Original Work

Post-Operative Antiemetic Use in Surgical Patients on Injectable GLP-1 Receptor Agonists

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Abstract

Background: Glucagon-like peptide 1 receptor agonists (GLP-1 RAs) are commonly prescribed for diabetes and obesity management. These agents can delay gastric emptying and may cause nausea and vomiting as adverse effects. The implications of GLP-1 RAs on surgical outcomes, particularly anesthesia type, post-operative nausea and vomiting (PONV), and recovery, are not well defined. This study evaluates the impact of GLP-1 RAs on perioperative drug selection, anesthesia type, and antiemetic use during the post-operative period.

Methods: A retrospective chart review was conducted to analyze surgical patients on injectable GLP-1 RAs compared to a cohort not receiving these agents. Data collection included the type of anesthesia administered during surgery and antiemetic medications used post-operatively. Statistical analyses were performed to identify differences in anesthesia type and antiemetic use between the two groups.

Results: Patients on GLP-1 RAs exhibited a statistically significant difference in the type of anesthesia used during surgery compared to those not on GLP-1 RAs. Post-operatively, patients receiving GLP-1 RAs required more antiemetics; however, this increase was not statistically significant. These findings highlight potential modifications to anesthesia protocols and post-operative care for patients on GLP-1 RAs to address the drugs' known gastrointestinal side effects.

Conclusions: Patients on GLP-1 RAs undergoing surgery may require tailored perioperative management due to the drugs' impact on gastric emptying and associated nausea. Further research is warranted to validate these findings and explore the mechanisms driving the observed differences in anesthesia and recovery.

Glucagon-like peptide 1 receptor agonists (GLP-1 RAs) are the United States Food and Drug Administration (FDA) approved medications for the treatment of type 2 diabetes mellitus (T2DM) and medication-assisted weight loss.[1] The mechanism of action is multimodal; they increase glucose-dependent insulin secretion, decrease inappropriate glucagon secretion, and slow gastric emptying. These factors help improve glycemic control and promote weight loss. Agents in this class have a high prevalence of nausea as an adverse effect, ranging from 8% to 44% of patients as reported in the injectable exenatide, semaglutide, and dulaglutide prescription drug label.[2-4] This may impact several aspects of patient care, including surgery. One common side effect following surgery is post-operative nausea and vomiting (PONV), which may be exacerbated by GLP-1 RAs. Limited literature exists describing this relationship or the impact of GLP-1 RAs in the surgical population.

Prior studies and case reports have shown patients on GLP-1 RAs have increased residual gastric contents measured through esophagogastroduodenoscopy under deep sedation or general anesthesia prior to procedure compared to patients not on GLP-1 RAs despite fasting for the instructed time, from 18 to 24 hours.[5-7] One study reported 24.2% of patients on weekly injectable semaglutide had residual gastric contents versus 5.1% of patients not on GLP-1 RAs.[5] Concerns exist that increased residual gastric contents despite proper pre-operative fasting instructions can increase the risk of adverse effects such as aspiration following surgery. As a result, a consensus-based guidance statement from the American Society of Anesthesiologists (ASA) published in June 2023 recommends holding weekly injectable GLP-1 RAs at least 7 days prior to surgery for elective procedures, which is different from the previous standard of care of typically holding medications the day of surgery.[8] This guidance was implemented within this institution on July 1, 2023.

A recent systematic review and meta-analysis reviewed the impact on GLP-1 RAs and periprocedural management focusing on gastric emptying and reviewed a solid diet and liquid diet prior to surgery.[9] The study demonstrated an approximate 36-minute gastric emptying delay for patients on GLP-1 RAs on a solid diet measured through scintigraphy; however, this delay was not meaningful given that the standard pre-operative fasting guidance is typically much longer. In addition, the liquid diet showed no difference in gastric emptying. With these findings, it was recommended to continue GLP-1 RAs, follow a liquid diet a day prior to procedure, and utilize standard pre-anesthesia fasting guidance.

There remains a gap in the literature exploring post-operative recovery for patients on GLP-1 RAs. With potential residual gastric contents present in the stomach, the project team questioned whether anesthesia and antiemetic practices differ for patients on GLP-1 RAs versus those who are not.

This study's primary objective was to investigate PONV for patients on GLP-1 RAs, measured indirectly through antiemetic administrations for patients on GLP-1 RAs compared to those who were not on these agents. Additional secondary objectives were to evaluate antiemetic administration for patients on GLP-1 RAs before and after implementation of the ASA consensus statement recommending holding weekly injectable GLP-1 RAs at least 7 days prior to surgery for elective procedures (July 1, 2023) to assess the impact of the updated guidance; to review anesthesia type used to evaluate if there are differences in

Key Points

Question: How do injectable glucagon-like peptide 1 receptor agonists (GLP-1 RAs) impact anesthesia type, post-operative nausea and vomiting (PONV), and recovery in surgical patients?

Findings: Patients on GLP-1 RAs had a statistically significant difference in anesthesia type used during surgery and required more antiemetics post-operatively, though the latter was not statistically significant.

Meaning: Perioperative management of patients on GLP-1 RAs may require tailored anesthesia protocols and proactive strategies to address potential gastrointestinal side effects.

TABLE 1. Baseline Characteristics (n=2779)

Category		*GLP-1 RA (N=105)*	*No GLP-1 RA (N=2674)*	*p-value*
Average age (years), mean ± SD		64.1 ± 11.5	63.6 ± 18.7	0.79
Sex as officially documented in medical record	Male	61 (58.1%)	1248 (46.7%)	0.021
	Female	44 (41.9%)	1426 (53.3%)	
Ethnicity	Hispanic or Latino	1 (1.0%)	49 (1.8%)	0.74
	Not Hispanic or Latino	103 (98.1%)	2606 (97.5%)	
	Unknown	1 (1.0%)	19 (0.7%)	
Race	American Indian/ Alaskan Native	1 (1.0%)	20 (0.7%)	0.35
	African	0	1 (0.0%)	
	Asian (Chinese, Laotian, Other, Thai, Vietnamese)	1 (1.0%)	23 (0.9%)	
	Black or African American	2 (1.9%)	17 (0.6%)	
	Native Hawaii/Pacific Islander	0	4 (0.1%)	
	White	100 (95.2%)	2593 (97.0%)	
	Other	0	7 (0.3%)	
	Unknown	1 (1.0%)	9 (0.3%)	
Weight (kg)		106 ± 26	88.5 ± 24.2	<0.001
Diabetes diagnosis %		86 (81.9%)	546 (20.4%)	<0.001
Prior to admission antiemetic use (% yes)		0	144 (5.4%)	0.006

**GLP-1 RA: Glucagon-like peptide-1 receptor agonists* anesthesia practices for patients on GLP-1 RAs compared to those who are not; and to assess the impact on patient length of stay.

Methods

This retrospective cohort study was conducted at Mayo Clinic Health System Northwest Wisconsin Region from November 1, 2022, to October 31, 2023. The study included adult surgical patients 18 years or older requiring at least one night stay and at least 12 hours in the hospital post-operatively. Identification of patients prescribed injectable GLP-1 RAs was completed using the prior to admission (PTA) medication list documented within the electronic health record. Patients were excluded if they were pregnant or had a prescription for an oral GLP-1 RA or glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 dual agonist. Information was collected from the electronic health record with assistance from an internal pharmacy informatics team. The study was approved by the appropriate Institutional Review Board (IRB), and the requirement for written informed consent was waived by the IRB.

Baseline information collected included age, ethnicity, race, sex as officially documented in medical record, weight at the time of surgery, presence of diabetes diagnosis, and prior to admission antiemetic use (Table 1). Surgical information collected included surgical service, surgical procedure, type of anesthesia ordered and administered, case request date and time, date and time of procedure, and hospital length of stay. Anesthesia types included general, regional, monitored anesthesia care, general with pain block, local, and moderate sedation. Data was collected through review of the surgical case request time and the actual surgery date to evaluate if the holding period implementation reduced PONV for patients on GLP-1 RAs. A determination was made if there were at least 7 days between the surgical request time and surgery date for patients on weekly injectable GLP-1 RAs or at least 24 hours if on a daily injectable. Antiemetics of interest collected included ondansetron, granisetron, palonosetron, prochlorperazine, haloperidol, fosaprepitant, aprepitant, promethazine, and metoclopramide for each group (Table 2). Pertinent order information, such as route of administration and order directions, was also collected. Administrations for the first 24 hours post-operatively were recorded for each antiemetic used during that period.

Data was summarized using frequencies and percentages for categorical data and either means and standard deviations or medians and interquartile ranges (IQR) for continuous data. Comparisons were made between groups using Chi-square or Fisher's exact tests for categorical data and either a t-test or Kruskal-Wallis test for continuous data. All analyses were performed using R version 4.1.2 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria).

Results

In total, 105 patients were included in the GLP-1 RA group with 2674 patients included in the non GLP-1 RA group (Table 3). The GLP-1 RA group had a higher percent of procedures for patients with at least one antiemetic administered within 24 hours post-operatively (21.0% versus 18.9%).

Of the 105 total patients in the GLP-1 RA group, 62 patients had their procedure prior to the new ASA guideline and 43 patients after the ASA guideline. Prior to the ASA guideline implementation, 24% of patients in the GLP-1 RA group had at least one antiemetic administered postoperatively. After the ASA guideline implementation, 26% of patients had at least one antiemetic administered postoperatively. Upon further analysis, for the 11 patients who

TABLE 2. Antiemetic Administered Post-Operatively

Antiemetic	*GLP-1 RA (n=124)*	*No GLP-1 RA (n=3199)*
Ondansetron	23 (18.5%)	497 (15.5%)
Granisetron	3 (2.4%)	8 (0.3%)
Palonosetron	0	0
Prochlorperazine	4 (3.2%)	101 (3.2%)
Haloperidol	4 (3.2%)	85 (2.7%)
Fosaprepitant	0	1 (0.0%)
Aprepitant	0	0
Promethazine	3 (2.4%)	36 (1.1%)
Metoclopramide	1 (0.8%)	26 (0.8%)

**GLP-1 RA: Glucagon-like peptide-1 receptor agonists*

TABLE 3. Post-Operative Antiemetic Administrations

	GLP-1 RA	*No GLP-1 RA*	*p-value*
Patients with antiemetics administered	26/105 (24.8%)	579/2674 (21.7%)	0.52
Procedures with antiemetics administered	26/124 (21.0%)	605/3199 (18.9%)	0.65
Antiemetic order administrations (total)	56	977	--
Median (IQR) administrations per person	1 (1, 2)	1 (1, 2)	0.14
Procedures with pre-procedure antiemetic given	9/124 (7.3%)	191/3199 (6.0%)	

**GLP-1 RA: Glucagon-like peptide-1 receptor agonists*

TABLE 4. GLP-1 RA Holding Period

Appropriate Hold Period	*Yes (N=19)*	*No (N=24)*	*p-value*
Procedures with antiemetic administrations	8 (42%)	3 (13%)	0.038
Antiemetic administrations	28	5	--
Median (IQR) administrations per person	3.5 (1, 5.3)	2 (1.5, 2)	0.53
Median (IQR) administrations per person	1 (1, 2)	1 (1, 2)	0.14

**GLP-1 RA: Glucagon-like peptide-1 receptor agonists*
***Hold periods defined as procedures for patients on GLP-1 RAs with case request time and surgery date ≥ 7 days apart, or appropriate depending on the medication after July 1, 2023.*

underwent surgery after the ASA guideline implementation and received at least one antiemetic postoperatively, eight patients (73%) met the criteria for adequate holding period. Three patients did not meet the criteria of holding more than 7 days for patients on weekly injectable GLP-1 RAs. The most notable reason for not meeting the hold period criteria was that it was an emergent surgery. Of the 8 patients meeting the holding period criteria, their procedures had a median of 3.5 (IQR 1, 5.3) antiemetic administrations per procedure, and for the 3 patients who did not meet the holding period criteria, there was a median of 2 (IQR 1.5, 2) administrations (p=0.53) (Table 4).

For the third objective, to review differences in anesthesia used between the groups, 82.3% of the GLP-1 RA group utilized general anesthesia compared to 69.3% in the No GLP-1 RA group. Surgical service performing the procedure was similar between groups (Table 6). Overall, there was a statistically significant difference in the type of anesthesia used for patients on GLP-1 RAs (p<0.001).

For the fourth objective, patients in the GLP-1 RA group had an average length of stay of 4.4 days versus 5.3 days for the No GLP-1 RA group (p=0.024) (Table 5).

TABLE 5. Inpatient Surgical Encounter (n=3323)

		GLP-1 RA (N=124)	*No GLP-1 RA (N=3199)*	*p-value*
Average length of stay (days), mean ± SD		4.4 ± 3.1	5.3 ± 4.4	0.024
Anesthesia Type, n (%)	General	102 (82.3%)	2216 (69.3%)	<0.001
	Regional	1 (0.8%)	291 (9.1%)	
	Monitored Anesthesia Care	15 (12.1%)	587 (18.3%)	
	General with Pain Block	6 (4.8%)	101 (3.2%)	
	Local	0	1 (0.05%)	
	Moderate Sedation	0	2 (0.1%)	
	Unknown (not documented)	0	1 (0.05%)	

**GLP-1 RA: Glucagon-like peptide-1 receptor agonists*
Total inpatient surgical encounters from November 1, 2022 to October 31, 2023 in Northwest Wisconsin Region Mayo Clinic

Discussion

No significant difference in antiemetic use post-operatively was found between patients in the GLP-1 RA group and the No GLP-1 RA group. Pre-procedure antiemetic administration was similar between groups. Patients were not matched by procedure type, but surgery service performing the procedure was collected and there were no major discrepancies among groups. However, differences in baseline characteristics, such as weight, presence of diabetes, and PTA antiemetic use, should be considered, as these factors may influence PONV. Prior to admission GLP-1 RA use may not predispose patients to increased PONV.

Implementation of the ASA guidance for holding GLP-1 RAs before procedures did not produce a significant difference in antiemetic administrations. Holding GLP-1 RAs prior to procedures did not impact PONV but may be important for preventing other adverse effects. Prior studies and case reports have demonstrated that patients on GLP-1 RAs may vomit residual gastric contents despite adhering to pre-operative fasting guidelines, raising

concerns that this may elevate the risk of aspiration and other complications following surgery.

There was greater use of general anesthesia in the GLP-1 RA group; however, this was not matched by type of procedure. It is unclear whether the GLP-1 RA group procedures required a higher use of general anesthesia based on the nature of the procedure, or whether general anesthesia was used more often due to patient-specific factors.

The GLP-1 RA group had a shorter average length of stay than patients in the No GLP-1 RA group. Length of stay is influenced by many factors, including procedure type, complications and other patient specific factors. Based on our study, it does not appear that GLP-1 RA use preoperatively contributes to hospital length of stay.

Limitations of the Study

This study does carry some limitations. Among the patients included, only 11 underwent surgery after the ASA guideline implementation and received at least one antiemetic postoperatively, limiting the ability to draw conclusions. This is a retrospective study with a small sample size and relied on chart review. As a result of these limitations, findings should be considered exploratory and correlational, not used to identify causation. Patients may have contraindications to specific antiemetic treatments, which may have limited the use of certain agents in this study. Patients may have other medications for comorbid conditions that may have antiemetic properties, such as olanzapine for mental health, which further complicates interpretation of the relationship between GLP-1 RA use and antiemetic administration. This consideration also resulted in a narrowed list of antiemetics for inclusion. Additional agents, such as olanzapine and dexamethasone, were excluded for this reason. In addition, patients may be prescribed medications for comorbid conditions that may increase nausea and vomiting, such as oral chemotherapy. Patients also may be predisposed to nausea and vomiting due to comorbid conditions. Certain surgical services utilize pre-operative antiemetics, which may impact post-operative administrations. This study also measures PONV indirectly through antiemetic administrations, which assumes the relationship, rather than directly measuring PONV. Only patients with an injectable GLP-1 RA on their PTA medication lists were included in the search for patients. This may have omitted patients obtaining GLP-1 RAs who did not self-report the prescription. Lastly, gastric content measurements are not a routine part of practice at this site, limiting the ability to collect that information for comparison to previous studies or assess the potential relationship with PONV.

Conclusion

This study provides preliminary insights into the post-operative effects of GLP-1 RA use, though further research is needed to draw definitive conclusions. Patients on GLP-1 RAs utilize more antiemetics post-operatively; however, the difference was not statistically significant. The holding period guidance implementation did not impact post-operative antiemetic use. GLP-1 RA patients did not have a longer length of stay post-operatively compared to the No GLP-1 RA group. Lastly, more general anesthesia was used in the GLP-1 RA group. Further studies are warranted to explore the relationships among GLP-1 RAs, gastric content measurements, and post-operative nausea and vomiting. Additionally, investigating whether pretreatment with antiemetics may improve post-operative outcomes in this population could provide valuable insight. An evaluation of the risks versus benefits of holding GLP-1 RAs for patients with diabetes and the potential impact on blood glucose levels a week prior to surgery could be useful to determine if there may be harm associated with holding the medication.

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TABLE 6. Surgical Service in Charge by Glucagon-like Peptide 1 Receptor Agonist (GLP-1 RA) (n=124) Versus No GLP-1 RA (n=3199) Group

	GLP-1 RA group %, (n)	No GLP-1 RA group %, (n)
Anesthesiology	0	4
Cardiovascular Disease	2.4 (3)	2.3 (72)
Cardiovascular Surgery	18.5 (23)	13 (416)
Electrophysiology	2.4 (3)	1.2 (39)
Family Medicine	0	0.1 (3)
Gastroenterology	9.7 (12)	14.3 (459)
General	26.6 (33)	17.7 (567)
Gynecologic	0	0.1 (3)
Interventional Radiology	0	0.1 (4)
Neurologic	7.3 (9)	7.8 (249)
Obstetrics/ Gynecology	0	7.1 (227)
Ophthalmic	0	0.1 (2)
Oral	0	0.3 (9)
Orthopedics	12.1 (15)	20 (639)
Orthopedics/Trauma	0	0.1 (2)
Orthopedics/ Podiatry	5.6 (7)	2.3 (72)
Head and neck	1.6 (2)	0.7 (22)
Plastic	0.8 (1)	0.2 (6)
Pulmonary	0	0.9 (29)
Trauma	0	0.03 (1)
Urology	4 (5)	4.7 (150)
Vascular	8.9 (11)	7 (224)

**GLP-1 RA: Glucagon-like peptide-1 receptor agonists*

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Disclosure: The authors declare no relevant relationships, real or potential, with ineligible companies or product(s) or services(s) mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria.

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