Hyperinsulinemia in African-American Adolescents Compared With Their American White Peers Despite Similar Insulin Sensitivity

A reflection of upregulated β-cell function?

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OBJECTIVE — African-American (AA) children are hyperinsulinemic and insulin resistant compared with American white (AW) children. Previously, we demonstrated that insulin secretion relative to insulin sensitivity was ~75% higher in AA compared with AW children, suggesting that hyperinsulinemia in AA children is not merely a compensatory response to lower insulin sensitivity. The aim of the present investigation was to assess whether glucose-stimulated insulin response is higher in AA versus AW adolescents who have comparable in vivo insulin sensitivity.

RESEARCH DESIGN AND METHODS — The hyperinsulinemic-euglycemic and hyperglycemic clamp techniques were utilized to assess first- and second-phase insulin secretion. Insulin secretion relative to insulin sensitivity was calculated as the glucose disposition index.

RESULTS — AA adolescents compared with their AW peers with comparable insulin sensitivity and body composition had higher first-phase insulin concentrations.

CONCLUSIONS — The quantitative relationship between insulin sensitivity and first-phase insulin appears to differ among AA and AW adolescents.

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African-American (AA) adolescents are hyperinsulinemic and at increased risk for type 2 diabetes when compared with American white (AW) adolescents; however, the mechanisms underlying the increased risk in AA adolescents are unclear. The objective of this study was to assess whether first- and second-phase insulin concentrations are higher in AA versus AW youth if insulin sensitivity is not different between the groups.

RESEARCH DESIGN AND METHODS

The study was approved by the University of Pittsburgh Institutional Review Board. Recruitment was done using posters, flyers, and newspaper advertisements. A total of 25 healthy AA adolescents (15 male and 10 female, aged 10.0–14.3 years) and 23 healthy AW adolescents (12 male and 11 female, aged 9.9–14.3 years), Tanner stages II–IV, participated. Findings from some of the participants have been reported (1). All subjects who participated in this study are included in this report. Exclusion criteria included ethnicity other than AA or AW, diabetes or other chronic diseases, and use of medications affecting glucose metabolism. Ethnicity was determined by self-report in three generations of the participants’ families.

Metabolic studies

Participants underwent a 3-h 40 mU/m² per min hyperinsulinemic-euglycemic clamp to assess insulin sensitivity and a 2-h hyperglycemic (12.5 mmol/l) clamp to assess insulin secretion, as described previously (2,3). Fasting hepatic glucose production was evaluated before the hyperinsulinemic-euglycemic clamp as described previously (2). Hepatic glucose production (4), insulin-stimulated glucose disposal (3), insulin sensitivity (3), insulin clearance (3), first- and second-phase insulin concentrations (2), and glucose disposition index (2) were calculated as previously reported. Fasting blood samples were obtained for lipid profile, insulin-like growth factor (IGF)-1, dehydroepiandrosterone sulfate (DHEA-S), estradiol in females, and testosterone in males.

Body composition analysis

Body composition was measured by dual-energy X-ray absorptiometry. Abdominal adiposity was assessed with a 10-mm single axial computed tomography scan at the level of L4–5 vertebrae (4).

Biochemical measurements

Plasma glucose and insulin were measured as previously described (2). IGF-1 levels were measured at Esoterix. Fasting lipid profile was measured using standards of the Centers of Disease Control and Prevention. Plasma free fatty acid levels and deuterium enrichment of glucose in the plasma were determined as previously reported (4). Stored plasma samples from the hyperglycemic clamp for C-peptide measurement were destroyed due to freezer malfunction. Fasting plasma samples for C-peptide from the euglycemic clamp were by immunochemiluminometric assay (Esoterix).

Statistical analysis

Comparisons between AA and AW adolescents were made using two-tailed Stu-
dent’s t test for continuous normally distributed variables. Appropriate nonparametric tests were otherwise used. Data are presented as means ± SEM.

RESULTS

Physical, hormonal, and metabolic characteristics
AA and AW adolescents had comparable body composition (BMI 21.1 ± 0.7 vs. 20.3 ± 0.8 kg/m², P = 0.45; percent body fat 21.0 ± 2.3 vs. 22.4 ± 2.2, P = 0.66; visceral adipose tissue 19.5 ± 2.9 vs. 24.9 ± 4.2 cm², P = 0.48; fat mass 11.2 ± 1.7 vs. 11.2 ± 1.6 kg, P = 0.96), hormonal profiles (estradiol 159 ± 47 vs. 126 ± 20 pmol/l, P = 0.53; testosterone 11.8 ± 2.0 vs. 12.4 ± 1.7 nmol/l, P = 0.83; DHEA-S 3,198 ± 465 vs. 2,962 ± 375 nmol/l, P = 0.85; IGF-1 55 ± 5 vs. 49 ± 3 nmol/l, P = 0.42), and fasting lipid profiles (cholesterol 4.09 ± 0.13 vs. 4.09 ± 0.18 mmol/l, P = 0.97; HDL cholesterol 1.30 ± 0.03 vs. 1.32 ± 0.05 mmol/l, P = 0.60; LDL cholesterol 2.41 ± 0.13 vs. 2.31 ± 0.13 mmol/l, P = 0.61; triglycerides 0.89 ± 0.01 vs. 1.01 ± 0.09 mmol/l, P = 0.30).

Basal metabolic data
Fasting glucose and insulin levels from the hyperinsulinemic-euglycemic and hyperglycemic clamps were averaged. Fasting insulin was not different (122 ± 11 vs. 120 ± 10 pmol/l, P = 0.89) and fasting glucose was lower (5.25 ± 0.05 vs. 5.44 ± 0.06 mmol/l, P = 0.02) in AAs. Fasting C-peptide (0.58 ± 0.05 vs. 0.58 ± 0.06 mmol/l, P = 0.93), free fatty acids (0.35 ± 0.04 vs. 0.34 ± 0.02 mEq/l, P = 0.81), and hepatic glucose production (3.1 ± 0.4 vs. 3.0 ± 0.1 mg·kg⁻¹·min⁻¹, P = 0.86) were not different.

Insulin sensitivity and clearance
During the hyperglycemic clamp, first- and second-phase glucose concentrations were not different (first-phase 11.9 ± 0.2 mmol/l in AA vs. 12.2 ± 0.1 mmol/l in AW, P = 0.25; second-phase 12.3 ± 0.1 mmol/l in AA vs. 12.4 ± 0.1 mmol/l in AW, P = 0.19). First-phase insulin concentration was higher in AAs (1,038 ± 126 vs. 636 ± 108 pmol/l, P = 0.002) (Fig. 1). Second-phase insulin concentration was not different (AA 1,068 ± 120 vs. AW 918 ± 174 pmol/l, P = 0.46). After controlling for insulin clearance, there remained a race difference in first-phase insulin (1,003 ± 121 vs. 647 ± 123 pmol/l, P = 0.05). The glucose disposition index was higher in AAs (10.3 ± 1.0 vs. 6.3 ± 0.7 μmol·kg⁻¹·FFM⁻¹·min⁻¹, P = 0.002).

CONCLUSIONS — Several studies have demonstrated that AA children have higher fasting and stimulated insulin levels than AW children (2,5–7); however, insulin sensitivity was lower in AA than in AW youth. Thus, the observed hyperinsulinemia in AAs was explained as a compensatory response to insulin resistance. In the current study, the observation of higher insulin secretion was made despite similar insulin sensitivity. Differences in insulin clearance could partly explain the differences in first-phase insulin concentrations; however, after adjusting for clearance, there remained a race difference in first-phase insulin concentration. Insulin clearance in AA adolescents was ~14% lower than in AWs, while first-phase insulin was ~63% higher.

Potential causes of insulin hypersecretion in AAs include dietary/lifestyle factors, genetic differences, and socioeconomic differences. Previously, we reported dietary differences including higher fat-to-carbohydrate ratio in AA children (2). Increased fat-to-carbohydrate ratio correlated negatively with insulin sensitivity and insulin clearance and positively with first-phase insulin levels across racial groups (2). Gower et al. (8) reported that genetic admixture was independently related to insulin sensitivity, fasting insulin, and acute insulin response to glucose, indicating that hyperinsulinemia in AAs has a genetic basis.

The present study demonstrates that AA adolescents have 1) ~63% higher first-phase insulin and 2) ~63% higher glucose disposition index even when they have insulin sensitivity comparable with that of their AW peers. There appears to be an upregulated β-cell function in AA adolescents, the mechanism(s) of which should be investigated.

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