

Liraglutide for management of adolescent obesity

Roya Kelishadi 

Available interventions for adolescents with obesity are based on behavioural therapy and lifestyle modification. A new randomized, controlled trial provides evidence of efficacy of a pharmacological therapy, liraglutide, for weight control in adolescent obesity. The indications for more widespread use of this medication in clinical practice are under discussion.

Refers to Kelly, A. S. et al. A randomized, controlled trial of liraglutide for adolescents with obesity. *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa1916038> (2020).

Childhood obesity has become a major global health problem at public and individual levels¹. The management of obesity, especially childhood obesity, is very difficult owing to its complex pathophysiology, which includes the interaction of socio-economic, familial and individual factors. Several family-based and school-based programmes have been implemented to tackle obesity in the paediatric age group; however, owing to the complex interaction of underlying factors, they have been of limited success². Still, not enough evidence exists to advocate any particular weight management treatment for obesity in children and adolescents. In general, the most successful programmes are those combining behavioural therapy and lifestyle modification³. Given that such programmes require the involvement of families and interventions that modify the lifestyles of families, as well as a change of established dietary or activity habits, they are often not completed in their entirety.

Although most physicians do not feel comfortable prescribing medications in the paediatric population, various investigations have been conducted on the efficacy of adding pharmacological treatment^{4,5} to lifestyle change in adolescents with obesity. In general, the effects of such medications (such as metformin or orlistat) have not been superior to lifestyle therapy⁶. Furthermore, some adolescents with severe obesity are even referred for bariatric surgery. Thus, more effective medications are under investigation.

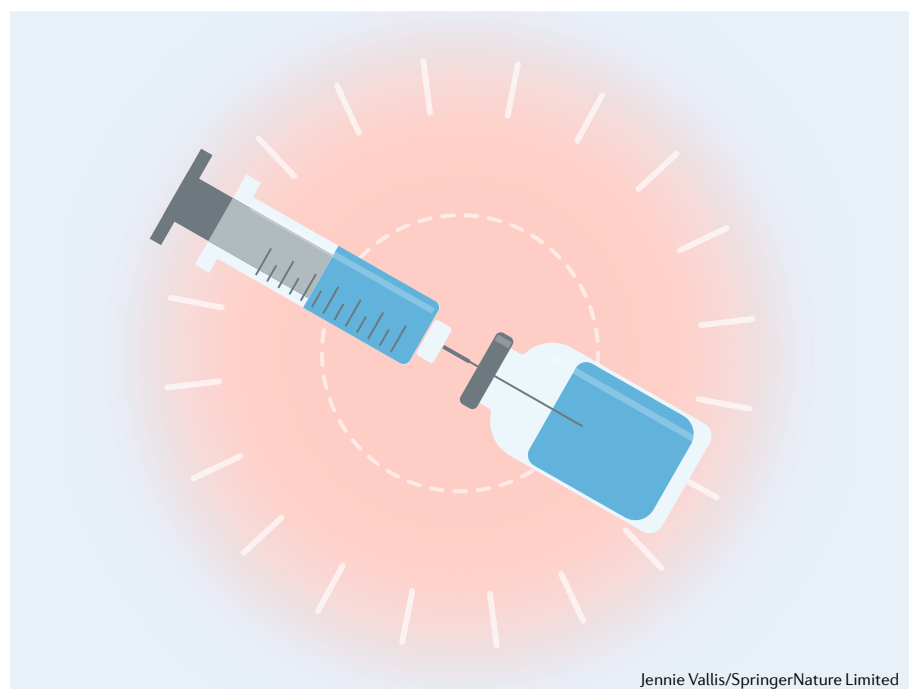
Liraglutide is a glucagon-like peptide 1 (GLP1) receptor agonist that increases the

release of insulin from the pancreas and also decreases excessive glucagon release. The drug has been used for management of diabetes mellitus as well as obesity⁷. Some trials used liraglutide in adolescents, mainly for treatment of type 2 diabetes mellitus⁸. Now, a new multi-centre randomized clinical trial carried out by Aaron Kelly and colleagues assessed the effects of using liraglutide in the management of obesity in adolescents⁹.

“The BMI standard deviation score ... had greater reduction in adolescents receiving liraglutide”

The present double-blind trial examined the effects of 56-week treatment and 26-week follow-up in adolescents who did not successfully lose weight after lifestyle therapy. In this trial, in addition to lifestyle consultation, daily subcutaneous liraglutide (3.0 mg) was administered to 126 participants and results were compared with 125 control participants receiving daily subcutaneous placebo. The BMI standard deviation score (BMI-SDS) had greater reduction in adolescents receiving liraglutide than in the placebo group. However, in the follow-up period, the liraglutide group had a greater increase in the BMI-SDS than participants who receive placebo⁹.

It is impressive that a medication could help in weight control of adolescents with obesity; however, the long-term effects need to be considered. For example, rapidly after discontinuation of liraglutide, adolescents with obesity faced weight gain⁹. Although the medication was shown to be effective at controlling weight, questions remain regarding



Jennie Vallis/SpringerNature Limited

“ rapidly after discontinuation of liraglutide, adolescents with obesity faced weight gain ”

whether adolescents with obesity would use this expensive and injectable medication for long periods of time. This study provides confirmatory evidence that the backbone for reaching weight control in adolescents is lifestyle modification. However, using liraglutide for 56 weeks did not have substantial effects in modifying cardiometabolic risk factors such as blood pressure or serum cholesterol and triglycerides⁹. The researchers suggested that this effect might be in part because participants did not have notably high levels of such risk factors at the beginning of the trial. However, abnormality of metabolic profile is highly prevalent in adolescents with obesity¹⁰. Management of cardiometabolic risk in this patient population is likely to be easier with lifestyle modifications rather than an expensive medication that comes with the potential adherence problems associated with daily injections.

The safety of liraglutide has been demonstrated in the present study⁹, and the only notable

adverse effects were gastrointestinal problems; however, owing to rare but potential serious adverse effects, such as thyroid cancer, post-marketing surveillance of this medication should be followed up over long periods of time.

In broader terms, the study of Kelly and colleagues⁹ provides promising evidence for the efficacy and safety of liraglutide in treatment of adolescents with obesity. The prescription and clinical use of this medication in adolescents with obesity would require further evaluation for safety concerns, as well as obtaining further efficacy data in the paediatric population.

However, liraglutide should not be used as a stand-alone approach for treatment of adolescents with obesity; it can be considered as an adjunct to behavioural therapy and lifestyle change. A more prudent use is to consider liraglutide for some adolescents who have morbid obesity or major complications of obesity.

Roya Kelishadi 

Child Growth and Development Research Center,
Research Institute for Primordial Prevention of
Non-Communicable Disease, Isfahan University
of Medical Sciences, Isfahan, Iran.

e-mail: Kelishadi@med.mui.ac.ir

<https://doi.org/10.1038/s41574-020-0371-7>

1. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* **390**, 2627–2642 (2017).
2. Kelishadi, R. et al. Controlling childhood obesity: A systematic review on strategies and challenges. *J. Res. Med. Sci.* **19**, 993–1008 (2014).
3. Bahia, L. et al. Overview of meta-analysis on prevention and treatment of childhood obesity. *J. Pediatr.* **95**, 385–400 (2019).
4. Srivastava, G. et al. Clinical considerations regarding the use of obesity pharmacotherapy in adolescents with obesity. *Obesity (Silver Spring)* **27**, 190–204 (2019).
5. Anderson, K. L. A review of the prevention and medical management of childhood obesity. *Child Adolesc. Psychiatr. Clin. N. Am.* **27**, 63–76 (2018).
6. Lentferink, Y. E. et al. Efficacy of metformin treatment with respect to weight reduction in children and adults with obesity: a systematic review. *Drugs* **78**, 1887–1901 (2018).
7. Lin, C. H. et al. An evaluation of liraglutide including its efficacy and safety for the treatment of obesity. *Expert Opin. Pharmacother.* **21**, 275–285 (2020).
8. Tamborlane, W. V. et al. Liraglutide in children and adolescents with type 2 diabetes. *N. Engl. J. Med.* **381**, 637–646 (2019).
9. Kelly, A. S. et al. A randomized, controlled trial of liraglutide for adolescents with obesity. *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa1916038> (2020).
10. Martinez, S. M. et al. Mechanisms linking childhood weight status to metabolic risk in adolescence. *Pediatr. Diabetes* **21**, 203–209 (2020).

Competing interests

The author declares no competing interests.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.