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Body Fat at Birth and Cord Blood Levels of Insulin, Adiponectin, Leptin, and Insulin-like Growth Factor-I in Small-for-Gestational-Age Infants

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Background. Low birthweight has been associated with an increased risk of obesity, insulin resistance, and diabetes in adulthood. The aim of this study was to evaluate IGF-I, adiponectin, insulin levels, and body fat in small-for-gestational-age (SGA) infants at birth.

Methods. We performed a transverse comparative study in SGA and appropriate-for-gestational-age (AGA) infants. The study was conducted at the Hospital of Gynecology and Obstetrics in Leon, Mexico. Weight, length, and percent of body fat were evaluated during the first 48 h of birth. Glucose, insulin, leptin, adiponectin, and IGF-I levels in cord blood were measured.

Results. We studied 100 infants (50 SGA and 50 AGA). A history of diabetes in a second-degree relative was higher in SGA infants than in AGA infants (48.0 vs. 30.0%, respectively; $p = 0.03$). Glucose, adiponectin, insulin and IGF-I levels were similar between the groups. Leptin levels and percentage of body fat were lower in SGA than AGA (15.3 vs. 23.4 ng/mL; $p = 0.003$, 11.1 vs. 12.7%; $p < 0.001$, respectively). Logistic regression analysis showed that length, percentage of body fat, and leptin levels were positively associated with birthweight. However, leptin levels were not independent of percentage of body fat.

Conclusions. Low body fat and leptin levels, but no evidence of increased metabolic risk at birth, were found in SGA infants.

Key Words: Small-for-gestational age, Insulin, Leptin, Adiponectin, IGF-I, Body fat.

Introduction

The thrifty phenotype hypothesis is one of the most relevant epidemiological statements in the last decades (1). It holds that low birthweight is causally related to the development of the metabolic syndrome and diabetes in adulthood (2). This concept of fetal programming is defined as an adaptive process to an adverse intrauterine environment that alters the fetal metabolic and hormonal milieu designed for survival in a fetal environment (3). Furthermore, it has been recognized that reduced insulin sensitivity, a hallmark in most small-for-gestational-age (SGA)-related conditions, may be present at early life (4,5).

Insulin and insulin-like growth factor I (IGF-I) are important regulators of fetal growth (6,7). IGF-I therapy is associated with increased insulin sensitivity in normal subjects as well as in patients with growth hormone (GH) deficiency, type 2 diabetes mellitus, and type A insulin resistance (8). Other hormones related to insulin resistance and adipose depots are adiponectin and leptin. The former has been described paradoxically reduced in obesity (9) and inversely related to leptin concentrations (10). Recently, adiponectin levels assessed in human cord blood specimens did not show expected physiological relations with adiposity in offspring of diabetic mothers (11).

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In Mexico, Hernández et al. (12) reported 24% prevalence of obesity in children and adolescents. No studies in our population with high risk of diabetes and obesity have evaluated insulin levels and other conditions associated with insulin resistance in newborns according to their birthweight. The aim of this study was to compare IGF-I, leptin, adiponectin, insulin levels, and insulin resistance index between SGA and appropriate-for-gestational-age (AGA) infants.

Materials and Methods

Subjects were recruited at birth from the neonatal unit of the Hospital of Gynecology and Obstetrics in Leon, Mexico. Fifty SGA (birth weight ≤2500 g) and 50 AGA infants (birthweight >2500 and <4000 g) were evaluated. We considered SGA infants if birthweight was <2500 g, consistent with previous studies (1,13). All infants had gestational age between 37 and 41 weeks, and nondiabetic mothers. Gestational age was determined by means of last menstrual period, obstetric ultrasound or both. Gestational age was also assessed by the neonatologists, and if discrepancy existed between the obstetric and pediatric gestational ages, the neonatal gestational age was used for this study. At birth, a clinical evaluation excluded those infants with significant medical, neurological, or genetic conditions. Data on clinical outcome, including mother's age, intercurrent medical conditions, and hypertensive disease of pregnancy were obtained by chart review.

The study protocol was approved by the local Ethics Committee. The study's purpose was fully explained to each pregnant woman, and written informed consent was obtained before enrollment.

Measurements

Supine length and weight were measured with SECA scales during the first 15 min of life by one investigator (HJ). Triceps, biceps, suprailiac, and subscapular skinfold thickness to estimate body composition (14) were performed on the second day of life without considering the feeding pattern.

A 15-mL venous blood sample was taken from the cord blood immediately after the separation of the placenta. Glucose was measured forthwith, whereas samples for insulin, leptin, adiponectin and IGF-I were aliquoted and frozen at −20°C until their processing (no longer than 6 months).

Assays

Blood glucose concentration was measured using the glucose oxidase method by a Vitros 250 analyzer (Ortho Clinical Diagnostics, Johnson & Johnson, Raritan, NJ).

Serum insulin was measured with a solid phase radioimmunoassay (Diagnostic Products Corporation, Los Angeles, CA). The intra-assay coefficient of variation (CV) was 5.2%, the inter-assay CV was 7.3%, and the sensitivity limit was 1.2 μIU/mL.

Serum leptin was measured by immunoradiometric assay (Diagnostic Systems Laboratories, Webster, TX). The intra-assay CV was 3.7%, the inter-assay CV was 5.2%, and the sensitivity limit was 0.10 ng/mL.

Adiponectin levels were measured by radioimmunoassay (Linco Research, St. Charles, MO). The intra-assay CV was 3.8%, the inter-assay CV was 8.4%, and the sensitivity limit was 1.0 ng/mL.

IGF-I was measured by immunoradiometric assay (Biocode-Hycel, Liege, Belgium). The intra-assay CV was 3.6%, the inter-assay CV was 9.1%, and the sensitivity limit was 1.25 ng/mL.

Insulin resistance was estimated by the HOMA-IR index with the following formula: fasting serum insulin (μIU/mL) × fasting plasma glucose (mmol/L)/22.5 (15).

Statistical Analysis

Results are expressed as mean ± SD. Differences between groups were assessed by χ^2 for proportions. The Mann-Whitney U test or Student's t-test was used for variables displaying non-normal or normal distribution, respectively. In addition, we performed ANCOVA test considering gender as covariable to compare leptin levels between SGA and AGA infants. We evaluated associations between hormones and different anthropometric variables by Pearson's correlation test. Logistic regression analysis considered the group as the dependent variable, and hormone levels, length and gender as regressor candidates. All data were analyzed using the STATISTICS software version 6.0 (Statsoft Inc., Tulsa, OK).

Results

One hundred infants were included. All mothers were nonsmokers during pregnancy. We did not find a history of diabetes in a first-degree relative; however, a history of diabetes in a second-degree relative was higher in SGA infants than in AGA infants (48.0 vs. 30.0%, respectively; $p = 0.03$). None of the infants presented moderate/severe jaundice, sepsis, or other major clinical complications.

In the group of SGA infants, length, gestational age, %BF, and leptin levels were lower than AGA infants. There was no difference in glucose, insulin, adiponectin and IGF-I levels between groups (Table 1) or difference in these variables according to gender.

Leptin levels in all infants correlated with %BF ($R = 0.27$; $p = 0.007$), weight ($R = 0.34$; $p = 0.0004$) and length ($R = 0.27$; $p = 0.007$). We did not find an association between leptin, insulin, adiponectin, and IGF-I levels. Furthermore, insulin, adiponectin, and IGF-I levels were not related to anthropometric measurements.