Efficacy and Tolerability of GLP-1 Receptor Agonists in Children and Adolescents with Obesity: A Meta-Analysis

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INTRODUCTION

• Prevalence of pediatric obesity is approaching 1 in 5 children and adolescents aged 2-19 years in the US.
• For these children, and particularly those with severe obesity, pediatricians have a paucity of safe, effective, and durable weight-reducing pharmacological interventions with high-grade evidence.
• While GLP-1 receptor agonists have proven to be effective in reducing weight and improving glucose control in adults, their effects in children and adolescents with obesity is less clear.

AIM

This meta-analysis study aimed to determine the:
1. Weight effects
2. BMI/BMI z-score effects
3. Cardiometabolic effects

METHOD

Databases & Searching
Web of Science, PubMed/MEDLINE, and Scopus databases were searched from 01/01/1994-01/01/2021 for randomized control trials examining the weight, BMI, cardiometabolic or gastrointestinal effects of GLP-1 receptor agonists in children and adolescents with obesity.

Data Abstraction
Data were extracted by two independent surveyors and a random effects model was applied to meta-analyze generic inverse variance outcomes.

Primary Outcomes
Related to weight and cardiometabolic profile, while secondary outcomes of interest were gastrointestinal-related treatment-emergent adverse events.

RESULTS

• 9 studies with 574 participants were identified, of which 3 involved exenatide and 6 involved liraglutide.
• Figure 1] GLP-1 receptor agonists caused a modest reduction in body weight (mean difference [MD], -1.50 [95% CI, -2.50; -0.50], P = 64%); BMI (MD, -1.24 [-1.71, -0.77] kg/m², P = 0%), and BMI z-score (MD, -0.14 [-0.23, -0.06], P = 43%).
• Figure 2] Glycemic control was improved in children with proven insulin resistance (HbA1c: MD, -1.05 [-1.92, -0.18%], P = 72%).
• Figure 3] Although no lipid profile improvements were noted, a modest decrease in systolic blood pressure was detected (MD, -2.30 [-4.11, -0.49] mmHg, P = 0%).
• Finally, analysis of gastrointestinal-related treatment-emergent adverse events revealed an increased risk of nausea (risk ratio 2.11 [1.44, 3.09]; P = 0%), without significant increases in other gastrointestinal symptoms.

CONCLUSIONS

• The two GLP-1RAs uncovered in the paediatric obesity literature were exenatide and liraglutide.
• In children and adolescents with obesity, GLP-1RAs:
1. Were effective in modestly reducing weight
2. Improved glycaemic control
3. Reduced systolic blood pressure
4. Are well tolerated despite increased nausea
5. Do not commonly cause pancreatitis or MTC
• This SRMA is limited by the fact that roughly half of the synthesised data arose from a single RCT.

INCLUDED RCTS

Mastrandrea et al. Longitudinal effects of exenatide (0.14 mg/kg) in weight reduction, diabetes, cardiovascular, and gastrointestinal parameters in adolescents and young adults with obesity: results of a 1-year, double-blind, placebo-controlled, open-label extension study. J Clin Endocrinol Metab. 2017;102:3577-87.

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