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Abstract—Although insulin sensitivity is correlated with high blood pressure in adults, it is unclear whether such a relationship exists in children across ethnic groups. Therefore, the aims of the study were to establish (1) if body composition and insulin sensitivity were related to blood pressure in children, and (2) if any differences in blood pressure between white and black children were explained by body composition and/or insulin sensitivity. Insulin sensitivity and the acute insulin response were established by the minimal model and body composition by dual-energy X-ray absorptiometry. Blood pressure was recorded in the supine position. Body composition, fasting insulin ($P<0.01$), and the acute insulin response ($P<0.05$) were positively related to systolic blood pressure but not to diastolic blood pressure, and insulin sensitivity ($P<0.001$) was negatively related to systolic blood pressure but not to diastolic blood pressure. Insulin sensitivity was negatively associated with systolic and diastolic blood pressure after adjustment for body composition ($P<0.01$). Black children had higher systolic (110 ± 9.2 versus 105 ± 8.5 mm Hg, $P=0.01$) and diastolic (59 ± 7.0 versus 54 ± 8.0 mm Hg, $P<0.01$) blood pressure than did white children. The ethnic difference in blood pressure was not explained by body composition, fasting insulin, acute insulin response, or insulin sensitivity. In conclusion, the relationship between insulin sensitivity and systolic blood pressure is evident early in life. Black ethnicity and low insulin sensitivity contribute independently to higher blood pressure in children. **(*Hypertension*. 2002; 40:18-22.)**

Key Words: insulin resistance ■ blood pressure ■ ethnicity ■ children

In adults, hypertension has been associated with insulin resistance and hyperinsulinemia, all of which are components of the insulin resistance syndrome.[1–4] It has been suggested that insulin resistance[3,5] and the compensatory hyperinsulinemia[6,7] may play a causal role in the development of hypertension.[8,9] Insulin resistance and hyperinsulinemia appear to develop in obese children at an early age,[10,11] as does the relationship between fasting insulin and blood pressure, which appears to be independent of adiposity.[12] It is less clear if a relationship between insulin sensitivity and blood pressure exists in children. In a small group of prepubertal white children, only diastolic blood pressure appeared to be correlated with insulin sensitivity after adjusting for percentage of body fat.[11]

The relationship between insulin resistance and hypertension has also been found in black adults.[9,13,14] Blacks are more insulin resistant[15] and have an increased prevalence of essential hypertension[16] compared with that of whites. However, the age at which ethnic differences in blood pressure emerge has not been clearly delineated. The Coronary Artery Risk Development in Young Adults (CARDIA) study has documented significant differences in blood pressure between blacks and whites in the young adult age group.[17] The results of studies in school-age children and adolescents have been mixed, with some showing higher blood pressure in black children compared with white children,[18,19] and others reporting no differences.[17,20]

The aims of the present study were therefore (1) to establish if blood pressure in prepubertal children was associated with fasting insulin, insulin sensitivity, and the acute insulin response, and if this relationship was independent of total body fat and lean mass; and (2) to establish if blood pressure was different between white and black children, and if any difference was explained by body composition, insulin sensitivity, and acute insulin response.

Methods

Subjects

Data for this analysis included measures from 101 children (58 whites and 43 blacks, 51 boys and 50 girls). These children were part of an ongoing longitudinal study of the etiology of obesity and associated disorders in children. A total of 220 children were initially recruited through newspaper and radio advertisements and word of mouth in the city of Birmingham, Alabama. The present study included data from only those subjects determined to be at Tanner

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TABLE 1. Subject Characteristics by Gender and Ethnic Group

	Whites (n=58)			Blacks (n=43)		
	Boys	Girls	Total	Boys	Girls	Total
Age, y	9.5±1.2	9.5±1.2	9.5±1.2	8.9±1.3	9.4±1.2	9.1±1.3
Height, cm	137.8±9.1	136.0±9.3	136.9±9.2	137.1±9.7	136.9±10.3	137.0±9.9
Weight, kg	38.1±10.6	37.5±13.8	37.8±12.2	37.0±10.5	36.0±12.1	36.5±11.2
Total fat mass, kg	10.1±6.9	11.2±8.8	10.6±7.9	9.1±7.0	10.4±7.2	9.8±7.1
Total lean mass, kg	25.2±41.1	24.0±54.4	24.6±48.2	25.9±43.1	23.7±52.5	24.8±48.6
% Body fat	24.8±11.6	27.7±10.8	26.3±11.2	22.4±11.4	26.7±9.8	24.5±10.7
Fasting insulin, pmol/L	75.7±27.8	89.6±62.5	82.6±48.6	84.7±49.3	92.4±50.7	88.2±50.0
Fasting glucose, mmol/L	94.5±6.0	92.4±4.7	93.5±5.5	94.5±5.7	93.2±6.8	93.9±6.2
Insulin sensitivity, $\times 10^{-4} \cdot min^{-1} \cdot pmol/L$*	55.6±31.3	49.3±33.3	52.8±31.9	36.1±16.7	27.8±18.8	31.9±18.1
Acute insulin response, pmol/L×10 min†	4237±2501	5007±4049	4625±3361	10 605±5445	11 105±5021	10 848±5188
Systolic blood pressure, mm Hg‡	106±9	104±8	105±9	111±9	109±9	110±9
Diastolic blood pressure, mm Hg‡§	57±7	52±8	54±8	60±7	58±7§	59±7

Values are mean±SD.
*$P<0.01$, †$P=0.001$, and ‡$P=0.01$ for ethnic difference; §$P<0.05$ for gender differences.

stage I by physician evaluation of both breast development and pubic hair in females and of genitalia in males, and it included children who had complete measures of blood pressure, body composition, and insulin sensitivity. In the event of multiple data being available for any child, we used the data from the initial study visit. Ethnicity was determined by self-report and based on both parents and both sets of grandparents reporting to be either white or black. The study was approved by the Institutional Review Board at the University of Alabama at Birmingham (UAB), and all procedures were in accordance with institutional guidelines. Written informed consent for the study was obtained from the parents. Subjects were healthy and were not taking any medication known to affect body composition or blood pressure.

Protocol

Children were admitted to the General Clinical Research Center (GCRC) for an overnight visit. Height and weight were recorded to the nearest 0.1 cm and 0.1 kg, respectively. On the morning after admission to the GCRC and after an overnight fast, subjects underwent a tolbutamide-modified frequently sampled intravenous glucose tolerance test, as described previously.[10] Blood pressure was recorded on 2 separate occasions after a 5-minute rest in the supine position with a Critikon Dynamap 8100 T (Critikon). The average of 2 measurements was used in the analysis.

Two weeks after visiting the GCRC, children came to the Energy Metabolism Laboratory in the Department of Nutrition Sciences at UAB for body composition (fat and lean mass) assessment by dual-energy X-ray absorptiometry (Lunar DPX-L densitometer; Lunar Radiation; Pediatric software, version 1.5). Subjects were scanned in light clothing while lying flat on their backs with arms at their sides.

Statistical Analysis

Ethnic and gender differences in physical and metabolic characteristics were examined by use of a general linear model. Variables that were not normally distributed (fasting insulin, insulin sensitivity, acute insulin response, body weight, and total fat mass) were log-transformed for this analysis only. Spearman correlation analysis was used to establish associations between blood pressure and measures of body composition, insulin, and glucose. Univariate linear regression analysis was used to further assess the relationship between blood pressure and measures of insulin, total fat mass, and total lean mass. Multivariate linear regression analysis was used to establish if (1) the relationships between measures of insulin and blood pressure were independent of body composition and (2) if the ethnic difference in blood pressure remained after adjusting for body composition and measures of insulin. In the linear regression analysis, systolic blood pressure or diastolic blood pressure were the dependent variables, whereas measures of insulin (fasting insulin, acute insulin response, insulin sensitivity) and body composition (total fat mass and total lean mass) were the independent variables. We did not adjust for other potentially confounding variables such as height and age, because these variables were not strongly correlated with blood pressure after controlling for body composition (data not shown). All analyses were performed using SPSS version 9.0 (SPSS Inc), with a type I error set at $P<0.05$.

Results

Physical Characteristics of Subjects

There were no differences in age, height, weight, or body composition between white and black children or between boys and girls (Table 1).

Ethnic Effect on Blood Pressure, Body Composition, Glucose, and Insulin Measures

As previously shown by our group,[10] black children had lower insulin sensitivity and a significantly higher acute insulin response than did white children; however, there were no differences in fasting glucose or fasting insulin (Table 1). Black children had higher systolic and diastolic blood pressure than did white children ($P<0.01$; Table 1). Boys had significantly higher diastolic ($P<0.05$) but not systolic blood pressure than did girls ($P>0.05$).

Spearman Correlation Analysis for Blood Pressure, Body Composition and Insulin Measures

All the body composition measures, age, height, fasting insulin, and the acute insulin response were positively correlated to systolic blood pressure but not to diastolic blood pressure (Table 2). Insulin sensitivity was negatively correlated to systolic blood pressure but not to diastolic blood pressure. Fasting glucose was not correlated to systolic or diastolic blood pressure (Table 2).

TABLE 2. Spearman Correlation Coefficients Between Blood Pressure and Measures of Body Composition, Insulin, and Glucose

	Systolic Blood Pressure	Diastolic Blood Pressure
Age	0.24*	0.03
Height	0.23†	0.04
Weight	0.27*	−0.01
Total fat mass	0.24*	−0.03
Total lean mass	0.27*	0.02
% Body fat	0.22†	−0.03
Fasting insulin	0.34‡	0.09
Fasting glucose	0.18	0.07
Insulin sensitivity	−0.35‡	−0.21†
Acute insulin response	0.28*	0.20†

Correlation analysis of non–log transformed data: *$P<0.01$, †$P<0.05$, and ‡$P<0.001$.

Univariate Regression Analysis for Systolic and Diastolic Blood Pressure

Univariate analysis indicated that fasting insulin, the acute insulin response, total fat mass, and total lean mass were positively related to systolic blood pressure but not to diastolic blood pressure. Insulin sensitivity was negatively related to both systolic and diastolic blood pressure, but this relationship was only significant for systolic blood pressure (Table 3).

Multiple Regression Analysis to Assess the Contribution of Insulin Measures and Body Composition on Blood Pressure

Fat mass and lean mass were not related to either systolic or diastolic blood pressure when entered into the same regression model (Table 4, model 1). Fasting insulin and the acute insulin response were no longer significantly related to systolic blood pressure after adjustment for body composition and were not related to diastolic blood pressure (Table 4, models 2 and 3). In contrast, insulin sensitivity remained significantly related to systolic blood pressure and became significantly related to diastolic blood pressure when adjusted for body composition (Table 4, model 4).

TABLE 3. Results of Univariate Regression Analysis to Assess the Relationship Between Systolic and Diastolic Blood Pressure and Measures of Insulin and Body Composition

	Systolic Blood Pressure		Diastolic Blood Pressure	
	$\beta\pm$SEE	P	$\beta\pm$SE	P
Model 1	$R^2=0.08$		$R^2=0.002$	
Fasting insulin	0.35±0.12	0.006	−0.04±0.11	NS
Model 2	$R^2=0.06$		$R^2=0.03$	
Acute insulin response	0.003±0.001	0.016	0.002±0.001	NS
Model 3	$R^2=0.14$		$R^2=0.04$	
Insulin sensitivity	−0.81±0.21	<0.001	−0.365±0.190	0.054
Model 4	$R^2=0.08$		$R^2=0.003$	
Total fat mass	0.35±0.12	0.003	−0.06±0.11	NS
Model 5	$R^2=0.08$		$R^2=0.0001$	
Total lean mass	0.54±0.18	0.004	0.036±0.16	NS

β, parameter estimate.

TABLE 4. Results of Multiple Regression Analysis to Assess the Contribution of Insulin Measures and Body Composition on Blood Pressure

	Systolic Blood Pressure		Diastolic Blood Pressure	
	$\beta\pm$SEE	P	$\beta\pm$SEE	P
Model 1	$R^2=0.10$		$R^2=0.01$	
Fat mass	0.21±0.16	NS	−0.13±0.14	NS
Lean mass	0.32±0.24	NS	0.17±0.22	NS
Model 2	$R^2=0.11$		$R^2=0.01$	
Fat mass	0.11±0.20	NS	−0.13±0.18	NS
Lean mass	0.31±0.24	NS	0.17±0.22	NS
Fasting insulin	0.16±0.19	NS	−0.01±0.17	NS
Model 3	$R^2=0.12$		$R^2=0.04$	
Fat mass	0.17±0.16	NS	−0.18±0.14	NS
Lean mass	0.28±0.24	NS	0.12±0.22	NS
Acute insulin response	0.002±0.001	NS	0.002 ±0.001	NS
Model 4	$R^2=0.17$		$R^2=0.08$	
Fat mass	0.01±0.17	NS	−0.30±0.15	NS
Lean mass	0.35±0.23	NS	0.19±0.21	NS
Insulin sensitivity	−0.67±0.24	0.006	−0.58±0.22	0.009

Gender coded as boys, 1; girls, 2. β indicates parameter estimate.

Multiple Regression Analysis to Assess the Contribution of Body Composition and Insulin Measures on the Ethnic Difference in Blood Pressure.

Multiple regression analysis indicated that systolic and diastolic blood pressure was different between the 2 ethnic groups ($P<0.01$), but only diastolic blood pressure was different between the 2 genders ($P<0.05$) (Table 5, model 1). Neither body composition nor insulin measures contributed to the ethnic difference in systolic blood pressure (Table 5, models 2 to 4). Insulin sensitivity (but not fasting insulin or the acute insulin response) remained related to systolic and diastolic blood pressure independently of ethnicity; however, this relationship was only significant for systolic blood pressure.(Table 5, models 2 to 4).

Discussion

The present study demonstrates that in healthy prepubertal black and white children, whole-body insulin sensitivity was negatively related to systolic blood pressure, and this relationship was independent of total body fat and lean mass. Furthermore, in this cohort, black children had higher systolic and diastolic blood pressure than did white children. The ethnic difference in blood pressure could not be explained by differences in body composition or insulin measures.

Previous studies have shown that in adults, hyperinsulinemia and decreased insulin sensitivity are correlated with blood pressure.[3,5,21] Although several large epidemiological studies in children have reported a positive relationship

TABLE 5. Results of Multiple Regression Analysis to Explore the Effect of Measures of Insulin and Body Composition on the Ethnic Difference in Blood Pressure

	Systolic Blood Pressure		Diastolic Blood Pressure	
	$\beta \pm$SEE	*P*	$\beta \pm$SEE	*P*
Model 1	R^2=0.08		R^2=0.13	
Ethnicity	4.6±1.8	0.009	4.5±1.5	0.003
Gender	−2.0±1.8	NS	−3.4±1.5	0.026
Model 2	R^2=0.18		R^2=0.13	
Ethnicity	4.9±1.7	0.005	4.5±1.5	0.003
Gender	−2.2±1.8	NS	−3.4±1.6	0.032
Fat mass	0.30±0.16	0.054	−0.01±0.14	NS
Lean mass	0.18±0.25	NS	−0.03±0.22	NS
Model 3	R^2=0.19		R^2=0.13	
Ethnicity	4.8±1.8	0.006	4.6±1.5	0.004
Gender	−2.2±1.8	NS	−3.4±1.6	0.036
Fat mass	0.23±0.20	NS	0.02±0.17	NS
Lean mass	0.16±0.25	NS	−0.02±0.22	NS
Fasting insulin	0.11±0.18	NS	−0.04±0.16	NS
Model 4	R^2=0.22		R^2=0.16	
Ethnicity	4.8±2.3	0.036	3.6±2.0	0.084
Gender	−2.2±1.7	NS	−3.6±1.6	0.024
Fat mass	0.19±0.18	NS	−0.13±0.16	NS
Lean mass	0.24±0.25	NS	−0.002±0.221	NS
Acute insulin response	−0.002±0.002	NS	−0.0005±.002	NS
Insulin sensitivity	−0.57±0.27	0.040	−0.43±0.25	0.080

Ethnicity coded as whites, 1; blacks, 2. Gender coded as boys, 1; girls, 2. Parameter estimate (β) for ethnicity represents the magnitude of the higher systolic blood pressure in blacks after controlling for the other variables in each model.

between fasting insulin and blood pressure,[22] there is a scarcity of data regarding the relationship between directly measured insulin sensitivity and blood pressure in children. In the present study, we found that fasting insulin and the acute insulin response were positively related to systolic blood pressure, and insulin sensitivity was negatively related to systolic blood pressure. After adjustment for differences in body composition, however, only insulin sensitivity remained significantly related to systolic blood pressure.

Our results are in agreement with previous epidemiological studies in children[22] that found that the relationship between fasting insulin and blood pressure was partially confounded by differences in body size, expressed as either body mass index[12] or body weight.[23,22] However, they disagree with 1 previous study[11] in white children only, in which insulin sensitivity adjusted for percentage body fat was correlated with diastolic but not systolic blood pressure. Differences between the current study and the previous one could be owing to the methods used to establish insulin sensitivity (intravenous glucose tolerance test versus hyperinsulinemic clamp) and body composition (dual energy X-ray absorptiometry versus $H_2{}^{18}O$ dilution). In addition, that study was performed in a small group (n=20) of lean prepubertal white children,[11] whereas the present study represented both prepubertal black and white children with a large variation in body composition.

In general, the lack of correlation between diastolic blood pressure and insulin measures in the present study is not surprising, because in children the correlation between fasting insulin and diastolic blood pressure has been shown to be quite weak, particularly once differences in body mass index are accounted for;[23,12,22]

The fact that fat mass, in the present study, was not independently related to systolic blood pressure in multivariate analysis suggests that the effect of adiposity on systolic blood pressure control is mediated by insulin resistance, as has been previously reported in adults.[24] Clearly, this conclusion is limited by the cross-sectional nature of the present data and is confined to normal prepubertal children of 2 distinct ethnic groups.

Whether insulin resistance per se leads to higher blood pressure can only be addressed through prospective studies. Several longitudinal studies have been performed in which the incidence of hypertension has been associated with fasting insulin[25,26] and postglucose challenge insulin levels[27] in whites. In addition, the CARDIA study explored the longitudinal relationship between fasting insulin and the incidence of hypertension in both white and black adults. Again, fasting insulin was related to the incidence of hypertension. However, this relationship was only true for blacks in univariate analysis.[25]

The nature of the relationship between insulin resistance and blood pressure has not been adequately explained. Nevertheless, a whole array of potential mechanisms by which insulin resistance and the accompanying hyperinsulinemia may alter blood pressure have been proposed and include the insulin-mediated effects on the sympathetic nervous system[28,29] and renal sodium reabsorption.[30] It has been suggested, on the one hand, that high blood pressure develops because of the lack of resistance to these secondary effects of insulin,[31] whereas on the other hand, insulin resistance may lead to endothelial dysfunction.[32] Alternatively, some unknown common factor might be responsible for both insulin resistance and high blood pressure. In this respect, several investigators have suggested that sympathetic overactivity may lead to structural changes in the microvasculature that not only raise blood pressure but also decrease peripheral glucose uptake with a concomitant decrease in insulin sensitivity.[33,34]

There is no doubt that black adults have an increased prevalence of essential hypertension[16] compared with that of whites; however, the age at which ethnic differences in blood pressure emerge is controversial.[20] We found that blood pressure was higher in black children than in white children, even after adjusting for total body fat and total body lean mass. Our results are in agreement with those obtained from the Third National Health and Nutrition Examination Survey.[18] This large national study included >7600 black, white, and Mexican American subjects between the ages of 6 to 24 years. Blood pressure in that study was measured in the sitting position and was adjusted for sex, age, and socioeconomic status. In contrast, our results are in disagreement with a recent report that pooled data from over 47 000 black and white children and adolescents between the ages of 5 to 17 years who participated in 8 different epidemiological studies. In that report, the investigators could not demonstrate any consistent ethnic differences in blood pressure after adjustment by sex, age, weight, and height.[17] The discrepancies

between studies could be caused by differences in the standardization of procedures, choice of instrument, number of measurements recorded, adjustment by confounding variables, and the age of the population studied, among others.[35]

Perspectives

This study is one of the first to explore the relationship between blood pressure and insulin sensitivity in a biethnic group of prepubertal children adjusting for both whole-body fat and lean mass. We found that in white and black children, insulin sensitivity was significantly related to systolic blood pressure after adjusting for total fat and total lean mass. Although the degree of obesity has typically been viewed as a major confounder in the relationship between insulin and blood pressure both in children and adults, our results point to the contrary and may suggest that insulin resistance is a more important determinant of systolic blood pressure in children than body fat. Furthermore, in this cohort, black children had higher blood pressure than did white children independent of body composition. It appears that black ethnicity and decreased insulin sensitivity are independently related to higher blood pressure even at an early age.

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