

A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity.

Kelly AS, Auerbach P, Barrientos-Perez M et al. N Engl J Med. 2020 May 28;382(22)

Background: There is a paucity of approved drugs for treatment of adolescent obesity. Liraglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist that increases the release of insulin and reduces excessive glucagon release, works by suppressing appetite and delaying gastric emptying and thus induces weight loss.

Methods: Randomised, double-blind, phase 3, placebo-controlled, multicentre trial

- 251 obese adolescents, aged 12 to less than 18 years, 32 sites in five countries
- Compared once-daily subcut. administration of liraglutide (3mg) with placebo
- Primary endpoint was change from baseline in the body-mass index (BMI) standard-deviation score at 56 weeks

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Results: Absolute change in BMI standard- deviation score from baseline at 56 wk was -0.23 ± 0.05 in the liraglutide group and -0.00 ± 0.05 in the placebo group.

- Estimated treatment difference was -0.22 (95% CI, -0.37 to -0.08 ; $P=0.002$) in favor of liraglutide.

- BMI fell by 1.39 kg/m^2 in the liraglutide group, compared with a 0.19 kg/m^2 increase in the placebo group.

Clinical outcomes: More participants in the liraglutide group than in the placebo group had gastrointestinal adverse events (64.8% vs. 36.5%, $P<0.001$)

- Adverse events led to discontinuation of liraglutide treatment in 10.4%

- After discontinuation, a greater increase in the BMI standard-deviation score was observed with liraglutide than with placebo (0.22 vs. 0.07)

Conclusion: In adolescents with obesity, the use of liraglutide plus lifestyle therapy led to a significantly greater reduction in the BMI standard-deviation score than placebo plus lifestyle therapy. The higher frequency of gastrointestinal adverse events observed with liraglutide suggests that this treatment may not be suitable for all patients.

Key message: Liraglutide was superior to placebo with regard to the change from baseline in the BMI standard-deviation score and the estimated treatment difference observed in this trial of liraglutide (-0.22) was greater than differences observed in trials of lifestyle therapy conducted by the U.S. Preventive Services Task Force (-0.17) and in an overview of six Cochrane reviews (-0.13).

EXPERT COMMENT

“This study provides evidence for the efficacy of liraglutide as an adjunct to lifestyle interventions for obesity in adolescents, but the gastrointestinal side effects of the drug and the rebound weight gain after discontinuation may limit its use. The bottom line is that behavioral therapy and lifestyle modification still remains the pillar of weight control therapy in adolescents.”

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With warm regards,

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Reference

Kelly AS, Auerbach P, Barrientos-Perez M, Gies I, Hale PM, Marcus C, Mastrandrea LD, Prabhu N, Arslanian S; NN8022-4180 Trial Investigators. A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity. N Engl J Med. 2020 May 28;382(22):2117-2128. doi: 10.1056/NEJMoa1916038