POEMs

Patient-Oriented Evidence That Matters

Semaglutide Once Weekly Helps Adolescents Lose Weight, but 4% Developed Acute Cholelithiasis

Clinical Question

Is a once-weekly injection of semaglutide a safe and effective way for adolescents with obesity to lose weight?

Bottom Line

Semaglutide helps adolescents lose a clinically significant amount of weight. It is unknown whether weight loss persists when the medication is discontinued, and there was a concerning increase in episodes of acute cholelithiasis, a known adverse effect of the drug. It is not clear whether the risk of acute cholelithiasis (also seen in a study of patients taking dulaglutide [Trulicity]) is caused by the medication or is a function of rapid weight loss. (Level of Evidence = 1b)

Synopsis

Semaglutide is a glucagon-like peptide-1 agonist that has been shown to help adults lose weight. The researchers recruited adolescents 12 to 17 years of age who were obese (i.e., body mass index [BMI] in the 95th percentile or higher) or overweight (i.e., BMI in the 85th percentile or higher) with at least one risk factor. After a 12-week run-in period, during which the 200 participants received lifestyle counseling, they were randomized in a 2:1 ratio to receive semaglutide subcutaneously once weekly or matching placebo. The dose started at 0.25 mg and was escalated as tolerated to a maximum dose of 2.4 mg during the first 16 weeks. The groups were balanced at the start of the study, and the analysis was by intention to treat. All participants and their families received lifestyle education throughout the trial. All but one participant were obese, with a mean pretreatment BMI of 37.7 in the semaglutide group and 35.7 in the placebo group. Only five patients were lost to follow-up or withdrew by the end of the 68-week trial. The primary outcome was a percentage change in BMI, which was significantly greater in the semaglutide group (–16.1% vs. 0.6%; $P < .001$). Significantly more patients in the semaglutide group had reductions in body weight of at least 5% (73% vs. 18%; number needed to treat [NNT] = 2), 10% (62% vs. 8%; NNT = 2), and 20% (37% vs. 3%; NNT = 3). Quality-of-life scores improved, especially in the physical comfort domain. Gastrointestinal symptoms were more common with semaglutide. Five patients in the treatment group had cholelithiasis (one also had cholecystitis) compared with none in the placebo group. Withdrawals due to adverse effects were similar between groups.

Study design: Randomized controlled trial (single-blinded)

Funding source: Industry

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Weghuber D, Barrett T, Barrientos-Pérez M, et al.; STEP TEENS Investigators. Once-weekly semaglutide in adolescents with obesity.* N Engl J Med. *2022;387(24):2245-2257.*

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No Benefit With Torsemide Over Furosemide for Posthospitalization Treatment of Heart Failure

Clinical Question

For patients discharged after hospitalization for acute heart failure, does long-term torsemide decrease all-cause mortality more than furosemide?

Bottom Line

There was no difference in all-cause mortality when comparing torsemide with furosemide in patients after hospitalization for acute heart failure. However, interpretation of the study results is limited because of loss to follow-up, crossover of trial participants, and nonadherence to study drugs. New changes in guideline-directed medical therapy for heart failure, specifically the addition of angiotensin receptor-neprilysin inhibitors and sodium-glucose cotransporter-2 inhibitors, may have affected outcomes and diuretic requirements over the course of the trial. (Level of Evidence = 1b–)

Synopsis

In this multicenter trial in the United States, investigators randomized patients hospitalized with acute heart failure (either

a new diagnosis or worsening of chronic heart failure) to treatment with torsemide (n = 1,431) or furosemide (n = 1,428) before discharge. Dosing and frequency of the study drugs were determined by the primary team in the hospital and then managed by outpatient clinicians at discharge. Data on outcomes were obtained via patient or proxy telephone interviews, medical record queries, death records, and the National Death Index. The two groups had similar baseline characteristics: median age was 65 years, 40% were women, 34% were Black, and 70% had a left ventricular ejection fraction of 40% or less. The median duration of follow-up was 17 months. Approximately 4% of patients in each group were lost to follow-up before completing the trial. There was a 7% crossover rate from torsemide to furosemide and 4% from furosemide to torsemide at hospital discharge. Almost 10% of patients were not taking any loop diuretic at the six-month follow-up. There was no significant difference detected in the primary outcome of all-cause mortality between the two groups (26% in both groups). All-cause mortality and hospitalization over 12 months were similar, with a rate of almost 50% for both groups.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Concealed

Setting: Inpatient (any location) with outpatient follow-up

Reference: *Mentz RJ, Anstrom KJ, Eisenstein EL, et al.; TRANSFORM-HF Investigators. Effect of torsemide vs furosemide after discharge on all-cause mortality in patients hospitalized with heart failure: the TRANSFORM-HF randomized clinical trial.* JAMA. *2023;329(3):214-223.*

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British Society of Gastroenterology Guidelines for the Evaluation and Management of Dyspepsia

Clinical Question

What are the latest evidence-based guidelines for the management of functional dyspepsia?

Bottom Line

The thoughtful, evidence-based guidelines provide a helpful framework for evaluating and treating patients with dyspepsia. The guidance regarding imaging and the use of upper endoscopy may be conservative for U.S. physicians. The authors acknowledge that approximately half of the recommendations are based on low- or very low-quality evidence. (Level of Evidence = 1a)

Synopsis

The 2022 guideline, last updated in 1996, was based on a series of systematic reviews and network meta-analyses. The authors recommend urgent evaluation of patients with upper gastrointestinal alarm symptoms, such as dysphagia in all patients, weight loss with dyspepsia, upper abdominal pain, or reflux in patients 55 years and older. Urgent evaluation is recommended for patients 40 years and older who are from a region where gastric cancer is common or have a family history of gastroesophageal cancer. Other alarm symptoms warranting a less urgent evaluation include hematemesis; treatment-resistant dyspepsia; dyspepsia; upper abdominal pain with elevated platelet count, low hemoglobin, and nausea or vomiting; and nausea or vomiting with weight loss, reflux, dyspepsia, or upper abdominal pain in patients who are 55 years and older. Patients without alarm symptoms who present with at least two months of epigastric burning or pain, early satiety, or postprandial fullness should be given a diagnosis of functional dyspepsia and told that it is a disorder of gut-brain interaction. As part of the initial evaluation in patients 55 years and older, a complete blood count with platelets should be obtained and those with overlapping irritable bowel symptoms should have celiac serology. Those 60 years and older with abdominal pain and weight loss should have abdominal computed tomography to evaluate for pancreatic cancer.

All patients with dyspepsia should be evaluated for the presence of *Helicobacter pylori* by obtaining a stool or breath test. If the results are abnormal, the patient should be treated to eradicate *H. pylori* (a recent study confirms that eradication not only reduces the risk of ulcer but is effective for functional dyspepsia). Confirmation of *H. pylori* eradication is recommended only for patients at increased risk of gastric cancer, although it should be considered in patients whose symptoms persist. The guidelines recommend against the routine use of gastric emptying tests or 24-hour pH monitoring. For patients who are negative for *H. pylori*, first-line treatment

includes acid-suppressive therapy with a histamine H_2 antagonist or proton pump inhibitor and regular aerobic exercise; the guidelines do not recommend specific diets such as a FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diet. Prokinetics may be an effective treatment, and the strongest evidence supports tegaserod. Second-line therapies include low to moderate dosages of tricyclic antidepressants (e.g., amitriptyline, 10 mg once daily, titrating to 30 to 50 mg). The authors recommend against selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and buspirone. Cognitive behavior therapy, psychodynamic interpersonal psychotherapy, stress management, and hypnotherapy may be effective. Patients with refractory or persistent symptoms should be referred to a gastroenterologist.

Study design: Practice guideline

Funding source: Foundation

Setting: Outpatient (any)

Reference: *Black CJ, Paine PA, Agrawal A, et al. British Society of Gastroenterology guidelines on the management of functional dyspepsia.* Gut. *2022;71(9):1697-1723.*

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Brief Behavior Therapy Improves Sleep in Older Adults With Chronic Insomnia

Clinical Question

Can brief behavior therapy improve sleep in older adults with insomnia?

Bottom Line

Although based on only a few studies, it appears that a brief four-week behavior therapy program will improve sleep quality in older adults with chronic insomnia. The findings underscore guidelines from the American College of Physicians and others to avoid drugs and use nonpharmacologic approaches for the initial management of insomnia.

This POEM aligns with the Canadian Geriatrics Society's Choosing Wisely Canada recommendation: do not use benzodiazepines or other sedative-hypnotics in older adults as first-choice therapy for insomnia, agitation, or delirium. Choosing Wisely Canada's hospital and primary care toolkits provide tools to reduce inappropriate use of benzodiazepines. (Level of Evidence = 2a)

Synopsis

The authors searched multiple databases and registries to identify randomized trials, systematic reviews, and meta-analyses that evaluated the effectiveness of brief behavior interventions in community-dwelling adults at least 60 years of age with chronic insomnia. They identified only four trials with 190 participants. Overall, the risk of bias was medium to low. In these studies, a four-week behavior intervention program had a large effect size on sleep quality based on the Pittsburgh Sleep Quality Index and the Insomnia Severity Index (standardized mean difference = –1.07; 95% CI, –1.43 to –0.71) and improved total sleep time by 25.7 minutes. The brief interventions improved several other measures of sleep efficiency. The authors found no heterogeneity among the data and did not report any data on daytime sleepiness, quality of life, or cognition.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Setting: Various (meta-analysis)

Reference: *Chen Y, Lu T, Ku E, et al. Efficacy of brief behavioural therapy for insomnia in older adults with chronic insomnia: a systematic review and meta-analysis from randomised trials.* Age Ageing. *2023;52(1):afac333.*

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