Trial Compares Glucose-Lowering Drugs for Type 2 Diabetes

Results from the Glycemia Reduction Approaches in Type 2 Diabetes: A Comparative Effectiveness (GRADE) Study could help clinicians and patients choose glucose-lowering medications.

The trial findings “close important gaps in knowledge” in achieving glycemic control among patients with type 2 diabetes who are at low risk of cardiovascular disease, according to an editorial that accompanied the results published in the New England Journal of Medicine.

The trial evaluated the comparative effectiveness of 4 commonly used glucose-lowering medications. It included 5047 patients who had type 2 diabetes for less than 10 years, had glycosylated hemoglobin levels of 6.8% to 8.5%, and were receiving metformin. Participants were randomly assigned to receive insulin glargine U-100, glimepiride, liraglutide, or sitagliptin.

After an average 5 years of follow-up, all 4 medications, when added to metformin, decreased glycosylated hemoglobin levels approximately 0.3 percentage points from baseline. Glargine and liraglutide were significantly but only modestly more effective than glimepiride and sitagliptin for achieving and maintaining targeted glycosylated hemoglobin levels. Sitagliptin was the least effective treatment.

Severe hypoglycemia was more prevalent with glimepiride than with glargine, liraglutide, or sitagliptin. The liraglutide group experienced greater weight loss but also had more frequent gastrointestinal adverse effects.

The similar effects of the 4 agents “is of great clinical importance,” the editorialists wrote. “The data confirm that older generic or biosimilar low-cost agents still have a role in the treatment of persons with early type 2 diabetes, who are at low cardiovascular risk.”

The investigators also analyzed the trial’s secondary outcomes. The incidences of microvascular complications and death were not substantially different among the treatment groups but there appeared to be small differences in rates of any cardiovascular disease.

“The different effects of these agents on microvascular complications, cardiovascular risk factors, and cardiovascular outcomes should be considered along with their glycemic effects when choosing therapies for type 2 diabetes,” the investigators wrote.

Vitamin D Supplements Don’t Reduce COVID-19 Risk

A trial found that adults who took oral vitamin D supplements during the SARS-CoV-2 pandemic when vaccine coverage was low were not protected against COVID-19 or any other acute respiratory tract infections.

The trial, conducted in the UK from December 2020 through June 2021, involved 6200 participants aged 16 years or older. Half the participants were offered a vitamin D blood test and, of this group, 86% had suboptimal vitamin D levels and received either 800 IU/d or 3200 IU/d of vitamin D supplements for 6 months. The other half of participants did not receive testing or supplements.

Neither of the vitamin D doses showed an effect on all-cause acute respiratory tract infections or COVID-19 cases specifically compared with the control group. At least 1 acute respiratory tract infection occurred in 5.7% of the lower-dose group, 5% of the higher-dose group, and 4.6% of the control group. Of 178 participants who developed COVID-19, 3.6% were in the lower-dose vitamin D group, 3% were in the higher-dose group, and 2.6% were in the control group. There were no differences in COVID-19 severity or prolonged symptoms between the 3 groups.

The results were reported in The BMJ along with those from a trial of cod liver oil, which contains low doses of vitamin D and vitamin A as well as omega-3 fatty acids. Nearly 35,000 adults in Norway were randomly assigned to receive either 5 mL of cod liver oil or 5 mL of placebo daily for 6 months. There were no differences in COVID-19 severity or prolonged symptoms between the 3 groups.

Large Treatment Effects With Automated Insulin Delivery System

An advanced hybrid closed-loop (AHCL) system improved glycemic control among individuals with type 1 diabetes who struggled to achieve target glucose levels compared with the standard of care in European countries.

The open-label Advanced Hybrid Closed Loop Study in Adult Population with Type 1 Diabetes (ADAPT) trial, conducted in France, Germany, and the UK, included patients with suboptimal glucose control who were using multiple daily injections of insulin plus intermittently scanned continuous glucose monitoring (isCGM) or real-time continuous glucose monitoring (rtCGM).

An article in The Lancet Diabetes & Endocrinology reported results for the trial’s cohort A, which consisted of 82 participants randomly assigned to receive AHCL therapy or to continue with multiple daily injections of insulin plus isCGM for 6 months.

At 6 months, average hemoglobin A1c (HbA1c) decreased by 1.54%, from 9% to 7.32%, in the AHCL group and by 0.2%, from 9.07% to 8.91%, in the group taking multiple daily injections of insulin plus isCGM. No diabetic ketoacidosis, severe hypoglycemia, or serious adverse events related to study devices occurred in either group. Other benefits of AHCL therapy...
included greater time in range and potentially reduced risk of long-term complications, suggesting that "AHCL should be considered at the early stages in the type 1 diabetes treatment pathway," the authors concluded.

Results for cohort B—AHCL therapy vs daily injections of insulin plus rtCGM—will be published separately.

**Sacubitril-Valsartan and Heart Function in End-stage Kidney Disease**

Trials have found that sacubitril-valsartan reduces heart failure hospitalizations and mortality for patients with heart failure with reduced ejection fraction (HFrEF). Now a study has evaluated the efficacy and safety of the angiotensin receptor-neprilysin inhibitor in patients with end-stage kidney disease (ESKD), who have the highest prevalence of heart failure, and concomitant HFrEF.

The case-control study included 49 patients with ESKD and HFrEF; 31 were undergoing hemodialysis and 18 were receiving peritoneal dialysis. Twenty-six participants received sacubitril-valsartan titrated to a dose of 200 mg twice daily. The other 23 participants received conventional treatment and maintained their regular medications. Fifteen echocardiographic parameters were compared before and after treatment.

After 1 year, sacubitril-valsartan significantly improved systolic and diastolic heart function, which was unchanged with conventional treatment. Sacubitril-valsartan did not increase hyperkalemia or hypotension risk in patients with ESKD. In their article published in the *Journal of the American Heart Association*, the authors call for larger-scale studies to determine whether the improvement in cardiac function translates to clinical outcomes. – Anita Slomski

**Note:** Source references are available through embedded hyperlinks in the article text online.