Short Communication

Anti-lipolytic Effects of Insulin in African American and White Prepubertal Boys

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Abstract

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Objective: Relative to whites, African Americans have lower circulating triglycerides (TG) and greater high-density lipoprotein cholesterol. The metabolic basis for this difference is not known. This study was conducted to test the hypothesis that insulin-induced suppression of free fatty acids (FFA) results in lower serum TG in African American versus white prepubertal children.

Research Methods and Procedures: Insulin, FFA, and TG were determined at baseline and during a frequently sampled, intravenous glucose tolerance test in eight African American and eight white prepubertal males pair-matched for whole-body insulin sensitivity.

Results: Baseline TG was lower in African Americans (0.43 ± 0.10 vs. 0.79 ± 0.37 mM/L; mean ± SD; $p < 0.01$). African Americans had higher peak insulin (218 ± 102 vs. 100 ± 30 pM/L; mean ± SD; $p < 0.01$) and a greater acute insulin response (9282 ± 4272 vs. 4230 ± 1326 pM/L × 10 minutes; mean ± SD; $p < 0.05$). FFA and TG values determined at the FFA nadir were lower in African Americans (0.26 ± 0.02 vs. 0.30 ± 0.03 mEq/L; mean ± SD; $p < 0.01$ for FFA nadir and 0.49 ± 0.07 vs. 0.77 ± 0.33 mM/L; mean ± SD; $p < 0.05$ for TG). Among all subjects, FFA nadir was correlated with peak insulin ($r = -0.54$; $p < 0.05$). After adjusting for FFA nadir, neither baseline nor postchallenge TG differed with ethnicity ($p = 0.073$ and 0.192, respectively). The ethnic difference in FFA nadir disappeared after adjusting for peak insulin ($p = 0.073$).

Discussion: These data suggest that hyperinsulinemia-induced suppression of FFA among African Americans is a determinant of lower TG in this group.

Key words: insulin, free fatty acids, triglyceride, ethnicity, children

Introduction

African Americans are more hyperinsulinemic than whites (1) but have a less atherogenic lipid profile (lower triglycerides [TG] and higher high-density lipoprotein [HDL] cholesterol) (2–4). Even among prepubertal children, the acute insulin response to glucose in African Americans is twice the magnitude of that in whites, despite statistical adjustment for insulin sensitivity, which is lower among African Americans (5,6). Thus, at any given level of whole-body insulin sensitivity, African Americans are likely to experience greater insulin action. The purpose of this study was to test the hypothesis that greater postchallenge insulin among African Americans versus whites resulted in lower circulating free fatty acids (FFA) and TG.

Research Methods and Procedures

Subjects were selected from a larger group of children involved in an ongoing study on body-fat distribution and disease risk factors. Before this study, insulin sensitivity and body composition had been measured during routine annual evaluations (6); methodology for the insulin sensitivity test is repeated below.

For this study, 16 prepubertal males (Tanner stage 1; eight African American males and eight white males) were selected to avoid confounding effects of gender and maturation. In addition, subjects were matched for whole-body insulin sensitivity (0% to 2% difference within a pair) to control for the 42% lower insulin sensitivity observed among African Americans in the larger cohort (6). The selected subjects provided a range of insulin sensitivity values from low to high across the distribution of values observed in the larger group. No subject was taking medication known to affect lipid or carbohydrate metabolism. The Institutional Review Board of the University of Ala-

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bama at Birmingham approved the study, and subjects and their parents gave written informed consent after being informed of the risks.

Frequently sampled, intravenous glucose tolerance tests (FSIGTs) were administered in the General Clinical Research Center at the University of Alabama at Birmingham. A cannula was introduced into a forearm or antecubital vein of each arm, and baseline blood samples were obtained. Glucose (25% dextrose; 11.4 g/m^2) was administered intravenously, and additional blood samples (2 mL) were collected at 2, 3, 4, 5, 6, 8, 10, 14, 19, 22, 25, 30, 40, 50, 70, 100, 140, and 180 minutes after glucose administration. At 20 minutes after glucose administration, tolbutamide (25 mg/m^2) was injected intravenously. Laboratory analyses of insulin, glucose, and lipids have been described previously (6). FFAs were assayed with "nonesterified fatty acids" reagents obtained from Wako Diagnostics (Richmond, VA). The assay was modified to accommodate a reduced sample volume (10 μL), and use of a microplate. The intra-assay coefficient of variation is 0.8%. Insulin sensitivity was determined with minimal modeling (7). Acute insulin response was determined as the incremental area under the curve during the first 10 minutes of the test.

The main outcome measures were baseline FFA, FFA nadir, baseline TG, and postchallenge TG. FFA nadir was determined for each subject as the lowest serum FFA concentration observed during their glucose tolerance test. Postchallenge TG was likewise determined as serum TG concentration at the FFA nadir.

Data were log-transformed to improve normality of distribution. Ethnic differences in the physical and metabolic characteristics of the subjects were examined by ANOVA. The ethnic differences in FFA and TG that were observed were further analyzed by analysis of covariance to determine whether differences remained significant after adjusting for confounding variables. Relationships between variables were determined using Pearson correlation analyses. All analyses were performed with SAS for Windows version 6.12 (SAS Inc., Cary, NC). Differences or relationships with a p value of <0.05 were considered statistically significant.

Results

Serum TG concentrations determined at baseline were ~50% lower in African Americans than in whites (Table 1). There were no significant between-group differences in baseline concentrations of insulin, FFA, total cholesterol, or HDL cholesterol. Baseline and postchallenge FFA are shown in Figure 1. FFA nadir and postchallenge TG were lower among African Americans, whereas peak insulin and the acute insulin response were higher (Table 1). In all subjects, FFA nadir was inversely related to peak insulin ($r = -0.54$; $p < 0.05$; Figure 2A), and the association with acute insulin response approached significance ($r = -0.45$; $p = 0.079$; Figure 2B). Baseline and postchallenge TG were correlated with FFA nadir ($r = 0.51$ and 0.58, respectively; $p < 0.05$ for both).

The ethnic differences in baseline and postchallenge TG were eliminated by adjustment for FFA nadir (baseline TG, 0.43 ± 0.07 vs. 0.69 ± 0.11 mM/L, $p = 0.073$; postchallenge TG, 0.52 ± 0.06 vs. 0.67 ± 0.08 mM/L, $p = 0.192$; adjusted mean ± SEM for African Americans and whites, respectively). The ethnic difference in FFA nadir was no longer significant after adjustment for peak insulin (0.26 ± 0.01 vs. 0.30 ± 0.01 mEq/L; $p = 0.073$; adjusted mean ± SEM for African Americans and whites, respectively).

Discussion

African Americans are reported to have lower TG and higher HDL cholesterol than whites. This study was conducted to test the hypothesis that greater postchallenge insulin among African Americans contributes to the less atherogenic lipid profile by suppressing lipolysis and thereby limiting the amount of FFA substrate available for TG synthesis. We found that FFAs were lower during a glucose tolerance test in African American subjects, FFA nadir was correlated with peak insulin, statistical adjustment for FFA nadir eliminated the ethnic differences in baseline and postchallenge TG, and statistical adjustment for peak insulin eliminated the ethnic difference in FFA nadir. These results support the hypothesis that greater postchallenge insulin among African Americans limits lipolysis and lowers FFA, which in turn limits TG synthesis. Because most individuals spend the majority of their day in the postprandial state, postprandial metabolism may play an important role in determining the lipid profile.

Our observation that postchallenge FFA concentrations were lower in African Americans is supported by the findings of Srinivasan et al. (8). These authors reported that among the adolescent offspring of both diabetic and nondiabetic parents, insulin-mediated suppression of FFA after a glucose load was greater in African Americans than in whites. In the present study, the ethnic difference in FFA nadir ($p < 0.01$) was reduced to below the level of statistical significance by adjusting for peak insulin ($p = 0.073$). Insulin may reduce FFA concentration through its anti-lipolytic effect on adipose tissue (9). Basal FFAs are also reported to be lower among African American versus white adolescents, presumably due to greater circulating insulin (10).

The present data suggest that ethnic differences in both baseline and postchallenge TG were dependent on the suppression of FFA during the FSIGTs. Similarly, McKeigue et al. (11) demonstrated that plasma TG was related to postchallenge FFA in South Asian and European men and women. Furthermore, insulin-mediated suppression of FFA has been shown to account for 66% of the variation in plasma TG in normotriglyceridemic and hypertriglyceridemic individuals (12). Be-

Table 1. Physical and metabolic characteristics of subjects*

	African American ($n = 8$)	White ($n = 8$)	p value
Age (years)	8.09 ± 1.41	9.82 ± 1.05	0.014
Height (cm)	129 ± 8	136 ± 12	0.199
Weight (kg)	29.47 ± 5.46	37.08 ± 15.00	0.995
Fat mass (kg)	5.70 ± 4.24	9.30 ± 8.84	0.532
Lean mass (kg)	22.29 ± 2.50	25.01 ± 5.67	0.293
Baseline insulin (pmol/L)	58 ± 35	59 ± 26	0.858
Baseline FFA (mEq/L)	0.47 ± 0.15	0.49 ± 0.14	0.740
Baseline TG (mmol/L)	0.43 ± 0.10	0.79 ± 0.37	0.004
HDL cholesterol (mmol/L)	1.29 ± 0.35	1.07 ± 0.26	0.172
Total cholesterol (mol/L)	3.87 ± 0.56	4.32 ± 0.70	0.193
Peak insulin (pmol/L)	218 ± 102	100 ± 30	0.007
Insulin sensitivity ($\times 10^{-4}$/min/[μU/mL])	6.30 ± 3.45	6.29 ± 3.42	1.000
Acute insulin response (pmol/l × 10 min)	9282 ± 4272	4230 ± 1326	0.011
FFA nadir (mEq/L)	0.26 ± 0.02	0.30 ± 0.03	0.006
Postchallenge TG (mmol/L)	0.49 ± 0.07	0.77 ± 0.33	0.014

* Mean ± SD.

cause concentrations of TG are closely related to those of HDL cholesterol (13), it is possible that greater suppression of FFA during postprandial conditions is indirectly responsible for the greater HDL cholesterol reported in African Americans relative to whites.

In summary, the hyperinsulinemia-induced suppression of FFA among African American prepubertal children may be a determinant of their lower serum TG. Our results suggest that among African Americans, development of an atherogenic blood lipid profile may be impeded by enhanced suppression of FFA by insulin. However, hyperinsulinemia is associated with negative health outcomes, such as development of type 2 diabetes, hypertension, and ischemic heart disease (14,15). The long-term effects of chronic

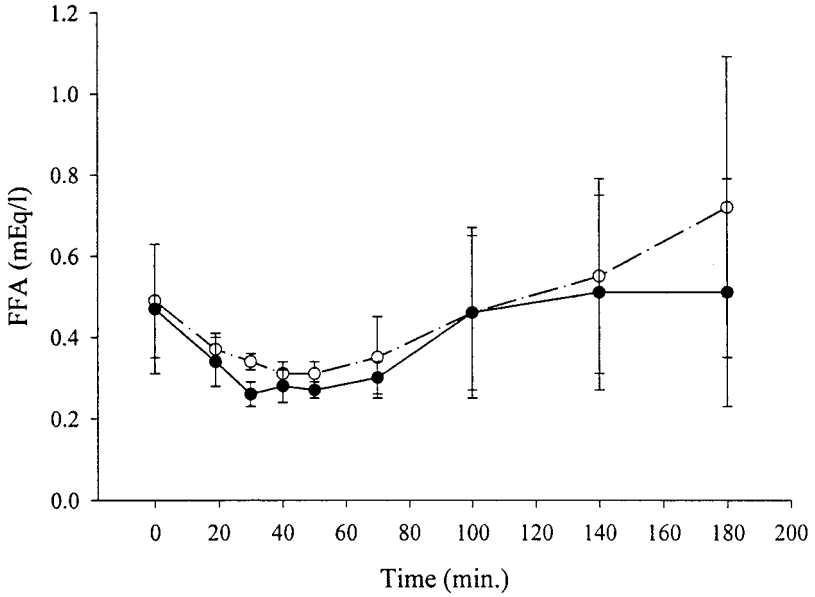

Figure 1. FFA at baseline and during the FSIGTs for African American (●) and white (○) boys. Mean ± SD.

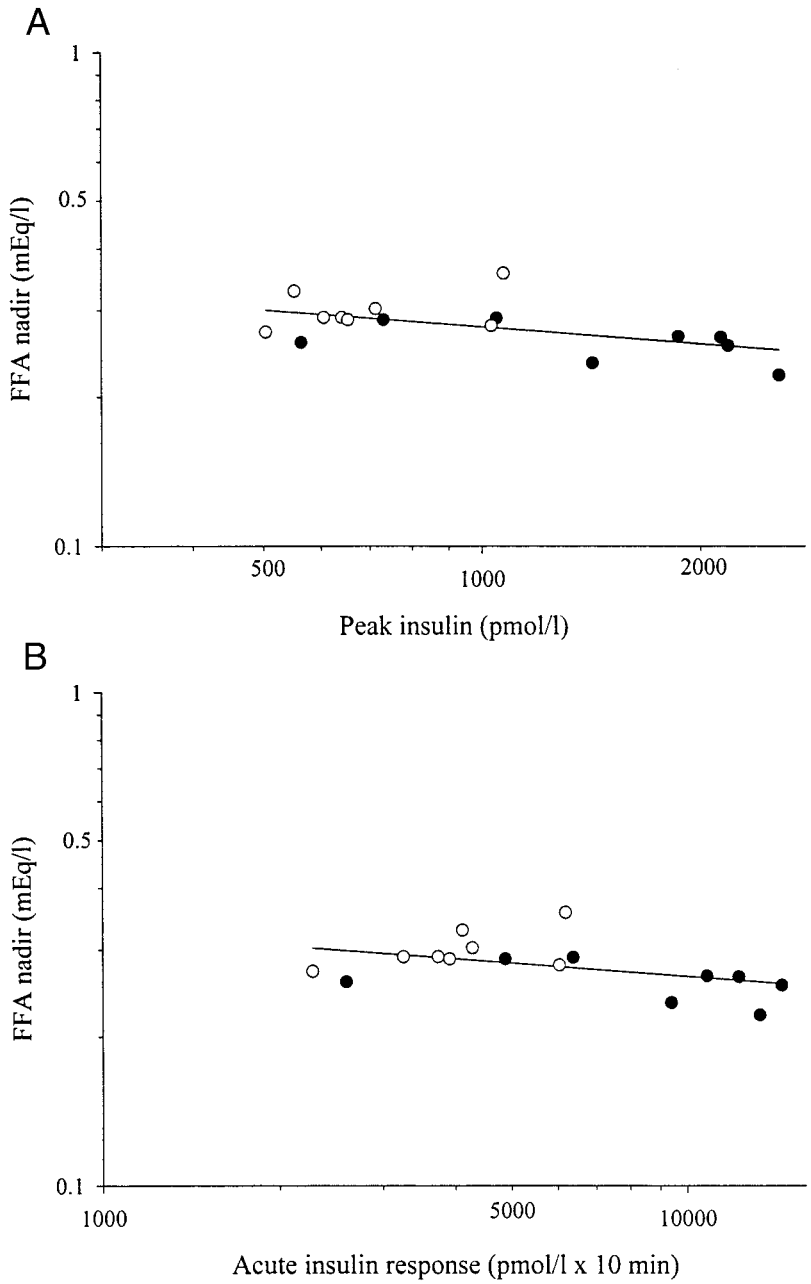

Figure 2. (A) FFA nadir versus peak insulin in African American (●) and white (○) boys; $R^2 = 0.29$, $p < 0.05$. (B) FFA nadir versus acute insulin response in African American (●) and white (○) boys; $R^2 = 0.20$, $p = 0.08$.

exposure to high levels of postprandial insulin among African Americans, National Institute of Child and Human Development remain to be determined.

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