ORIGINAL ARTICLE

Efficacy of metoclopramide with dexamethasone in comparison with metoclopramide alone for postoperative vomiting after open laparoscopic cholecystectomy

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Abstract

Background: Post operative vomiting is one of the most undesirable events in general anaesthesia that causes discomfort and irritation after surgery. Factors that increase the incidence include female gender, smoking, age, duration of surgery, intraoperative use of opioids and nitrous oxide. Metoclopramide acts centrally asdopamine receptor antagonist and peripherally as cholinomimetic at specific muscarinic receptors. Dexamethasone probably acts by prostaglandin antagonism, serotonin inhibition in gut, release of endorphins and by its anti-inflammatory membrane stabilizing effect. Single dose of Dexamethasone has no side effects.

Objective:To determine the anti-emetic efficacy of metoclopramide plus dexamethasone compared to metoclopramide alone in terms of postoperative vomiting in patients undergoing elective open/laparoscopic cholecystectomy.

Methods:Total 110 patients who have undergone elective open/ laparoscopic cholecystectomy were divided into two equal groups. Patients were intubated with endotracheal tube. Patients were observed for post-operative vomiting during first 24 hours. Descriptive statistics were calculated and stratification was done. Chi-square test was applied, P-value ≤0.05 was considered as significant.

Results:In both Group-A and Group-B 41.8% had open while 58.2% patients had laparoscopic cholecystectomy. In Group-A, vomiting was observed in 40.0% patients and 47.3% in Group-B. In Group-A, mild vomiting episodes were observed in 25.5%, moderate in 9.1%, and severe in 5.5% cases. In Group-B, mild in 16.4%, moderate in 18.2%, and severe in 12.7% episodes were observed. The efficacy was 85.5% in group-A, and 69.1% in Groups. The association was significant with p=0.041.

Conclusion:It was concluded that combination of metoclopramide and dexamethasone is superior in preventing postoperative vomiting.

Key Words:anti-emetic efficacy, metoclopramide, dexamethasone, post operative vomiting, open/laparoscopic Cholecystectomy

Introduction:

Post operative vomiting is one of the most undesirable events in general anaesthesia that causes discomfort and irritation after surgery. Its estimated incidence is 25% to 30%.[1] Post operative vomiting prolongs stay in hospital. Factors affecting it include female gender, smoking, age, duration of surgery, intraoperative use of opioids, nitrous oxide and propofol.[2] Complications of vomiting include dehydration, electrolyte imbalance, wound dehiscence, pulmonary aspiration and esophageal rupture.[3] Those patients who are undergoing cholecystectomy especially laproscopic cholecystectomy are at increased risk of vomiting and in these patients the incidence of vomiting is 50-70%.[4]

Postoperative nausea and vomiting is very distressing for the patient. These symptoms predispose to aspiration of gastric contents, increased intraocular pressure, psychological distress, and delayed recovery and discharge times.[5] Anaesthesia is given worldwide to more than 75 million surgical patients annually. Out of these one third patients suffer from either postoperative nausea or vomiting, or both (PONV).[6] PONV is often described as "Big Little Problem".[4] According to patients avoidance of PONV is of greater

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concern than avoidance of postoperative pain.[7]

Metoclopramide enhances gastric emptying, intestinal transit and lower esophageal sphincter pressure. It is one of the commonly used antiemetics and its side effects are extra pyramidal reactions.[8] Dexamethasone is also used for prevention of vomiting. It acts probably by prostaglandin antagonism, serotonin inhibition in gut, release of endorphins and by its anti-inflammatory membrane stabilizing effect.[9] No single therapy has been proved to be effective in prevention of PONV because of the several emetic centers, all of which may be blocked by different groups of drugs and the diverse risk factors which act alone or in combination to cause vomiting.[10] It is better to use multi-modal approach with combination of anti-emetics of different groups.[11]

Prevention of PONV is especially significant in ambulatory surgeries, which comprise more than 60% of the combined 56.4 million ambulatory and inpatient surgery visits in the United States. It is because ambulatory patients spend very brief time in health care facilities.[12] Strategies to reduce incidence of PONV include the use of regional anesthesia and propofol for induction and maintenance of anesthesia, maintaining adequate hydration and intra-operative FiO2 of >60% along with avoidance of nitrous oxide and volatile anesthetics, and minimization of intra-operative and post-operative opioids and neostigmine.[13]

Material & Method:

This randomized control trial was conducted at the Department of Anaesthesiology, Jinnah Postgraduate Medical Center, Karachi from January to May 2016. Sample size was calculated by the help of WHO sample size calculator. Patients with risk of aspiration or vomiting, pregnant, full stomach, obese, with history of acid peptic disease, history of motion sickness, history of taking steroids, history of extrapyramidal effects with metoclopramide, history of contraindication to metoclopramide or steroids, and history of allergy were excluded. The study wasconducted after the approval from institutional ethical and review committee. The written and informed consent was also taken from the patient or caretaker of the patient. Patients with age 20-50 years with ASA class-I-II who underwent elective open/laparoscopic cholecystectomy were included in the study.

The patients were divided into two groups by random allocation based on table of random numbers. Group A were given injection Metoclopramide 150µg/kg intravenously alone and Group B were given Metoclopramide 150µg/kg with Dexamethasone 100µg/kg, half an hour before induction of anaesthesia. Induction of anaesthesia was done with Nalbuphine 0.1mg/kg, Propofol 2mg/kg and Succinylcholine 1.5mg/kg. Patients were intubated with endotracheal tube of appropriate size. Anaesthesia was maintained by mixture ofisoflurane and muscle relaxation. Patients were monitored for blood pressure, heart rate, oxygen saturation and electrocardiogram. At the end of surgery, on return of muscle power, residual neuromuscular blockade was reversed by injection Neostigmine 30µg/kg along with Atropine 15µg/kg intravenously. Patients were extubated and after complete recovery from anaesthesia patients were shifted to intensive care unit where they were observed for postoperative vomiting during first 24 hours. Any evidence of vomiting was recorded by the trainee researcher or an equivalent postgraduate trainee. The anti-emetic efficacy of drugs was assessed by observing the number of episodes of vomiting within 24 hours post operatively. Episode of nausea/ vomiting per patients was classified as No POV (absence of vomiting), Mild POV(one episode of vomiting), Moderate POV (2 episode of vomiting), Severe POV (>2 episode of vomiting). The Positive Efficacy was considered when No or mild POV was observed and Negative efficacy was considered when Moderate or severe POV was observed.

All the data were compiled and analyzed using SPSS. The quantitative variables i.e. age and episode of vomiting were described by mean±SD. The qualitative variables like gender, smoking, type of procedure (open/laproscopic cholecystectomy), postoperative vomiting, and efficacy

Table 1: *Frequency distribution of gender,smoking and type of procedures*

	Group-A (n=55)		Group-B (n=55)	
	Frequency	%	Frequency	%
Gender				
Male	34	61.8%	31	56.4%
Female	21	38.2%	24	43.6%
Type of Procedures				
Open Cholecystectomy	23	41.8%	23	41.8%
Laparoscopic Cholecystectomy	32	58.2%	32	58.2%
Smoking				
Yes	32	58.2%	34	61.8%
No	23	41.8%	21	38.2%

Table 2: *Descriptive statistics of age and episodes of vomiting*

	Age (years)		**Episodes of Vomiting**	
	Group-A	Group-B	Group-A	Group-B
Mean±SD	34.02±7.31	35.87±9.31	0.64±0.98	1.02±1.36
95% CI (min-max)	32.04 to 36.00	33.35 to 38.39	0.37 to 0.90	0.65 To 1.39
Median (IQR)	32(9)	35(19)	0.00(1)	0.00(2)
Range	28	28	4	5
Minimum	22	22	0	0
Maximum	50	50	4	5

Table 3: *Frequency and association of vomiting and episodes of vomiting with treatment groups.*

	Group-A (n=55)		**Group-B (n=55)**		**P-value**
	Frequency	%	Frequency	%	
Vomiting					
Yes	22	40.0%	26	47.3%	0.442
No	33	60.0%	29	52.7%	
Episodes of Vomiting					
No	33	60.0%	29	52.7%	
Mild	14	25.5%	9	16.4%	0.203
Moderate	5	9.1%	10	18.2%	
Severe	3	5.5%	7	12.7%	

Table 4: *Mean difference of no. of vomiting among two treatment groups*

	Episodes of Vomiting		
	Mean±SD	Mean Difference	P-value
Group-A	0.64±0.98	0.382	0.096
Group-B	1.02±1.36		

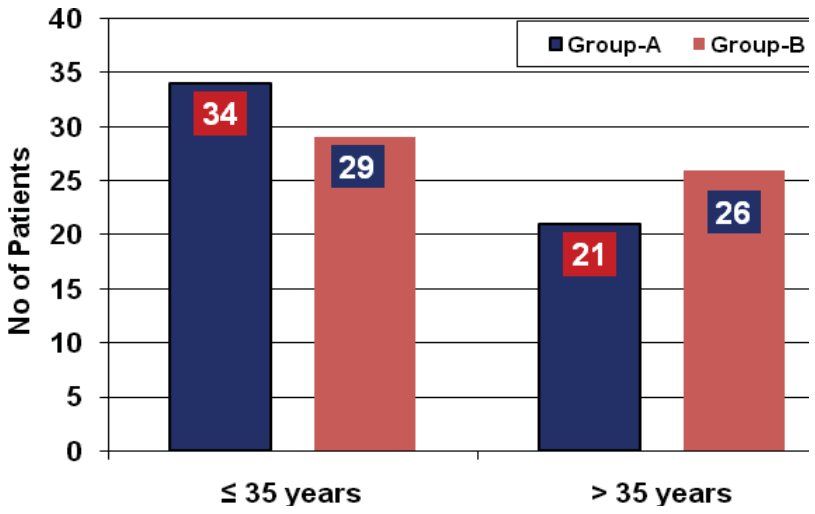
Table 5: *Frequency and association of efficacy with treatment groups*

	Group-A (n=55)		Group-B (n=55)	
	Frequency	%	Frequency	%
Efficacy				
Yes	47	85.5%	38	69.1%
No	8	14.5%	17	30.9%

Table 6: *Frequency and association of efficacy according to stratified groups with treatment groups*

		Group-A (n=55)		Group-B(n=55)		P-value
	Efficacy	Frequency	%	Frequency	%	
Male						
	Yes	28	82.4%	17	54.8%	0.016*
	No	6	17.9%	14	45.2%	
Female						
	Yes	19	90.5%	21	87.5%	0.751
	No	2	9.5%	3	12.5%	
≤ 35years						
	Yes	30	88.2%	24	82.8%	0.536
	No	4	11.8%	5	17.2%	
> 35 Years						
	Yes	17	81.0%	14	53.8%	0.051
	No	4	19.0%	12	46.2%	
Open						
	Yes	20	87.0%	16	69.6%	0.153
	No	3	13.0%	7	30.4%	
Laproscopic						
	Yes	27	84.4%	22	68.8%	0.140
	No	5	15.6%	10	31.2%	
Smoking						
	Yes	26	81.3%	22	64.7%	0.131
	No	6	18.7%	12	35.3%	
No smoking						
	Yes	21	91.3%	16	76.2%	0.171
	No	2	8.7%	5	23.8%	

* Significant at 0.05 levels



were presented by their frequency and percentage. Stratification was done with regards to age, gender, smoking, and type of procedures to see the effect of these modifiers. Chi square test was applied to observe the association of efficacy among the two groups and p-value ≤0.05 was considered as significant. The mean difference of vomiting episodes was also assessed among two groups using student t-test and p-value ≤0.05 was considered as significant.

Results:

The results were calculated according to the two treatment groups. The results showed that there were 34 male and 21 female patients in Group A while 31 male and 24 female patients in group B. In Group A, smoking was found positive in 58.2% patients and in Group B it was found positive in 61.8% patients. Among 55 study subjects of Group A, 41.8% patients had open cholecystectomy while rest of 58.2% patients had laparoscopic cholecystectomy. Similarly in Group B, 41.8% patients also had open cholecystectomy while rest of 58.2% patients also had laparoscopic cholecystectomy. The detailed frequency distributions are presented in Table-1.

The mean age of study subjects of Group A was 34.02±7.31 years and mean age of study subjects of Group B was 35.87±9.31 years. The vomiting episodes within 24 hours were observed and it was evaluated that mean vomiting episodes was 0.64±0.98 in Group-A and 1.02±1.36 in Group-B. The detailed results are presented in Table-2.

The age of both treatment groups were stratified into groups. In group-A, 61.8% patients were aged ≤35 years and 38.2% patients were aged >35 years. In groups-B, 52.7% patients were aged ≤35 years and 47.3% patients were aged >35 years. The frequencies were presented in Graph-1.

In Group A, vomiting was observed in 40.0% patients and in Group B it was observed in 47.3% patients.The vomiting episodes were categorized and the results showed that in Group-A, no vomiting was observed in 60.0% cases, mild episodes were observed in 25.5% cases, moderate episodes were observed in 9.1% cases, and severe episodes were observed in 5.5% cases. While in Group-B, no vomiting was observed in 52.7% cases, mild episodes were observed in 16.4% cases, moderate episodes were observed in 18.2% cases, and severe episodes were observed in 12.7% cases. The Chi square test was applied to evaluate the association of vomiting and episodes of vomiting with treatment groups. The results showed no significant association of vomiting and episodes of vomiting with the treatment groups with p-value > 0.05. The results are presented in Table-3.

The mean difference of no. of episodes was observed among two treatment groups. It was observed that the mean difference was also not significant among study groups with p-value <0.05. The results are presented in Table-4.

Stratification with respect to gender, age, type of procedure, and smoking was done to see the effect of these modifiers on outcome by applying chi square, considering p-value ≤0.05 as significant. The results showed that the significant association of efficacy with the treatment groups was also observed in male patients (p=0.016). No significant association was observed with female (p=0.751), age ≤35 years (p=0.536), age >35 years (p=0.068), open procedure (p=0.153), laparoscopic procedure (p=0.140), smoking (p=0.131), and no-smoking (p=0.171). The detailed results are presented in Table-6.

Discussion:

Researches show that nausea and vomiting are feared far more in comparison to postoperative pain, and PONV is ranked as a major concern by most surgical patients. Persistent vomiting after surgery can result in dehydration, electrolyte imbalance and metabolic alkalosis. Vomiting increases the risk of esophagealperforation, bleeding and pulmonary aspiration. During emesis there is increase in abdominal pressure that may cause tension on suture lines resulting in incisional hernias. Traditional antiemetics, used for the control of PONV includes anticholinergics (e.g. scopolamine), antihistamines (e.g. dimenhydrinate), phenothiazines (e.g. promethazine), butyrophenones (e.g. droperidol), and benzamide (e.g. metoclopramide). Nowadays most commonly used treatment modalities for prevention of PONV are dopamine antagonists, dexamethasone, HT3 receptor antagonists and NK-1receptor antagonists. Dexamethasone is well known for its antiemetic effect and review of literature shows multiple studies supporting its antiemetic efficacy. However there are very few studies that show controversial results. Dexamethasone is cost effective and is easily available in hospitals so it can safely used as antiemetic for prevention of PONV in cholecystectomy. Our study was a comparative study in which we compared two groups of drugs that is metoclopramide alone and combination of metoclopramide and dexamethasone for prevention of PONV.

In one study, incidence of PONV was studied in patients undergoing laproscopic cholecystectomy by using placebo, metoclopramide, dexamethasone and their combination. The total incidence of PONV was 60% with placebo, 45% with metoclopramide, 23% with dexamethasone, and 13% with the combination of dexamethasone plus metoclopramide. None of the dexamethasone plus metoclopramide group patients and one dexamethasone group patient required antiemetictreatment, however four patients in the metoclopramide group and six patients in the placebo group required antiemetic. So combination of metoclopramide and dexamethasone was superior to metoclopramide or dexamethasone alone for prevention of PONV.[14]

In another study done at Nishtar Hospital Multan incidence of PONV was studied by using metoclopramide alone and combination of metoclopramide and dexamethasone. In first 6 hours of postoperative period 33% patients in metoclopramide group experience vomiting while only 10% patients in combination group experience vomiting.[9] So results of this study were comparable to our study.

Another study done at Jordan University Hospital, Amman, an incidence of PONV was studied in patients undergoing laproscopic cholecystectomy by using 4mg ondansetron, 8mg dexamethsone and normal saline.The incidences of PONV were 32% in the ondansetron group, 30% in the dexamethasone group, and 33% in the saline group. There were no significant differences among the groups ($p > 0.05$). So it was concluded that addition of dexamethasone to anaesthetic technique does not add any benefit for prevention of PONV.[15]

Study Limitations:A limitation of our study was that male gender predominated in our survey. Therefore, one should be cautious in extra-polating our findings to women. One of the limitations in this study is that, study was conducted on a small scale and at urban environment therefore, the findings might not be generalizable to larger populations.

Conclusion:
we conclude that combination of metoclopramide with dexamethasone is superior to metoclopramide alone in preventing post-operative vomiting among patients undergoing cholecystectomy.

Role and contribution of authors:

Dr Muhammad Nadeem Muneer, assistant professor, JPMC, selection of topic, collection of references, writing the discussion and conclusion.

Dr Shoaib Malik, assistant professor, JPMC, collection of references and compilation of results.

Dr Abdul Majeed, collection of data and their statistical analysis and compilation of results

Conflict of Interest: None

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