

# A Comparative Study between Aprepitant only versus Combined Ondansetron and Aprepitant as Antiemetic Therapy, Regarding Efficacy and Duration, in Patients Undergoing Laparoscopic bariatric Surgery Double-blinded, Randomized Control Clinical Trial

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## Abstract

**Background:** Post-operative nausea and vomiting (PONV) are a common problem associated with general anesthesia. The incidence in high-risk patients can be about 80%.

**Objective:** The objective was to compare aprepitant versus ondansetron and aprepitant combination antiemetic therapy as regards the efficacy and duration of the combination of dexamethasone-ondansetron as a gold standard and dexamethasone-aprepitant versus dexamethasone-ondansetron-aprepitant in patients undergoing laparoscopic bariatric surgery.

**Patients and Methods:** A prospective, double-blinded, randomized control clinical trial, for evaluation of 150 laparoscopic bariatric surgery patients receiving a standardized general anesthetic; patients in the dexamethasone-ondansetron Group A (Group DO, n=50) received oral placebo identical to aprepitant 2 hours before the induction of anesthesia then ondansetron 4 mg IV within the last 30 minutes of operation. In the dexamethasone-aprepitant Group B (Group DA, n=50) the patients received 80 mg orally aprepitant 2 hours before the induction of anesthesia and 2 ml saline intravenously (IV) within the last 30 minutes of surgery. Patients in the dexamethasone-ondansetron-aprepitant Group C (Group DOA, n=50) received oral aprepitant 2 hours before the induction of anesthesia and then 4 mg ondansetron IV within the last 30 minutes of operation. We were given 8 mg dexamethasone IV after the induction of anesthesia to all patients. The primary outcome measured the severity of nausea with complete response (no PONV and no rescue antiemetics) up to 48 h postoperatively. The secondary outcome measure was the amount of rescue postoperative antiemetics given during the first 48 h postoperatively.

**Result:** Nausea severity was higher in Group A (the Group DO) more than Group B (Group DA) more than Group C (Group DOA). The mean of nausea verbal rating score in the Group B was lower than Groups A, but no statistically significant but, in the Group C was more lower and statistical significance in compared with Group A and B at 4 h, 8 h, 12 h, 16 h, 20 h, 24 h and 48 h ( $p < 0.05$ ). In compared with Group A and Group B received rescue antiemetic within 48 hours after surgery was no statistical difference but in compared of both Groups with Group C was significant ( $p = 0.05$ ) complete response was also among the Group A (60%) and Group B (72%) and Group C (94%).

**Conclusion:** In patients undergoing laparoscopic bariatric surgery, the addition of aprepitant to ondansetron significantly decreased postoperative vomiting rates and nausea severity and increased complete response for up to 48 hours postoperatively. Dexamethasone-aprepitant decreased postoperative vomiting rates and nausea severity in compared to dexamethasone-ondansetron but insignificantly. Finally, Oral aprepitant, when combined with intravenous ondansetron and dexamethasone, was effective in suppressing early PONV up to 48 h postoperatively.

**Keywords:** Aprepitant; Ondansetron; PONV; Laparoscopy; Dexamethasone

## Introduction

Postoperative nausea and vomiting (PONV) are one of the most common problems related to surgery and anesthesia that happen within 24 hours after operations [1]. In the absence of pharmacological management, the incidence of PONV ranges between 20% and 30% in the general surgical population and increases up to 80% in high-risk

surgical patients [2,3]. The incidence of PONV is generally accepted to be 50% to 80% after craniotomy and 40% to 80% after laparoscopic surgery [4]. The Apfel score is a simplified risk score for predicting PONV incidence. It includes four variables and assigns one point for each: female sex, history of PONV and/or motion sickness, nonsmoking status, and using of opioids in the postoperative. Present of factors, 0, 1, 2, 3 or 4 increases; the risk of PONV is 10%, 20%, 40%, 60%, or 80%, respectively [2]. In addition to forecited risks pointed in Apfel score, increased intra-abdominal pressure during laparoscopic procedures can increase the risk of PONV [5].

The nonsmoking status, female gender, a history of PONV and/or motion sickness, the type of the operation, a longer duration of operation, the use of inhalational anesthetic agents and reversal of the neuromuscular blockade at recovery, nitrous oxide, postoperative pain and the use of postoperative opioids can affect the incidence of PONV also [5]. Many antiemetic drugs used for the treatment of PONV. The first one [Dexamethasone] can decrease the incidence of PONV [6]. However, some authors emphasize that the combination of antiemetic drugs can further reduce PONV compared to single-agent treatment [7,8] especially for high-risk patients [1]. The dexamethasone-ondansetron combination effectively reduced the overall incidence of PONV for approximately 50% in high-risk and very high-risk patients when compared to a control Group [9]. Aprepitant considered a neurokinin-1 (NK-1) receptor antagonist and is defined as an alternative to prevent PONV [10]. Aprepitant blocks the emetic effects of substance P (SP) neurokinin-1 receptors in the gastrointestinal tract. Another mechanism for their action is through inhibiting signals received from the chemoreceptor trigger zone by the nucleus tractus solitarius in the brainstem [11]. In recent, several studies have demonstrated that aprepitant is useful for preventing PONV, especially when combined with other antiemetics, particularly corticosteroids and 5-hydroxytryptamine (5-HT<sub>3</sub>) receptor blockers. Aprepitant is notably expensive when compared with other antiemetics, which may limit its use in some situations. The typical dose is 40 mg orally preoperatively, most commonly given within two h of surgery [12].

Some studies showed that aprepitant is significantly more effective than ondansetron for the prevention of postoperative vomiting in open abdominal surgery [13,14]. Some authors showed that the dexamethasone-aprepitant combination was more effective than the dexamethasone-ondansetron combination for the prevention of postoperative vomiting in adults undergoing craniotomy under general anesthesia [15]. Aprepitant can use with other antiemetic drugs to increase antiemetic efficiency. In this study, we examined PONV, the severity of nausea with a complete response up to 48 h postoperatively in two Group dual therapy [Group A control Group], [Group B study Group] and one Group triple therapy [Group C]. The secondary outcome measure was the amount of rescue postoperative antiemetics are given and complete response for up to 48 hours postoperatively.

## Methods

All patients between 18 and 60 years of age with American Society of Anesthesiology I to II status who considered at high risk for postoperative nausea and vomiting and who were undergoing a laparoscopic bariatric surgery under general anesthesia of at least 1-hour duration were eligible for this prospective, randomized, double-blind control clinical trial in Aswan and Benha university from September 01 to March 08, 2019. Subjects recruited on the day of operation during the preoperative evaluation by study investigators who were anesthesiologists already involved in the patients care.

## Inclusion criteria

In this study were significant postoperative nausea and vomiting patient-related risk factors (1) female gender, (2) history of postoperative nausea and vomiting as a complication or history of motion sickness, (3) nonsmoking status, and (4) postoperative use of opioids [16,17]. Patients have two or more risk factors, eligible for the study. All patients who scheduled for 48-hour observation included in the survey as depending on the time of day.

## Exclusion criteria

This study included patient refusal to participate in the study, patients who had received other antiemetics before their procedure, history of allergy or sensitivity to study drugs, pregnancy, and a history of chronic opioid use (chronic pain syndrome). Women of reproductive age routinely screened for pregnancy, and patients who were pregnant were informed and excluded from the study. The local institutional investigational review board approved the study and written informed consent was obtained from each subject by one of the study investigators. Patients were randomized by a computer-generated number table which used to allot patients to one of three Groups [Group A]: oral placebo plus intravenous 4 mg of ondansetron or [Group B]: 80 mg of oral aprepitant plus 2 ml of intravenous normal saline or [Group C]: 80 mg of oral aprepitant plus 4 mg of ondansetron intravenously. The oral aprepitant or placebo was given within 2 hours before their scheduled operation. The placebo and study drug was identical in appearance; hence, both the investigators and the patients were blinded to the patient's study Group, eliminating any potential bias. The authors were free to publish their results regardless of the study outcome. We give 8 mg dexamethasone iv after the induction of anesthesia to all patients.

The general anesthetic consists of premedication (2 mg of midazolam intravenously for anxiolysis). After the application of standard American Society of Anesthesiology monitors, all patients were intravenously induced with 2 to 3 mg/kg of propofol, 1 to 1.5 mg/kg of succinylcholine or 0.6 to 0.8 mg/kg of rocuronium to facilitate endotracheal intubation. Maintenance of general anesthesia consisted of 1.5 to 2.5 percent sevoflurane in oxygen and fentanyl as needed for analgesia (not to exceed 10 µg/kg). Incremental doses of rocuronium used as necessary for muscle relaxation. Muscle relaxation reversed at the end of surgery with 0.01 mg/kg of glycopyrrolate and 0.05 mg/kg of neostigmine. Criteria for reversal with neostigmine were standardized to avoid the possibility of a repeated dose of the neostigmine, which in repeated doses is known to cause vomiting [18].

Patients experiencing postoperative nausea and vomiting in the post anesthesia care unit, regardless of treatment Group, could receive any of the following medications on formulary as part of our institutions' guidelines for postoperative nausea and vomiting (in vomiting or nausea more than 10 minutes). Intravenous rescue antiemetics include 4 mg of ondansetron, 4 mg of dexamethasone, 10 mg of metoclopramide, 1 mg of granisetron. Patients with continuing postoperative nausea and vomiting refractory to these modalities were admitted to the hospital for 24-hour observation by the surgical service. A standard post anesthesia care unit hospital protocol was also available for the treatment of postoperative pain. Analgesics were titrated to patient comfort based on the postoperative standardized protocol to have a verbal pain score (0-no pain to 10-worst pain ever) less than four patient discharges. Intravenous medications available on formulary included fentanyl, morphine, paracetamol, ketorolac, and meperidine. Oral analgesics available included ibuprofen and acetaminophen. All doses of antiemetics and analgesics recorded.

Patients were evaluated postoperatively for nausea using a verbal rating scale (0-no nausea to 10-worst nausea ever) [12-15]. The presence of retching or vomiting was evaluated as a binary outcome (yes or no). A study investigator do not know type of the drug in the treatment Group, just recorded the occurrence of nausea and vomiting in the preoperative period, on admission to the post anesthesia care unit, one hourly interval until 4 hours then every 4 h while awake for

up to 24 hours after the first day of surgery, and every 8 hours while awake during the second day after surgery (48 hours).

### Data collection

Nausea defined as the subjectively unpleasant sensation associated with the awareness of the urge to vomit. The forceful expulsion the contents of the stomach through the mouth this is definition of vomiting. Retching defined as an attempt to vomit, not productive of stomach contents. A complete response defined as no postoperative nausea (VRS<4), no retching or no vomiting, and no need for rescue antiemetic. Nausea was rated on an 11-point verbal rating scale (VRS) with 0 equal to 'no nausea' and ten equal to 'nausea as bad as it could be.' Nausea, retching, and vomiting were assessed immediately on return to the recovery room at 0, 1 hour, 4 hours and every 4 hours postoperatively for 24 hours then every 8 hours for 48 hours. Complete response recorded for 0-48 hours. Demographic data, duration of the surgery, risk factors for PONV, and postoperative use of rescue antiemetic recorded. Rescue medication was presented to patients who requested it, had an episode of vomiting or had nausea lasting longer than 10 minutes. All patients were treated with 4 mg of ondansetron, 4 mg of dexamethasone, 10 mg of metoclopramide, 1 mg of granisetron. Observation of any adverse events such as headache, dizziness, sedation, delayed passage of flatus, and pruritus. The primary target of this study was a complete response that is, no nausea (VRS<4), no vomiting, no retching, and no rescue therapy from 0 to 48 hours after the operation. The secondary target was a decreasing incidence of nausea, vomiting, retching.

### Statistical analysis

Statistical analyses performed with SPSS (version 16.0, Chicago, Ill.) and Minitab (version 15, State College, Pa). Using a chi-square test (Query 4.0, Statistical Solutions, Saugus, Mass.) with an alpha value of

0.05 and power of 80 percent, power analysis showed that a sample size of 50 patients for each Group was necessary to detect a significant decrease. To allow for patients who might not complete the study, 55 patients per Group (165 total patients) were enrolled. Baseline Group demographics compared with chi-square t-test, as appropriate. Comparison of Group response utilized the following tests: interval data were analyzed using the t-test, nominal data with the chi-square test, and ordinal data with the Mann-Whitney rank sum test. An intention-to-treat approach calculated the relative risk reduction, and along-rank chi-square analysis accompanied the Kaplan-Meier hazards plot. Comparison of nausea severity was performed in two ways. In those patients who exhibited nausea, verbal rating scale more significant than 0, the worst nausea score for each patient defined as the highest nausea score recorded over the 48 hours. The Mann-Whitney rank sum test was used to compare worst nausea scores. Multivariate analysis of variance was used to determine whether the mean verbal rating scale score over time was significant.

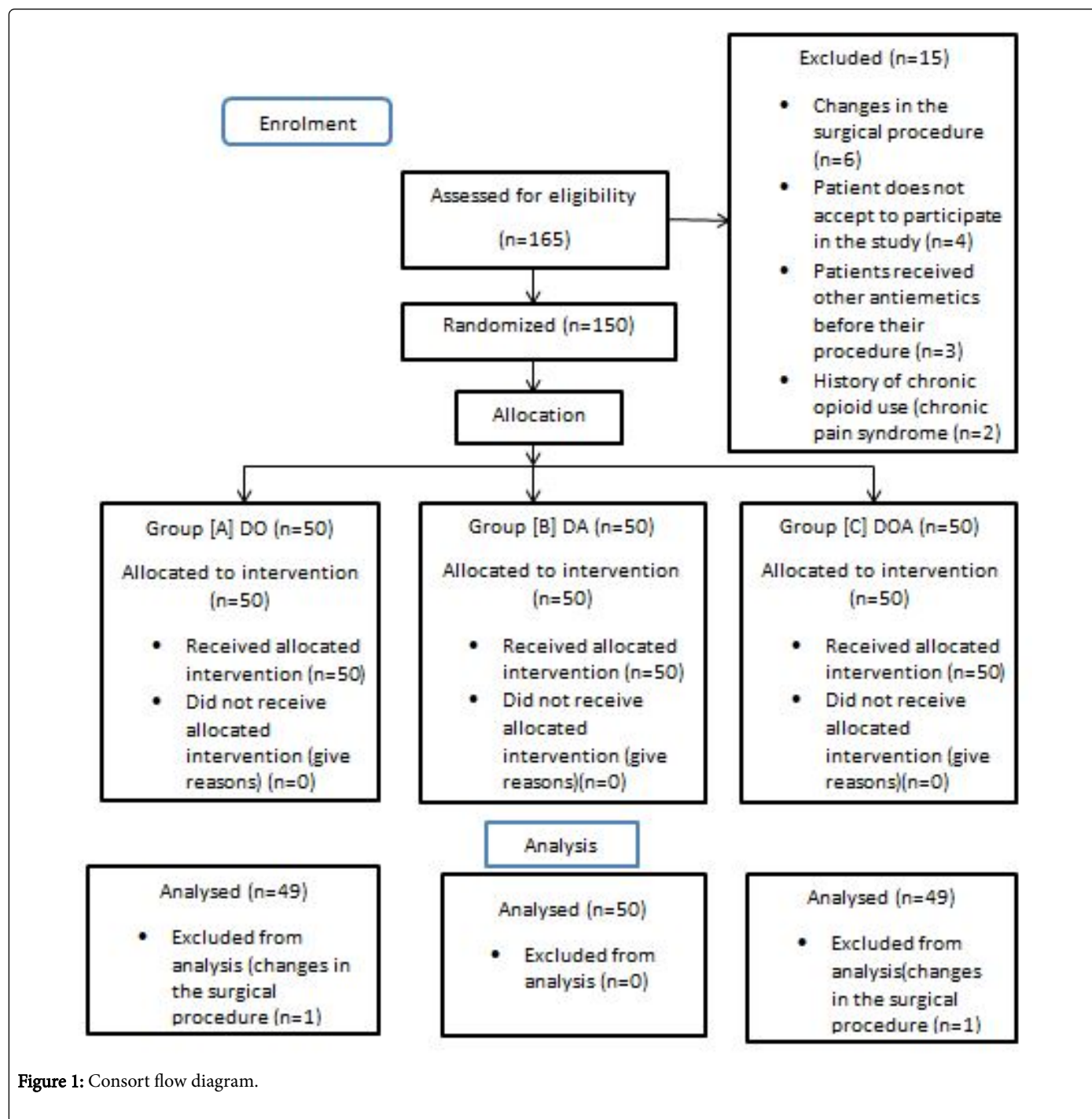
### Results

One hundred sixty-five patients included in this study. Fifteen patients excluded from the study due to changes in the surgical procedure from laparoscopy to laparotomy during the surgery (six patients), patient refusal to participate in the study (4 patients), patients received other antiemetics before their procedure (3 patients) and history of chronic opioid use (chronic pain syndrome)(2 patients). Therefore, 150 patients (in Group [A] DO [n=50], in Group [B] DA [n=50]) and in Group[C] DOA [n=50] completed the study (Figure 1).

One hundred, and eleven of the patients who completed the study were female as opposed to 39 male patients there was no difference in the patient Apfel risk factors for PONV, duration of surgery and demographics data between the two Groups (Table 1).

Variables	Group DO (n=50)	Group DA (n=50)	Group DOA (n=50)	P-value
Age (year)	35.3 ± 7.9	40 ± 10.9	37 ± 11.7	0.823
Weight (kg)	66.8 ± 14.3	66.9 ± 13	66.9 ± 13	0.973
Height (cm)	166.6 ± 8	166.3 ± 8	166.9 ± 7	0.982
<b>Apfel's risk score</b>	<b>Group DO (n=50)</b>	<b>Group DA (n=50)</b>	<b>Group DOA (n=50)</b>	<b>P-value</b>
0	0	0	0	
1	8	11	9	0.745
2	12	13	14	0.854
3	17	15	13	0.645
4	13	11	16	0.698
<b>Gender</b>	<b>Group DO (n=50)</b>	<b>Group DA (n=50)</b>	<b>Group DOA (n=50)</b>	<b>P-value</b>
Male	12	14	13	0.908
Female	38	36	37	0.897
Duration of surgery (min)	67.1 ± 24.5	74.8 ± 29.4	75.7 ± 27.5	0.605

**Table 1:** Patient demographics, characteristics and intraoperative data.



**Figure 1:** Consort flow diagram.

Nausea severity was higher in Group A (the Group DO) more than Group B (Group DA) more than Group C (Group DOA). The mean of nausea verbal rating score was  $(3.82 \pm 3.93)$  in the Group DO, and  $(3.53 \pm 3.62)$  in the Group DA There was no statistical difference but  $(1.75 \pm 3.00)$  in the Group DOA that statistical significance at 4 h ( $p=0.01$ ). Also at 8 h was  $(2.47 \pm 3.38)$  in the Group DO and  $(2.39 \pm 3.22)$  in the Group DA There was no statistical difference but  $(1.30 \pm 2.60)$  in the Group DOA that statistical significance ( $p=0.01$ ). Also, at 12 h was  $(1.85 \pm 2.89)$  in the Group DO, and  $(1.62 \pm 2.75)$  in the Group DA There was no statistical difference but  $(0.66 \pm 1.63)$  in the Group DOA that statistical significance ( $p=0.03$ ) Also, at 16h was  $(1.06$

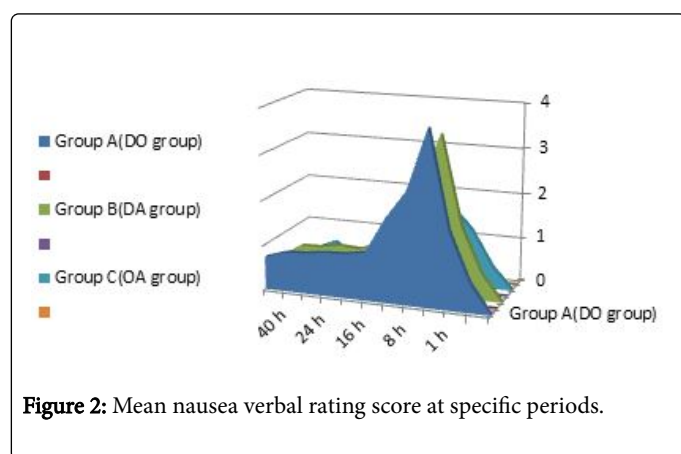
$\pm 2.08)$  in the Group DO, and  $(1.01 \pm 1.98)$  in the Group DA There was no statistical difference but  $(0.53 \pm 1.35)$  in the Group DOA that statistical significance ( $p=0.03$ ). Also, at 20 h was  $(0.98 \pm 2.06)$  in the Group DO, and  $(0.85 \pm 1.95)$  in the Group DA There was no statistical difference but  $(0.41 \pm 1.11)$  in the Group DOA that statistical significance ( $p=0.02$ ). Also at 24 h was  $(0.96 \pm 1.99)$  in the Group DO and  $(0.88 \pm 1.74)$  in the Group DA. There was no statistical difference but  $(0.35 \pm 0.97)$  in the Group DOA that statistical significance ( $p=0.01$ ), Also at 48 h was  $(0.73 \pm 1.74)$  in the Group DO, and  $(0.50 \pm 1.68)$  in the Group DA There was no statistical difference but  $(0.33 \pm$



1.05) in the Group DOA that statistical significance ( $p=0.04$ ), (Table 2 and Figure 2).

Nausea VRS				
Period (hr)	Group A (n=50)	Group B (n=50)	Group C (n=50)	P-value
PACU admission	0.62 ± 2.04	0.58 ± 1.92	0.49 ± 1.48	0.31
1 h	1.68 ± 3.00	1.59 ± 2.51	1.26 ± 2.47	0.18
4 h	3.82 ± 3.93	3.53 ± 3.62	1.75 ± 3.00	0.01*
8 h	2.47 ± 3.38	2.39 ± 3.22	1.30 ± 2.60	0.01*
12 h	1.85 ± 2.89	1.62 ± 2.75	0.66 ± 1.63	0.03*
16 h	1.06 ± 2.08	1.01 ± 1.98	0.53 ± 1.35	0.03*
20 h	0.98 ± 2.06	0.85 ± 1.95	0.41 ± 1.11	0.02*
24 h	0.96 ± 1.99	0.88 ± 1.74	0.35 ± 0.97	0.01*
32 h	0.90 ± 1.97	0.80 ± 1.89	0.69 ± 1.84	0.24
40 h	0.87 ± 1.89	0.79 ± 1.73	0.50 ± 1.53	0.09
48 h	0.73 ± 1.74	0.50 ± 1.68	0.33 ± 1.05	0.04*

**Table 2:** Mean nausea verbal rating score at specific periods.



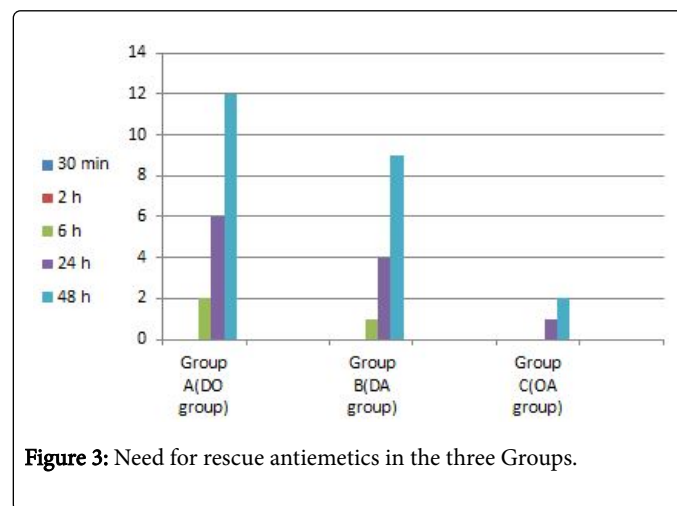
**Figure 2:** Mean nausea verbal rating score at specific periods.

Eight patients (16%) in Group DO, and five patients (10%) in Group DA received rescue antiemetic within 24 hours after surgery that was no statistical difference but 1 patient (2%) in Group DOA which was significant ( $p=0.05$ ). Also after 24 h 12 patients (24%) in Group DO, and 9 patients (18%) in Group DA received rescue antiemetic that was no statistical difference but 2 patients (4%) in Group DOA which was significant ( $p=0.05$ ). Complete response was also among the DO (60%) and DA (72%) Groups and the DOA (94%) over the 48 hours (Table 3 and Figure 3).

Time	Group A (n = 50) DO Group	Group B (n = 50) DO Group	Group C (n = 50) DO Group	P
30 min	0 (0-0)	0 (0-0)	0 (0-0)	1
2 h	0 (0-0)	0 (0-0)	0 (0-0)	1
6 h	2 (0-2)	1 (0-1)	0 (0-0)	0.05*

24 h	6 (4-7)	4 (1-3)	1 (0-1)	0.05*
48 h	12 (5-8)	9 (3-5)	2 (0-1)	0.001*

**Table 3:** Need for rescue antiemetics in the three Groups.



**Figure 3:** Need for rescue antiemetics in the three Groups.

## Discussion

Post-operative nausea and vomiting are considered the side effect related to the patient anesthetic and surgical factors. There are many medications to prevent PONV, such as metoclopramide, dimenhydrinate, serotonin antagonists and dexamethasone. Although antiemetic prophylaxis might not eliminate the risk of PONV, it can significantly reduce the incidence of nausea and vomiting [19]. However, no single excellent medication or method will be described.

Dexamethasone well documented as an effective antiemetic. A single dose of dexamethasone administered perioperative is rarely associated with significant side effects [20]. Using of dexamethasone 8 mg significantly reduces PONV and the use of rescue antiemetic [21,22]. Karanicolas et al. [23] published a systematic review and meta-analysis of 17 randomized controlled trials that evaluated the impact of prophylactic corticosteroid administration on PONV. The authors concluded that prophylactic dexamethasone decreases the incidence of nausea and vomiting. Some study show, using dexamethasone (8-16 mg) are more effective than smaller treatments (2-5 mg) in patients undergoing laparoscopic cholecystectomy [23]. So, we administered dexamethasone 8 mg IV to all patients in our study. Dexamethasone usually takes a long time for the onset of the effect [24]. Wang et al. [25] evaluated the impact of timing of dexamethasone administration on its efficacy as a prophylactic antiemetic for PONV. The prophylactic dexamethasone iv, when given immediately before the induction of anesthesia, is more effective compared to the administration at the end of the operation in preventing nausea and vomiting after significant abdominal surgery [25]. Therefore, dexamethasone is recommended to administer before or after the induction of anesthesia [24]. Consequently, in our study, we preferred to apply dexamethasone after tracheal intubation.

Prophylactic antiemetic therapy is useful, but combinations of antiemetics recommended for patients who are at high risk of PONV [26,27]. Furthermore, patients with a moderate risk of PONV should be given antiemetic combinations with one or more prophylactic drugs

from different classes [19]. A combination of dexamethasone with other antiemetics is more effective than any single drug alone [24]. Kawano et al. [28] concluded that aprepitant and dexamethasone combined were more effective than dexamethasone alone to prevent postoperative vomiting for the patients at high-risk PONV. According to these data, we preferred to combine dexamethasone with an antiemetic therapy for the management of PONV.

Ondansetron is considered as serotonin (5-HT<sub>3</sub>) receptor antagonist, and it can be used effectively in PONV. However, it might not eliminate PONV, probably because it acts through the blockage of one receptor [25]. The efficacy of an ondansetron-dexamethasone combination is superior to mono-therapy in PONV [25]. For this reason, in our study, we preferred to apply the ondansetron-dexamethasone combination instead of a mono-therapy as a control Group. White et al. [29] recommended combination drug therapy for routine antiemetic prophylaxis with a steroid and a 5-HT<sub>3</sub> antagonist for high-risk patients. If a 5-HT<sub>3</sub> antagonist used, it should give toward the end of the surgery [29]. So we used ondansetron within the last 30 minutes of operation. Also, Kim et al. [9] showed that the antiemetic prophylaxis with the dexamethasone-ondansetron combination is effective in reducing PONV in both high-risk and very high-risk patients [9]. However, in this study, despite the prophylactic administration of the antiemetic drug in very high-risk patients, the occurrence of PONV was around 30% [9]. Aprepitant is considered a new selective NK-1 receptor antagonist antiemetic drug, able to alleviate the emetic effects of substance P [30]. Some recent studies showed that it is effective in reducing the incidence of PONV up to the first 48 hours after anesthesia following the preoperative oral administration [31].

Kakuta et al. [32] showed that aprepitant could effectively decrease PONV and the amount of pain medication required by patients in laparoscopic gynecological surgical procedures. In this study, all patients received 80 mg of aprepitant orally. However, Dilorio et al. [33] concluded that a single pre-operative oral aprepitant dose of 40 mg reduces the percentage of patients with PONV and the need for additional antiemetic drugs after total joint arthroplasty. Gan et al. [13] published a multicentre, double-blind trial, involving 805 patients. In this study, even though the efficacy of aprepitant for nausea control, the need for rescue antiemetic and complete response were similar, aprepitant was significantly more effective than ondansetron in the prevention of postoperative vomiting in the first 48 hours after open abdominal surgery. Hartrick et al. [34] found that even though aprepitant significantly reduced the incidence of PONV compared to a combination therapy, when it used alone, it did not eliminate PONV. Same authors also indicated that to have optimal prophylaxis for PONV, at least one other antiemetic agent should be added to aprepitant. Relying on the findings of these aforementioned researchers, we combined aprepitant with dexamethasone in our study.

Habib et al. [15] found prophylaxis with dexamethasone and aprepitant to be more effective than the combination of dexamethasone and ondansetron for the prevention of postoperative vomiting in adult patients undergoing craniotomy. However, the occurrence or severity of nausea, the need for rescue antiemetic and a complete response did not differ between the two Groups, as in our study. Also, this result is similar to the Gan et al. [13] effect. In our study, the incidence of rescue antiemetic was 8 patients (16%) in Group DO, and five patients (10%) in Group DA received within 24 hours after surgery that was no statistical difference but 1 patient (2%) in Group DOA which was significant ( $p=0.05$ ). Also after 24 h, 12

patients (24%) in Group DO, and nine patients (18%) in Group DA received rescue antiemetic that was no statistical difference but 2 patient (4%) in Group DOA which was significant ( $p=0.05$ ). This occurrence was lower than in the study of Habib et al. [15] (14% for the aprepitant Group and 36% for the ondansetron Group at 24 hours). The timing of antiemetic therapy and antiemetic drugs were similar in both studies. In our study, in Group A and B, the incidence or severity of nausea, the need for rescue antiemetic and a complete response did not differ between the two Groups as shown in the previous study [15] but, in the Group C had statistically different.

By the studies mentioned above, we administered 80 mg aprepitant preoperatively, 4 mg ondansetron at the end of the surgery and 8 mg dexamethasone to all patients during the induction period. Gan et al. [13] designed a multi-center study in that they found that complete response was similar 4 mg ondansetron (42%) and the 40 mg aprepitant (45%) among treatment Groups after the open abdominal surgery. In our study, there is a complete response also similar among the DA (60%) and DO (72%) Groups and the DOA Group (94%). Gan et al. [13] reported similar results for aprepitant and ondansetron. We also as in our study did not found a significant difference between our Groups for a complete response. However, the percentage of total effect was much better in our study than Gan et al.'s study [13], and this finding could be related to the additive effect of the combined therapy. However, more studies are required to evaluate the additional effect of aprepitant and dexamethasone on PONV with or without the combination of these drugs [35]. In our research, combining aprepitant and ondansetron did not increase the incidence of adverse events such as headache, dizziness, sedation, delayed passage of flatus, and pruritus. This finding is consistent with previous studies [12-14].

## Conclusion

In patients undergoing laparoscopic bariatric surgery, the addition of aprepitant to ondansetron significantly decreased postoperative vomiting rates and nausea severity and increased complete response for up to 48 hours postoperatively. Dexamethasone-aprepitant decreased postoperative vomiting rates and nausea severity in compared to dexamethasone-ondansetron but insignificantly. Finally, Oral aprepitant, when combined with intravenous ondansetron and dexamethasone, was effective in suppressing early PONV up to 48 h postoperatively.

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