Gain Changers: New Generation of Weight Loss Medications

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Hosting the 95th Academy Awards, Jimmy Kimmel opened his monologue by saying, “Everybody looks so great! When I look around this room, I can’t help but wonder, ‘Is Ozempic right for me?’”

Semaglutide (Ozempic, Wegovy, and Rybelsus) is boosting new social media trends because it works (Diabetes Obes Metab 2017;19:1242-51; Lancet 2018;392:637-64; N Engl J Med 2021;384:899-1002; N Engl J Med 2021;384:1066-7; N Engl J Med 2022;387:2245-57; Nat Med 2022;28:2083-91; Obesity 2023;31:703-15; JAMA 2021;325:1414-25). Patients on semaglutide typically lose 15% of their weight during the first month or two. It should be mentioned that recent news stories have uncovered cases of severe gastroapoptosis that may have been caused by patients’ weight loss, but no scientific conclusions have been reached as of this publication date (asamonitor.pub/3BFkxjx). On June 29, the ASA Task Force on Preoperative Fasting released consensus-based guidance on the preoperative management of patients taking GLP-1 receptor agonists, which included recommendations to hold dosing up to a week before surgery (asamonitor.pub/3Q9to4O).

GLP-1 receptor agonists share a block box warning about thyroid C-cell tumors because they cause thyroid tumors in rats. A case control study of 2,562 patients with thyroid cancer and 45,184 matched controls found a hazard ratio of 1.6 for thyroid cancer in patients treated with GLP-1 receptor agonists (Diabetes Care 2023;46:84-390).

Because GLP-1 receptor agonists delay gastric emptying, there is a possibility of aspiration risk in patients taking semaglutides (Anaesthesia July 2023). Regurgitation of large gastric volumes following aspiration induction in a fasted patient on semaglutide has been recently documented (Can J Anaesth March 2023). Because these drugs are often given as weekly injections, reducing the risk of aspiration may require withholding them for a week or more prior to elective surgery (asamonitor.pub/3Q9to4O).

The indirect mechanism of action for GLP-1 inhibitors would theoretically make hypoglycemia less likely than for drugs that directly decrease blood glucose levels. The risk of hypoglycemia in patients on GLP-1 receptor agonists – including semaglutide – is very low in clinical trials, approaching zero in randomized controlled trials for obesity where both active and control groups are not taking additional medications to reduce blood glucose (Advances in Therapy 2021;38:1470-82). As of this writing, hypoglycemia has not been documented during anesthesia in patients on GLP-1 receptor agonists.

The success of GLP-1 receptor agonists in treating obesity has led to additional research. As recently documented in Nature News, another generation of obesity medications is in development (Nature 2023;619:19). A problem with the existing GLP-1 receptor agonists is that they are peptides that must be given by injection. Owftoglipron is a nonpeptide GLP-1 receptor agonist that can be given as a daily oral tablet. Randomized controlled trials demonstrate efficacy similar to semaglutide (N Engl J Med June 2023; Lancet 2023;S0140-6736).


Obesity is a global health concern, estimated to affect more than 40% of the U.S. population including more than 17% of children and adolescents (Obes 2022;2022:765248; Mol Diagn Ther 2020;24:653-63). Obesity is a cause of major health care disparities, disproportionately affecting minorities and lower socioeconomic groups (Curr Diab Rep 2015;15:95). Obesity increases the risk of diabetes, cardiovascular diseases, certain cancers, sleep apnea, osteoarthritis, and mental health conditions (Sensors (Basel) 2020;20:2734; Comprat Metab Med 2021;136:104754). It is also a risk factor for surgical complications and increased hospital stays (BMJ Open Diabetes Res Care 2016;4:e002200). In the United States, obesity has been estimated to account for $147 billion in additional health care expenses and lost productivity (Diabetes Metab Syndr Obes 2010;3:285-95).

The high cost of GLP-1 receptor agonists must be weighed against the health care and economic costs of obesity. GLP-1 receptor agonists are currently primarily used in patients whose diabetes cannot be managed with generic medications. However, from what we know now, the efficacy of these drugs, documented in both the peer-reviewed literature and publicized on social media, will increasingly draw attention to their benefits. Given the personal and societal costs of obesity, we will increasingly see these drugs in our patients.

So yes, Jimmy Kimmel, Ozempic might be right for you.