Adiposity Outcomes and Linear Growth Trajectories in Children and Adolescents with Obesity and/or Type 2 Diabetes Using Glucagon-Like Peptide-1 Receptor Agonists

Pareeta Kotecha, PharmD, MS, Yao An Lee, MS, Angelina V Bernier, MD, Sarah C Westen, PhD, Tamara S. Hannon, MD, Sarah E. Wiehe, MD, MPH, Emily N. Israel, PharmD, Ephrem Abebe, PhD, Yi Guo, PhD, Jiang Bian, PhD, Steven M Smith, PharmD, MPH, Jingchuan Guo, MD, PhD

ABSTRACT

Importance: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly used to treat pediatric obesity and type 2 diabetes (T2D), raising concerns about potential effects on growth due to reduced appetite and nutritional intake. However, real-world evidence on adiposity and linear growth remains limited.

Objective: To evaluate longitudinal adiposity and linear growth trajectories among children and adolescents initiating GLP-1 RAs compared with prevalent metformin users.

Methods: This retrospective cohort study used OneFlorida+ electronic health records data (January 2019-January 2024) to emulate a target trial among children aged 6 to younger than 18 years with obesity or T2D. Each GLP-1 RA initiation defined an exposure set and an index date; prevalent metformin users with no evidence of GLP-1 RA use within ±45 days of that date were identified as potential comparators and were assigned the corresponding index date. Within each exposure set, eligible GLP-1 RA users were matched 1:2 to eligible metformin users using time-conditional propensity scores accounting for duration of metformin use and 18 months of baseline demographic, clinical, medication, and health care utilization characteristics. Individuals with pregnancy, gestational diabetes, type 1 diabetes, end-stage renal disease, medullary thyroid carcinoma, multiple endocrine neoplasia, or active malignancy were excluded. Outcomes included height-for-age z-score (HAZ) for linear growth and percentage of the 95th BMI percentile (%BMIp95), BMI z-score, modified BMI z-score, and BMI for adiposity. Outcome-specific cohorts required an eligible measurement within 6 months before or on the index date and at least 1 follow-up measurement; clinically or algorithmically identified biologically implausible values were excluded. Longitudinal treatment differences were estimated using mixed-effects models with treatment-by-time interactions and inverse probability of censoring weighting. Sex-stratified analyses were also conducted.

Results: The matched linear growth cohort included 1338 episodes (446 GLP-1 RA; 892 metformin) and 6098 HAZ measurements; the adiposity cohort included 1017 episodes (339 GLP-1 RA; 678 metformin) and 4975 BMI measurements. HAZ declined over time, but trajectories did not differ between groups (β, -0.01; 95% CI, -0.03 to 0.01; P = .376). GLP-1 RA use was associated with greater annual reductions in %BMIp95 (β, -1.34; 95% CI, -2.05 to -0.63; P = .0002), modified BMI z-score (β, -0.05; 95% CI, -0.09 to -0.01; P = .01), and BMI (β, -0.32 kg/m²; 95% CI, -0.52 to -0.11; P = .002). BMI z-score trajectories did not differ significantly (β, -0.023; 95% CI, -0.046 to 0.001; P = .056). Sex-stratified analyses suggested significant adiposity reductions among females across all outcomes. HAZ trajectories differed in direction by sex.

Conclusions and Relevance: Among children and adolescents with obesity or T2D, GLP-1 RA use was associated with greater reductions in several adiposity measures compared with prevalent metformin use, without evidence of a differential HAZ trajectory.