IFSO

ORIGINAL CONTRIBUTIONS

The impact of Aprepitant on Nausea and Vomiting following Laparoscopic Sleeve Gastrectomy: A Blinded Randomized Controlled Trial

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Abstract

Introduction Laparoscopic sleeve gastrectomy (LSG) is associated with postoperative nausea and vomiting (PONV). We aimed to compare the effects of aprepitant on the incidence of PONV after LSG.

Methods In this double-blind, randomized controlled trial, the case group received the standard care regimen for PONV (dexamethasone 10 mg, ondansetron 4 mg, and metoclopramide 10 mg) plus prophylactic oral aprepitant 80 mg 1 h pre-operatively. The control group received standard care plus a placebo. Comparative analyses using the Rhodes index were performed at 0, 6, 12, and 24 h postoperatively.

Results A total of 400 patients (201 in the aprepitant group and 199 in the placebo group) underwent LSG. The groups were homogeneous. The aprepitant group experienced less PONV: early, 69 (34.3%) vs. 103 (51.7%), $p \le 0.001$; 6 h, 67 (33.3%) vs. 131 (65.8%), $p \le 0.001$; 12 h, 41 (20.4%) vs. 115 (57.8%), $p \le 0.001$; and 24 h, 22 (10.9%) vs. 67 (33.7%), $p \le 0.001$. Fewer patients in the aprepitant group vomited: early, 3 (1.5%) vs. 5 (2.5%), $p = 0.020$; 6 h, 6 (3%) vs. 18 (9%), $p = 0.020$; 12 h, 2 (1%) vs. 17 (8.5%), $p = 0.006$; and 24 h, 1 (0.5%) vs. 6 (3%), $p = 0.040$. Patients in the aprepitant group required less additional PONV medication: early, 61 (30.3%) vs. 86 (43.2), $p = 0.008$; 6 h, 7 (3.5%) vs. 34 (17%), $p = 0.001$; 12 h, 6 (3%) vs. 31 (15.6%), $p \le 0.001$; and 24 h, 5 (2.5%) vs. 11 (5.5%), $p \le 0.001$.

Conclusions Prophylactic aprepitant improved PONV between 0 h (early) and 24 h postoperatively in patients undergoing LSG.

Keywords Aprepitant · Laparoscopic sleeve gastrectomy · Obesity · Bariatric surgery · Ponv · Postoperative nausea and vomit · Bariatric anesthesia

Key Point
- Laparoscopic sleeve gastrectomy is associated with postoperative nausea and vomiting.
- The study compared aprepitant to placebo in a blinded-randomized fashion.
- Aprepitant improved postoperative nausea and vomiting between 0 and 24 h post-LSG.

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Introduction

Obesity, a chronic condition with numerous manifestations, has become a global epidemic [1].

Over the past decade, significant progress has been made in laparoscopic sleeve gastrectomy (LSG) for the treatment of morbid obesity. However, LSG is associated with postoperative nausea and vomiting (PONV) in approximately 48% of cases [2]. PONV may prolong a patient's discharge from the post-anesthesia care unit, increasing medical costs [3]. The use of anesthetics and opioids to treat postoperative pain, type of surgery, and patient characteristics contribute to PONV. PONV can lead to many complications, such as increased intragastric pressure, hemorrhage, suture dehiscence, leakage, dehydration, and electrolyte imbalances, which lengthen the hospital stay due to delayed recovery [4, 5].

PONV remains one of the most significant causes of patient dissatisfaction with the perioperative experience. PONV rates are predicted to decrease with the use of various pharmacological agents [6]. Aprepitant is a selective neurokinin-1 (NK1) receptor antagonist with a half-life of 9–12 h that effectively prevents opioid-induced vomiting. It is used to prevent PONV and chemotherapy-induced nausea and vomiting [7]. It is also safe for use in patients with obesity undergoing anesthesia and surgery [8].

This randomized, double-blind study aimed to evaluate the efficacy of a combination of ondansetron, metoclopramide, dexamethasone, and aprepitant versus ondansetron, metoclopramide, dexamethasone, and placebo as PONV prophylaxis in patients with obesity undergoing LSG.

Materials and Methods

This randomized, double-blind (participants and care providers) study included patients who underwent LSG at a private center. The candidates were recruited between December 2022 and January 2023. This study aimed to determine the effects of aprepitant on PONV from the early postoperative period to 24 h postoperatively. A total of 400 consecutive patients were enrolled and randomized in a 1:1 ratio. The case group received a standard care regimen for PONV during surgery (dexamethasone 10 mg, ondansetron 4 mg, and metoclopramide 10 mg) plus a single oral dose of 80 mg of aprepitant 1 h preoperatively. The control group received the same standard of care and an oral placebo. A comparative analysis of the demographic, anthropometric, and perioperative factors was performed. The primary objective was to evaluate PONV using the Rhodes index at 0, 6, 12, and 24 h postoperatively (Appendix Table 6). The Rhodes index, which was designed to measure nausea frequency and duration, and vomiting quantity, is an eight-item instrument that uses a five-point Likert scale and consists of three subscales: nausea (range, 0–12), vomiting (range, 0–12), and retching (range, 0–8). These ranges provide a severity rating of 0–4 for each item [9]. Rescue medications were administered to patients with moderate or severe PONV at the discretion of the postoperative care physician. The treatment options included ondansetron 4 mg, dexamethasone 8 mg, and diphenidol 40 mg.

The sample size calculation aimed to detect a clinically significant difference in PONV incidence between the two groups. We anticipated a 20% reduction in PONV incidence in the intervention group compared to the control group, based on preliminary findings and previous studies suggesting a potential decrease in PONV with aprepitant use [6]. Assuming a standard deviation (SD) of 0.5 for the Rhodes index score, to detect this difference with 95% confidence and 80% power, the calculation required a minimum of 278 participants, or 139 per group. We performed this calculation using G*Power software, version 3.1.9.7, selecting the sample size analysis for independent means tests with specific parameters: an interest mean difference (d = 0.4), derived from the expected 20% difference and the SD, a significance level (α) of 0.05, and a statistical power (1-β) of 0.80.

Randomization was conducted using a computer-generated sequence obtained from the website www.randomizer.org. For blinding, we used a placebo capsule closely resembling the active medication in appearance. To further ensure the integrity of the blinding process, the administration of both the study drug and the placebo was carried out by hospital staff who were not involved in the study, thus maintaining impartiality, and minimizing bias. The placebo consisted of a commercially sourced inert capsule, matched in color, size, and shape to the aprepitant capsule, and filled with 10 mg of fructose to mimic the weight and consistency of the active drug. The commercial name is "Vegan Empty Pill Capsules", manufactured by XPRS Nutra, white color and size of 14 × 5x5 mm. The inclusion criteria were adults aged 18–65, non-smoking status, and a body mass index (BMI) > 35 kg/m^2, with or without comorbidities. Exclusion criteria included documented hypersensitivity to any component of the study regimen, treatment with pimozide, terfenadine, astemizole, or cisapride, allergies to drugs used in the protocol, a history of drug or alcohol abuse, and a history of prior bariatric procedures. Smoking status was an exclusion criterion due to scientific evidence suggesting that smoking may influence the incidence of PONV. Specifically, the protective effect of smoking on PONV has been recognized in several studies, with research indicating that smokers have a reduced risk of PONV, potentially due to the pharmacokinetic effects associated with smoking [10]. This study was approved by the local ethics committee and registered at www.ClinicalTrials.gov (NCT05772676).

Surgical Technique

The patient was placed in the supine position under general anesthesia, and access to the peritoneal cavity was initiated 20 cm below the xiphoid process. The five-trocar technique was used. The gastroepiploic vessels were located 2–5 cm from the pylorus, the short gastrosplenic vessels were identified on the greater curvature, and the fundus was dissected using a harmonic scalpel until the left pillar was visualized. A 36-Fr calibration bougie was used, and stapling was performed every 60 mm based on the gastric wall thickness. The staple line was reinforced with 2-0 non-absorbable sutures.

Statistical Analysis

The results are expressed as percentages, means, and standard deviations. Normal data distribution was confirmed

using the Kolmogorov-Smirnov test. Comparative analysis of continuous variables was performed using the Student's t-test, while categorical variables were analyzed using the chi-squared test. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using the SPSS for Mac (version 25; SPSS Inc., Chicago, IL, USA).

Results

A total of 400 patients fulfilled the inclusion criteria and underwent LSG; 201 received aprepitant, and 199 received a placebo. The baseline demographic information was homogeneous between the groups (Table 1). Most of the patients (94%) were women. The mean age of the patients was 38 years. The mean BMI was 42.2 kg/m^2 in the aprepitant group and 42 kg/m^2 in the placebo group. The results of the perioperative analysis are presented in Table 1. Overall, complications occurred in six patients (1.5%); there were no cases of mortality, conversion to open surgery, or reoperation.

In the early postoperative evaluation (T0), the aprepitant group displayed significantly reduced rates of nausea (34.3% vs. 51.7%, $p < 0.001$) and vomiting (1.5% vs. 2.5%, $p = 0.020$) and rescue medication use (30.3% vs. 43.2%, $p = 0.008$) (Table 2). At the 6-h assessment, patients continued to experience less nausea (33.3% vs. 65.8%, $p < 0.001$), vomiting (3% vs. 9%, $p < 0.001$), and the need for rescue medication (3.5% vs. 17%, $p < 0.001$) (Table 3). Similarly, at 12 h postoperatively, the aprepitant group showed lower levels of nausea (20.4% vs. 57.8%, $p < 0.001$), vomiting (1% vs. 8.5%, $p < 0.001$), and rescue medication requirements (3% vs. 15.6%, $p < 0.001$) (Table 4). Finally, at the 24-h evaluation, the aprepitant group continued to experience less nausea (10.9% vs. 33.7%, $p < 0.001$), vomiting (0.5% vs. 3%, $p < 0.001$), and the need for rescue medication (2.5% vs. 5.5%, $p < 0.001$) (Table 5). Complete analyses of each

time point and all the measured parameters are shown in Tables 2, 3, 4, and 5.

Discussion

In this randomized controlled trial involving patients who underwent LSG, the use of prophylactic aprepitant significantly reduced the symptoms and discomfort associated with PONV, thereby reducing postoperative complications. Furthermore, appropriate use decreases the need for rescue medications to manage PONV and contributes to a more comfortable and less distressing patient recovery process. PONV is associated with significant perioperative morbidity in the form of dehydration, electrolyte imbalance, venous hypertension, and potential broncho-aspiration, with a higher risk of rehospitalization and emergency department visits [11]. Compared to the general surgical population, patients undergoing bariatric surgical procedures have a much higher incidence of PONV [11]. Moreover, patients undergoing LSG are twice as likely to develop PONV than those undergoing laparoscopic Roux-en-Y gastric bypass, attributable to factors such as stomach manipulation, patient-specific characteristics, and the anesthetic techniques [12]. Involvement of stomach pace disruption and inflammation might be implicated, but there is a lack of scientific data supporting this. Nonetheless, the inclusion of aprepitant in antiemetic regimens can significantly decrease the occurrence of PONV in this population. In our study, 42.2% of patients experienced PONV within the 24-h follow-up, a lower proportion than in previous studies on bariatric surgery [13–15].

Multimodal antiemetic therapy involves the simultaneous use of different antiemetics acting through different physiological pathways to produce effective synergistic antiemetics with fewer side effects [16]. In our study, we added

Table 1 Baseline demographic, comorbidity, and perioperative analysis

	Placebo ($n=199$)	Aprepitant ($n=201$)	Total ($n=400$)	p value
Female; n(%)	186 (93.5%)	190 (94.5%)	376 (94%)	**0.550**
Age (years); mean ± SD	39 ± 9.7	37 ± 9.7	38 ± 9.8	**0.750**
Weight (kg); mean ± SD	116.4 ± 21.7	116.7 ± 24.2	116.5 ± 22.9	**0.660**
Height (m); mean ± SD	1.67 ± 0.1	1.65 ± 0.1	1.66 ± 0.1	**0.110**
BMI (kg/m^2); mean ± SD	42 ± 7.2	42.2 ± 8.7	42.1 ± 8	**0.930**
Diabetes; n(%)	25 (12.5%)	31 (15.4%)	56 (14%)	**0.430**
Hypertension; n(%)	40 (20.1%)	37 (18.4%)	77 (19.2%)	**0.780**
Surgical time (min); mean ± SD	43 ± 13.3	46 ± 14.5	44 ± 1	**0.950**
Liquid diet start (hours); mean ± SD	5.7 ± 3.3	5.5 ± 3.8	5.6 ± 2.9	**0.590**
In-hospital stay (hours); mean ± SD	49.2 ± 0.2	48.8 ± 0.4	49 ± 0.5	**0.730**
Early major complications; n(%)	4 (2%)	2 (1%)	6 (1.5%)	**0.580**

Homogeneity of variance analysis with Levene's Test

SD Standard deviation

Table 2 Early postoperative evaluation (0 h)

	Placebo ($n = 199$)	Aprepitant ($n = 201$)	p value
Patients with retching; $n(\%)$	23 (11.6%)	9 (4.5%)	**< 0.001**
Retching episodes; mean $\pm$ SD	2.2 $\pm$ 1.1	1.5 $\pm$ 0.3	**< 0.001**
Retching discomfort; $n(\%)$	23 (11.6%)	9 (4.5%)	**0.040**
Mild; $n(\%)$	10 (5%)	8 (4%)	**0.040**
Moderate; $n(\%)$	10 (5%)	1 (0.5%)	**0.040**
Major; $n(\%)$	3 (1.6%)	0	**0.040**
Patients with nausea; $n(\%)$	103 (51.7%)	69 (34.3%)	**< 0.001**
Nausea episodes; mean $\pm$ SD	2.2 $\pm$ 1.3	1.8 $\pm$ 0.6	**< 0.001**
Nausea discomfort; $n(\%)$	100 (50.2%)	66 (32.8%)	**0.020**
Mild; $n(\%)$	62 (31.1%)	42 (20.9%)	**0.020**
Moderate; $n(\%)$	34 (17.1%)	24 (11.9%)	**0.020**
Major; $n(\%)$	4 (2%)	0	**0.020**
Vomiting patients; $n(\%)$	5 (2.5%)	3 (1.5%)	**0.020**
Vomit episodes; mean $\pm$ SD	2 $\pm$ 0.6	1 $\pm$ 0.1	**0.020**
Minimal vomit (< 120 ml); $n(\%)$	5 (2.5%)	3 (1.5%)	0.240
Vomiting discomfort; $n(\%)$	5 (2.5%)	3 (1.5%)	0.380
Mild; $n(\%)$	2 (1%)	3 (1.5%)	0.380
Moderate; $n(\%)$	2 (1%)	0	0.380
Major; $n(\%)$	1 (0.5%)	0	0.380
Use of rescue medication; $n(\%)$	86 (43.2%)	61 (30.3%)	**0.008**

Chi-squared test for categorical variables, Student's t-test for continuous variables

SD Standard deviation

aprepitant, a long-acting antagonist of the substance P/neurokinin 1 receptor with little or no affinity for selective serotonin receptors, corticosteroid receptors, or dopamine receptors, and targets of existing antiemetics for PONV. However, it has a high selective affinity for the human substance P NK1 receptor antagonist present in the brainstem regions involved in emesis [17, 18]. The mechanisms of chemotherapy-induced nausea and vomiting (CINV) and postoperative nausea and vomiting (PONV) after bariatric surgery differ significantly. CINV is primarily attributed to the activation of the serotonin and substance P/neurokinin-1 (NK1) pathways, leading to stimulation of the chemoreceptor trigger zone [19]. Aprepitant acts as an NK1 receptor antagonist, effectively managing CINV by blocking substance P signaling. In contrast, PONV, particularly after bariatric surgery, involves factors like surgical manipulation, anesthesia, and individual patient characteristics. Despite these differences, the involvement of NK1 receptors in both CINV and PONV underlies the effectiveness of aprepitant in managing these conditions [20, 21]. We noted a significant reduction in episodes of nausea and vomiting compared to the traditional multimodal ondansetron plus dexamethasone scheme. These results are similar to those reported in a systematic review and meta-analysis [22] that analyzed 15 clinical trials, including four on laparoscopic surgery and one on bariatric surgery, and showed a clear advantage of aprepitant (alone or in combination) in reducing PONV on postoperative day 1.

Diemunsch et al. [4] reported that aprepitant was more effective using five evaluation criteria: absence of significant nausea (56.4% vs. 48.1%); no nausea (39.6% vs. 33.1%); no vomiting (86.7% vs. 72.4%); no nausea or vomiting (38.3% vs. 31.4%); and no nausea, vomiting, or rescue medication use (37.9% vs. 31.2%). Our study used the Rhodes index, which includes six evaluation criteria: the presence and number of retching episodes (4.7% vs. 11.6%), nausea (24.7% vs. 52.25%), vomiting (1.5% vs. 5.7%), and discomfort caused by each (4.7% vs. 11.6%, 24.3% vs. 51.8%, and 1.5% vs. 5.7%, respectively). We found superiority of aprepitant for all parameters over the traditional regimen; however, not all differences were statistically significant ($p < 0.05$).

A similar study [23] reported that aprepitant was not inferior to palonosetron in terms of complete response at 0–48 h postoperatively (74% vs. 77%). At 0 and 2 h after administration, nausea severity was significantly lower with aprepitant 40 mg than palonosetron 75 mg. In contrast, we found a statistically significant reduction in the use of rescue medication at every time point of analysis, considering that 90% of the patients in our study were at high risk according to Apfel's criteria [6] (greater use of rescue antiemetics). Sinha et al. [24] found that in populations with obesity, the cumulative incidence of vomiting at 72 h was significantly lower in the aprepitant 80 mg group (3%) than in the ondansetron 4 mg group (15%). The combined results of the parameters in our study showed a lower incidence of nausea

Table 3 Evaluation at 6 postoperative hours

	Placebo ($n = 199$)	Aprepitant ($n = 201$)	*p value*
Patients with retching; $n(\%)$	39 (19.6%)	18 (9%)	**0.030**
Retching episodes; mean $\pm$ SD	2.6 $\pm$ 1.5	1.6 $\pm$ 0.7	**0.030**
Retching discomfort; $n(\%)$	39 (19.6%)	18 (9%)	**< 0.001**
Mild; $n(\%)$	12 (6%)	12 (6%)	**< 0.001**
Moderate; $n(\%)$	23 (11.6%)	6 (3%)	**< 0.001**
Major; $n(\%)$	4 (2%)	0	**< 0.001**
Severe; $n(\%)$	1 (0.5%)	0	**< 0.001**
Patients with nausea; $n(\%)$	131 (65.8%)	67 (33.3%)	**< 0.001**
Nausea episodes; mean $\pm$ SD	3.78 $\pm$ 1.9	2.73 $\pm$ 0.8	**< 0.001**
Duration of nausea; mean (min) $\pm$ SD	110.2 $\pm$ 26.5	36.8 $\pm$ 13.7	**< 0.001**
Nausea discomfort; $n(\%)$	131 (65.8%)	67 (33.3%)	**< 0.001**
Mild; $n(\%)$	70 (35.2%)	41 (20.3%)	**< 0.001**
Moderate; $n(\%)$	51 (25.6%)	24 (12%)	**< 0.001**
Major; $n(\%)$	8 (4%)	1 (0.5%)	**< 0.001**
Severe; $n(\%)$	2 (1%)	1 (0.5%)	**< 0.001**
Vomiting patients; $n(\%)$	18 (9%)	6 (3%)	**0.020**
Vomit episodes; mean $\pm$ SD	2.27 $\pm$ 0.63	1.66 $\pm$ 0.75	**0.020**
Minimal vomit (< 120 ml); $n(\%)$	15 (7.5%)	6 (3%)	**0.040**
Moderate vomit (120–480 ml); $n(\%)$	3 (1.5%)	0	**0.040**
Vomiting discomfort; $n(\%)$	18 (9%)	6 (3%)	0.110
Mild; $n(\%)$	7 (3.5%)	3 (1.5%)	0.110
Moderate; $n(\%)$	9 (4.5%)	3 (1.5%)	0.110
Major; $n(\%)$	2 (1%)	0	0.110
Use of rescue medication; $n(\%)$	34 (17%)	7 (3.5%)	**< 0.001**

Chi-squared test for categorical variables, Student's t-test for continuous variables

SD Standard deviation

and vomiting episodes in the aprepitant versus the traditional regimen group with a 2.1- and 3.8-times lower probability of nausea and vomiting, respectively.

Most studies of PONV and aprepitant have used doses ranging from 40 to 125 mg without significant adverse effects [8, 25, 26]; however, one study reported dizziness using 125 mg versus 80 mg [26]. Other side effects include asthenia, hiccups, dehydration, diarrhea, gastritis, elevation in liver function tests, and thrombocytopenia. Such effects are challenging to evaluate in a patient undergoing a sleeve gastrectomy since the primary surgery itself can induce these problems. A limitation of our study includes a lack of information in terms of laboratory tests and specific information about related side effects. Despite the above, our finding aligns with the literature indicating that aprepitant is generally well-tolerated. A meta-analysis by Liu et al. (2023) [27] supports the safety of aprepitant, showing no significant difference in the incidence of major side effects compared to control groups. A homogeneous dose of 80 mg was administered to all patients in this study. For comparison, another group of patients should be randomized to receive a 125 mg dose in a future study. When comparing our findings with the established global benchmarks for Sleeve Gastrectomy

(SG) [28], which are a 90-day complication rate of 6.2% and a readmission rate of 5.5%, our study contributes important insights into one specific aspect of postoperative recovery: the management of PONV. While the benchmark study provides broader surgical outcome metrics, our study's focus on PONV offers a critical perspective on enhancing patient recovery and comfort, key components of overall surgical success. The observed reduction in PONV rates in our study could potentially contribute to broader goals of reducing postoperative complications and readmissions, as effective PONV management is closely linked with patient well-being and satisfaction in the immediate postoperative period. Our findings suggest that incorporating aprepitant into the postoperative care regimen for SG patients could be instrumental in achieving or even surpassing these global benchmarks, thereby enhancing the quality of care in bariatric surgery.

The limitations of this study include the timing of aprepitant administration and the start of the surgical procedure, which may have varied in some cases owing to logistics. Some assessments were performed early in the morning, which interrupted the patients' sleep and had unknown effects. Our study also acknowledges the cost of aprepitant as a potential limitation. The total costs, including the

Table 4 Evaluation at 12 postoperative hours

	Placebo (n=199)	Aprepitant (n=201)	p value
Patients with retching; n(%)	22 (11%)	7 (3.5%)	**0.020**
Retching episodes; mean ± SD	2.3 ± 0.4	1 ± 0	**0.020**
Retching discomfort; n(%)	22 (11%)	7 (3.5%)	**< 0.001**
Mild; n(%)	11 (5.5%)	1 (0.5%)	**< 0.001**
Moderate; n(%)	9 (4.5%)	5 (2.5%)	**< 0.001**
Major; n(%)	2 (1%)	1 (0.5%)	**< 0.001**
Patients with nausea; n(%)	115 (57.8%)	41 (20.4%)	**< 0.001**
Nausea episodes; mean ± SD	3.9 ± 1.3	3.6 ± 0.9	**< 0.001**
Duration of nausea; mean (min) ± SD	96.3 ± 30.7	29.7 ± 8.3	**< 0.001**
Nausea discomfort; n(%)	115 (57.8%)	41 (20.4%)	**< 0.001**
Mild; n(%)	67 (33.6%)	27 (13.4%)	**< 0.001**
Moderate; n(%)	38 (19.2%)	10 (5%)	**< 0.001**
Major; n(%)	6 (3%)	4 (2%)	**< 0.001**
Severe; n(%)	4 (2%)	0	**< 0.001**
Vomiting patients; n(%)	17 (8.5%)	2 (1%)	**< 0.001**
Vomit episodes; mean ± SD	2.5 ± 0.5	1 ± 0	**< 0.001**
Minimal vomit (< 120 ml); n(%)	15 (7.5%)	2 (1%)	**< 0.001**
Moderate vomit (120–480 ml); n(%)	2 (1%)	0	**< 0.001**
Vomiting discomfort; n(%)	17 (8.5%)	2 (1%)	**< 0.001**
Mild; n(%)	8 (4%)	2 (1%)	**< 0.001**
Moderate; n(%)	7 (3.5%)	0	**< 0.001**
Major; n(%)	2 (1%)	0	**< 0.001**
Use of rescue medication; n(%)	31 (15.6%)	6 (3%)	**< 0.001**

Chi-squared test for categorical variables, Student's t-test for continuous variables

SD Standard deviation

Table 5 Evaluation at 24 postoperative hours

	Placebo (n=199)	Aprepitant (n=201)	p value
Patients with retching; n(%)	9 (4.5%)	4 (2%)	0.130
Retching episodes; mean ± SD	2.1 ± 0.3	1 ± 0	0.130
Retching discomfort; n(%)	9 (4.5%)	4 (2%)	0.350
Mild; n(%)	3 (1.5%)	3 (1.5%)	0.350
Moderate; n(%)	4 (2%)	1 (0.5%)	0.350
Major; n(%)	2 (1%)	0	0.350
Patients with nausea; n(%)	67 (33.7%)	22 (10.9%)	**< 0.001**
Nausea episodes; mean ± SD	3.9 ± 1	2 ± 0.7	**< 0.001**
Duration of nausea; mean (min) ± SD	57 ± 19.9	10.6 ± 5.1	**< 0.001**
Nausea discomfort; n(%)	67 (33.7%)	22 (10.9%)	**< 0.001**
Mild; n(%)	51 (25.6%)	15 (7.4%)	**< 0.001**
Moderate; n(%)	12 (6%)	6 (3%)	**< 0.001**
Major; n(%)	4 (2%)	1 (0.5%)	**< 0.001**
Vomiting patients; n(%)	6 (3%)	1 (0.5%)	**0.040**
Vomit episodes; mean ± SD	1.5 ± 0.5	1 ± 0	**0.040**
Minimal vomit (< 120 ml); n(%)	6 (3%)	1 (0.5%)	**0.030**
Vomiting discomfort; n(%)	6 (3%)	1 (0.5%)	**0.040**
Mild; n(%)	5 (2.5%)	1 (0.5%)	**0.040**
Moderate; n(%)	1 (0.5%)	0	**0.040**
Use of rescue medication; n(%)	11 (5.5%)	5 (2.5%)	**< 0.001**

Chi-squared test for categorical variables, Student's t-test for continuous variables

SD Standard deviation

intervention, placebo, and other associated expenses such as data collection and analysis, were entirely covered by the research team. The cost for one dose of aprepitant was approximately 45 USD, resulting in a total of 9,045 USD for the 201 participants. Additionally, the cost for the placebo and other research-related expenses were also fully funded by the investigators. It is important to note that our study did not receive any sponsorship or support from any pharmaceutic, ensuring an unbiased approach in our research methodology and analysis. This financial aspect is an important consideration for the practical application of our findings in clinical settings. Another limitation is that smoking status and cannabis consumption reduced PONV. These were among the exclusion criteria; this decision was based on scientific evidence suggesting that smoking may influence the incidence of PONV. The protective effect of smoking on PONV has been recognized in several studies. For instance, a study published by Habib AS et al. [10] showed that smokers have a reduced risk of PONV, which might be attributed to the pharmacokinetic effects associated with smoking. Therefore, including smokers in our study could have introduced a significant confounding variable, potentially skewing the results and affecting the validity of

our conclusions regarding the efficacy of the intervention in preventing PONV. By excluding smokers, our study aimed to provide a clearer assessment of the intervention's effectiveness in a population not influenced by this protective factor; however, they were based only on patient interrogation, and no special laboratory tests were performed. Despite these limitations, this is the first randomized study to demonstrate the substantial improvement of prophylactic aprepitant for PONV in patients undergoing LSG. This approach has significantly transformed our routine clinical practice, leading to a more comfortable postoperative recovery for patients, characterized by fewer surgical discomforts. Additionally, it has facilitated an enhanced tolerance to a liquid diet post-surgery.

Conclusions

Compared to the standard of care, preoperative aprepitant significantly improved PONV in patients who underwent LSG. This effect was observed in the early postoperative period and persisted for up to 24 h postoperatively.

Appendix

Table 6 Rhodes index for PONV (evaluation at 0, 6, 12, 24 h)

Number of retching episodes (no vomiting):	7 or more	5–6	3–4	2–1	No
Experiences Discomfort from Retching:	Severe	Major	Moderate	Mild	No
Experiences Nausea / Upset Stomach:	>6 h	3–6 h	2–3 h	<1 h	No
Number of Instances with Nausea / Upset Stomach:	7 or more	5–6	3–4	2–1	No
Experiences Discomfort Due to Nausea:	Severe	Major	Moderate	Mild	No
Vomited:	7 or more	5–6	3–4	1–2	No
Each Vomiting Episode Results in:	Too much (+ 3 cups)	High (2–3 cups)	Moderate (½ -2 cups)	Low (<½ cups)	No vomit
Experiences Discomfort Caused by Vomiting:	Severe	Major	Moderate	Mild	No

Required Additional Medication for Nausea and Vomiting Control? If yes, specify:

Medication and Dosage:

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