Preoperative Aprepitant Decreases Postoperative Nausea After Laparoscopic Sleeve Gastrectomy

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ABSTRACT

BACKGROUND: Postoperative nausea is common following bariatric surgery despite the use of enhanced recovery protocols for perioperative care.

OBJECTIVES:

- To determine the prevalence of postoperative nausea in our sleeve gastrectomy population.
- To administer preoperative aprepitant and track postoperative nausea after laparoscopic sleeve gastrectomy.

METHODS: Beginning in September 2022, a retrospective cohort study was conducted. We added 80 mg of oral aprepitant to a standard prophylactic antiemetic regimen, which included scopolamine, dexamethasone, and ondansetron. Utilizing an existing database at our institution, we reviewed the records of patients who underwent laparoscopic sleeve gastrectomy before and after the addition of aprepitant to the standard prophylactic antiemetic regimen. We assessed the severity and frequency of postoperative nausea and vomiting qualitatively (endorsed in postoperative-day-one house-staff note) and quantitatively (number of postoperative antiemetic doses administered beyond standard protocol).

RESULTS: One hundred thirty-four (134) laparoscopic sleeve gastrectomies were performed between March and November 2022. Sixty-four patients (64) received aprepitant preoperatively, while 70 did not. Groups were similar in age, BMI, and ASA class. In the aprepitant group, we noted a 41.60% reduction in nausea reported on postoperative-day-one (29.20% vs 50.00%, P=0.013) and a 30.5% reduction in absolute number of additional antiemetic doses (2.98 vs 4.29, P= 0.013). Additional antiemetics included ondansetron, metoclopramide, prochlorperazine, diphenhydramine, haloperidol, and lorazepam. Length of stay was not significantly different.

CONCLUSIONS: The addition of preoperative aprepitant to a multimodal protocol can reduce nausea after laparoscopic sleeve gastrectomy.

KEYWORDS: Aprepitant, Postoperative Nausea and Vomiting (PONV), Bariatric Surgery, Enhanced Recovery After Surgery (ERAS)

INTRODUCTION

Postoperative nausea and vomiting (PONV) is a major cause of patient dissatisfaction with perioperative care.[1-3] It contributes to a variety of postoperative problems, including delayed oral intake, dehydration, electrolyte abnormalities, aspiration, and increased length of hospital stay.[3-5,9] The incidence of PONV is common following bariatric surgery.[3,5,8,9]

To decrease the risk of PONV among bariatric patients, our institution's enhanced recovery protocols for surgery (ERAS) includes a standard prophylactic antiemetic regimen for every patient. While our ERAS protocol has been effective in reducing PONV among laparoscopic gastric bypass patients, we observed many laparoscopic sleeve gastrectomy patients continued to experience significant PONV. To better define and address this problem, our surgical team partnered with anesthesiology to refine our ERAS protocol for laparoscopic sleeve gastrectomy patients.

Based on existing data demonstrating the efficacy of aprepitant as an antiemetic, we added the medication to our ERAS regimen. Aprepitant is a long-acting neurokinin-1 (NK-1) receptor antagonist without sedative effect or risk of tardive dyskinesia and has been approved by the FDA for the prophylaxis of chemotherapy-related nausea and PONV.[6] Several studies and meta-analyses have demonstrated its efficacy as a prophylactic agent to reduce PONV, though none have focused specifically on laparoscopic sleeve gastrectomy.[3,5,7]

In our study, we assess the efficacy of adding prophylactic aprepitant to an existing ERAS protocol for the prevention of PONV after laparoscopic sleeve gastrectomy.

METHODS

With appropriate Institutional Research Board (IRB) approval, a retrospective cohort study was conducted, including all patients who underwent laparoscopic sleeve gastrectomy from March 2022 to November 2022 at our institution. All patients received a pre-existing, standardized prophylactic antiemetic regimen, which included preoperative scopolamine patch placed the day prior to surgery, a single dose of intra-operative dexamethasone, and 24 hours of standing postoperative ondansetron. Beginning September 2022, 80 mg oral aprepitant administered three hours prior to induction of anesthesia was added to the standard prophylactic antiemetic regimen.

Utilizing a pre-existing, quality improvement database within the Center for Bariatric Surgery, the records of all patients who underwent laparoscopic sleeve gastrectomy between March 2022 and November 2022 were reviewed. Variables already included in the pre-existing database included medical record number (MRN), patient age, body mass index (BMI), American Society of Anesthesiologists Physical Status Classification (ASA I-VI), date of surgery, discharge date, and length of stay (LOS) as measured in days. Additional variables collected from the electronic medical record of each patient included documentation of preoperative scopolamine patch application, time of aprepitant administration, number of postoperative antiemetic doses administered in addition to the standard prophylactic regimen, and documentation of nausea as subjectively reported on postoperative-day one (POD#1).

To determine whether a scopolamine patch was applied preoperatively, each patient's medication dispense report was queried and peri-anesthesia nursing notes reviewed. Patients who received a prescription for scopolamine prior to surgery, or those who had a scopolamine patch applied in preoperative holding, were considered to have received the medication unless nursing notes documented otherwise. The application of a scopolamine patch at any time on the day of surgery, regardless of whether the patient had applied one previously, was not considered an additional antiemetic dose.

Time of aprepitant administration as documented in a patient's medication administration record (MAR) was used to determine if a patient received aprepitant preoperatively, postoperatively, or both. Patients who received aprepitant preoperatively were included in the aprepitant group, while those who did not were included in the control group. Postoperative administration of aprepitant was considered an additional antiemetic dose, regardless of whether the patient received aprepitant preoperatively or not.

The total number of antiemetic doses administered beyond the standard prophylactic regimen was determined by reviewing each patient's MAR. Any postoperative antiemetic administered, other than 24 hours of standing ondansetron as included in the standard prophylactic regimen, was considered an additional dose, whether it was ordered as needed or as a one-time dose. A medication was considered to be an antiemetic if it was ordered with an indication of nausea or vomiting. Any medication commonly used to treat postoperative nausea, unless ordered with a different specified indication, was also included. Antiemetics included ondansetron, metoclopramide, prochlorperazine, diphenhydramine, haloperidol, and lorazepam.

Reported postoperative nausea was determined by reviewing POD#1 notes from resident and attending physicians, nutritionists, and nurses. Any documented complaint of nausea or emesis, including those noted to be "minimal," "controlled," "improving," or "resolved," was considered to represent clinically significant postoperative nausea. If there was no mention of nausea or emesis in any notes, the patient was considered not to have clinically significant postoperative nausea.

Statistical Analysis

Statistical analysis was performed using STATA Version 15 (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC). Two groups were compared – those who received preoperative aprepitant (aprepitant group) and those who did not (control group). Demographic data between groups was compared using Student's two-sample *t*-test (age, BMI) and Pearson's chi-squared test (ASA). Wilcoxan rank sum test was used to compare LOS and number of additional antiemetic doses, while Person's chi-squared test was used to compare rates of reported POD#1 nausea between groups.

RESULTS

One hundred thirty-four (134) laparoscopic sleeve gastrectomies were performed between March and November 2022. Sixty-four (64) patients received aprepitant preoperatively (aprepitant group), while 70 did not (control group). Other than one 17-year-old patient (BMI 50 kg/m^2), all patients were adults ages 18-69 years old with a mean BMI of 43.6 kg/m^2 [34–64 kg/m^2]. On statistical analysis, groups were similar in age, BMI, and ASA class [**Table 1**].

Clinically significant nausea was reported on POD#1 by 29.2% (19/64) of patients who received aprepitant, and 50.0% (35/70) of those who did not (p=0.013). This represented a 41.60% relative reduction in reported PONV on POD#1 in the aprepitant group. The mean number of antiemetic doses required in addition to the standard prophylactic regimen was 2.98 [1–20] in those who received aprepitant preoperatively, compared to 4.29 [1–28] in those who did not (p= 0.0027). This represented a 30.5% relative reduction in unplanned postoperative antiemetic doses in the aprepitant group. There was no significant difference in length of stay between groups, which both had a median LOS of 1 day

Table 1. Demographics, Reported Nausea, and Number of Additional Antiemetic Doses

	Control (n=70)	Aprepitant (n=64)	P-value
Age (years)	39.31	41.59	0.2506
BMI (kg/m^2)	43.89	43.27	0.5708
Median ASA	3	3	0.410
Median LOS	1	1	0.6348
POD#1 nausea	50.00%	29.20%	0.013
Antiemetic doses	4.29	2.98	0.0027

BMI=body mass index. ASA=American Society of Anesthesiologists Physical Status Classification. LOS=length of stay. POD#1=postoperative day 1. Antiemetic doses= unplanned doses of antiemetics beyond standard prophylactic regimen.

(p=0.6348). LOS ranged from one to three days in the aprepitant group, and one to four days in the control group.

Of the 70 patients who did not receive aprepitant preoperatively, 15 received the medication postoperatively. This subset of control group patients required more antiemetic doses than either the aprepitant group or the remainer of the control groups, with a mean of 9.8 [4–28] additional antiemetic doses. Two patients in the aprepitant group received a second dose of aprepitant on POD#1, which was included as an additional antiemetic dose beyond the prophylactic regimen. One of these patients required a total of three additional antiemetic doses, while the other required a total of 20.

DISCUSSION

The addition of preoperative aprepitant to an existing ERAS protocol for the prevention of PONV after laparoscopic sleeve gastrectomy proved to be effective in reducing PONV both quantitatively and qualitatively when compared to the existing ERAS protocol alone. Compared to the control group, patients who received prophylactic aprepitant required fewer additional antiemetic doses (2.98 vs 4.29, p=0.0027) and reported less nausea/vomiting on POD#1 (29.2% vs 40.0%, p=0.013). While these results are consistent with previous studies demonstrating the efficacy of aprepitant as a prophylactic antiemetic for patients undergoing bariatric surgery, they suggest the medication's efficacy is more pronounced following laparoscopic sleeve gastrectomy as opposed to other types of bariatric surgery.

Two prior studies have demonstrated aprepitant's prophylactic efficacy in reducing emesis after bariatric surgery, though both studies included predominantly gastric bypass patients, and neither study demonstrated a reduction in patient-reported nausea.[3,5] Sinha et al performed a double-blind, placebo-controlled study of 125 participants undergoing bariatric surgery, 98 (79%) of whom underwent a bypass procedure, while the remaining 26 underwent gastric banding. Compared to the placebo group, those who received prophylactic aprepitant had a significantly lower rate of emesis at 72 hours (3.1% vs 15.0 %, p=0.021), though verbal rating scores of nausea were no different between groups (p=0.675).[3] Therneau et al performed a retrospective analysis of 338 patients undergoing bariatric surgery, 257 (76%) of whom underwent malabsorptive procedures, while 62 underwent sleeve gastrectomy and 19 underwent gastric banding. Compared to the control group, there was a lower cumulative incidence of emesis in the aprepitant group over 48 hours (6% vs 13%, p=0.04), though there was no difference in reported nausea or additional antiemetics required.[5]

While we did not quantify cumulative episodes of emesis, our study demonstrated a significant reduction in both patient-reported nausea/vomiting and antiemetic doses required. This finding suggests that laparoscopic sleeve gastrectomy patients benefit from prophylactic aprepitant for the prevention of PONV more than those undergoing other types of bariatric surgery. Following completion of our project, these findings have been replicated in a randomized controlled trial performed by Ortiz et al.[10] This group demonstrated improvement in PONV over the first 24 hours postoperatively after laparoscopic sleeve gastrectomy using a validated assessment scale.

There are several proposed mechanisms for why sleeve gastrectomy patients have increased rates of PONV. This may be due to anatomy, with the pylorus remaining intact and the stomach unable to distend after sleeve gastrectomy is performed, leading to overdistension with smaller amounts of intraluminal contents. Removal of the gastric fundus and its stretch receptors may temporarily slow gastric emptying immediately after surgery. It is also known that enterochromaffin cells release 5-hydroxytryptamine in response to gastric surgery. This hormone and is associated with nausea and vomiting and appears to have a greater effect on the obese population.[8]

Limitations

It is important to note that our assessment of subjective nausea was restrained by the limitations of a retrospective study design – no standardized or validated tool was used to assess nausea. Rather, we relied on documentation from various providers in the electronic medical record of each patient. While this heterogeneity lends some degree of uncertainty to our findings, the relative reduction in reported nausea/vomiting (41.6% RRR) and antiemetic dose requirement (30.5% RRR) were similar. Because antiemetics were ordered as PRN or one-time doses with an indication of nausea, a patient's antiemetic requirement can be assumed to be a reasonable proxy for subjective nausea, and our data adequately reliable.

CONCLUSION

PONV is a prevalent problem after laparoscopic sleeve gastrectomy. The addition of preoperative aprepitant to an existing ERAS protocol is effective in reducing PONV. Patients undergoing this procedure appear to benefit more from the prophylactic antiemetic effects of aprepitant than those undergoing other bariatric surgeries (e.g., gastric bypass) based on comparison with previous studies.[3,5,10] Our results were limited by heterogenous documentation of subjective nausea, though appear to be reliable based on concordance between reported nausea/vomiting and number of antiemetic doses required. Future research should work on treatment options for non-responders, those patients with persistent nausea despite use of our current protocols.

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