PREDICTORS OF RESPONSE TO METFORMIN IN YOUTH WITH TYPE 1 DIABETES (T1D) AND OBESITY OR OVERWEIGHT

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Background: Metformin used as adjuvant therapy in obese or overweight adolescents with T1D decreased insulin requirements and insulin resistance, but not hemoglobin A1c (A1c), in the T1D Exchange Metformin Study (NCT01881828). Yet, the factors that explain heterogeneity in response are not known. Here, we aimed to test the hypothesis that baseline measures can predict response to metformin therapy in youth with T1D and obesity or overweight.

Materials/Methods: We conducted our analysis using data from participants in the metformin treatment arm of the T1D Exchange Metformin Study. Data were available on 61 adolescents (median age 15.3 years, range 12–18.9; 36% males; 72% non-Hispanic whites, 98% overweight or obese; median diabetes duration 7.4 years, range 1.7–15). We assessed baseline age, sex, diabetes duration, race/ethnicity, BMI z-score, waist circumference, body fat percentage (BF%, as measured by dual-energy X-ray absorptiometry [DEXA] scan), serum adiponectin, and serum leptin levels. Outcome measures included changes in A1c, total daily insulin dose, and BF% at 13 and 26 weeks. After adjusting for baseline values, multiple linear regression models were used to identify predictors associated with the outcome measures.

Results: Decreases in total daily insulin dose at 13 and 26 weeks showed a significant negative association with baseline leptin ($p=0.0008$, $p=0.004$, respectively). In addition, decreases in BF% by DEXA at 26 weeks were positively associated with baseline BMI z-score ($p=0.03$) and negatively associated with baseline BF% ($p=0.0002$). Lastly, increase in HbA1c at 26 weeks trended towards a positive association with baseline BF% ($p=0.07$) and a negative association with baseline adiponectin ($p=0.06$). We also observed sex-based differences in response. Compared to females, males showed a significant reduction in BF% at 26 weeks ($p<0.0001$) and trended towards a reduction in total daily insulin dose at 13 weeks ($p=0.06$).

Conclusions: In adolescents with T1D and overweight or obesity treated with metformin as adjuvant to insulin, baseline leptin was the strongest predictor of decrease in total daily insulin dose at 13 and 26 weeks. Baseline BMI z-score and BF% were significant predictors for changes in BF%. These findings can help identify individuals likely to respond to metformin and facilitate a precision medicine approach in this population.

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