



Plasma non-esterified fatty acid levels in children and their relationship with sex steroids



Lorena Ortega^a, Alicia Garcia-Angueta^a, Pía Riestra^a, Henar Ortega^b, Leandro Soriano-Guillén^c, Miguel A. Lasunción^b, Manuel de Oya^a, Carmen Garcés^{a,*}

^a Lipid Metabolism Research Laboratory, IIS-Fundación Jiménez Díaz, Madrid, Spain

^b Servicio de Bioquímica-Investigación, Hospital Ramón y Cajal Madrid, and CIBER de Fisiología de la Obesidad y Nutrición (CIBERObn), Spain

^c Department of Pediatrics, IIS-Fundación Jiménez Díaz, Madrid, Spain

ARTICLE INFO

Article history:

Received 28 August 2013

Received in revised form 30 May 2014

Accepted 4 June 2014

Available online 16 June 2014

Dedicated to the late Prof. Manuel de Oya, as the warmest homage to his memory.

Keywords:

Children

Hormone levels

Insulin

Non-esterified fatty acids

SHBG

ABSTRACT

Objective: Puberty is associated with decreased insulin sensitivity. Sexual hormones have been related with the onset of insulin resistance, but their relationship with non-esterified fatty acids (NEFA) remains unexplored. The aim of this study was to evaluate circulating NEFA levels in population-based samples of prepubertal children and adolescents and to analyze the association of NEFA with obesity, insulin resistance, and sexual hormones in adolescents.

Experimental: The studied population included 854 randomly selected 6–8-year-old children and 822 children aged 12–16 years. NEFA levels were determined using a commercial kit. Testosterone and estradiol levels were determined by RIA, and insulin and sex hormone binding protein by IRMA. HOMA was calculated as an indicator of insulin resistance.

Results: NEFA levels were lower in adolescents than in 6–8-year-old children, and decreased progressively with age between 12-year-olds and 16-year-olds. No significant differences in NEFA levels were observed between obese and non-obese adolescents. NEFA were not correlated with insulin or HOMA in 12–16-year-old girls, and appear negatively correlated with these variables in boys. Insulin and HOMA were negatively correlated with SHBG levels in both sexes adjusting by age but NEFA levels were not.

Conclusions: NEFA levels decrease with age in adolescents and are not significantly increased in obese children, supporting the fact that the decreased insulin sensitivity at this age is not affecting NEFA metabolism. Although SHBG is related to insulin and HOMA independently of age in both sexes, SHBG levels are not associated with NEFA.

© 2014 Elsevier Inc. All rights reserved.

1. Introduction

It has been established that obesity is related to the onset of insulin resistance [1]. Among other reasons, obesity determines this onset of insulin resistance by impairing insulin signaling, interfering in glucose transport or decreasing insulin clearance related with elevated non-esterified fatty acids (NEFAs) [1]. Inhibition of NEFA release is the most sensitive action of insulin in normal conditions. In adults, it is believed that NEFA could be the main link between obesity and insulin resistance [2]. NEFA levels are

increased in most obese adults due to an increase in the rate of lipolysis from the increased fat cell mass and elevated plasma NEFA concentrations trigger peripheral and hepatic insulin resistance [3]. In children and adolescents, on the other hand, although obesity has also been associated with impaired glucose tolerance and insulin resistance [4–6], the role of NEFA in the onset of insulin resistance remains unclear. In a previous study by our group, including 6–8-year-old obese children, NEFA levels were not different between obese and non-obese boys, and were significantly lower in obese girls [7].

Puberty is associated with decreased insulin sensitivity and increased insulin levels [8–12]. The role of sex hormones in insulin sensitivity has been studied, and a relationship between sex hormones and insulin resistance has been suggested in adults [13–15]. Sex hormone levels have been associated with insulin sensitivity in some studies in children [9,16] but not in others

Abbreviations: BMI, body mass index; NEFA, non esterified fatty acids; SHBG, sex hormone binding protein.

* Corresponding author. Address: Lipid Research Laboratory, IIS-Fundación Jiménez Díaz, Avda. Reyes Católicos, 2, 28040 Madrid, Spain. Tel./fax: +34 91 5432880.

E-mail address: cgarces@fjd.es (C. Garcés).

<http://dx.doi.org/10.1016/j.steroids.2014.06.007>

0039-128X/© 2014 Elsevier Inc. All rights reserved.

[11,17]. Besides, to our knowledge, the relationship between hormones and NEFA levels has not been investigated in a general population of adolescents. Thus, we aimed to determine whether NEFA levels are related to sexual hormones during sexual development.

In our study we have analyzed NEFA levels in two cohorts of 6–8-year-old and 12–16-year-old children, respectively, evaluating their association with obesity, insulin, HOMA, testosterone, estradiol, and SHBG in our population-based sample of healthy 12–16-year-old boys and girls, in order to assess the possible association between hormones and NEFA levels in adolescents.

2. Experimental

2.1. Study subjects

The studied population included two population-based samples comprising 854 (416 boys and 438 girls) 6–8-year-olds, and 822 (393 boys and 429 girls) 12–16-year-olds. Children were participants of a cross-sectional study designed to analyze cardiovascular risk factors in Spanish schoolchildren, and were selected by means of random cluster sampling in schools. Parents were required to provide written consent for their children to participate in the study. All children reported by their parents to be suffering from chronic diseases were excluded. The study protocol complied with Helsinki Declaration guidelines and Spanish legal provisions governing clinical research on humans, and was approved by the Clinical Research Ethics Committee of the Fundación Jiménez Díaz in Madrid.

2.2. Data collection and study variables

At each school, data were collected by a field team, comprised of a physician, several nurses, and a group of persons purpose-trained for taking anthropometric measurements.

2.2.1. Anthropometric variables

Measurements were taken with the children lightly dressed and barefoot. Height and weight were recorded, and body mass index (BMI) was computed based on these measurements. Children were categorized as obese according to the age- and sex-specific BMI cut-off points proposed by Cole et al. [18].

2.2.2. Biochemical variables

Fasting (12-h) venous blood samples were obtained by venipuncture into Vacutainer tubes. Plasma glucose was measured by the glucose oxidase method. NEFA levels were measured by using the Wako NEFA-C kit (Wako Industries, Osaka, Japan). Testosterone and estradiol were determined by coated tube radioimmunoassay (RIA), using commercial kits (DSL-4000 Active® Testosterone and DSL-43100 Active® Estradiol, respectively; Diagnostic Systems Laboratories, Inc., Webster, Texas, USA). Sex hormone binding globulin (SHBG) was measured using an Immunoradiometric Assay (IRMA) kit (DSL-7400 Active® SHBG; DSL, Inc., Webster, Texas, USA). Serum insulin concentration was also measured by IRMA using a commercial kit (BI-Insulin IRMA, Bio-Rad, France). Insulin resistance was estimated using the homeostasis model assessment for insulin resistance (HOMA; fasting insulin [$\mu\text{U/ml}$] \times fasting glucose [mmol/L]/22 \times 5).

2.3. Statistical analysis

All statistical analyses were conducted using the statistical package SPSS v9.0 (SPSS Inc, Chicago, IL). Differences in NEFA levels by age were evaluated by ANOVA and the appropriate post-hoc test. Differences in the studied variables between sexes and

between non-obese and obese children were analyzed by *t*-test or Mann–Whitney test depending on the distribution of the variable. Partial correlation coefficients were estimated after adjusting by age to evaluate the relationships between insulin-resistance variables and hormone levels.

3. Results

Our study sample comprises of 76 obese children (35 boys and 41 girls) aged 6–8 years old, and 50 obese children (26 boys and 24 girls) aged 12–16 years old.

NEFA levels in 6–8-year-old and 12–16-year-old boys and girls are shown by age in Table 1. No significant differences in NEFA levels between boys and girls were observed in adolescents, but NEFA levels were higher in girls than in boys at the age of 6 and 7. Mean NEFA levels were lower in 12–16-year-olds than in 6–8-year-old children. In addition, NEFA levels decreased gradually with age in 12–16-year-old boys and girls (Table 1). Furthermore, NEFA levels were negatively correlated with days of life in both boys ($-.302$, $p < 0.001$) and girls ($-.282$, $p < 0.001$). BMI, insulin, and HOMA were significantly correlated with days of life in boys but not in girls. Days of life correlated positively with testosterone in boys and estradiol in girls, and negatively with SHBG in both sexes.

Insulin levels and HOMA were significantly higher in obese than in non-obese 12–16-year-old boys and girls (Table 2). However, no significant differences in plasma glucose and NEFA levels were found between obese and non-obese 12–16-year-old children, although obese girls showed slightly higher NEFA levels than non-obese girls (Table 2).

Partial correlations, after adjusting by age, between BMI, plasma sex hormones, and insulin resistance-related parameters were evaluated in our 12–16-year-old children (Table 3). BMI correlated positively with insulin and HOMA in both genders, but not with NEFA. In boys, NEFA levels correlated negatively with insulin levels and HOMA, although this correlation was not present in girls (Table 3). SHBG levels were significantly and negatively related to insulin and HOMA in boys and girls, after adjusting by age, but the correlations were more substantial in girls. No significant correlations were observed between testosterone or estradiol and the studied variables. No correlation was found when analyzing partial correlation coefficients between NEFA and hormone levels after adjusting by age (Table 3).

4. Discussion

In our study, we report data on the distribution of NEFA levels by age in Spanish children, describing that NEFA concentrations are lower in 12–16-year-old children than in prepubertal children. In addition, we show a progressive decrease of NEFA levels with age in the age interval studied, between 12 and 16 years of age. Lower NEFA levels in pubertal than in prepubertal children have also been described in other pediatric populations [12,19] even though, as discussed previously, a decrease in insulin sensitivity associated with the onset of puberty is accepted [8–12]. It has been reported that pubertal insulin resistance is associated with decreased insulin stimulated glucose and decreased insulin suppression of NEFA oxidation [20]. In our study, no positive correlations have been found between insulin and HOMA and NEFA; in fact, in boys, significant negative correlations were detected. A negative correlation between insulin and NEFA was also found for 13-year-old girls and 16-year-olds of both sexes in the study of Allard et al. [19]. No relationships or negative associations between insulin and NEFA have been found in studies in prepubertal children [21,22].

Download English Version:

<https://daneshyari.com/en/article/2027879>

Download Persian Version:

<https://daneshyari.com/article/2027879>

[Daneshyari.com](https://daneshyari.com)