POEMs

Patient-Oriented Evidence That Matters

Similar Long-Term Morbidity and Mortality with Human Insulin and Analogue Insulin

Clinical Question

Is there a difference in the long-term morbidity and mortality in adults with type 2 diabetes mellitus who are treated with human insulin vs. analogue insulin?

Bottom Line

This study found no difference in long-term patient-oriented outcomes between human and analogue insulins in adults with type 2 diabetes. Recent evidence also found no difference in the rates of severe hypoglycemia. The best evidence shows no proven benefit to using analogue insulins instead of the older human insulins, and potential harm because the higher cost of analogue insulins may prohibit patient acquisition. (Level of Evidence = 2b)

Synopsis

The investigators analyzed data from four large integrated health care delivery systems in the United States, specifically identifying adults who filled a first insulin prescription from January 1, 2005, through December 31, 2013. Continuous treatment with the same insulin therapy was determined based on prescription refill dates. A total of 127,600 participants met eligibility criteria, including having type 2 diabetes and an initial date of insulin therapy. The individuals who assessed outcomes obtained vital statistics from hospital records, state registries, and national registries. Adjustments occurred in outcomes to control for potential confounders, including patient demographics, comorbid conditions, medication use, smoking, and socioeconomic variables. Adjusted hazard ratios for continuous exposure to analogue vs. human insulin demonstrated no significant differences in all-cause mortality, mortality due to cardiovascular disease, myocardial infarction, and congestive heart failure hospitalization.

Study design: Cohort (retrospective)

Funding source: Government

Setting: Population-based

Reference: *Neugebauer R, Schroeder EB, Reynolds K, et al. Comparison of mortality and major cardiovascular events among adults with type 2 diabetes using human vs analogue insulins.* JAMA Netw Open. *2020;3(1):e1918554.*

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Denosumab No Better than Bisphosphonates for Preventing Fracture, and the Cost Is Much Higher

Clinical Question

What is the comparative effectiveness of denosumab (Prolia) and bisphosphonates in adults with osteoporosis?

Bottom Line

This meta-analysis found no evidence that the monoclonal antibody denosumab reduces the risk of fracture more than bisphosphonates. A one-year supply of denosumab costs $2,453 in the United States (http://www.goodrx.com; accessed January 29, 2020) and $758 in Canada (https://www.formulary.health.gov.on.ca/formulary/; accessed January 29, 2020). (Level of Evidence = 1a–)

Synopsis

This meta-analysis of randomized trials compared the monoclonal antibody denosumab with a bisphosphonate. The authors searched the usual databases but do not report looking for unpublished studies; this is especially important when the research is largely funded by industry. They identified 10 studies that compared denosumab with one of four bisphosphonates, most often alendronate (Fosamax) (n = 6). There were a total of 5,361 patients, with a mean age ranging from 63 to 78 years; 99% were women. Only 13% had a previous fracture, and 29% had experienced no previous treatment for osteoporosis. It is not clear whether treatment-naive patients would have had different results than those already taking a bisphosphonate. All patients were also concomitantly taking calcium and vitamin D supplements. The authors did a limited assessment of risk

of bias (not judging the overall risk of bias of each study), but found a number of flaws: open-label design in five studies, masked outcome assessment in only three studies, failure to conceal allocation in three studies, and no description of how randomization was performed in two studies. These biases would tend to favor the novel therapy. The authors found that denosumab leads to a greater increase in bone density. Regarding primary patient-oriented outcomes, there was no significant difference in the risk of any fracture based on five studies with 3,540 patients. The trend was toward more fractures with denosumab (relative risk = 1.32; 95% CI, 0.93 to 1.87; pooled absolute risks were 4.0% vs. 3.1%). There was also no difference in the risk of osteoporotic fracture at 12 months based on reporting from three studies with 1,999 patients (relative risk = 0.92; 95% CI, 0.39 to 2.15). There was no difference between groups in adverse events or severe adverse events. The authors estimate that up to three unpublished negative trials may be out there.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Setting: Various (meta-analysis)

Reference: *Lyu H, Jundi B, Xu C, et al. Comparison of denosumab and bisphosphonates in patients with osteoporosis: a meta-analysis of randomized controlled trials.* J Clin Endocrinol Metab. *2019;104(5):1753-1765.*

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ACR Guideline for Managing Patients with Degenerative Joint Disease of the Hand, Knee, and Hip

Clinical Question

What are the key approaches to managing patients with degenerative joint disease involving the hand, knee, or hip?

Bottom Line

This guideline underscores that we have multiple options to help patients with degenerative joint disease be more comfortable and functional, but we still have significant limitations based on the available evidence. For many of our patients, exercise, adaptive devices, and comfort measures will be the best approaches. (Level of Evidence = 5)

Synopsis

The American College of Rheumatology (ACR) convened a guideline development panel. Panel members, many of whom reported ties to industry, followed an explicit process of identifying key questions, conducting systematic literature reviews, and synthesizing recommendations based on the available data. The ACR had a panel of patients and an intraprofessional voting panel of rheumatologists, an internist, and occupational and physical therapists. On the basis of their own reviews of the available literature (rather than using systematic reviews conducted by other entities), the panel issued strong or conditional recommendations based on a 70% consensus among the voting panel members, typically according to the quality of the supporting data. The use of their own reviews rather than others is important in that some systematic reviews come to differing conclusions for some of their recommendations, such as intra-articular steroid injections. The panel made strong recommendations for a comprehensive approach that includes exercise, self-efficacy programs, weight loss, tai chi, and assistive devices (e.g., canes, tibiofemoral knee braces, thumb splints), as well as topical, oral, and intra-articular steroids (for knee and hip). The panel made conditional recommendations in favor of education, cognitive behavior therapy, and other forms of exercise. They made conditional recommendations in favor of taping, other types of splints and braces, acetaminophen, tramadol, duloxetine (Cymbalta), chondroitin (hand), topical capsaicin (knee), and acupuncture. They made strong recommendations against the use of transcutaneous electrical nerve stimulation (knee, hip), bisphosphonates, glucosamine, hydroxychloroquine (Plaquenil), methotrexate, biologics, platelet-rich plasma or stem cell injections, chondroitin (knee, hip), and intra-articular hyaluronic acid (hip). The panel made conditional recommendations against many other measures, including chondroitin (hand), hyaluronic acid injections (hand, knee), topical capsaicin (hand, hip), botulinum toxin, prolotherapy, colchicine, nontramadol opioids, fish oil, vitamin D, massage, and wedged insoles or modified shoes. Some of the negative recommendations were based on a lack of reasonable-quality evidence of benefit as

opposed to an abundance of reasonable-quality evidence of the absence of benefit. Some of these areas will continue to evolve.

Study design: Practice guideline

Funding source: Foundation

Setting: Outpatient (any)

Reference: *Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee.* Arthritis Rheumatol. *2020;72(2):220-233.*

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Fecal Microbiota Transplant Effective for Irritable Bowel Syndrome

Clinical Question

Does a fecal microbiota transplant safely improve symptoms in patients with irritable bowel syndrome?

Bottom Line

This is the largest and best study to date of fecal microbiota transplant for irritable bowel syndrome (IBS)—with impressive results. The authors argue that the quality of donor stool is an important factor and may explain the differences in results (one previous study had positive findings, the other did not). Although findings persisted and even improved between one and three months posttransplant, it is unclear how long the benefits will persist. (Level of Evidence = 1b)

Synopsis

When we call something a syndrome, that often means we do not know what causes it or how to treat it. It seems like bacteria in the gut may have something to do with IBS. These authors identified 200 Norwegian patients who met the Rome IV criteria for IBS and who had no red flags for inflammatory bowel disease or malignancy. A 12-week course of dietary manipulation therapy had been ineffective. At baseline, a stool sample was taken. After excluding 35 patients, largely because of withdrawal of consent or declining participation, the authors randomized the remaining 165 patients to one of three groups: placebo (transplant with 30 g of their own stool), 30-g fecal microbiota transplant, or 60-g fecal microbiota transplant. The fecal microbiota transplants were administered via upper endoscopy. The average age of participants was 40 years, 81% were women, and most had constipation- or diarrhea-predominant IBS rather than mixed. The donor was a healthy, nonsmoking male who had received only three courses of antibiotics in his life and ate a healthy diet. A variety of IBS-specific scores were measured, and a response was defined as a reduction in the IBS Severity Scoring System score of at least 50 points at three months' follow-up. This occurred in 24% of the patients who received placebo, 77% who received the 30-g fecal microbiota transplant, and 89% who received the 60-g fecal microbiota transplant. These differences were statistically and clinically significant, with a number needed to treat of 2 for one person to benefit. The benefit was similar for subgroups by type of IBS, sex, and duration of IBS symptoms. Patients reported improvements in quality of life, fatigue, and abdominal symptoms using validated survey instruments. The authors also analyzed the stool specimens after treatment and saw significant differences in some species.

Study design: Randomized controlled trial (double-blinded)

Funding source: Foundation

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *El-Salhy M, Hatlebakk JG, Gilja OH, et al. Efficacy of faecal microbiota transplantation for patients with irritable bowel syndrome in a randomised, double-blind, placebo-controlled study.* Gut. *2020;69(5):859-867.*

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