

# Comparing the Effect of Ondansetron–dexamethasone and Metoclopramide–dexamethasone on Postoperative Nausea and Vomiting after Gynecological Laparoscopy: A Randomized Double-blind Clinical Trial

## Abstract

**Background:** Nausea and vomiting is a common complication after gynecological surgeries, especially laparoscopy, which can lead to discomfort and restlessness in the patients. The aim of the study was to compare the effect of ondansetron–dexamethasone and metoclopramide–dexamethasone on postoperative nausea and vomiting following gynecological laparoscopy. **Materials and Methods:** In this double-blind clinical trial, 68 females scheduled for gynecological laparoscopy and age range of 18–40 years were randomly divided into two groups. Group OD received ondansetron 4 mg plus dexamethasone 8 mg and group MD received metoclopramide 10 mg plus dexamethasone 8 mg, 15 min before the end of surgery. The incidence of nausea and vomiting and need for rescue medication was assessed during the recovery period, as well as at 2, 4, 6, 12, and 24 h after surgery. The data were analyzed using STATA software version 12 and a significance level of  $<0.05$  was considered in this research. **Results:** The incidence of nausea in ondansetron and metoclopramide groups was 23.3% and 33.3%, respectively, and the frequency of vomiting was 10% and 16.6%, respectively, which showed no significant difference ( $P > 0.05$ ). The highest incidence of nausea and vomiting in patients belonged to the metoclopramide group inside 4–6 h after surgery. **Conclusion:** Our study showed that no significant difference was observed in the incidence of nausea and vomiting between ondansetron–dexamethasone and metoclopramide–dexamethasone groups following laparoscopic gynecological surgery; however, the number of patients with nausea and vomiting was lower in the ondansetron–dexamethasone group.

**Keywords:** Laparoscopy, metoclopramide, ondansetron, postoperative nausea and vomiting

## Introduction

Nausea and vomiting is known as the second most adverse and problematic event after surgery,<sup>[1]</sup> which occurs after general, regional, and even local anesthesia.<sup>[2]</sup> The incidence of postoperative nausea and vomiting is nearly 30%, which increases to 70% in patients with certain risk factors.<sup>[3–5]</sup> The type of surgery is not necessarily the most important cause of postoperative nausea and vomiting, which is mostly due to factors related to the patient and anesthesia; however, female gender, laparoscopic surgery, and opioids are influential factors in this regard.<sup>[5–8]</sup>

Postoperative nausea and vomiting can cause dehydration, electrolyte disturbances, hypertension, aspiration of gastric contents, postoperative hypoxemia,

hematoma at the site of surgical resection or suturing, metabolic disorders such as metabolic alkalosis, decreased activity and postoperative patient's dissatisfaction, prolonged hospitalization, longer nursing care, and increasing treatment costs.<sup>[7,9,10]</sup>

Laparoscopic surgery, including gynecological operations such as ovarian cyst surgery, is used to diagnose and treat several diseases.<sup>[11]</sup> Injection of CO<sub>2</sub> into the peritoneal space during laparoscopy can stimulate the vagus nerve and thus increases the likelihood of nausea and vomiting.<sup>[12]</sup> For unknown reasons, the incidence of nausea and vomiting in women is 2–3 times that of men, which is increased when gynecological and laparoscopic surgeries are combined.<sup>[6,7]</sup> To prevent and reduce nausea and vomiting, various suggestions have been presented such as

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gastric emptying, nonadministration of N<sub>2</sub>O, administration of antiemetic drugs, use of short-acting anesthetics, and less manipulation during surgery.<sup>[13]</sup>

Metoclopramide is the most common drug for the control and prevention of nausea and vomiting that should be used with caution due to extrapyramidal side effects.<sup>[14]</sup> Ondansetron, a competitive antagonist of peripheral 5-hydroxytryptamine receptor at vagus nerve terminals as well as intestinal and central neurons in chemoreceptor trigger zone (CTZ), is a relatively newer drug with fewer side effects that has recently been considered in various studies.<sup>[15]</sup> The use and administration of dexamethasone for the prevention and treatment of nausea and vomiting is recommended in researches.<sup>[7]</sup> In a number of studies, the combination of dexamethasone with an antiemetic drug, including ondansetron or metoclopramide, has been associated with better efficacy.<sup>[16-19]</sup>

Choosing an appropriate and timely method for the prevention and treatment of nausea and vomiting leads to patient satisfaction, improves the level of activities and recovery, and reduces treatment costs.<sup>[8]</sup> The aim of this study was to compare the effect of ondansetron–dexamethasone and metoclopramide–dexamethasone on postoperative nausea and vomiting following laparoscopic gynecological surgery.

## Materials and Methods

### Design

This randomized double-blind controlled trial was approved by the Institutional Clinical Research Ethics Committee of Kurdistan University of Medical Sciences, and the study was registered at the Iranian Registry of Clinical Trials (IRCT code: IRCT20171216037910N2). All patients provided written informed consent to participate in the study.

In this randomized double-blind controlled trial, 68 patients who were candidates for ovarian cyst surgery by laparoscopic method and who underwent general anesthesia in Besat Hospital (Sanandaj, Iran) with inclusion criteria of age range 18–40 years, classified as American Society of Anesthesiologists physical status I or II, were enrolled in the study. Non-inclusion criteria are as follows: diabetes, history of motion sickness, gastroesophageal reflux disease, body mass index (BMI) >30, previous history of postoperative nausea and vomiting, history of opioid use or drug addiction, breastfeeding, contraindication to acetaminophen use, and exclusion criteria were as change of surgical procedure to open surgery, and need for administration of opioids in the postoperative period. The patients were divided into two groups by computer-generated random numbers. Based on computer-generated random numbers, odd numbers were in the ondansetron group and even numbers were in the metoclopramide group.

### Interventions

After entering the theatre room, intravenous (IV) line (G18) was established. Electrocardiography, pulse oximetry, pulse rate, and noninvasive blood pressure cuff were attached to the patient for monitoring. 500 ml of Ringer's lactates was infused. Fluid therapy was based on the period of fasting preoperatively, surgery time, and surgical losses. For the induction of anesthesia, fentanyl (2 µg/kg), propofol (2 mg/kg), and atracurium (0.4 mg/kg) were administered for all the patients. After intubation, anesthesia was maintained in both groups using 4 L/min oxygen and 1.2% isoflurane. Metoclopramide and ondansetron were prepared in equal volumes (2 mL syringe) by an anesthesia nurse who did not participate in the study. Fifteen minutes before the end of surgery (as reported by the surgical team), the first group (O group) received 4 mg ondansetron plus 8 mg dexamethasone and the second group (M group) received 10 mg metoclopramide plus 8 mg dexamethasone by an anesthesiologist who was not involved in the research. At the end of the surgery, the effects of muscle relaxation were reversed using atropine (15 µg/kg) and neostigmine (40 µg/kg). The patients were transferred to the postanesthesia care unit after. In case of vomiting or severe and prolonged nausea more than 5 min in patients, metoclopramide (10 mg) was administered intravenously. For pain relief, IV acetaminophen was administered at a rate of 1 g/100 ml of saline 0.9% for 20 min.

### Assessment

The incidence rate of nausea and vomiting was recorded by an anesthesia nurse who was not aware of the grouping and type of medication during the recovery period. The patients were also followed for nausea and vomiting by a nurse at 2, 4, 6, 12, and 24 h after surgery. The need for antiemetic drugs was recorded over a 24-h period. The mean arterial pressure and heart rate of patients were recorded by bedside monitoring.

### Data analysis

The collected data were analyzed using STATA version 12 (StataCorp LLC, College Station, Texas, USA) as well as mean and frequency tests, variance, and Mann–Whitney test. 95% confidence interval and significance level of < 0.05 were considered in this research.

### Results

From ninety-one patients investigated in this study based on the inclusion and noninclusion criteria, 68 were selected to participate in the study, but at the end, 61 patients were analyzed. The group randomization according the CONSORT is shown in Figure 1.

There was no significant difference according to the age, heart rate, mean arterial pressure (MAP), body mass index (BMI), and duration of surgery between the two groups [Table 1].

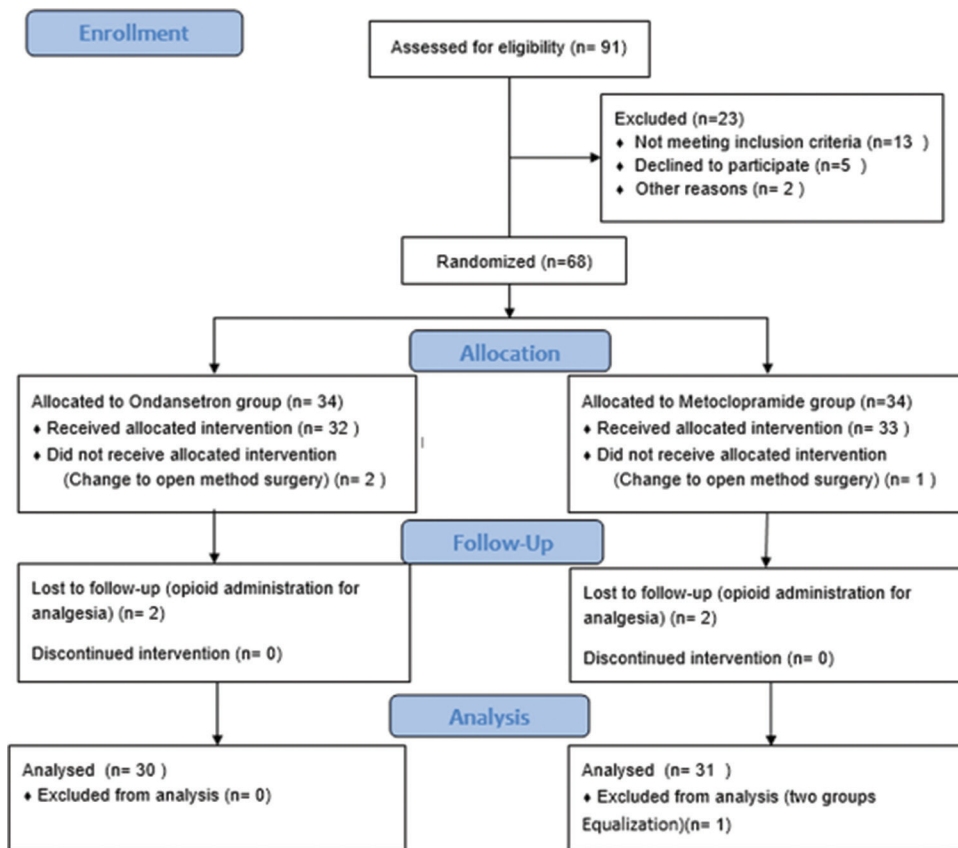


Figure 1: Group randomization according to the Consolidated Standards of Reporting Trials 2010<sup>[20]</sup>

**Table 1: Demographic variables and clinically data of the participants in two groups**

Variable	Ondansetron-dexamethasone group	Metoclopramide-dexamethasone group	P
Age	29.35±4.71	27.90±4.97	0.24
BMI	26.03±2.76	26.71±2.12	0.53
Heart rate	85.54±6.68	83.71±6.42	0.31
MAP	92.89±5.65	91.97±6.78	0.21
Duration of surgery	71.39±19.76	65.57±17.10	0.09

Analysis of variance test was used to compare the variable, data presented as mean±SD. BMI: Body mass index, MAP: Mean arterial pressure, SD: Standard deviation

All patients stated that they had no history of smoking. The mean age of patients participating in the study was 28.63 ± 4.85 years, which was 29.35 ± 4.71 and 27.90 ± 4.97 in ondansetron and metoclopramide groups, respectively ( $P > 0.05$ ).

Using Mann–Whitney test, the incidence of nausea in ondansetron and metoclopramide groups was 23.33% and 33.33%, respectively ( $P > 0.05$ ). Moreover, the incidence of vomiting in ondansetron and metoclopramide groups were 10% and 16.6%, respectively ( $P > 0.05$ ); however, there was no significant difference in the incidence of nausea and vomiting between the two groups, although it was lower in the ondansetron group. The highest rate

of nausea and vomiting in both study groups was in the 6<sup>th</sup> h after surgery. The need for complementary antiemetic drugs was 10% in the ondansetron group and 20% in the metoclopramide group. Although the general incidence of nausea and vomiting and the need for rescue medication was not significantly different between the two study groups ( $P > 0.05$ ), it was lower in the ondansetron group [Table 2].

## Discussion

The incidence of nausea and vomiting within the first 24 h after surgery and the need for antiemetic drugs were the main outcomes examined in our study. A number of studies show that ondansetron administration has been more effective than metoclopramide in reducing nausea and vomiting,<sup>[21,22]</sup> while others have revealed that the two drugs were not different in control and reduction of nausea and vomiting.<sup>[15,23]</sup> In our study, both ondansetron–dexamethasone and metoclopramide–dexamethasone in general decreased the incidence of nausea and vomiting. In a study of 100 patients undergoing laparoscopic cholecystectomy, that was conducted by Mortazavi *et al.* in 2014, the incidence of nausea and vomiting was assessed in the two groups receiving metoclopramide (10 mg)–dexamethasone (8 mg) and ondansetron (4 mg)–dexamethasone (8 mg) within the first 4 h after surgery, 38% and 28% incidence of nausea was

**Table 2: Incidence of postoperative nausea and vomiting and the need for rescue medication**

Groups Time	Ondansetron-dexamethasone group, n (%)	Metoclopramide-dexamethasone group, n (%)	P
Recovery			
Nausea	1 (3.3)	1 (3.3)	>0.999
Vomiting	Nil	Nil	>0.999
Rescue administration	Nil	Nil	>0.999
2 h after surgery			
Nausea	1 (3.3)	3 (10%)	0.448
Vomiting	Nil	1 (3.3)	0.985
Rescue administration	Nil	1 (3.3)	0.985
4 h after surgery			
Nausea	2 (6.6)	2 (6.6)	>0.999
Vomiting	1 (3.3)	2 (6.6)	0.894
Rescue administration	1 (3.3)	1 (3.3)	>0.999
6 h after surgery			
Nausea	2 (6.6)	3 (10%)	>0.999
Vomiting	2 (6.6)	2 (6.6)	>0.999
Rescue administration	1 (3.3)	1 (3.3)	>0.999
12 h after surgery			
Nausea	1 (3.3)	1 (3.3)	>0.999
Vomiting	1 (3.3)	1 (3.3)	>0.999
Rescue administration	Nil	1 (3.3)	>0.999
24 h after surgery			
Nausea	Nil	Nil	>0.999
Vomiting	Nil	Nil	>0.999
Rescue administration	Nil	Nil	>0.999
Total			
Nausea	7 (23.3)	10 (33.3)	0.336
Vomiting	3 (10)	5 (16.6)	0.422
Rescue administration	3 (10)	6 (20)	0.183

Data presented as, n (%), Mann-Whitney test was used to compare the variable

observed in the metoclopramide and ondansetron groups, respectively, and the incidence of vomiting was 30% and 16%, respectively, indicating no significant difference in the reduction of nausea and vomiting.<sup>[24]</sup> Although the rate of nausea in this study was in line with ours, higher incidence of vomiting was reported in it, which may be due to the difference in type of surgery. Metoclopramide and ondansetron drugs were assessed in the study of Isazadehfar *et al.* on 60 patients undergoing laparoscopic gallbladder surgery in 2017. The incidence of nausea and vomiting in the metoclopramide and ondansetron groups was 43.3% and 33.3% as well as 20% and 26.6%, respectively. Besides, the highest rate of nausea in the metoclopramide and ondansetron groups was 43.3% and 23.3%, respectively, and the highest incidence of vomiting in the metoclopramide and ondansetron groups was 16.7% and 20% during the first 6 h after surgery, respectively.<sup>[15]</sup> In our study, the highest rate of nausea and vomiting was observed in the 6<sup>th</sup> h after surgery. While in the study of Isazadehfar, the rate of vomiting was generally higher in the ondansetron group, the incidence of vomiting was higher in the metoclopramide group of our research, and the difference in results could be due to the administration

of dexamethasone for patients. The timing of medications also varied between the two studies.

In a study by Farhat *et al.* that was performed on 150 female patients who underwent laparoscopic gallbladder surgery, the effect of intravenous administration of metoclopramide (10 mg) and ondansetron (8 mg) was evaluated before the induction of anesthesia.<sup>[11]</sup> In this study, the incidence of nausea and vomiting was significantly lower in the ondansetron group than in the metoclopramide group ( $P > 0.05$ ); therefore, the need for a antiemetic drug to treat nausea and vomiting was higher in the metoclopramide group.<sup>[11]</sup> Although there was no significant difference between the two groups in our study, the variation in our results with those of Farhat *et al.* could be due to the administration of dexamethasone along with ondansetron and metoclopramide. Furthermore, the timing of drug administration was different, which may cause variations in results.

In the study by Sahabi *et al.*, 80 female patients subject to abdominal hysterectomy and general anesthesia were studied. In this investigation, the patients were divided into two groups receiving metoclopramide–dexamethasone and

ondansetron–dexamethasone. The drug was administered at the end of the operation and the patients were examined for nausea and vomiting at intervals of 2 and 6 h after surgery and no significant differences were observed between the two groups ( $P > 0.05$ ); however, the rate of nausea and vomiting was lower in the ondansetron group after 6 h ( $P < 0.001$ ).<sup>[18]</sup> While the differences between the incidences of nausea and vomiting were significant in the study of Sahabi *et al.*, it can be generally stated that the results were in line with our results as a whole and confirmed our findings.

Although metoclopramide is an older and cheaper drug than ondansetron, it seems that ondansetron can be used as the first drug of choice to prevent nausea and vomiting in laparoscopic gynecological surgeries under general anesthesia due to the effectiveness of ondansetron, the reduction of the need for another antiemetic, and the side effects of further nausea and vomiting with metoclopramide.

## Conclusion

Although the results of our study indicated no significant difference between ondansetron plus dexamethasone with metoclopramide plus dexamethasone in reducing nausea and vomiting after laparoscopic gynecological surgery, the incidence of nausea and vomiting was lower in the ondansetron group in laparoscopic gynecological surgery under general anesthesia.

## Limitation

In our study, the dose of medication prescribed was administered to all patients regardless of body weight that can be a limitation.

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## Conflicts of interest

There are no conflicts of interest.

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