# Comparative study between Ondansetron, Alizapride and Dexamethasone in Prevention of Postoperative Nausea and Vomiting in Laparoscopic Surgery

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## ABSTRACT

**Background:** Post-operative nausea and vomiting (PONV) is a common cause of post-operative discomfort with incidence ranges from (50%-70%) after laparoscopic surgery.

**Objective:** To compare the effectiveness of dexamethasone, ondansetron and alizapride as monotherapy administered intravenously in postoperative nausea and vomiting prophylaxis for patients with moderate to high risk for nausea and vomiting undergoing laparoscopic surgery under general anesthesia.

**Patients and Methods:** The study population was 120 Egyptian patients from both sexes undergoing laparoscopic surgery under general anesthesia with endotracheal intubation at Al-Azhar University Hospitals (El Hussein Hospital and Bab Al-Sharya Hospital). Approval of the study was taken from the Ethics Committee of Al-Azhar University. Prior to initiation of the study, written informed consent of the patient was obtained after full explanation of elements contained in the research protocol. There were 4 study groups; Control group, ondansetron group, alizapride group and dexamethasone group.

**Results:** Age, sex, smoking history, related history, duration of surgery, type of surgery,
vital signs and postoperative pain severity did not have any significant value in our study. Comparing the 4 studied groups according to postoperative nausea and vomiting presence, time of incidence and number of episodes had a significant value.

**Conclusion:** Intravenous 0.1 mg/kg of ondansetron is very safe and highly significant in control of postoperative nausea and vomiting (PONV), it is even more effective than using 50 mg of intravenous alizapride or 8 mg of intravenous dexamethasone as prophylaxis. Dexamethasone is slightly better than alizapride in control of postoperative nausea and vomiting.

**Keywords:** Dexamethasone, Ondansetron, Alizapride, laparoscopic surgery, post-anesthetic care unit**.**

## INTRODUCTION

Postoperative nausea and vomiting (PONV) is a common cause of postoperative discomfort and its incidence rate ranges from (50%-70%) after laparoscopic surgery [(1)]. Risk factors include opioid analgesic drugs, postoperative pain, the anesthetic agent or anesthesia technique, sudden movement or positional changes of the patient, a history of motion sickness, hypotension, the site of surgical operation, day of menstrual cycle and estrogen level[(2)].

The best scoring system for PONV has been argued. The Apfel score; age<50 years, female, non-smoking, and history of PONV, and opioid administration has become highly accepted [(3)].

The Sinclair score includes duration and type of surgery as well**.** The risk factors for PONV also been assessed by Apfel group. These include female patients, younger than 50 years, history of nausea and/or vomiting after anesthesia and opioid intake [(4)].

Hypotension and bradycardia may trigger emesis [(5)]. A liberal crystalloid regime reduces PONV risk [(6)]**.** Fasting 6 hours for food and 2 hours for clear liquor exhibits explicit benefits, e.g. reduced PONV[(7)].

Complete opioid free anesthesia has a reducing effect of PONV [(8)]. A long surgical period may have a great impact on PONV in women who undergo laparoscopic surgery [(9)].

The duration of nitrous oxide exposure seems to have an impact; less than 1 hour use as part of the fresh gas has not been shown to increase the risk [(10)].

The relative risk of nausea and vomiting is four times higher during menses; days one to eight of the menstrual cycle [(11)]. Female gender is associated to more PONV than men [(12)]. Non-smoking and younger age are well-known high risk factors for PONV [(13)].

Ondansetron is a selective 5-hydroxytryptamine receptor antagonist with potent antiemetic activities. Its clearance half-time is 3.2-3.9 hours and a single dose of ondansetron provides long antiemetic effects. Ondansetron is effective in preventing post-operative nausea and vomiting (PONV) after laparoscopic, orthopedic, gynecologic, thyroid, and ophthalmic surgeries. The best dose for PONV prophylaxis is a single 4 mg bolus of I.V. ondansetron[(14)].

The $D_2$-receptor antagonist alizapride is a methoxy-2-benzamide derivative structurally related to metoclopramide [(15)]. Alizapride is a well-established antiemetic which is widely used in oncology and perioperative medicine [(16)].

Since the mid 1980s, studies have stated that dexamethasone can decreases vomiting in patients after chemotherapy [(17)]**.** Subsequent studies have also found that dexamethasone effectively



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prevents PONV induced by epidural morphine which is used to reduce post-operative pain [18].

## AIM OF THE WORK

To compare the effectiveness of dexamethasone, ondansetron and alizapride as monotherapy administered intravenously in post-operative nausea and vomiting prophylaxis for patients with moderate to high risk for nausea and vomiting undergoing laparoscopic surgery under general anesthesia.

## PATIENTS AND METHODS

**Patients:** The study population was 120 Egyptian patients from both sexes undergoing laparoscopic surgery under general anesthesia with endotracheal intubation at Al-Azhar University Hospitals (El Hussein Hospital and Bab Al-Sharya Hospital): Approval of the study was taken from the Ethics Committee of Al-Azhar University. Prior to initiation of the study, written informed consent of the patient was obtained after full explanation of elements contained in the research protocol.

**Study design:** This is a single-center, open-label, double blinded prospective, randomized study. The patients, health care providers included in the patient care, the person who collected and analyzed data, and the outcome adjudicators were unaware of the treatment group allocation.

**Randomization:** Randomization was done through opaque and well-sealed envelopes. The sequence generation was done by computer. Number was written on envelope and group was written on the card within it along with the serial number. When a patient comes, an envelop was opened to see the group to be allotted. Patients were randomly allocated to receive a single dose of ondansetron, alizapride, dexamethasone or normal saline.

**Study Groups: - Control group**: received 10 ml of normal saline. **Ondansetron group**: received 0.1 mg/kg of ondansetron. **Alizapride group**: received 50 mg of alizapride. **Dexamethasone group**: received 8 mg of dexamethasone.

**Assignment of Interventions:** Medications were administered in a 10 ml syringe. Syringes were labeled with a study-specific identification i.e. a number for each patient. The anesthetist administered the study medication and was unaware of the distribution of the treatment groups.

**Inclusion Criteria**: Patients with age between 18-60 years. Weight between 50-120 kg. Patients who were planned for laparoscopic surgery under GA. American Society of Anesthesiologists (ASA) I-II.

**Exclusion Criteria** Patients with history of gastrointestinal hemorrhage. Patients who developed nausea and vomiting on the last day on prior surgery. Patients who received antiemetic drugs within 24 hours on prior surgery. Conversion to open cholecystectomy. Patients with previous history of drug reaction to any of the drug used in the present study. Patients with less than 6 hours fasting. Patients who were taking corticosteroids. Patients with any pathology that causes preoperative nausea or vomiting. Patients with ASA score III or more. Patients below 18 years and above 60 years old. Patients with history of severe hypotension.

**Patients' assessments:** All patients were subjected to perioperative assessment which will include: -Preoperative assessment (In outpatient clinic center). Intraoperative assessment (After induction of anesthesia). Postoperative assessment (In postoperative care unit).

**Preoperative assessment**: - Age. Sex. Diagnosis. Type of laparoscopic surgery. History of motion sickness, taking anti-emetic drugs, repeated nausea and vomiting, any pathology that increases or decreases the risk of PONV, and smoking.

**Intraoperative assessment:** Oxygenation. Blood pressure. Pulse. Duration of surgery. Unusual intraoperative events during the surgery.

**Postoperative assessment: -** Presence of nausea. Presence of vomiting. Amount and frequency of vomiting. Specific characters of vomitus. Time of vomiting incidence. Presence of postoperative pain. Intensity of postoperative pain. Amount of rescue anti-emetics needed postoperatively. Amount of analgesics needed postoperatively.

### *Data analysis*

All the observed parameters and results were carefully recorded and analyzed statistically. Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**.** **(**Armonk, NY: IBM Corp**):** Qualitative data were described using number and percent. Significance of the obtained results was judged at the (5%) level.

**The used tests were:- Chi-square test:** For categorical variables, to compare between different groups. **Monte Carlo correction:** Correction for chi-square when more than (20%) of the cells have expected count less than 5. **F-test (ANOVA):** For normally distributed quantitative variables, to compare means of more than 2 groups.

## RESULTS

**Table (1):** Distribution of the studied cases

| | No. | % |
|---|---|---|
| **Total** | **120** | **100.0** |
| **Included patients** | **100** | **83.3** |
| Saline | 25 | 20.8 |
| Ondansetron | 25 | 20.8 |
| Alizapride | 25 | 20.8 |
| Dexamethasone | 25 | 20.8 |
| **Excluded patients** | **20** | **16.7** |
| ASA (III& IV) | 10 | 8.3 |
| Lost follow | 2 | 1.7 |
| Refused to participate | 8 | 6.7 |

**Table (2): Comparison between the four studied groups according to sex**

| Groups / Variables | Control group (n = 25) | Ondansetron group (n = 25) | Alizapride group (n = 25) | Dexamethasone group (n = 25) | $\chi^2$ | P-value |
|---|---|---|---|---|---|---|
| **Sex** | | | | | | |
| Male | 9 (36.0%) | 12 (48.0%) | 8 (32.0%) | 10 (40.0%) | 1.471 | 0.689 |
| Female | 16 (64.0%) | 13 (52.0%) | 17 (68.0%) | 15 (60.0%) | | |

$\chi^2$: Chi square test Data presented as number (n) and percentage (%)
P: p value for comparing between the four studied groups

**Table (3): Comparison between the four studied groups according to age**

| Groups / Variables | Control group (n = 25) | Ondansetron group (n = 25) | Alizapride group (n = 25) | Dexamethasone group (n = 25) | F | P - value |
|---|---|---|---|---|---|---|
| **Age (years)** | | | | | | |
| Mean ± SD. | 34.64 ± 10.76 | 39.04 ± 10.04 | 39.16 ± 8.72 | 37.92 ± 9.74 | 1.148 | 0.334 |

F: F for ANOVA test , P: p value for comparing between the four studied groups
Data presented as mean ± standard deviation (M ± SD)

**Table (4): Comparison between the 4 studied groups according to related history.**

| Groups / Variables | Control group (n = 25) | Ondansetron group (n = 25) | Alizapride group (n = 25) | Dexamethasone group (n = 25) | $\chi^2$ | P - value |
|---|---|---|---|---|---|---|
| **ASA Score** | | | | | | |
| I | 10 (40.0%) | 9 (36.0%) | 13 (52.0%) | 8 (32.0%) | 2.333 | 0.506 |
| II | 15 (60.0%) | 16 (64.0%) | 12 (48.0%) | 17 (68.0%) | | |
| **Surgery type** | | | | | | |
| Lap Chol. | 21 (84.0%) | 21 (84.0%) | 21 (84.0%) | 22 (88.0%) | 0.388 | $^{MC}p=$ 1.0 |
| Gastric sleeve | 4 (16.0%) | 4 (16.0%) | 4 (16.0%) | 3 (12.0%) | | |
| **Motion sickness history** | 7 (28.0%) | 5 (20.0%) | 10 (40.0%) | 10 (40.0%) | 3.309 | 0.346 |
| **Antiemetics history** | 7 (28.0%) | 5 (20.0%) | 10 (40.0%) | 10 (40.0%) | 3.309 | 0.346 |
| **Frequent nausea and vomiting history** | 7 (28.0%) | 5 (20.0%) | 10 (40.0%) | 10 (40.0%) | 3.309 | 0.346 |
| **Smoking history** | 5 (20.0%) | 11 (44.0%) | 7 (28.0%) | 8 (32.0%) | 3.506 | 0.320 |

$\chi$2: Chi square test MC : Monte Carlo test Data presented as number (n) & percentage (%), P: p value for comparing between the four studied groups

**Table (5): Comparison between the four studied groups according to intraoperative assessment**

| Variables \ Groups | Control group (n = 25) | Ondansetron group (n = 25) | Alizapride group (n = 25) | Dexamethasone group (n = 25) | Test of Sig. | P-value |
|---|---|---|---|---|---|---|
| **Systolic blood pressure (mmHg)** Mean ± SD. | 96.40 ± 4.90 | 96.0 ± 5.0 | 96.0 ± 5.0 | 96.0 ± 5.0 | F= 0.040 | 0.989 |
| **Diastolic blood pressure (mmHg)** Mean ± SD. | 56.40 ± 4.90 | 56.0 ± 5.0 | 56.0 ± 5.0 | 56.0 ± 5.0 | F= 0.040 | 0.989 |
| **Duration of surgery** 1 hour | 21 (84.0%) (16.0%) | 21 (84.0%) (16.0%) | 21 (84.0%) 16.0%) | 22 (88.0%) 3 (12.0%) | $\chi^2$= 0.388 | $^{MC}p$= 1.0 |

$\chi^2$: Chi square test MC : Monte Carlo test F: F for ANOVA test
P: p value for comparing between the four studied groups

Data presented as mean ± standard deviation (M ± SD) and number (n) and percent (%)

**Table (6): Comparison between the four studied groups according to postoperative nausea**

| Variables \ Groups | Control group (n = 25) | Ondansetron group (n = 25) | Alizapride group (n = 25) | Dexamethasone group (n = 25) | $\chi^2$ | P-value |
|---|---|---|---|---|---|---|
| **Presence** | 13(52.0%) | 4(16.0%) | 7(28.0%) | 6(24.0%) | 8.571* | 0.036* |
| **Sig. bet. Groups** | $p_1$=0.007*,$p_2$=0.083,$p_3$=0.041*,$p_4$=0.306,$p_5$=0.480,$p_6$=0.747 | | | | | |
| **Time** 1st 2nd | 11(84.6%) 2 (15.4%) | 3(75.0%) 1 (25.0%) | 6(85.7%) 1 (14.3%) | 4(66.7%) 2(33.3%) | 1.491 | $^{MC}p$= 0.789 |
| **Episodes number** 1 | 13 (100.0%) | 4 (100.0%) | 7(100.0%) | 6 (100.0%) | - | - |

$\chi^2$: Chi square test MC : Monte Carlo test Data presented as number (n) and percentage (%)
P: p value for comparing between the four studied groups
p1: p value for comparing between control group and Ondansetron group
p2: p value for comparing between Saline group and Alizapride group
p3: p value for comparing between Saline group and Dexamethasone group
p4: p value for comparing between Ondansetron group and Dexamethasone group
p5: p value for comparing between Ondansetron group and Alizapride group
p6: p value for comparing between Dexamethasone group and Alizapride group
*: Statistically significant at $p \leq 0.05$

**Table (7): Comparison between the four studied groups according to postoperative vomiting.**

| Groups / Variables | Control group (n = 25) | Ondansetron group (n = 25) | Alizapride group (n = 25) | methasone group (n = 25) | $\chi^2$ | P- value |
|---|---|---|---|---|---|---|
| **Presence** | 13(52.0%) | 4(16.0%) | 7(28.0%) | 6(24.0%) | 8.571* | 0.036* |
| **Sig. bet. Grps** | $p_1$=0.007*,$p_2$=0.083,$p_3$=0.041*,$p_4$=0.306,$p_5$=0.480,$p_6$=0.747 | | | | | |
| **Time** | | | | | | |
| 1st | 11(84.6%) | 3(75.0%) | 6(85.7%) | 4(66.7%) | 1.491 | MCp= 0.789 |
| 2nd | 2(15.4%) | 1(25.0%) | 1(14.3%) | 2(33.3%) | | |
| **Episodes number** | | | | | | |
| 1 | 11(84.6%) | 3(75.0%) | 6(85.7%) | 5(83.3%) | 0.894 | MCp= 1.000 |
| 2 | 2(15.4%) | 1(25.0%) | 1(14.3%) | 1(16.7%) | | |
| **Rescue anti-emetics** | 13(52.0%) | 4(16.0%) | 7(28.0%) | 6(24.0%) | 8.571* | 0.036* |
| **Sig. bet. Grps** | $p_1$=0.007*,$p_2$=0.083,$p_3$=0.041*,$p_4$=0.306,$p_5$=0.480,$p_6$=0.747 | | | | | |

$\chi^2$: Chi square test MC: Monte Carlo test Data presented as number (n) & percentage (%)
P: p value for comparing between the four studied groups
p1: p value for comparing between control group and Ondansetron group
p2: p value for comparing between control group and Alizapride group
p3: p value for comparing between control group and Dexamethasone group
p4: p value for comparing between Ondansetron group and Dexamethasone group
p5: p value for comparing between Ondansetron group and Alizapride group
p6: p value for comparing between Dexamethasone group and Alizapride group
*: Statistically significant at $p \leq 0.05$

**Table (8): Comparison between the four studied groups according to postoperative pain severity**

| Groups / Variables | Control group (n = 25) | Ondansetron group (n = 25) | Alizapride (n = 25) | Dexamethasone group (n = 25) | $\chi^2$ | P-value |
|---|---|---|---|---|---|---|
| **Severity** | | | | | | |
| No | 0 (0.0%) | 0 (0.0%) | 1(4.0%) | 0 (0.0%) | | |
| Mild to moderate | 16 (64.0%) | 22 (88.0%) | 16 (64.0%) | 15 (60.0%) | 8.759 | 0.123 |
| Severe | 9 (36.0%) | 3 (12.0%) | 8 (32.0%) | 10 (40.0%) | | |
| **Rescue analgesic** | 9 (36.0%) | 3 (12.0%) | 8 (32.0%) | 10 (40.0%) | 5.524 | 0.137 |

$\chi$2: Chi square test Data presented as number (n) & percentage (%)
P: p value for comparing between the four studied groups

**Table (9): Relation between PONV and risk factors.**

| | Nausea and Vomiting | | $\chi^2$ | P |
|---|---|---|---|---|
| | No (n = 70) | Yes (n = 30) | | |
| **Motion sickness history** | 8(11.4%) | 24(80.0%) | 45.378* | <0.001* |
| **Anti-emetics history** | 8(11.4%) | 24(80.0%) | 45.378* | <0.001* |
| **Frequent nausea & vomiting history** | 8(11.4%) | 24(80.0%) | 45.378* | <0.001* |
| **Non-smoking history** | 41(58.6%) | 28(93.3%) | 11.864* | 0.001* |
| **Severity**: No | 0(0.0%) | 1(3.3%) | 40.936* | MCp <0.001* |
| Mild to moderate | 62(88.6%) | 7(23.3%) | | |
| Severe | 8(11.4%) | 22(73.3%) | | |
| **Surgery duration:** 1 hour | 69(98.6%) | 16(53.3%) | 33.707* | FEp <0.001* |
| 2 hour | 1(1.4%) | 14(46.7%) | | |
| **Sex**: Male | 36(51.4%) | 3(10.0%) | 15.150* | <0.001* |
| | 34(48.6%) | 27(90.0%) | | |

$\chi^2$: Chi square test Data presented as number (n) & percentage (%) MC : Monte Carlo test
P: p value for comparing between the four studied groups

## DISCUSSION

In our study, age did not constitute a significant risk factor. Neither did we observe that the incidence of PONV depended on the gender, type of laparoscopic surgery, ASA score or surgery duration. History of motion sickness, frequent vomiting, anti-emetics intake or smoking did not show any significant difference in our study.

**Masoomeh *et al.*** [19] found in a similar study that age and surgery duration did not show any significant difference.

It was noted that PONV occurred less frequently in the groups administered antiemetic drugs than in the control group. Patients of control group had the highest rate of PONV and requested rescue anti-emetics in 13 patients out of 25 with percentage of (52%). Our results are congruent with a previous study by **Langevin *et al.*** [20]

The best results were obtained in the group in which we administered ondansetron, whereas the worst results were observed in the control group that received normal saline.

In ondansetron group only (16%) of patients had postoperative nausea and vomiting. In dexamethasone group (24%) of patient presented with nausea and vomiting. In alizapride group (28%) of patients had postoperative nausea and vomiting.

Similar results were reported by **Masoomeh *et al.*** [19] 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.

In a study by **Ho *et al.*** [21] the occurrence of vomiting and nausea was the most common in the control group compared with the dexamethasone, ondansetron and the granisetron groups, and the lowest rate was observed in dexamethasone group. **Wu *et al.*** [22] reported that ondansetron was the most effective in the prevention of nausea and vomiting.

## CONCLUSION

Intravenous 0.1 mg/kg of ondansetron is very safe and highly significant in control of PONV. It is even more effective than using 50 mg of intravenous alizapride or 8 mg of intravenous dexamethasone as prophylaxis. Dexamethasone is slightly better than alizapride in control of postoperative nausea and vomiting. Both alizapride and dexamethasone are definitely better than using normal saline. The highest rate of PONV was among the control group of normal saline.

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