

Comparative Study of the Effectiveness of Ondansetron, Metoclopramide and Low Dose Dexamethasone to Prevent Postoperative Nausea and Vomiting in Females who Undergo Laparoscopic Cholecystectomy

Masoomeh Tabari¹; Hossein Shabahang²; Alireza Tavasoli²; Hassan Abbaspour³; Mohammad Alipour^{1,*}

¹Department of Anesthesiology, Ghaem Hospital, Endoscopic and Minimally Invasive Research Center, Mashhad University of Medical Sciences, Mashhad, IR Iran

²Department of General Surgery, Endoscopic and Minimally Invasive Surgery Research Center, Ghaem Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran

³Department of Anesthesiology, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, IR Iran

*Corresponding author: Mohammad Alipour, Department of Anesthesiology, Ghaem Hospital, Endoscopic and Minimally Invasive Research Center, Mashhad University of Medical Sciences, Mashhad, IR Iran. Tel: +98-05118012612, E-mail: alipourm@mums.ac.ir

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Background: Despite progress in surgical and anesthetic techniques, postoperative nausea and vomiting are among the most common surgical complications. Prevention and suitable treatment of postoperative nausea and vomiting can decrease the length of hospital stay, hospitalization cost and increase patient satisfaction.

Objectives: The aim of this study is to assess the effectiveness of three antiemetic drugs in postoperative nausea and vomiting prevention on female patients who undergo laparoscopic cholecystectomies.

Patients and Methods: This prospective randomized double-blind clinical trial enrolled 126 women, aged 20 to 65 years, who had American Society of Anesthesiologists I and II classifications and were scheduled for elective laparoscopic cholecystectomy. All patients received the same induction and care with propofol-based total intravenous anesthesia. After general anesthesia, patients were randomly divided into four groups: dexamethasone (5 mg; n = 31), ondansetron (4 mg; n = 32), metoclopramide (10 mg; n = 31), and normal saline (n = 32). The patients were assessed for incidence and severity of nausea and vomiting at intervals of 0-1, 1-6, and 6-24 hours after extubation.

Results: The incidence of nausea was as follows among patients: 72 (20.8%) in the ondansetron group, 23.6% in the dexamethasone group, 25.0% in the metoclopramide group, and 30.5% in the control group. Vomiting was found in 49 patients with an incidence rate of 8.1%, 16.3%, 36.7% and 38.7%, in ondansetron, dexamethasone and metoclopramide groups, respectively. The highest incidence of the initial nausea symptom occurred at the 1-6 hour interval in all groups (P = 0.034). Only ondansetron (P = 0.005) and dexamethasone (P = 0.019) were effective in preventing nausea at the 0-1 hour interval. The severity of nausea in patients who received dexamethasone was less.

Conclusions: Ondansetron was more effective than dexamethasone and metoclopramide in preventing vomiting after laparoscopic cholecystectomy at intervals of 0-1 and 1-6 hours. Ondansetron delayed the interval of the first onset of nausea and vomiting.

Keywords: Ondansetron; Dexamethasone; Metoclopramide; Laparoscopic Cholecystectomy; Postoperative Nausea and Vomiting

1. Background

Postoperative nausea and vomiting (PONV) is one of the most common adverse effects of anesthesia and surgery, particularly among women following laparoscopy surgery (1). Prevention and suitable treatment of PONV can reduce the duration and cost of hospitalization and increase patient satisfaction. Various studies have shown that 20% to 30% of the general population is at risk for PONV, however in patients who undergo laparoscopy the risk is 53% to 72% and in children over three years of age, PONV is greater than 40% (2, 3).

Laparoscopic gallbladder surgery (cholecystectomy) is a standard treatment for patients with symptomatic gallstones and it has replaced open cholecystectomy. The application of this technique has spread worldwide due to the advantages of decreased pain and faster recovery times (4). Practically, in the treatment and prevention of PONV, it is preferred that antiemetic drugs be admin-

istered based on the Apfel simplified risk score. Of note the application of a regional risk score strategy is effective and accompanied by significant reductions in nausea and vomiting (5, 6). Hence, increased knowledge and updated information about PONV enable physicians to demonstrate better daily clinical skills, particularly with regards to treatment of PONV.

2. Objectives

The aim of this study was to compare the effectiveness of three popular regimens for prevention of PONV in females who underwent the laparoscopic cholecystectomy procedure.

3. Patients and Methods

After obtaining agreement from the Ethics Committee

of Mashhad University of Medical Sciences, we enrolled 126 female patients (20 to 65 years old) with American Society of Anesthesiologists (ASA) I and II classifications. Patients were candidates for elective laparoscopic cholecystectomy in this randomized double blind study. Enrollment was contingent upon patients meeting the inclusion criteria and signing the informed consent form. Patients were excluded from the study if they had an allergy history or contraindications to the prescribed medications, a positive history of chronic nausea and vomiting, presence of nausea and vomiting 24 hours before anesthesia, were prescribed antiemetic drugs 24 hours before surgery, a body mass index (BMI) > 35, ages > 65 and ≤ 20 years, pregnancy, positive history of illegal drug or cigarette abuse, mobility problems, and migraines. Following general anesthesia, the patients were randomly assigned to one of the four study groups: metoclopramide (10 mg; n = 31), ondansetron (4 mg; n = 32), dexamethasone (5 mg; n = 31), and the control group that received normal saline (n = 32).

All patients received 10 cc/kg of crystalloid prior to anesthesia induction. Patients subsequently received 0.04 mg/kg of midazolam, 3 µg/kg of fentanyl, 2 mg/kg of propofol and 0.5 mg/kg of atracurium induction while a nasal gastric tube was inserted for suction of gastric secretions. The anesthesia process was continued by administration of 100 to 150 µg/kg/minute of propofol, 0.1 µg/kg/minute of intravenous remifentanyl, and 6 L/minute of 100% oxygen. Atracurium, at a 0.15 mg/kg dose every 20 to 30 minute, was used when necessary for muscle relaxation until the end of the surgery. Morphine at a dose of 0.1 mg/kg was administered intravenously to all patients half an hour before the end of surgery to reduce pain caused by the operation. During surgery blood pressure, heart beat, electrocardiography (ECG), SpO₂, and exhaled carbon dioxide (ETCO₂) were monitored. All patients received 0.04 mg/kg of neostigmine and 0.02 mg/kg of atropine to reverse muscle relaxation.

After extubation, we recorded the manifestation and severity of nausea [without nausea, nausea with visual analog scale (VAS) ≤ 4, and nausea with VAS > 4], and vomiting (positive or negative) in patients at interval periods of 0-1, 1-6, and 6-24 hours after surgery. Following the ethic principles in our study, suitable treatment and care were taken for all patients. No patients were withdrawn from the study because of reported adverse effects.

For post-surgical pain control, patients received diclo-

enac sodium suppositories every 6 to 8 hours depending on patients' needs. In cases of vomiting and nausea after surgery, antiemetic drugs from different drug classes with appropriate doses were administered intravenously.

Collected data was inserted in a special check list and analyzed by SPSS software version 14. We used the chi-square test, Fisher's exact test, and ANOVA or its equivalent Kruskal-Wallis nonparametric test. The significance level was set at 5% for all tests.

4. Results

Nausea was found in 72 out of 126 patients with an incidence rate of 20.8% in the ondansetron, 23.6% in the dexamethasone, 25.0% in the metoclopramide, and 30.5% in the control groups. Vomiting was found in 49 patients with an incidence rate of 8.1%, 16.3%, 36.7% and 38.7% in ondansetron, dexamethasone, metoclopramide and control groups, respectively. The mean age of patients was 41.79 ± 11.88 years which was similar between groups (P = 0.216). Mean duration of anesthesia was 98.29 ± 32.8 minutes, which did not show any significant differences in the four main study groups (P = 0.269; Table 1).

The antiemetic drugs showed a significant effect when we simultaneously compared the manifestation and severity of nausea in the 0-1 hour (P = 0.003) and 1-6 hour (P = 0.034) subgroups of the four study groups. In a comparison of the manifestation and severity of nausea of each group with the control group, we observed that only in the 0-1 hour time interval was there a significant effect by dexamethasone (P = 0.019) and ondansetron (P = 0.005; Table 2).

There was a significant effect by antiemetic drugs when we compared the presence of vomiting in the 0-1 hour (P = 0.003), 1-6 h (P = 0.015), and 6-24 hour (P = 0.002) subgroups. However in a comparison of onset of vomiting in each medication group with the control group we observed that only metoclopramide at 0-1 hour (P = 0.026) as well as ondansetron at 0-1 hour (P = 0.005) and 1-6 hour (P = 0.006) were significant (Table 3).

A simultaneous comparison of the time interval of the first nausea (P = 0.036) and vomiting (P < 0.001) episodes in the four study groups was significant. Moreover, a comparison of the time interval of the first nausea and vomiting manifestations in each group separately with the control group showed that in the dexamethasone group the time interval of the first vomiting episode was significant (P = 0.047). In the ondansetron group the time

Table 1. Duration of Anesthesia and Age of Participants ^{a,b}

	Total	DXM	MCP	OND	Control	P Value ^c
Age, y	41.79 ± 11.88	41.16 ± 12.34	44.97 ± 11.31	42.37 ± 11.49	38.75 ± 12.08	0.22
Duration of anesthesia, min	98.29 ± 32.8	96.45 ± 31.58	99.84 ± 24.85	90.47 ± 38.49	106.41 ± 34.04	0.27

^a Data are presented as Mean ± SD.

^b Abbreviations: **DXM**: Dexamethasone; **MCP**: Metoclopramide; **OND**: Ondansetron

^c One-way ANOVA F-test

interval of the first vomiting ($P = 0.009$) and nausea ($P < 0.001$) manifestations were significant (Tables 4 and 5). The highest incidence of the first nausea was observed during the 1-6 hour interval in all groups. Only ondansetron and dexamethasone were more effective compared to the other groups in preventing nausea at the 0-1 hour interval. The severity of nausea in patients who received dexamethasone was less.

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Table 2. Manifestation and Severity of Nausea During the Study Time Intervals ^{a,b}

Study group	Total	DXM	MCP	OND	Control	P Value ^c
0-1 hours						0.003
Without nausea	115 (91.3)	30 (96.8)	29 (93.5)	32 (100)	24 (75.0)	
Nausea with VAS ≤ 4	4 (3.2)	1 (3.2)	1 (3.2)	0 (0.0)	2 (6.3)	
Nausea with VAS > 4	7 (5.6)	0 (0.0)	1 (3.2)	0 (0.0)	6 (18.8)	
1-6 hours						0.034
Without nausea	75 (59.5)	17 (54.8)	21 (67.7)	19 (59.4)	18 (56.3)	
Nausea with VAS ≤ 4	20 (15.9)	10 (32.3)	3 (9.7)	1 (3.1)	6 (18.8)	
Nausea with VAS > 4	31 (24.6)	4 (12.9)	7 (22.6)	12 (37.5)	8 (25.0)	
6-24 hours						0.069
Without nausea	87 (69)	22 (71)	17 (54.8)	27 (84.4)	21 (65.6)	
Nausea with VAS ≤ 4	14 (11.1)	5 (16.1)	4 (12.9)	0 (0.0)	5 (15.6)	
Nausea with VAS > 4	25 (19.8)	4 (12.9)	10 (32.3)	5 (15.6)	6 (18.8)	

^a Data are presented as No. (%).

^b Abbreviations: VAS: Visual analog scale; DXM: Dexamethasone; MCP: Metoclopramide; OND: Ondansetron

^c Chi-square test

Table 3. Total Manifestation of Vomiting ^{a,b}

Study group	Total	DXM	MCP	OND	Control	P Value ^c
0-1 Hours	11 (8.7)	2 (6.5)	1 (3.2)	0 (0.0)	8 (25)	0.003
1-6 Hours	25 (19.8)	5 (16.1)	9 (29)	1 (3.1)	10 (31.3)	0.015
6-24 Hours	28 (22.2)	3 (9.7)	14 (45.2)	4 (12.5)	7 (21.9)	0.002

^a Data are presented as No. (%).

^b Abbreviations: DXM: Dexamethasone; MCP: Metoclopramide; OND: Ondansetron.

^c Chi-square test between positive and negative vomiting manifestations in the four therapeutic groups for each evaluation interval.

Table 4. Initial Onset of Nausea ^{a,b}

Study group	Total	DXM	MCP	OND	Control	P Value ^c
0-1 Hours	11 (8.7)	1 (3.2)	2 (6.5)	0 (0)	8 (25)	0.036
1-6 Hours	46 (36.5)	13 (41.9)	9 (29)	13 (40.6)	11 (34.4)	
6-24 Hours	15 (11.9)	3 (9.7)	7 (22.6)	2 (6.3)	3 (9.5)	

^a Data are presented as No. (%).

^b Abbreviations: DXM: Dexamethasone; MCP: Metoclopramide; OND: Ondansetron.

^c Chi-square test between different intervals of nausea onset.

Table 5. Initial Onset of Vomiting ^{a,b}

Study group	Total	DXM	MCP	OND	Control	P-value ^c
0-1 Hours	11 (8.7)	2 (6.5)	1 (3.2)	0 (0)	8 (25)	0.001
1-6 Hours	19 (15.1)	3 (9.7)	8 (25.8)	1 (3.1)	7 (21.9)	
6-24 Hours	19 (15.1)	3 (9.7)	9 (29)	3 (9.4)	4 (12.5)	

^a Data are presented as No. (%).

^b Abbreviations: DXM: Dexamethasone; MCP: Metoclopramide; OND: Ondansetron.

^c Chi-square test between different intervals of vomiting onset.

5. Discussion

The study groups were similar in terms of age and average stage of anesthesia. In general, dexamethasone, metoclopramide, and ondansetron were effective after surgery to reduce the amount of nausea manifestation and severity during the 0-1 hour ($P = 0.003$) and 1-6 hour ($P = 0.034$) time intervals. The severity of nausea was less with dexamethasone. In a comparison with the control group, only dexamethasone ($P = 0.019$) and ondansetron ($P = 0.005$) were effective after surgery to reduce the severity of nausea and its manifestation during the 0-1 hour time interval.

In general, the evaluated drugs were effective after surgery in reducing vomiting during the 0-1 hour ($P = 0.003$), 1-6 h ($P = 0.015$), and 6-24 h ($P = 0.002$) time intervals. In a comparison to the control group, metoclopramide was effective in the first hour and ondansetron was effective in the 0-1 hour and 1-6 hour intervals in reducing vomiting after surgery ($P = 0.001$, $P = 0.005$ and $P = 0.006$, respectively).

Initial appearance of nausea for all groups primarily occurred during the 1-6 hour time interval. The highest amount of onset of vomiting in the dexamethasone group occurred equally during the time intervals of 1-6 and 6-24 hours; in the ondansetron and metoclopramide groups initial vomiting episodes primarily occurred during the 6-24 hour time interval. In the control group the initial onset of vomiting primarily occurred 0-1 hours after surgery. Ondansetron delayed the onset of both vomiting ($P = 0.009$) and nausea ($P < 0.001$) episodes. Dexamethasone delayed the occurrence of the onset of vomiting ($P = 0.047$).

The study results of Mayeur et al. showed that nausea and vomiting incidents after surgery in the 8 mg dexamethasone group was 30%, for the ondansetron group it was 32%, and in the control group it was 33% which showed no difference between the study groups (7). However, in the current study the onset of vomiting in the ondansetron group was later than the other groups. Kaki et al. reported that the frequency of vomiting and nausea after surgery was similar in both the control and metoclopramide groups (28%). This frequency was less in the ondansetron group (20%) (5), which was similar to the current study results.

In a study by Erhan et al. and Ho et al. the occurrence of vomiting and nausea was more common in the control group compared with the ondansetron and the granisetron groups, and the lowest rate was observed in dexamethasone group. These drugs were relatively effective in reducing nausea and vomiting after surgery (6, 8), while in the current study ondansetron was more effective in reducing vomiting. Wu et al. reported that ondansetron was more effective in the prevention of nausea and vom-

iting compared to metoclopramide, which was similar to the current results (9, 10).

In cases that necessitate the use of an antiemetic drug to prevent nausea and vomiting after surgery, according to basic patient risk, ondansetron is preferable compared to dexamethasone and metoclopramide. We recommend dexamethasone in cases where a second drug is required. Major surgeries with longer periods of anesthesia have increased incidences of nausea and vomiting after surgery. In the current study, the average anesthesia period for all study patients was 98.9 ± 32.8 minutes. Possibly, nausea and vomiting manifestations after surgery can be decreased by reducing the anesthesia duration. Considering the duration effect of ondansetron, we recommend more comparison studies with antiserotonin drugs that have longer duration effects such as palonosetron, granisetron, and aprepitant.

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