

Impact of Dexamethasone in Improving Outcomes of Laparoscopic Cholecystectomy: A Case- Control Study

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Abstract

Background: Postoperative nausea and vomiting (PONV) remains a matter of concern for surgeons as they induce dehydration, metabolic abnormalities, delayed recovery, and other problems. It has been shown that dexamethasone can contribute to the reduction of postoperative symptoms. Therefore, this study aimed to evaluate the protective role of dexamethasone in reducing postoperative nausea and vomiting in patients who underwent laparoscopic cholecystectomy (LC) through comparison with antiemetic metoclopramide.

Patients and methods: About 153 patients who underwent cholecystectomy in surgical unit of Tikrit Teaching Hospital (Iraq) during the period between August 2021 and October 2022 participated in this prospective clinical case-control study. The patients were divided into three groups as follow: Group (DEX) patients were dosed with intravenous dexamethasone (8mg) at induction of general anesthesia; Group (MET) patients were treated with metoclopramide (10mg) intravenously; while normal saline solution (2ml) was administrated to control patients (CON) as a placebo. The incidence of postoperative nausea and/or vomiting in the three groups was recorded and compared.

Results: The data confirmed the significant differences between the post-operative outcomes between the two drug comparison groups with regard to PONV.

Conclusion: Dexamethasone (8 mg) is considered more effective and safe than metoclopramide in reducing postoperative nausea and vomiting after laparoscopic cholecystectomy.

Keywords: Cholecystectomy, dexamethasone, nausea, vomiting.

Introduction

Currently, the laparoscopic technique has replaced the open technique in several common operations, including routine cholecystectomy [1-4]. Laparoscopic cholecystectomy (LC) is clearly defined as a minimally invasive surgical procedure to remove an inflamed gallbladder resulting from symptomatic cholelithiasis, gallstone, gallbladder masses, and benign tumors [5-7]. Postoperative nausea and vomiting (PONV) is defined as any nausea, retching, or vomiting that occurs within the first 24-48 hours after surgery in an inpatient setting. They are among the most common causes of patient dissatisfaction after anesthesia, with an incidence of 30% in all postoperative patients and up to 80% in high-risk patients [8,9]. Although serious adverse events are uncommon after laparoscopic cholecystectomy, approximately (50- 75%) of patients develop a postoperative nausea and vomiting [10].

In general, vomiting center in the lateral reticular formation of the medulla oblongata coordinates vomiting, while chemoreceptor trigger zone (CTZ) is located in the postnatal region. Peripheral and central stimuli can affect both the vomiting center and the CTZ area [11]. The etiology of PONV is multifactorial, including factors related to the patient, medicine, surgery, and anesthesia. Certain surgeries are associated with an increased risk of PONV such as laparoscopy, breast augmentation, shoulder orthopedic, strabismus surgeries, and varicose vein stripping [12-14]. The mechanisms that produce PONV after LC may differ from those that produce this complication after other operations. Therefore, drugs that are effective in other cases may not have the same effect after LC. After corticosteroids were shown to be effective in chemotherapy-induced nausea and vomiting, they were used in anesthesia as a prophylaxis against PONV [15]. The mechanism of action of antiemetic corticosteroids is not known, but prostaglandin antagonism has been suggested to be the mechanism, and release of endorphins is another suggested explanation for this action. It has also been speculated that the mechanism of action is related to the anti-inflammatory and membrane-stabilizing effect [16]. The antiemetic mechanism of dexamethasone is not fully understood. However, central inhibitions of prostaglandin synthesis, inhibition of endogenous opioid release, and

changes in the permeability of the blood-brain barrier for serum proteins have been suggested. It may also exert its antiemetic effect through some peripheral mechanisms [17]. As a corticosteroid, it has potent anti-inflammatory effects and can significantly reduce inflammation of the tissues around the surgical sites thus decreasing ascending parasympathetic impulses to the vomiting center and reducing PONV [18]. The aim of the study was to evaluate the role of prophylactic dexamethasone administration in reducing postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy and to compare its effect with that of the well-known antiemetic metoclopramide.

Methods and patients

This prospective case control study was conducted on 153 patients attending the surgical ward at Tikrit Teaching Hospital, Iraq during the period from August 2021 to October 2022. Inclusion criteria included adult patients with symptoms of cholelithiasis underwent elective LC. In contrast, exclusion criteria included patients with diabetes mellitus, acute cholecystitis, gastric and duodenal ulcers, history of a hypersensitivity reaction to metoclopramide, and previous upper abdominal surgery. The study was carried out after obtaining the informed consent of each participating patient, in addition to the approval of the local health directorate. All patients received a similar type of standardized anesthesia regimen induction with propofol, maintenance with isoflurane, relaxation with aturacurionium and reverse with neostigmine. A reverse trendelenberg was performed with the right side up and a pneumothorax established at the port site above the umbilicus, using the open technique. During laparoscopy, intra-abdominal pressure was maintained at 12 - 13 mm Hg and at the end of surgery; CO₂ was removed by manual abdominal pressure. The LC is performed using standard 4-port technology with two 10mm ports and two 5mm ports. The gallbladder was extracted through the epigastric port and the fascial defect of the 10 mm port was closed using 2/0 Vicryl. The participants were divided into three equal groups as follow: Group DEX was given (8 mg) intravenously dexamethasone at induction of G.A., group (MET) was given (10 mg) of metoclopramide intravenously. Whereas, (2 ml) of normal saline was given to the control group (CON) as a placebo. Nausea and/or vomiting, after 6 and 24 hours, were recorded in the three postoperative groups. Grades of vomiting can be categorized as follows: Grade 0: no vomiting, grade 1: (1-4) episodes/24 hours, grades 2: >4 episodes/24 hours. Then all data were analyzed using SPSS (version 20) software, and statistical analysis included descriptive statistics and Z-test for comparisons between qualitative variables. In this analysis, statistical significant correlation was determined, and $p < 0.05$ was considered significant.

Results

Of 153 patients enrolled in this study, 145 (94%) were females and 9 (6%) males. Ages of patients ranged from (19-74) years with mean age (45) years, their weights ranged between (50 - 92) kg, mean weight was (76) kg as shown in (Table 1).

Table 1: Baseline characteristics of the participating patients .

Characters	Study groups		
	DEX N= 51	MET N= 51	CON N= 51
Mean of Age (years)	46	45	47
Gender (Female: Male)	48:3	49:2	47:4
Mean of body weight (Kg)	77	76	77
Mean of operation time (minutes)	45	45	45

Incidence of PONV

In DEX group, eight patients (15.7%) reported nausea and 6 patients (12%) had episodes of vomiting. So total incidence of PONV observed in 14 patients (27.7%) . This means that 72.3% of patients are free of PONV and this has a significant P value. In MET group, total incidence of PONV occurred in 21 patients (41%). Twelve

patients (23, 5%) reported nausea and 9 patients (17.5%) developed vomiting that is 59% had no PONV. In CON group, PONV had been recorded in 36 patients (70%), as nausea in 19 cases (37 %), while 17 patients (33 %) had vomiting (Table 2).

Table 2: Incidence of PONV among study groups .

Groups	PONV		Total	P value
	Nausea	Vomiting		
DEX	8 (15.7%)	6 (12%)	14 (27.7%)	0.018*
MET	12 (23.5%)	9 (17.5%)	21(41%)	0.118
CON	19 (37%)	17(33%)	36 (70%)	/

Frequency of vomiting

Grade 1 (1-4) episodes/24 hrs : It occurred in 5 of 6 patients (83%) in group DEX. It was reported in 5 out of 9 patients (55.5%) in group MET, & reported in 9 out of 17 patients (53%) in group CON as shown in (table 3).

Grade 2 (>4) episodes/24 hrs: It had been reported in 1patient (17 %), 4 patients (45.5%), 8 patients (47%) in the groups DEX, MET, and CON respectively. So, most of patients (83%) who developed vomiting in group DEX are of low grade (grade 1), in contrast to MET and CON groups.

Table 3: Grades of vomiting among study groups .

Groups	Vomiting grades			
	Grade 1	P- value	Grade 2	P- value
DEX	5 (83%)	0.001**	1 (17%)	0.001*
MET	5(55.5%)	0.839	4 (44.5%)	0.800
CON	9 (53%)	/	8 (47%)	/

Time onset of vomiting

Regarding the time onset, we found that group DEX reported the least percentage of late onset of vomiting, i.e. among the 6 patients who developed vomiting, 4 of them (66, 6%) had within the first 6 hours, & 2 patients (33.3%) had late onset vomiting (6-24 hrs).In group MET, 4 out of 9 (44,5%) stated late onset of vomiting. About group CON, 9 out of 17 (53%) reported vomiting after 6 hours. Statistical analysis revealed no significant difference between groups DEX & MET, as shown in table (Table 4).

Table 4: Time onset of vomiting among study groups .

Groups	Vomiting time				
	Total	Within 6 hrs.	P- value	(6-24) hrs.	P- value
DEX	6	4 (66.6%)	0.048*	2 (33.3%)	0.047*
MET	9	5 (55.5%)	0.392	4(44.5%)	0.420
CON	17	8(47%)	/	9 (53%)	/

Requirements for rescue antiemetic

In those how develop vomiting, two patients in group DEX (33.3 %), while in groups MET there were 5 patients (55.5 %) and 12 patients in group CON (70%) required rescue antiemetic as shown in table (5).

Table 5: Number & percentage of patients required rescue antiemetic.

Group	DEX	MET	CON
Patients	2 (33.3%)	5 (55.5%)	12 (70%)
P- value	DEX & MET		0.262*
	DEX & CON		0.003*
	MET & CON		0.133

Complete response

It was 72.5 % ,60 % , and 30 % in groups DEX, MET, and CON respectively (Table 6).

Table 6: Percentage of complete response among study groups .

Group	DEX	MET	CON
Patients	(37)72.3%	(30)59%	(15)30%
P- value	DEX & MET		0.160
	DEX & CON		0.001*
	MET & CON		0.004*

Discussion

Several studies report that dexamethasone reduces postoperative pain and fatigue and improves outcomes along with reducing PONV in patients undergoing LC, and recommend its routine use [19,20]. This is supported by the results of our current study, as the total incidence of PONV reached (70%) at 24 hours post-operative in patients underwent laparoscopic cholecystectomy without receiving prophylactic antiemetic. In a recent similar study by Jamil and Qaisar (2022) on 160 patients underwent laparoscopic cholecystectomy under general anesthesia. They concluded that the mean pain score was significantly lower in the group of laparoscopic cholecystectomy patients dosed with a single dose of dexamethasone at a dose of 0.1 mg/kg intravenously at induction of anesthesia than in placebo group and thus can be considered effective for postoperative pain control[21]. In another study by Rabie and Abdelfattah (2022) involving sixty patients, they concluded that intravenous infusion of 0.6 µg/kg/hour of dexmedetomidine before anesthesia induction attenuated the hemodynamic stress response as well as PONV incidence, and postoperative analgesic requirements in patients undergoing laparoscopic cholecystectomy [22]. Ahmad and colleagues (2023), in their study of 150 patients with symptoms of gallstones, concluded that a combination of metoclopramide with dexamethasone had better results for the prevention of PONV in laparoscopic cholecystectomy patients than metoclopramide alone [23]. This supported our findings, as the incidence of PONV in the current study in patients who dosed with dexamethasone was lowest than other patients (27.7%). Regarding frequency of vomiting, we found in the present study that dexamethasone besides reducing PONV it also lowered the frequency of vomiting in patients. In a study by Rekei et al. (2021) recommended the use of a combination of dexmedetomidine (25mg) and dexamethasone (4 ml/2 mg) to reduce nausea and vomiting after surgical laparoscopic cholecystectomy [24]. After a thorough literature search, we were unable to find a report of side effects associated with the use of a single dose of dexamethasone. Besides this distinctive therapeutic efficacy of dexamethasone, the cost of use is added,

avoiding unnecessary expenses on anti-emetics with their undesirable effects and saving nursing care efforts [25,26].

Conclusion

A single prophylactic dose of dexamethasone (8mg) is safe and effective in prevention of postoperative nausea and vomiting for laparoscopic cholecystectomy. Also, it is more effective than metoclopramide in reducing PONV following LC, with no observed adverse effects.

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