Communication in Brief

Differences in Stimulated Androgen Levels in Black and White Obese Adolescent Females

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A B S T R A C T

Study Objective: Little is known about racial differences in androgen levels among obese children. The objective of this pilot study was to compare basal and stimulated androgen levels in a cross-sectional sample of obese black and white pubertal females.
Study Design, Setting, and Participants: This was cross-sectional study of obese (body mass index ≥ 95th percentile) but otherwise healthy female adolescents (10 black and 12 white; age range 8.8-13.9 y) who underwent adrenocorticotropic hormone stimulation testing at an academic medical center as part of a protocol for the study of obesity-related conditions.
Main Outcome Measures: Basal and stimulated androgen levels.
Results: White and black participants were similar with regard to pubertal stage, body mass index, percentage body fat, and fasting glucose and insulin levels. Black girls had lower stimulated levels of 17-hydroxyprogesterone, and the differences between basal and stimulated levels of 17-hydroxyprogesterone and androstenedione were lower in black girls. Body mass index was negatively correlated with stimulated cortisol in blacks only (r = -0.69, P = .03).
Conclusion: There appear to be race-related differences in stimulated androgen levels in obese adolescent females. These differences deserve further study, as measurements of androgen levels are commonly used in clinical practice and research.
Key Words: ACTH stimulation test, Race, Cortisol, Obesity, Overweight, Androstenedione, 17-Hydroxyprogesterone, Testosterone, 17-Hydroxypregnenolone, Dehydroepiandrosterone

Introduction

Measurement of basal and stimulated androgen levels is often performed during the evaluation of conditions related to obesity and insulin resistance, such as premature adrenarche and polycystic ovary syndrome. However, little is known about the clinical significance of potential racial differences in androgen levels among obese children. The objective of this pilot study was to compare basal and adrenocorticotropic (ACTH)-stimulated androgen levels in a cross-sectional sample of obese black and white pubertal females.

Methods

The study was approved by the University of Pittsburgh Institutional Review Board and was performed in the Pediatric Clinical and Translational Research Center at Children's Hospital of Pittsburgh. After obtaining informed consent, 22 obese (body mass index [BMI] ≥ 95th percentile) but otherwise healthy female adolescents (10 black and 12 white; age range 8.8 − 13.9 y) participated in the collection of baseline measures prior to further treatment for obesity at the Weight Management and Wellness Center at Children's Hospital of Pittsburgh. Power calculations indicate that at least 26 participants per group would be required to demonstrate a 30% difference between groups in stimulated androgen levels (based on estimates of a 100 ±35 ng/dL increase in 17 OH-progesterone). However, this was a pilot study with limited resources allowing for analysis of data from 22 subjects to generate pilot data. Exclusion criteria were chronic diseases or medications that could interfere with endocrine function or glucose regulation, neurologic/psychiatric disorders, and syndromic obesity.

A fasting blood sample was obtained for measurement of baseline androgens (total and free testosterone, sex hormone-binding globulin [SHBG]; Esoterix, Inc.), insulin (Luminex-200 system, Luminex Corporation), and lipid profile. Adrenocorticotropic hormone stimulation testing was performed by administering cosyntropin (Cortrosyn TM, Amphastar Pharmaceuticals) (0.25 mg, iv) over 1 minute. Blood samples were obtained for 17-hydroxypregnenelone, 17-hydroxyprogesterone, androstenedione, and dehydroepiandrosterone (DHEA) before administration of Cortrosyn and 30 minutes post-infusion.[1] Homeostasis model assessment-insulin resistance (HOMA-IR = fasting insulin

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[μU/mL[× fasting glucose [mmol/L] divided by 22.5) was calculated to express basal insulin resistance. Body composition was measured by air displacement plethysmography (BOD POD; COSMED, Concord CA).

Two-sided *t* tests were used to compare continuous variables between black and white participants. Mann-Whitney *U* tests were used for non-normally distributed outcomes. Pearson correlation coefficients were calculated to quantify the association between BMI and outcome variables after log transformation of non-normally distributed data, and partial correlations were calculated after controlling for race or BMI. Data are expressed as the mean ± SEM unless otherwise noted.

Results

The anthropometric and metabolic characteristics of participants according to race are shown in Table 1. Age and pubertal stage (mean Tanner stage = 4 ± 1 for breasts and pubic hair) did not differ between the groups. Three white and 2 black participants were post-menarcheal. Testing was scheduled to target the follicular phase of the menstrual cycle; however, 1 black and 1 white participant had progesterone levels > 200 ng/dL on the day of testing. Body mass index, percentage body fat, fasting glucose, lipids, glycosylated hemoglobin (HbA1C), fasting insulin and C-peptide, HOMA-IR, total/free testosterone, and sex hormone binding globulin (SHBG) were not significantly different among white and black participants.

Baseline and stimulated adrenal hormone levels according to race are shown in Figure 1. Stimulated 17-hydroxyprogesterone levels were 32% lower in black girls. The response to ACTH stimulation in 17-hydroxyprogesterone (Δ 17-hydroxyprogesterone) was 28% lower in black girls, and Δ androstenedione was 42% lower in black compared with white girls. There were no significant differences according to race in baseline or stimulated cortisol, DHEA, or 17-hydroxypregnenelone.

Stimulated cortisol and Δ cortisol were negatively correlated with BMI (r = -0.434, P = .04 and r = -0.478, P = .03). After controlling for race, correlations with BMI were no longer significant for the study group as a whole (stimulated cortisol r = -0.369, P = .15; Δ cortisol r = -0.397, P = .11). When the correlation analysis was performed separately for blacks and whites, BMI was negatively correlated with stimulated cortisol in blacks only (Figure 2, r = -0.6934, P = .03).

Delta cortisol was negatively correlated with both fasting insulin (r = -0.478, P = .02) and HOMA-IR (r = -0.431, P = .05). Sex hormone binding globulin was negatively correlated with fasting insulin (r = -0.434, P = .04). However, after controlling for BMI, these correlations were no longer significant. After controlling for race, SHBG was negatively correlated with BMI (r = -0.517, P = .03) and positively associated with stimulated androstenedione (r = 0.484, P = .05) for the study group as a whole. Neither BMI nor percentage body fat were significantly correlated with other measures from the ACTH stimulation test.

Table 1
Anthropometric and Metabolic Characteristics of Participants According to Race

	White Girls (N=12)	Black Girls (N=10)	*P*
Age (yr)	11.8 ± 0.4	11.2 ± 0.5	0.36
BMI (kg/m^2)	28.4 ± 1.1	31.2 ± 1.9	0.21
BMI SDS	2.30 ± 0.22	3.17 ± 0.35	0.42
Percent body fat (%)	35.6 ± 1.8	39.1 ± 2.5	0.24
Fat mass (kg)	25.5 ± 2.0	30.1 ± 4.9	0.37
Lean mass (kg)	46.3 ± 3.3	44.2 ± 3.3	0.67
Triglycerides (mg/dL)	121 ± 22	80 ± 7	0.10
Cholesterol (mg/dL)	141 ± 10	128 ± 8	0.35
LDL (mg/dL)	85 ± 8	79 ± 7	0.64
HDL (mg/dL)	37 ± 4	35 ± 2	0.75
VLDL (mg/dL)	19 ± 3	13 ± 1	0.12
TG/HDL	3.9 ± 0.8	2.4 ± 0.2	0.11
Non-HDL cholesterol (mg/dL)	104 ± 9.4	92 ± 7.7	0.37
HbA1C (%)	5.2 ± 0.1	5.3 ± 0.1	0.81
Fasting glucose (mg/dL)	87 ± 2.2	84 ± 1.7	0.36
Fasting insulin (μU/mL)*	34.7 ± 5.5	32.4 ± 5.1	0.74
Fasting C-peptide (ng/mL)*	3.07 ± 0.38	2.50 ± 0.40	0.32
HOMA-IR*	7.56 ± 1.34	6.72 ± 1.06	0.64
Testosterone (ng/dL)*	18.0 ± 4.2	20.9 ± 9.7 (n=9)	0.80
Free testosterone (pg/mL)*	2.33 ± 0.49	3.29 ± 1.87 (n=9)	0.67
Percent free testosterone (%)	1.37 ± 0.12	1.28 ± 0.14 (n=9)	0.63
SHBG (nmol/L)	30.5 ± 4.1	26.3 ± 4.1	0.43

* Data not normally distributed. Mann Whitney U test for non-parametric data was used to compare differences between groups.

Discussion

The results of this study suggest that in obese adolescent females, there are race-related differences in stimulated androgen levels. Black race was associated with lower stimulated levels of 17-hydroxyprogesterone and a smaller magnitude of increase 17-hydroxyprogesterone and androstenedione in response to ACTH. Stimulated cortisol levels were negatively associated with BMI in black females. Our results are in agreement with (1) studies in adults showing black women to have lower androstenedione levels than white women, although the black women had higher BMI[2,3]; and (2) a cross-sectional survey of healthy children (n = 360 girls; 6-18 y), which showed that black girls had lower serum AM androstenedione levels than white girls with similar weights and Tanner staging.[4] We are unaware of similar studies that have compared stimulated androgens in black and white women or children. The physiological significance of this racial difference in androstenedione is unknown, but differences in body fat distribution, insulin resistance, and genetic factors may be contributory.

We did not observe a significant relationship between measures of adiposity and androgen levels, likely because all of the participants in this study were obese. Other cohort studies have shown obese prepubertal and pubertal girls to have significant hyperandrogenemia and low SHBG as compared with lean girls, and that weight loss promotes decreases in testosterone levels.[5] In the present study, the participants did not have clinical evidence of hyperandrogenism. Thus, characteristics of the obese but otherwise healthy study population may have decreased the apparent relationship between androgen excess and adiposity.

The relationship between measures of adrenocortical activity and adiposity among developing children is confounded by environmental and socioeconomic factors that also have an impact on cortisol levels. Moreover, race differences in stimulated cortisol response in obese black