Indian Academy of Pediatrics (IAP)

nRICH

Newer **R**esearch and recommendations **I**n **C**hild **H**ealth

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UNDER THE AUSPICES OF THE IAP ACTION PLAN 2023

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Dear fellow IAPans,

nRICH

Newer **R**esearch and recommendations **I**n **C**hild **H**ealth-aims to bring you the abstracts of some of the breakthrough developments in pediatrics, carefully selected from reputed journals published worldwide.

Expert commentaries will evaluate the importance and relevance of the article and discuss its application in Indian settings. nRICH will cover all the different subspecialities of pediatrics from neonatology, gastroenterology, hematology, adolescent medicine, allergy and immunology, to urology, neurology,vaccinology etc. Each issue will begin with a concise abstract and will represent the main points and ideas found in the originals. It will then be followed by the thoughtful and erudite commentary of Indian experts from various subspecialties who will give an insight on way to read and analyze these articles.

I'm sure students, practitioners and all those interested in knowing about the latest research and recommendations in child health will be immensely benefitted by this endeavor which will be published online on every Monday.

Happy reading!

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A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity

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BASED ON ARTICLE

Kelly AS, Auerbach P, Barrientos-Perez M, Gies I, Hale PM, Marcus C, Mastrandrea LD, Prabhu N, Arslanian S. A randomized, controlled trial of liraglutide for adolescents with obesity. New England Journal of Medicine. 2020 May 28;382(22):2117-28.

SUMMARY

Background: Obesity is a chronic disease with limited treatment options in paediatric patients. Liraglutide may be useful for weight management in adolescents with obesity.

Methods: In this randomized, double-blind trial, which consisted of a 56-week treatment period and a 26-week follow-up period, we enrolled adolescents (12 to <18 years of age) with obesity and a poor response to lifestyle therapy alone. Participants were randomly assigned (1:1) to receive either liraglutide (3.0 mg) or placebo subcutaneously once daily, in addition to lifestyle therapy. The primary endpoint was the change from baseline in the body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) standard deviation score at week 56.

Results: A total of 125 participants were assigned to the Liraglutide group and 126 to the placebo group. Liraglutide was superior to placebo with regard to the change from baseline in the BMI standard deviation score at week 56 (estimated difference, −0.22; 95% confidence interval [CI], −0.37 to −0.08; P = 0.002). A reduction in BMI of at least 5% was observed in 51 of 113 participants in the Liraglutide group and 20 of 105 participants in the placebo group (estimated percentage, 43.3% vs. 18.7%), and a reduction in BMI of at least 10% was observed in 33 and 9, respectively (estimated percentage, 26.1% vs. 8.1%). A greater reduction was observed with Liraglutide than with placebo for BMI (estimated difference, −4.64 percentage points) and for body weight (estimated difference, −4.50 kg [for absolute change] and −5.01 percentage points [for relative change]). After discontinuation, a greater increase in the BMI standard deviation score was observed with Liraglutide than with placebo (estimated difference, 0.15; 95% CI, 0.07 to 0.23). More participants in the Liraglutide group than in the placebo group had gastrointestinal adverse events (81 of 125 [64.8%] vs. 46 of 126 [36.5%]) and adverse events that led to discontinuation of the trial treatment (13 [10.4%] vs. 0). Few participants in either group had serious adverse events (3 [2.4%] vs. 5 [4.0%]). One suicide, which occurred in the Liraglutide group, was assessed by the investigator as unlikely to be related to the trial treatment.

Conclusions: In adolescents with obesity, the use of Liraglutide (3.0 mg) plus lifestyle therapy led to a significantly greater reduction in the BMI standard deviation score than placebo plus lifestyle therapy. (Funded by Novo Nordisk; NN8022-4180 ClinicalTrials.gov number, NCT02918279.)

Commentary: Globally, including in India, childhood obesity is a major concern and more so after the Covid-19 pandemic (1,2). The incidence of childhood obesity has gone up post-COVID across all countries (3). Some of the reasons are schools getting shut down, lockdowns restricting physical activity, increased screen time, and also mental health issues due to lockdowns. When it comes to the management of obesity, lifestyle, and nutritional modifications are the sheet anchor of treatment. The harsh reality is that lifestyle modification & dietary management are easier said than done as it requires perpetual adherence, great willpower, and good social, medical & family support. Obesity management needs a multidisciplinary approach consisting of a team of a paediatrician, paediatric endocrinologist, dietician, psychologist, and social worker.

When it comes to pharmacotherapy for obesity the options are limited and not many are very promising (4) and there are concerns about adverse effects. In the paper by Kelly AS, Auerbach P et al there was a significant weight loss (5%) in obese adolescents when treated with Liraglutide as compared with the placebo group, both groups also received nutritional and lifestyle intervention. Liraglutide a Glucagon-like peptide -1 (GLP-1) analogue increases the postprandial insulin level in a glucose-dependent manner, lowers glucagon secretion, delays gastric emptying, and induces weight loss through reductions in appetite and energy intake. The trial has shown a 5% reduction in the BMI in 45% in the Liraglutide group vs 19% in the placebo group at the end of 56 weeks of therapy. In terms of actual numbers that means for a 100 kg adolescent, it is 5 kg weight loss in about 1 year of therapy.

It is to be noted that once the drug was stopped obesity rebounded. At the end of 26 weeks following the trial, the rate of weight gain was marginally higher in those who received therapy vs the placebo group. This suggests that obesity is a chronic condition that requires continued lifestyle intervention and multidisciplinary management than short-term pharmacotherapy. The above study has demonstrated reasonable safety for the use of Liraglutide in adolescents. Recently a weekly injectable preparation of GLP-1 analog (Semaglutide) has been approved in adolescents with obesity & oral Semaglutide is under trial (5).

The most common adverse effect included gastrointestinal events, like nausea, vomiting, and diarrhea, which are well known. These adverse effects mostly occurred during dose escalation and then became less frequent. Liraglutide was not tolerated in all the patients as there was a discontinuation of the trial in 13 patients. While the trial showed some encouraging results during the trial period, post-trial rebound weight gain is disheartening. It also highlights the fact that obesity which is a lifestyle disease needs a multidisciplinary approach more focused on permanent change of lifestyle and nutrition rather than a pharmacological agent. The role of pharmacological agents in the long-term management of obesity needs further exploration.

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