Diabetes Drug Significantly Cuts Body Weight In Adults With Obesity

Obesity is a prevalent and serious health concern, both in the United States and globally. The Centers for Disease Control and Prevention (CDC) report that the prevalence of obesity in the U.S. increased substantially from 30.5% in 1999–2000 to 42.4% in 2017–2018, with severe obesity rising from 4.7% to 9.2%.

Doctors often use body mass index (BMI) — which a person can calculate by dividing their weight in kilograms (kg) by the square of their height in meters — to determine whether a person's weight is healthy. A BMI of 25 to <30 falls within the overweight range in adults, while those with obesity have a BMI of ≥30.

A serious health concern

Obesity reduces life expectancy and is a major risk factor for cardiovascular disease, type 2 diabetes, non-alcohol-related fatty liver disease, and certain cancers, including breast, ovarian, endometrial, prostate, liver, and colon cancer.

Currently, a combination of diet and exercise is the mainstay of obesity treatment. If these lifestyle interventions prove ineffective over 6 months, clinical guidelines recommend medications for people with a BMI of ≥30 or those with a BMI of ≥27 who have other related health conditions.

Effectiveness, cost, and safety issues limit the use of currently available medications. Injectable semaglutide

is a drug that the Food and Drug Administration (FDA) have approved for adults with type 2 diabetes and cardiovascular disease.

Semaglutide is an analog of the naturally occurring human glucagon-like peptide-1 (GLP-1) hormone in the body. The body releases GLP-1 from the gut into the bloodstream after meals, increasing satiety and reducing hunger and cravings.

In a phase 2 clinical trial involving adults with type 2 diabetes and obesity, injectable semaglutide treatment resulted in weight loss.

This result led investigators to conduct a global phase 3 trial called Semaglutide Treatment Effect in People with Obesity (STEP) to investigate the safety and effectiveness of semaglutide in participants aged 18 years and older.

The participants had either a BMI of ≥30 or a BMI of ≥27 and weight-related health conditions. A group of the participants received a placebo instead of the treatment.

The trial excluded people who had diabetes, had previously undergone obesity surgery, or had used medications to treat obesity in the 90 days before enrollment. However, the participants had some weight-related health conditions, including hypertension, high cholesterol, obstructive sleep apnea, and cardiovascular disease.

The researchers randomly assigned a total of 1,961 participants to receive either semaglutide (as an injection under the skin with a dose of 2.4 milligrams) or placebo, with both groups also receiving lifestyle interventions.

Over 68 weeks, 1,306 participants received semaglutide and 655 participants received the placebo on a weekly basis.

At baseline, the average body weight was 105.3 kg, the average age was 46 years, and the average BMI was 37.9. In addition, 75% of the participants had at least one coexisting condition.

‘Game-changing’ findings

On average, participants in the semaglutide group significantly decreased their body weight by 14.9% (-15.3 kg) from baseline compared with 2.4% (-2.6 kg) in the placebo group.

The trial demonstrated significant weight reductions of:

- 5% or more in 86.4% of participants in the semaglutide group vs. 31.5% in the placebo group
- 10% or more in 69.1% of participants in the semaglutide group vs. 12% in the placebo group
- 15% or more in 50.5% of participants in the semaglutide group vs. 4.9% in the placebo group

Study participants receiving semaglutide also had greater reductions in waist circumference, blood pressure, fasting lipid levels, and blood glucose than those receiving the placebo. In

addition, they had increased self-reported physical functioning scores.

The most common adverse effects included mild-to-moderate nausea and diarrhea that usually subsided with time. More participants stopped treatment due to gastrointestinal side effects in the semaglutide group (4.5%) than in the placebo group (0.8%).

Study limitations

The trial had some limitations, including its short duration and the exclusion of people with diabetes.

The majority of the participants were white (75.1%) and female (74.1%) and, therefore, not reflective of the general population with obesity. This limits the generalizability of the findings.

Additionally, people with a phobia of needles may not wish to use an injectable drug in the long term.

One of the main authors of the study, Rachel Batterham, M.B., B.S., Ph.D., a professor of obesity, diabetes, and endocrinology at the Centre for Obesity Research at University College London (UCL) and the UCL Hospitals Centre for Weight Management, comments on the findings:

"No other drug has come close to producing this level of weight loss — this really is a gamechanger. For the first time, people can achieve through drugs what was only possible through weight loss surgery."

Based on these trial results, Novo Nordisk, the pharmaceutical company funding the clinical trial, submitted a request for regulatory approval for injectable semaglutide to treat obesity to the FDA, the European Medicines Agency, and the National Institute for Health and Care Excellence.

Although the trial results seem promising, head-to-head trials comparing semaglutide with other standard-of-care pharmacologic and surgical treatment options will be necessary to determine its eventual role in treatment.

Dr. Batterham adds, "The impact of obesity on health has been brought into sharp focus by COVID-19, where obesity markedly increases the risk of dying from the virus, as well as increasing the risk of many life limiting serious diseases, including heart disease, type 2 diabetes, liver disease, and certain types of cancers."

"This drug could have major implications for U.K. health policy for years to come."