Drug, Lifestyle Combo Promotes Weight Loss

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Pramlintide treatment combined with lifestyle intervention resulted in sustained weight loss at 12 months in a single-blind, placebo-controlled extension study.

Pramlintide (Symlin) is an injectable synthetic analogue of human amylin, a peptide hormone that is naturally cosecreted with insulin in response to meals. Pramlintide has been shown to reduce caloric intake and promote weight loss in obese individuals.

The drug has been approved for the treatment of type 1 and type 2 diabetes and is currently under investigation by its manufacturer Amylin as a potential treatment for obesity.

In the company's initial 4-month randomized, double-blind, placebo-controlled dose-escalation study conducted at 24 centers, 411 obese subjects were randomized to receive placebo three times daily or pramlintide in doses of 120, 240, or 360 mcg either two or three times daily. (Those participants randomized to twice-daily pramlintide received placebo at midday meals.) All subjects participated in a lifestyle intervention program in which they were encouraged to reduce their caloric intake by 500 kcal/day and to increase their steps to 10,000/day with the aid of a digital pedometer.

In the 8-month single-blind extension, all of the pramlintide subjects except for the lowest dose (120 mcg) either maintained their weight or continued to lose.

Subjects were nondiabetic adults aged 18-70 years with a body mass index between 30 and 50 kg/m^2 and waist circumference greater than 102 cm for men and greater than 88 cm for women. Of 270 patients who were evaluable at 4 months, 77% opted to participate in a single-blind 8-month extension of the initial study that included continuation of the lifestyle intervention. There were 146 evaluable subjects at the end of 12 months, Dr. Steve R. Smith and his associates reported in Diabetes Care (2008;31:1816-23).

At 4 months, weight loss in the evaluable pramlintide groups ranged from 3.9 to 5.7 kg, compared with 2.6 kg in the placebo group. The results were significant for the 120-mcg b.i.d. and 360-mcg t.i.d. and b.i.d. groups, compared with placebo. Within those arms, 44%-47% of evaluable participants achieved a weight loss of 5% or greater, compared with just 28% of the placebo participants. Reductions in weight appeared to be dose-dependent for the pramlintide twice-daily but not the thrice-daily arms, said Dr. Smith, of the Pennington Biomedical Research Center, Baton Rouge, La.

In the 8-month single-blind extension, most of the placebo subjects gained weight while all the pramlintide subjects except for the lowest dose (120 mcg) either maintained their weight or continued to lose. Excluding that one group, weight loss from baseline to month 12 ranged from 6.0 to 7.9 kg among the evaluable subjects, compared with 1.1 kg with placebo. Weight loss was statistically significant for the thrice-daily 120-, 240- and 360-mcg groups and the twice-daily 360-mcg group. In those arms, 41%-65% achieved weight loss of 5% or greater from baseline to 12 months, compared with just 18% in the placebo group.

Similar to the 4-month results, reductions at 8 months in weight appeared to be dose dependent for the twice-daily but not thrice-daily arms, the researchers said.

Pramlintide was generally safe and well-tolerated, with no novel safety concerns identified. Nausea was the only adverse event, occurring in 5% or more of study subjects and more frequently than with placebo, and was the reason for withdrawal in 12 participants. At 4 months, the incidence of nausea ranged from 9% for the 240-mcg t.i.d. group to 29% in the 360-mcg t.i.d. group, versus 2% with placebo. Nausea was generally mild to moderate and decreased over time. Weight loss was dissociated from nausea, as subjects who did not report nausea achieved body weight reductions similar to those in the overall study population, they said. ■