

ISMP Canada Safety Bulletin

Volume 23 • Issue 9 • September 27, 2023

Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists: Risk of Aspiration during Anesthesia

Pulmonary aspiration of regurgitated gastric contents during anesthesia is a serious complication that may cause pneumonitis, aspiration pneumonia, or other lung injury. It has the potential to cause long-term complications, morbidity, and even death.¹ A major risk factor for aspiration during anesthesia is the presence of food or fluid contents in the stomach. This bulletin describes a reported incident, also shared with the Canada Vigilance Program, in which a patient experienced pulmonary aspiration of regurgitated gastric contents during anesthesia. The patient was taking a glucagon-like peptide-1 (GLP-1) receptor agonist. Raising awareness about this newly identified risk provides an opportunity to develop medication safety strategies and prevent patient harm.

INCIDENT DESCRIPTION

A patient who was taking semaglutide injections once weekly for weight loss underwent orthopedic surgery. The semaglutide dose had been increased approximately 2 weeks before the surgery, with the last dose given 7 days before surgery. The patient had then followed the preoperative fasting instructions and had not ingested solid food for 12 hours before anesthesia.

At the time of endotracheal extubation, the patient vomited a large volume of undigested food while waking from anesthesia. Suction was applied and supplemental oxygen given. There was no

evidence of significant pulmonary aspiration, although the patient required additional oxygen in the postanesthesia care unit.

BACKGROUND

GLP-1 receptor agonists are a relatively new class of medications used to manage type 2 diabetes. Their physiological effects include delayed gastric emptying that slows the postprandial increase in blood glucose.² Currently, certain semaglutide and liraglutide products (specifically Wegovy [not yet marketed in Canada] and Saxenda³, respectively) also have an indication for weight management, as approved by Health Canada. Other GLP-1 receptor agonist products are used off-label for weight loss.

GLP-1 Receptor Agonists Marketed in Canada (Brand Names)

dulaglutide (Trulicity)

liraglutide (Victoza, Saxenda)

lixisenatide (Adlyxine, Soliqua)

semaglutide (Ozempic, Rybelsus)

Additional Cases Reported in the Literature

Three published case reports describe patients who followed a recommended fasting protocol^{4,5} but had residual food or fluid in their stomach at the time of the procedure.⁶⁻⁸ The first 2 case reports involved patients who were taking semaglutide for weight loss. One of these patients had a substantial amount of food discovered in the stomach during endoscopy; suctioning and rapid intubation were required.⁶ The other patient had stopped semaglutide 2 days before the procedure, however, they regurgitated a large volume of clear gastric contents upon induction of anesthesia.⁷ In the third case report, tirzepatide for weight loss (a GLP-1/glucose-dependent insulinotropic polypeptide receptor agonist that is available in the United States) had been held for 2 days before their procedure; the patient vomited a large amount of undigested food during emergence from general anesthesia.⁸ All 3 patients recovered.

An additional published case report described a patient who was scheduled for magnetic resonance imaging under sedation, had held their semaglutide for weight loss starting 7 days before the procedure, and had fasted for 18 hours. However, point-of-care gastric ultrasonography performed before the imaging showed solid gastric contents. The imaging was cancelled because of the risk of aspiration during anesthesia.⁸

DISCUSSION

Fasting procedures and holding of medications that delay gastric emptying can help to mitigate the risk of regurgitation and aspiration. In the cases summarized above, the patients adhered to fasting recommendations, but gastric contents remained in the stomach at the time of the procedure.

One small study showed that patients who took semaglutide within the previous 30 days had approximately 5 times greater risk for the presence of residual gastric contents at the time of the procedure than those who had not taken semaglutide, despite following fasting instructions.⁹ Although delayed gastric emptying is a known effect of GLP-1 receptor

agonist used for any indication, the incidents described all occurred in patients who were using the medication for weight management. The higher doses used for weight loss relative to the doses used for diabetes management are hypothesized to prolong gastric emptying, however this association has not yet been confirmed.¹⁰

RECOMMENDATIONS

In June 2023, the Canadian Anesthesiologists' Society circulated a communication amongst their members highlighting the risk for patients using GLP-1 receptor agonists.¹¹ It is important to have a shared decision-making approach among the care team that begins early, when procedures are being scheduled, rather than in the days leading up to the procedure.

The Canadian Journal of Anesthesiology recently published an editorial that included some recommendations.¹² The editorial's authors recommended the following:

- Consider holding the GLP-1 receptor agonist for at least 3 half-lives ahead of the procedure to clear approximately 88% of the drug. For example, semaglutide has a half-life of 1 week and would therefore need to be held for 3 weeks.
 - For patients taking a GLP-1 receptor agonist for *weight loss*, hold the GLP-1 receptor agonist for at least 3 half-lives ahead of the procedure.
 - For patients taking a GLP-1 receptor agonist for *type 2 diabetes*, consult with the endocrinologist about the risks and benefits of holding the drug for at least 3 half-lives ahead of the procedure.
- If the patient is unable to hold the GLP-1 receptor agonist for at least 3 half-lives before the procedure,
 - consider rapid-sequence induction of general anesthesia, to reduce the risk of aspiration, and
 - consider the use of point-of-care gastric ultrasonography, where available, to check for residual gastric content.
- Prolongation of the fasting period in this situation is not recommended, given the lack of safety evidence.
- Use a shared decision-making approach with patients to openly discuss the risks and benefits of each option before the procedure.

According to the American Society of Anesthesiologists' consensus guidelines, if the patient has reported gastrointestinal side effects of nausea or vomiting due to a GLP-1 receptor agonist, they must be considered at increased risk for complications requiring "full-stomach" precautions for anesthesia.¹³

Preoperative Risk Assessment Clinicians

(e.g., pre-operative assessment clinicians, anesthesiologists)

Preprocedural/Pre-imaging Risk Assessment Clinicians

(e.g., interventional radiologists, proceduralists, gastroenterologists, anesthesia team)

- Ask specifically about the patient's use of GLP-1 receptor agonists and document the dose and indication when conducting a best possible medication history for patients requiring gastric emptying and sedation.
 - Remind patients to bring all their medications to the appointment, or a detailed list of their medications (which includes, at a minimum, the medication name, dose, and directions for use).
 - Note: GLP-1 receptor agonists may not appear on the provincial electronic record in provinces where these medications are not covered. Some patients may take semaglutide (Ozempic) off-label for weight loss.
- Document on a standardized assessment checklist the dates when the GLP-1 receptor agonist was started, when the last dose was given, and any recent dose increases. Patients who have recently started taking a GLP-1 receptor agonist may be at greater risk of delayed gastric emptying than those who have been taking one of these medications for a longer period.¹³
- Ask if the patient is experiencing, or has ever experienced, nausea and vomiting because of the GLP-1 receptor agonist therapy, and if so, document this information in the patient record. Patients previously experiencing gastrointestinal symptoms from GLP-1 receptor agonists, including nausea, vomiting, or abdominal distension, have a greater risk of increased residual gastric contents and should be treated as if they had a full stomach, regardless of fasting.¹³

- Alert the anesthesia and surgical teams to consider aspiration risk reduction strategies for the following patients:

- those unable to hold the GLP-1 receptor agonist for 3 half-lives before the procedure
- those who have recently started the medication or increased their dose
- those who have reported gastrointestinal side effects from GLP-1 receptor agonists.

Risk reduction strategies may include postponement/cancellation of the procedure, ingestion of a clear fluid diet for some period of time before the "nothing by mouth" period, avoidance of deep sedation/general anesthesia if possible, and use of rapid-sequence induction if general anesthesia is required.¹¹

- Consult an endocrinologist for recommendations to bridge antidiabetic therapy if GLP-1 receptor agonists prescribed for diabetes management are to be held for longer than the next scheduled dosing time.¹³
- Use point-of-care ultrasonography, where available, for inspection of residual gastric contents, to guide decision-making.^{12,14}

Manufacturer/Sponsor

- In consultation with Health Canada, review current data and consider inclusion of the risk of delayed gastric emptying in the "Serious Warnings and Precautions" box in the product monograph, as well as in any consumer-facing information.

Primary Care Practitioners/Specialists

(e.g., family physicians, nurse practitioners, gastroenterologists, endocrinologists, bariatric specialists, surgeons, endoscopists, dentists)

- Share the risk of aspiration associated with delayed gastric emptying and provide information about fasting and holding of the medication for all patients who are taking GLP-1 receptor agonists and undergoing procedures or imaging for which anesthesia is required.
- Seek advice from specialists about optimal blood glucose management for patients who are using

these medications to treat diabetes and who need an alternative regimen before procedures requiring anesthesia.

Pharmacists

- When counselling patients who are starting a GLP-1 receptor agonist, inform them of the potential for delayed gastric emptying and the associated risk if they are to undergo any procedures or imaging that involves anesthesia (for which a fasting period or empty stomach is required).
- Instruct patients to inform all health care providers, including the preprocedure assessment team and the anesthesiologist, about their use of GLP-1 receptor agonists, and suggest that they proactively ask for recommendations to reduce the risk of aspiration.

Provincial/Regional Health Authorities and Hospitals

- Send out a provincial, regional, or hospital alert to all staff, including anesthesia teams, about the increased risk of aspiration for patients who are taking GLP-1 receptor agonists, especially when used for weight loss.

Pharmacy Informatics Specialists

- Include a drug–drug interaction (or drug-procedure interaction) between GLP-1 receptor agonists and medications used for general anesthesia in the computerized prescribing, pharmacy, and medication administration systems, to alert practitioners of the aspiration risk.

CONCLUSION

Although more research and consensus are needed to determine the optimal length of time for holding GLP-1 receptor agonists before a procedure requiring anesthesia, it is important for practitioners and

patients to be aware of the increased risks for aspiration and to consider strategies to mitigate harm. Share this bulletin with your team. Incidents related to aspiration or regurgitation of gastric contents after appropriate fasting, can be reported to the Canada Vigilance Program at <https://www.canada.ca/en/health-canada/services/drugs-health-products/med-effect-canada/adverse-reaction-reporting/drug.html>, or to ISMP Canada through the Individual Practitioner Reporting portal at https://www.ismp-canada.org/err_ipr.htm.

ACKNOWLEDGEMENTS

*ISMP Canada gratefully acknowledges the consumers, health care providers, and organizations that report medication incidents for analysis and learning. The expert review of this bulletin by the following individuals (in alphabetical order) is also recognized and appreciated: **Sharon Capogna** BScN, Charge Nurse, Surgical Assessment Clinic, Oak Valley Health; **Pascal Daigle**, Respiratory Therapist, Clinical Coordinator, CHUS, Sherbrooke, QC; **Sandra Marlow** BScN, Patient Care Manager, Surgical Assessment Clinic, Outpatient Procedure Suite, and Outpatient Procedure Suite Day Surgery, Oak Valley Health; **Conor Mc Donnell** MB MD BCh, Medication Safety Physician Lead, The Hospital for Sick Children; **Lindsay Yoo** BSc, BScPhm, RPh, CDE, BCGP, PharmD.*

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Natural Health Products: Mandatory Reporting of Serious Adverse Drug Reactions

The *Protecting Canadians from Unsafe Drugs Act*, also known as Vanessa's Law, is intended to increase patient safety by improving the reporting of serious adverse drug reactions (serious ADRs)* and medical device incidents (MDIs)† by hospitals.^{1,2}

Mandatory reporting by hospitals, which came into effect on December 16, 2019, applies to therapeutic products, including pharmaceuticals (prescription and nonprescription drugs), biologic drugs (including vaccines), radiopharmaceutical drugs, disinfectants, and medical devices.¹ As of June 22, 2023, the definition of therapeutic products has been revised in the *Food and Drugs Act* to include natural health products (NHPs).³

Natural health products include products such as probiotics, herbal remedies, vitamins and minerals, homeopathic medicines, traditional medicines (such as traditional Chinese medicines), and other products like amino acids and essential fatty acids.⁴

The inclusion of NHPs in Vanessa's Law gives Health Canada the immediate authority to take action and protect Canadians if an NHP presents a serious or imminent risk of injury to human health. These actions include ordering a recall and requiring a label change or package modification.³

- **Mandatory reporting of serious ADRs involving NHPs will come into effect when regulations specific to NHPs are developed.**
 - Hospitals can begin to prepare their staff and systems to do so:
<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>
 - Other health care organizations and individual practitioners are encouraged to report serious ADRs to help Health Canada optimize the safe use of all therapeutic products, including NHPs.

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* A **serious ADR** is "a noxious and unintended response to a drug that occurs at any dose and that requires in-patient hospitalization or prolongation of existing hospitalization, that causes congenital malformation, that results in persistent or significant disability or incapacity, that is life threatening or that results in death."²

† An **MDI** is an incident "related to a failure of the device or a deterioration in its effectiveness, or any inadequacy in its labelling or in its directions for use; and has led to the death or a serious deterioration in the state of health of a patient, user or other person, or could do so were it to recur."²



The Canadian Medication Incident Reporting and Prevention System (CMIRPS) is a collaborative pan-Canadian program of Health Canada, the Canadian Institute for Health Information (CIHI), the Institute for Safe Medication Practices Canada (ISMP Canada) and Healthcare Excellence Canada (HEC). The goal of CMIRPS is to reduce and prevent harmful medication incidents in Canada.



The Healthcare Insurance Reciprocal of Canada (HIROC) provides support for the bulletin and is a member owned expert provider of professional and general liability coverage and risk management support.



The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent national not-for-profit organization committed to the advancement of medication safety in all healthcare settings. ISMP Canada's mandate includes analyzing medication incidents, making recommendations for the prevention of harmful medication incidents, and facilitating quality improvement initiatives.

Report Medication Incidents

(Including near misses)

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Phone: 1-866-544-7672

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