POEMs

Low-Carb Diets May Produce Short-Term Diabetes Remission

Clinical Question

What is the usefulness of low-carbohydrate or very low-carbohydrate diets for people with type 2 diabetes mellitus?

Bottom Line

Patients with type 2 diabetes can try cutting out bread and pasta, leaving the skin on chicken, or eating nuts and avocados to lower their blood glucose levels. Six months of a low-carbohydrate diet (less than 26% of calories from carbohydrates) was more likely than other diets or usual diet to reduce A1C level to less than 6.5% or a fasting blood glucose level to less than 126 mg per dL (7.0 mmol per L), with or without continued medication therapy. A very low-carbohydrate diet (less than 10% of calories from carbohydrates) worked for those who were able to stay on it. Body weight and serum triglyceride levels decreased over six months, but the difference was not sustained. The studies combined in this analysis were not great, and the numbers of studies and study participants were small. (Level of Evidence = 1a–)

Synopsis

The researchers searched Cochrane CENTRAL, four other databases, and three trial registries for published and unpublished randomized trials in any language that compared low-carbohydrate diets with low-fat diets or no specific diet (wait-listing) in patients with type 2 diabetes. Two authors independently selected articles for inclusion, abstracted the data, and assessed the research for risk of bias. They identified 23 small studies. Compared with control diets in eight studies of 264 patients, some of whom were receiving diabetes medication, low-carbohydrate diets achieved diabetes remission after six months in an additional 32 participants for every 100 treated (number needed to treat = 4; 95% CI, 2 to 6). Longer-term data are not available. Patients not receiving medication did not have a greater likelihood of remission than patients in the control group. Body weight and serum triglyceride levels (but not other lipid levels) decreased over six months, but the difference disappeared at 12 months. Participants who were able to follow a very low-carbohydrate diet—50% to 80% of participants enrolled in those studies, even with behavioral support—had similar weight loss as patients on a low-carbohydrate diet. Most of the research had moderate to high risk of bias, and there was moderate heterogeneity among the studies. There is evidence of publication bias regarding weight loss.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Foundation

Setting: Various (meta-analysis)

Reference: *Goldenberg JZ, Day A, Brinkworth GD, et al. Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: systematic review and* meta-analysis *of published and unpublished randomized trial data.* BMJ. *2021;372:m4743.*

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Single-Dose Opioid Analgesics Offer No Benefit over Nonopioid Analgesia for Musculoskeletal Pain

Clinical Question

What oral analgesic provides the best, immediate relief for acute muscle pain?

Bottom Line

A single dose of opioid analgesics provides similar acute pain relief compared with a single dose of a combination of acetaminophen and ibuprofen in patients with acute musculoskeletal pain in the emergency department. Opioids increase the

likelihood of nausea or vomiting. There was no added benefit of 800 mg of ibuprofen compared with 400 mg. The study did not investigate the effect of an injectable analgesic, possibly because of the placebo effect. These results are similar to those of previous studies of opioids and different doses of ibuprofen. (Level of Evidence = 1b)

Synopsis

The researchers enrolled 600 adults, primarily Latino, presenting to two emergency departments with a sprain, strain, fracture, or other musculoskeletal extremity pain, excluding back pain. The patients were randomly assigned, using concealed allocation, to receive a single dose of one of five combinations of analgesics: 1,000 mg of acetaminophen with either 400 mg or 800 mg of ibuprofen, 300 mg of acetaminophen with 30 mg of codeine, 300 mg of acetaminophen with 5 mg of hydrocodone, or 325 mg of acetaminophen with 5 mg of oxycodone. Pain scores before treatment were mostly 8 to 10 on a scale of 0 to 10 (with 10 being the worst pain). Pain scores dropped an average of three points in every group by 60 minutes after the medication dose, with no statistical difference among the groups. Within two hours, the decrease from baseline was an average 4.3 to 4.7 points, with no significant differences among the groups. A similar percentage of patients in each group (24%) received rescue pain medication within the first two hours. The likelihood of nausea or vomiting was significantly higher among patients who received an opioid analgesic, with one additional patient experiencing these adverse effects for every 25 patients treated with an opioid (number needed to treat = 20; 95% CI, 12 to 59). The study had the power to detect a difference of 1.3 points between treatments, if one existed.

Study design: Randomized controlled trial (double-blinded)

Funding source: Foundation

Allocation: Concealed

Setting: Emergency department

Reference: *Bijur PE, Friedman BW, Irizarry E, et al. A randomized trial comparing the efficacy of five oral analgesics for treatment of acute musculoskeletal extremity pain in the emergency department.* Ann Emerg Med. *2021;77(3):345-356.*

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Once-Weekly Semaglutide Is an Effective Adjunct for Weight Loss in Adults without Diabetes Who Are Overweight or Obese

Clinical Question

Is once-weekly subcutaneous semaglutide (Ozempic) an effective adjunct to intensive behavioral therapy for adults without diabetes mellitus who are overweight or obese?

Bottom Line

Once-weekly subcutaneous semaglutide used as an adjunct to intensive behavioral therapy significantly improves the likelihood that adults without diabetes who are overweight or obese will lose at least 5% of their baseline body weight compared with placebo (number needed to treat = 2.4). (Level of Evidence = 1b)

Synopsis

Although semaglutide helps reduce weight and improve glucose control in adults with type 2 diabetes, its effectiveness as an adjunct for weight loss in adults without diabetes who are overweight or obese is uncertain. The investigators identified adults without diabetes, 18 years or older, who reported at least one unsuccessful dietary effort to lose weight and had a body mass index (BMI) of 27 kg per m^2 or higher with at least one weight-related comorbidity (e.g., cardiovascular disease, hyperlipidemia, hypertension, obstructive sleep apnea) or a BMI of 30 kg per m^2 or higher. Most patients were women (81%) and White (76%) with a mean age of 46 years and mean BMI of 38 kg per m^2. Eligible patients (n = 611) randomly received (concealed allocation assignment) once-weekly subcutaneous semaglutide (initially 0.25 mg, with dose titrated as tolerated every four weeks to a target dosage of 2.4 mg per week at week 16) or matched placebo. Participants also received a low-calorie diet (1,000 to 1,200 kcal per day) for the first eight weeks, followed by 1,200 to 1,800 kcal per day for the remainder of the 68 weeks. In addition, all participants received an exercise prescription and 30 individual intensive behavioral visits with a dietitian. Complete follow-up occurred for 92.8% of participants at 68 weeks.

Using intention-to-treat analysis, participants in the semaglutide group lost significantly more weight than in the placebo group (estimated mean body weight change from baseline: –16.0% for semaglutide vs. –5.7% for placebo). More

participants treated with semaglutide lost at least 5% of baseline body weight compared with participants treated with placebo (86.6% vs. 47.6%, respectively; number needed to treat = 2.4; 95% CI, 2.1 to 3.0). Significantly more participants treated with semaglutide achieved weight losses of at least 10% and 15% compared with participants treated with placebo.

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Wadden TA, Bailey TS, Billings LK, et al.; STEP 3 Investigators. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: the STEP 3 randomized clinical trial.* JAMA. *2021;325(14):1403-1413.*

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Cryoablation Preferred as Initial Therapy for Paroxysmal Atrial Fibrillation

Clinical Question

Is cryoablation more effective than drug therapy to prevent recurrence of paroxysmal atrial fibrillation (AF)?

Bottom Line

Initial cryoablation for patients with paroxysmal AF is superior to initial antiarrhythmic drug therapy. Another study in the same issue of *New England Journal of Medicine* (2021;384[4]:316-324) compared cryoablation with medical therapy and had similar findings. (Level of Evidence = 1b)

Synopsis

The researchers identified 303 adults with paroxysmal AF and randomized them to receive initial therapy with cryoablation or an antiarrhythmic drug chosen by the treating physician (most commonly flecainide). Groups were balanced at baseline with a mean age of 58 years and a median duration of paroxysmal AF of one year. Patients were followed for one year. Patients recorded episodes of symptomatic AF and wore an implantable cardiac monitor to detect any episodes of tachyarrhythmia. Patients were able to cross over from medication to cryotherapy if an episode of tachyarrhythmia had occurred after the first 90 days, the episode warranted a change in therapy, and the patient was taking a therapeutic dose of the antiarrhythmic. This occurred in 24% of patients in the drug therapy group. Analysis was by intention to treat, and outcomes were assessed by a committee masked to treatment allocation. At one year, the likelihood of any episode of atrial tachyarrhythmia was lower in the ablation group (42.9% vs. 67.8%; hazard ratio = 0.48; 95% CI, 0.35 to 0.66; number needed to treat = 4). Symptomatic episodes were significantly less common in the ablation group (11.0% vs. 26.2%; hazard ratio = 0.39; 95% CI, 0.22 to 0.68; number needed to treat = 7). There was a slightly greater improvement in an AF-specific quality of life score (10-point difference at six months, 8 points at 12 months), but this is of borderline clinical significance on a 100-point scale. Serious adverse events were similar between groups, although hospitalizations were more common in the drug therapy group (13 vs. 5).

Study design: Randomized controlled trial (single-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Andrade JG, Wells GA, Deyell MW, et al.; EARLY-AF Investigators. Cryoablation or drug therapy for initial treatment of atrial fibrillation.* N Engl J Med. *2021;384(4):305-315.*

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