Weekly Adjunctive Semaglutide Augments Weight Loss in Non-Diabetic Overweight Adults

New study reveals weekly semaglutide 2.4 mg leads to 10.3% additional weight loss in individuals with obesity.
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September 27, 2023 – In a recent study, individuals without diabetes who were overweight/obese and received semaglutide 2.4 mg in addition to intensive behavior therapy and a low-calorie diet experienced 10.3% additional weight reduction compared to placebo.

Thomas A Wadden, PhD with the Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, and colleagues reported their findings in the April 13, 2021, issue of *JAMA*.

Obesity has become a global health crisis. CDC reports a rise in prevalence of obesity from 30.5% in 2000 to 41.9% in 2020. The estimated annual medical expenditure related to obesity in the United States is approximately 173 billion dollars. Pharmacological treatments have long been recognized as a valuable addition to lifestyle interventions. However, until recently, the available agents only provided a moderate weight loss over that provided by lifestyle alone.

Semaglutide, a long-acting glucagon-like peptide 1 receptor agonist, was originally approved by the FDA at a lower dose for the treatment of type 2 diabetes in adults in 2017. It decreases both fasting and postprandial glucose levels by increasing insulin secretion, inhibiting glucagon release, and suppressing hepatic gluconeogenesis. Its effect on the central nervous system has also been shown to delay gastric clearing, stimulate satiety, and reduce hunger and appetite.

One of the largest, phase 3 clinical trial programs Semaglutide Treatment Effect in People with Obesity (STEP 1-5) assessed the efficacy and safety of 2.4 mg of semaglutide administered subcutaneously weekly. The STEP 3 randomized clinical trial enrolled adults without diabetes who had either obesity (BMI >30 kg/m^2) or overweight (BMI >27kg/m^2) with at least one comorbidity. Of 611 participants, 407 were randomly assigned to receive semaglutide, while the remaining 204 received a placebo. Treatment was initiated with semaglutide 0.25 mg, then

increased every 4 weeks until a target dose of 2.4 mg/week was reached. Additionally, both groups received an initial 8 weeks of a low-calorie meal replacement diet (1000-1200 kcal/day) followed by a hypocaloric conventional diet (1200-1800 kcal/day) for 60 weeks and intensive behavioral therapy for 68 weeks. Subjects were also encouraged to exercise regularly, starting with 100 min/week to a goal of 200 min/week.

At week 68, participants receiving semaglutide experienced a mean weight loss of 16% vs 5.7% for placebo (difference: -10.3 percentage points, [95% CI, −12.0 to −8.6]; *P*<.001). Furthermore, a significantly higher proportion of participants who received semaglutide lost at least 5% of their baseline body weight compared to those in the placebo group (86.6% vs. 47.6%, respectively, *P*< .001).

The semaglutide group was also found to have a higher likelihood of achieving weight reduction of ≥10%, ≥15%, and ≥20% by week 68 compared with the placebo group (75.5% vs 27%, 55.8% vs 13.2 %, and 35.7 % vs 3.7% respectively, *P* < .001). Furthermore, individuals in the semaglutide arm reported a significantly higher reduction in waist circumference and blood pressure, BMI, glycated hemoglobin, C-reactive protein, total cholesterol, and LDL at week 68 than with placebo.

Gastrointestinal adverse events such as nausea, constipation, diarrhea, and vomiting were more prevalent in the semaglutide group (82.8%) compared to the placebo group (63.2%). Although these events were typically mild to moderate in severity and transient, they resulted in a higher discontinuation rate of 3.4% in the semaglutide group versus 0% in the placebo group.

“The present findings suggest that the addition of Semaglutide to intensive behavioral therapy may help patients achieve more than the average 5 to 10% reduction in body weight typically produced by behavioral interventions at 6 to 12 months,” reported Wadden and colleagues.

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