POEMs

Patient-Oriented Evidence That Matters

Closed-Loop System Improves Glycemic Control but Not Hypoglycemia for Young Children With Type 1 Diabetes Mellitus

Clinical Question

Does a closed-loop system offer benefits over sensor-augmented pump therapy in children one year to seven years of age?

Bottom Line

A closed-loop system that automatically adjusts the delivery rate of an insulin pump increases the time in the target glucose range without any other measurable benefits over the short study period. There may be quality of life benefits for parents and children because of less need for hands-on decision-making, but in this study there was one episode of severe hypoglycemia. This seems like an opportunity for shared decision-making. (Level of Evidence = 1b–)

Synopsis

Sensor-augmented pump therapy uses continuous monitoring of blood glucose combined with an insulin pump. A closed-loop system (sometimes called an artificial pancreas) takes the human out of the loop and uses an algorithm to adjust insulin delivery. The authors identified 74 children, one year to seven years of age, who had type 1 diabetes mellitus for at least six months and a glycated hemoglobin level of 11% or lower. Those 74 children were randomized into two groups. The mean age of the children was 5.6 years, the two groups were balanced at the beginning of the study, and the analysis was by intention to treat. Group A began with the closed-loop system; group B began with the sensor-augmented pump therapy. After 16 weeks, they had a one- to four-week washout period before they crossed over to receive the other therapy for 16 weeks. During the closed-loop period, children were more likely to be in the target glucose range of 70 to 180 mg per dL (3.89 to 9.99 mmol per L; 71.6% vs. 62.9%; $P < .001$; number needed to treat = 11) and their mean glycated hemoglobin level was a bit lower (6.4% vs. 7.0%; $P < .001$). There was no difference in the time spent with low blood sugar (defined as less than 54 mg per dL [3.0 mmol per L], 63 mg per dL [3.5 mmol per L], or 70 mg per dL) or insulin use, and only a very small reduction in the percentage of time spent with a glucose level higher than 300 mg per dL (16.65 mmol per L; 2.0% vs. 3.1%; 95% CI for the difference, –1.6% to –0.6%). Overall adverse events were similar, but there was one severe episode of hypoglycemia in the closed-loop group compared with zero in the sensor-augmented pump therapy group.

Study design: Crossover trial (randomized)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *Ware J, Allen JM, Boughton CK, et al.; KidsAP Consortium. Randomized trial of closed-loop control in very young children with type 1 diabetes.* N Engl J Med. *2022;386(3):209-219.*

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Several Drugs Are Effective for Weight Loss in Obese or Overweight Adults; It Is Unclear Whether They Improve Health Outcomes

Clinical Question

Are any medications effective for weight loss and improving health in adults who are obese or overweight?

Bottom Line

Several medications are more effective than lifestyle modification in achieving short-term weight loss at the expense of adverse events. Although quality of life scores are improved, it is unclear if weight loss with medication results in fewer adverse health events. (Level of Evidence = 1a–)

Synopsis

The authors searched PubMed, EMBASE, the Cochrane Library, and ClinicalTrials.gov to identify randomized trials of various medications that promote weight loss in adults who are overweight or obese. The included trials

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This series is coordinated by Sumi Sexton, MD, editor-in-chief.

A collection of POEMs published in *AFP* is available at https://www.aafp.org/afp/poems.

SUMMARY TABLE

Agent	Number needed to treat to achieve at least 5% weight loss	Number needed to treat to achieve at least 10% weight loss	Number needed to harm for discontinuation
Phentermine/topiramate (Qsymia)	3	3	17
Glucagon-like peptide-1 receptor agonists	3	3	20
Naltrexone/bupropion (Contrave)	3	4	14
Pramlintide (Symlin)	No significant difference	No significant difference	No significant difference
Sodium-glucose cotransporter-2 inhibitors (SGLT-2)	5	No significant difference	No significant difference
Orlistat (Xenical)	5	9	31
Metformin	6	No significant difference	No significant difference

did not have to include people with comorbid conditions but had to compare a medication with lifestyle modification with or without a placebo. The studies had to report weight loss–related data and quality of life scores but did not have to report other health outcomes (e.g., gastrointestinal symptoms, body image, changes in blood pressure, changes in laboratory parameters such as glycated hemoglobin, lipid levels). The authors also accepted data that were not necessarily analyzed by intention to treat. They included 143 unique trials with 49,810 participants, 75% of whom were women. The median length of the trials was 24 weeks. The authors identified a high risk of bias due to protocol deviations and missing outcome data, and they had concerns about how adverse events were assessed. They decided to perform a network meta-analysis. They found that phentermine/topiramate (Qsymia) was the most effective medication for achieving at least a 5% weight loss (odds ratio [OR] = 8.02; 95% CI, 5.24 to 12.27), followed by glucagon-like peptide-1 (GLP-1) receptor agonists (OR = 6.33; 95% CI, 5 to 8). The order of effectiveness in achieving at least a 10% weight loss was the same. Although effective in achieving weight loss, most drugs had significant discontinuation rates due to adverse events: naltrexone/bupropion (Contrave; OR = 2.69; 95% CI, 2.11 to 3.43), phentermine/topiramate (OR = 2.40; 95% CI, 1.69 to 3.42), GLP-1 receptor agonists (OR = 2.17; 95% CI, 1.71 to 2.77), and orlistat (Xenical; OR = 1.72; 95% CI, 1.44 to 2.05). Quality of life scores improved to a greater degree for phentermine/topiramate (standardized mean difference [SMD] = 0.42), followed by naltrexone/bupropion (SMD = 0.36), and GLP-1 receptor agonists (SMD = 0.29). The authors reported that compared with lifestyle modification, medications caused greater degrees of lower glycated hemoglobin and lipid levels but not systolic blood pressure. For most of the data, the authors report significant heterogeneity. They do not report on other important outcomes, such as mortality, cardiac events, development or regression of diabetes, and so forth.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Foundation

Setting: Various (meta-analysis)

Reference: *Shi Q, Wang Y, Hao Q, et al. Pharmacotherapy for adults with overweight and obesity: a systematic review and network meta-analysis of randomised controlled trials.* Lancet. *2022;399(10321):259-269.*

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All-Cause Mortality Is Comparable in Patients With Left Main Coronary Artery Disease Treated With PCI or CABG

Clinical Question

Is mortality improved in patients with left main coronary artery disease that is managed with coronary artery bypass grafting (CABG) or percutaneous interventions (PCI) with drug-eluting stents?

Bottom Line

The five- and 10-year all-cause mortality rates are similar in people with left main coronary artery disease whether it is managed with PCI with drug-eluting stents or with CABG. (Level of Evidence = 1a)

Synopsis

The team searched several databases and identified four randomized trials that compared PCI (n = 2,197) with

CABG (n = 2,197) in adults with left main coronary artery disease and reported five-year mortality outcomes. The authors were able to obtain the data on the individual participants in these trials. Three of the trials recruited only people with left main disease. Although the fourth trial included people with multivessel disease, the authors were able to isolate the subgroups with left main disease. After five years, there was no significant difference in all-cause mortality between the two groups (slightly more than 10%), and no significant difference in cardiovascular and noncardiovascular deaths. The authors found no significant difference in 10-year mortality (slightly more than 20%). The patients whose left main coronary artery disease was managed by PCI had slightly more spontaneous myocardial infarctions (6.2% vs. 2.6%; number needed to harm = 31; 95% CI, 23 to 47) and subsequent revascularizations (18.3% vs. 10.7%; number needed to harm = 14; 95% CI, 11 to 19).

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: *Sabatine MS, Bergmark BA, Murphy SA, et al. Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis.* Lancet. *2021; 398(10318):2247-2257.*

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Proton Pump Inhibitor Use Associated With an Increased Risk of Gastric Cancer

Clinical Question

Is there an association between gastric cancer and the use of proton pump inhibitors (PPIs)?

Bottom Line

This is the strongest evidence to date that there is a small but clinically significant increase in the risk of gastric cancer for patients taking a PPI (number needed to harm = 1,191 over 10 years). Physicians initiating antacid therapy should begin with a histamine H_2 receptor antagonist and, if prescribing a PPI, should use the lowest dose and duration possible. Another study using data from a Korean registry produced similar findings (*Gut*. 2021;70:2066-2075). (Level of Evidence = 2b)

Synopsis

PPIs cause hypergastrinemia and can lead to hyperplasia of the gastric mucosa. Several studies have shown an association between PPI use and gastric cancer. This study is the largest and most methodologically sound; it addresses several potential sources of confounding better than previous studies. The authors identified more than 1.1 million people who had received a new prescription for a PPI between 1990 and 2018, and another 220,825 people who had received a new prescription for an H_2 receptor antagonist during the same period. This is a better comparison group than the general population because it avoids confounding by indication (i.e., patients who take PPIs may have different risk factors and health habits than patients who do not). People with a familial syndrome associated with gastric cancer or a history of gastric cancer, and those who had less than one year of follow-up were excluded, leaving 973,281 patients who take PPIs and 198,306 patients who take an H_2 receptor antagonist. The authors matched patients using propensity scores that incorporated an array of potential confounders, including age, comorbidities, tobacco and alcohol use, and medications. In the fully adjusted model, the authors found a significantly increased risk of gastric cancer in patients taking PPIs compared with patients taking an H_2 receptor antagonist (hazard ratio [HR] = 1.45; 95% CI, 1.06 to 1.98; numbers needed to harm = 2,121 after five years and 1,191 after 10 years). The Kaplan-Meier survival analysis showed that the risk increased linearly with the duration of PPI use. Greater doses were associated with increased risk: HR = 1.22 for less than 14,600-mg cumulative omeprazole (Prilosec) dose equivalents; HR = 1.81 for 14,600-mg to 28,199-mg dose equivalents; and HR = 2.03 for 29,200-mg and higher dose equivalents (although the CIs overlap).

This POEM aligns with the Choosing Wisely Canada recommendation that advises not to maintain long-term PPI therapy for gastrointestinal symptoms without stopping at least once per year in most patients. Choosing Wisely Canada's toolkit provides tools for deprescribing PPIs.

Study design: Cohort (retrospective)

Funding source: Government

Setting: Population-based

Reference: *Abrahami D, McDonald EG, Schnitzer ME, et al. Proton pump inhibitors and risk of gastric cancer: population-based cohort study.* Gut. *2022;71(1):16-24.*

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