# GLP-1 Drugs in Anesthesia

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The latest rage in new medications that has raised serious concerns among anesthesia providers has been the availability of GLP-1 agonists, analogues of a naturally occurring hormone, GLP-1, that is secreted primarily from the small bowel. This hormone augments insulin release to modulate the plasma glucose concentration. To exploit the action of this hormone for diabetes, medications were developed in the laboratory following two paths: 1. Those that inhibit the enzyme that rapidly inactivates GLP-1, known as DPP-4 (eg. Januvia®) and 2. Those that mimic GLP-1 to increase the amount of GLP-1 in the body (eg., Ozempic®). The primary indication for their use is to modulate fluctuations in plasma glucose concentration in prediabetics and type II diabetics. However, a secondary and seemingly more popular indication that became apparent during clinical trials is the rapid weight-loss that occurs coincidental with their use. Now indicated for weight-loss, the use of GLP-1 drugs has exploded resulting in many more patients than diabetics taking these drugs.

**Pharmacology:** Approved for use in adults and adolescents, these drugs are delivered parenterally, with a frequency that ranges between daily and weekly. The mechanism by which GLP-1 agonists induce weight-loss is several-fold: delayed gastric emptying (GE), increased satiety and decreased appetite. Delayed GE is what has led these drugs to become feared by every anesthesiologist. In the past 2 years, multiple case reports in adults, both diabetic and non-diabetic, have chronicled instances of massive gastric regurgitation and in some cases, pulmonary aspiration despite having fasted for periods greater than those mandated, eg., up to 20h after solids. Fortunately, to date no deaths have occurred. The silver lining in the effect of GLP-1 agonists on GE is that tachyphylaxis has been demonstrated after prolonged use. The delay in GE that is apparent immediately and during the first 6 weeks after starting to take a GLP-1 agonist begins to wane after 3 months of chronic use. However, there is no definite cutoff time after which GE returns to normal whether continuing or after discontinuing these medications. In fact, GE may never return to normal even after stopping the medication especially if there is another cause for delayed GE and gastroparesis (eg., diabetes)

**Clinical care:** Approaching the patient who is taking GLP-1 agonist for either sedation or general anesthesia raises the specter of the risk of regurgitation and aspiration. To that end, the American Society of Anesthesiologists recommended in June 2023 that the agonist be held for one dose (whether given on a daily or weekly basis) and if held for more than one dose, the patient should seek further guidelines to manage their glucose homeostasis from their endocrinologist.

**Recommendations:** As a clinician scientist, I was disappointed that the ASA recommendations were so limited in highlighting the dangers of these medications and offering specific strategies to guide clinicians to mitigate risks. I submit that:

1. Holding a single dose of a GLP-1 drug or any drug for that matter, does not eliminate the drug from the body. Four to five half-lives are required to reduce the blood concentration to concentrations <5%. On the other hand, holding these specific medications for such prolonged periods is not a viable option.
2. There is no evidence to support holding GLP-1 drugs for a period in order that GE returns to normal. There is no time interval for return of the GE to normal after discontinuing a GLP-1 drug. In diabetics, gastroparesis may be permanent.
3. A gastric ultrasound is a useful tool to identify the presence of food in the stomach, which will assist in planning whether to proceed with the surgery and if so, the optimal strategy to secure the airway.
4. In these patients, I recommend that the airway is secured using a rapid sequence induction with tracheal intubation for deep sedation and general anesthesia because of the unknown risk of delayed GE and regurgitation. Specifically, I recommend against the use of an LMA in these patients.
5. If elective surgery can be deferred, it may be prudent to consider waiting until the patient has been using the GLP-1 medication for more than 3 months to reduce the likelihood of delayed GE and if available, use a gastric ultrasound to document an empty stomach before embarking on anesthesia with an open airway or an LMA.
6. If urgent or emergent surgery is required, a rapid sequence induction should be undertaken in patients taking GLP-1 medications, especially if a gastric ultrasound has not been performed.

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