 0.055). The low incidence of PONV in the diabetic patients in the two treatment groups may be attributed to the different physiological properties of the patients, including the possibility of gastroparesis.

The present study demonstrated PONV incidence of 14.3% in combination therapy group compared to 30.6% in metoclopramide alone group (p=0.053), which is consistent with findings reported by Ahmad H *et al.*¹⁴ who observed PONV in 13.33% patients receiving combination therapy versus 34.7% with metoclopramide alone (p=0.002). Similarly, Afzal MA *et al.*¹⁵ and Amer M *et al.*¹⁶ reported that 26% patients in combination group experienced PONV compared to 64% in metoclopramide alone group in first 24 hours, showing more pronounced difference than current findings. This variation in magnitude of difference could be attributed to different dosing regimens used, as these studies utilized 5 mg metoclopramide with 4 mg dexamethasone while present study employed standard doses of both medications. The synergistic antiemetic effect through dual mechanism of dopamine antagonism and anti-inflammatory action explains superior efficacy of combination therapy across all studies. The most significant finding in present study was complete prevention of PONV in patients with BMI >25 kg/m² receiving combination therapy 0 (0%) versus 22.9% in monotherapy group (p=0.007). However, this specific BMI stratification was not reported in comparable studies by Ahmad H *et al.*¹⁴ Afzal MA *et al.*¹⁵ or Amer M *et al.*¹⁶ making direct comparison impossible. The enhanced efficacy in overweight patients may be related to improved pharmacokinetic and anti-inflammatory properties of

dexamethasone which counteracts obesity-related inflammatory mediators that contribute to PONV.

Rasheed MA *et al.*¹⁷ studied similar combination in cesarean section patients and found 95% full responders in combination group at first hour postoperatively compared to 75% with metoclopramide alone ($p=0.025$), demonstrating even better efficacy than present study. This superior outcome might be explained by different surgical population and procedure type, as cesarean section has different PONV risk profile compared to laparoscopic cholecystectomy. Alkaissi A *et al.*¹⁸ reported 16.7% nausea incidence in combination group using higher doses of metoclopramide (20 mg) and dexamethasone (8 mg), which is comparable to current findings despite different dosing strategy. Naghibi KH *et al.*¹⁹ investigated pediatric population undergoing strabismus surgery and found only 6.1% PONV in combination group versus 18.2% with metoclopramide alone, showing better efficacy than present study possibly due to different age group and surgical procedure with inherently higher emetogenic potential. Conversely, Rab A *et al.*²⁰ compared metoclopramide and dexamethasone as monotherapies in abdominal surgeries and found no significant difference between groups ($p=0.971$), suggesting that combination approach is necessary to achieve superior antiemetic effect. Interestingly, Waqas A *et al.*²¹ reported that ondansetron was more effective than metoclopramide-dexamethasone combination, with 61.7% patients having no PONV in late postoperative period compared to 35% in combination group. This contrasts with general trend favoring combination therapy and suggests that ondansetron may be preferred choice in certain clinical scenarios despite higher cost. Ahsan A *et al.*²² compared combination therapy with dexamethasone alone and found significantly lower vomiting rates with combination 1.94% versus 8.39% ($p=0.010$), supporting concept that multiple antiemetic mechanisms provides superior prophylaxis.

The current study has a number of limitations that must be discussed. First, it is a single-center study that may not be generalizable in the context of other healthcare facilities that may not use similar patient populations or perform

similar surgical procedures. Second, the number of patients selected was small, that is, only 49 in each group; thus, they may have contributed to the findings of the current study that only achieved borderline significance ($p = 0.053$) for the primary evaluation. Third, the current study was not long-term in that it only evaluated the periods immediately after the surgical procedures. It may be that there were cases of postoperative nausea and vomiting that were delayed in occurrence. Fourth, there are other factors that may influence PONV that are not controlled for in the current evaluation.

CONCLUSION

Based on the findings, it may be concluded that the co-administration method of metoclopramide and dexamethasone is more effective compared to metoclopramide alone for preventing patients undergoing the laparoscopic cholecystectomy procedure from nausea and vomiting. The administration method was more effective as it effectively inhibited the development of PONV, especially among obese patients.

Disclaimer

Not applicable.

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Ethical Permission

This research was approved by the concerned ethics committee. All procedure were carried out by following the committee guidelines and principles of the Helsinki declaration.

Patient Consent

Written permission was taken from all patient before including them in the study. Patients were informed that their personal data would remain confidential and they were free to withdraw at any stage.

Conflict of Interest

The authors declare that there was no personal or financial conflict involved in this research.

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