Insulin Sensitivity and Blood Pressure in Black and White Children

Martha L. Cruz, Terry T-K. Huang, Maria S. Johnson, Barbara A. Gower, Michael I. Goran

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 resistance3,5 and the compensatory hyperinsulinemia6,7 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 resistant15 and have an increased prevalence of essential hypertension16 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...
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 accor-
dance 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. 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
UBA 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 character-
istics 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, 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 corre-
lated to systolic blood pressure but not to diastolic blood
pressure (Table 2). Insulin sensitivity was negatively corre-
lated to systolic blood pressure but not to diastolic blood
pressure. Fasting glucose was not correlated to systolic or
diastolic blood pressure (Table 2).

### Table 1. Subject Characteristics by Gender and Ethnic Group

<table>
<thead>
<tr>
<th></th>
<th>Whites (n=58)</th>
<th></th>
<th>Blacks (n=43)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boys</td>
<td>Girls</td>
<td>Total</td>
<td>Boys</td>
</tr>
<tr>
<td>Age, y</td>
<td>9.5±1.2</td>
<td>9.5±1.2</td>
<td>9.5±1.2</td>
<td>8.9±1.3</td>
</tr>
<tr>
<td>Height, cm</td>
<td>137.8±9.1</td>
<td>136.0±9.3</td>
<td>136.9±9.2</td>
<td>137.1±9.7</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>38.1±10.6</td>
<td>37.5±13.8</td>
<td>37.8±12.2</td>
<td>37.0±10.5</td>
</tr>
<tr>
<td>Total fat mass, kg</td>
<td>10.1±6.9</td>
<td>11.2±8.8</td>
<td>10.6±7.9</td>
<td>9.1±7.0</td>
</tr>
<tr>
<td>Total lean mass, kg</td>
<td>25.2±41.1</td>
<td>24.0±54.4</td>
<td>24.6±48.2</td>
<td>25.9±43.1</td>
</tr>
<tr>
<td>% Body fat</td>
<td>24.8±11.6</td>
<td>27.7±10.8</td>
<td>26.3±11.2</td>
<td>22.4±11.4</td>
</tr>
<tr>
<td>Fasting insulin, pmol/L</td>
<td>75.7±27.8</td>
<td>89.6±62.5</td>
<td>82.6±48.6</td>
<td>84.7±49.3</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>94.5±6.0</td>
<td>92.4±4.7</td>
<td>93.5±5.5</td>
<td>94.5±5.7</td>
</tr>
<tr>
<td>Insulin sensitivity, ×10^-4 · min^-1 · pmol/L*</td>
<td>55.6±31.3</td>
<td>49.3±33.3</td>
<td>52.8±31.9</td>
<td>36.1±16.7</td>
</tr>
<tr>
<td>Acute insulin response, pmol/L×10 min†</td>
<td>4237±2501</td>
<td>5007±4049</td>
<td>4625±3361</td>
<td>10 605±5445</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg‡</td>
<td>106±9</td>
<td>104±8</td>
<td>105±9</td>
<td>111±9</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg§</td>
<td>57±7</td>
<td>52±8</td>
<td>54±8</td>
<td>60±7</td>
</tr>
</tbody>
</table>

Values are mean±SD. *P<0.01, †P<0.001, and ‡P=0.01 for ethnic difference; §P<0.05 for gender differences.
TABLE 2. Spearman Correlation Coefficients Between Blood Pressure and Measures of Body Composition, Insulin, and Glucose

<table>
<thead>
<tr>
<th></th>
<th>Systolic Blood Pressure</th>
<th>Diastolic Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.24*</td>
<td>0.03</td>
</tr>
<tr>
<td>Height</td>
<td>0.23†</td>
<td>0.04</td>
</tr>
<tr>
<td>Weight</td>
<td>0.27‡</td>
<td>-0.01</td>
</tr>
<tr>
<td>Total fat mass</td>
<td>0.24*</td>
<td>-0.03</td>
</tr>
<tr>
<td>Total lean mass</td>
<td>0.27*</td>
<td>0.02</td>
</tr>
<tr>
<td>% Body fat</td>
<td>0.22†</td>
<td>-0.03</td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>0.34‡</td>
<td>0.09</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>0.18</td>
<td>0.07</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>-0.35‡</td>
<td>-0.21†</td>
</tr>
<tr>
<td>Acute insulin response</td>
<td>0.28*</td>
<td>0.20†</td>
</tr>
</tbody>
</table>

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, but this relationship was only significant for systolic blood pressure (Table 3).

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

<table>
<thead>
<tr>
<th></th>
<th>Systolic Blood Pressure</th>
<th>Diastolic Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β±SEE</td>
<td>P</td>
</tr>
<tr>
<td></td>
<td>β±SE</td>
<td>P</td>
</tr>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>0.35±0.12</td>
<td>0.006</td>
</tr>
<tr>
<td>Model 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute insulin response</td>
<td>0.003±0.001</td>
<td>0.016</td>
</tr>
<tr>
<td>Model 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>-0.81±0.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total fat mass</td>
<td>0.35±0.12</td>
<td>0.003</td>
</tr>
<tr>
<td>Model 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total lean mass</td>
<td>0.54±0.18</td>
<td>0.004</td>
</tr>
</tbody>
</table>

β, parameter estimate.

Acute insulin response 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 systolic blood pressure (Table 5, model 2) was significant when adjusted for body composition (Table 4, model 4).

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. Although several large epidemiological studies in children have reported a positive relationship
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 children22 that found that the relationship between fasting insulin and blood pressure was partially confounded by differences in body size, expressed as either body mass index12 or body weight.23,22 However, they disagree with 1 previous study11 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 H218O 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 insulin25,26 and postchallenge glucose challenge insulin levels27 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.

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 resistance and the accompanying hyperinsulinemia may alter blood pressure (Table 5). 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 resistance and the accompanying hyperinsulinemia may alter blood pressure. 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.
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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References
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