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Original article

Body composition and metabolic risk in small for gestational age children treated with growth hormone[☆]

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A R T I C L E   I N F O

A B S T R A C T

Background and objectives: Small for gestational age (SGA) children are at increased risk of metabolic syndrome. Our objective is to evaluate changes in body composition produced by growth hormone (GH) treatment.

Patients and method: A group of 28 SGA children without catch-up growth and undergoing treatment with GH was selected for evaluation. Over the course of 3 years from the beginning of the treatment with GH, the children's body composition variables (bone mineral density [BMD], fat and lean body mass proportion) were evaluated annually with dual-energy X-ray absorptiometry. A study of correlation between metabolic and body composition variables was also made.

Results: Treatment with GH produces a reduction in fat mass proportion in relation to lean body mass, decreasing from $25.94 \pm 6.09\%$ to $22.88 \pm 5.38\%$ ($P = .034$). In the abdominal regions we observe an increase in lean mass, from 1356.91 ± 426.71 to 2570.96 ± 814.36 g ($P = .000$) and a tendency for visceral fat deposits to decrease. BMD in lumbar vertebrae improved from -1.55 ± 0.68 to -0.90 ± 0.79 Z ($P = .019$).

Conclusions: Treatment with GH produces changes in body composition, improving BMD and increasing the proportion of lean body mass with a reduction in fat mass. If these changes persisted into adulthood, they may cause a reduction in the metabolic and cardiovascular risk in this group of patients.

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Composición corporal y riesgo metabólico en niños pequeños para la edad gestacional en tratamiento con hormona del crecimiento

R E S U M E N

Antecedentes y objetivos: Los niños pequeños para la edad gestacional (PEG) constituyen un grupo de riesgo para desarrollar síndrome metabólico. El objetivo de este estudio es evaluar las modificaciones que produce el tratamiento con *growth hormone* (GH, «hormona de crecimiento») en la composición corporal.

Pacientes y método: Se analizan diversas variables antropométricas y de riesgo metabólico en una muestra de 28 niños PEG sin crecimiento recuperador. De forma anual desde el inicio del tratamiento con GH y durante 3 años se miden, mediante densitometría, diferentes variables de composición corporal: densidad mineral ósea (DMO), proporción de masa magra y masa grasa corporal y en la región abdominal. Se ha realizado un estudio de correlación entre variables metabólicas y de composición corporal.

Resultados: El tratamiento con GH produce una disminución de la proporción de masa grasa con respecto a la masa magra en el cuerpo entero, con una disminución del porcentaje de grasa total desde 25,94 ± 6,09 hasta 22,88 ± 5,38% (p = 0,034). En la región abdominal se observa un aumento de la masa magra desde 1.356,91 ± 426,71 hasta 2.570,96 ± 814,36 g (p = 0,000) y una tendencia a disminuir el depósito de grasa visceral. La DMO en la región lumbar mejora desde −1,55 ± 0,68 hasta −0,90 ± 0,79 Z (p = 0,019).

Conclusiones: El tratamiento con GH produce cambios en la composición corporal con mejoras en la DMO y un aumento de la masa magra a expensas de la masa grasa. Estas modificaciones, de persistir en la edad adulta, podrían disminuir el riesgo metabólico y cardiovascular de estos pacientes.

Introduction

The small-for-gestational-age (SGA) child is defined as a newborn whose weight and/or height is more than 2 standard deviations (SD) below the mean established for his/her gestational age according to data from the reference population.[1]

SGA children are a risk group regarding the development of alterations in body composition as well as pubertal disorders and neurodevelopmental delays, among other conditions. A decreased total body fat, lean body mass and bone mineral content has been described for this group when compared appropriate-gestational-age (AGA) children.[2] It has also been observed that they are patients with a tendency to central fat deposition. This fat deposition at truncal and visceral level is a major risk factor for the development of metabolic syndrome in adulthood.[3] The highest incidence of metabolic syndrome in this group of patients increases their likelihood of cardiovascular disease.[4]

Treatment with *growth hormone* (GH) is approved for SGA patients, after 4 years of age, have not experienced a catch-up growth. Because of its anabolic properties, administration of GH also causes changes in body composition, with changes in the proportions of lean and fat mass.[5,6]

Taking all of the above into account, it is important to monitor body composition changes occurring in this group of patients. One of the most popular methods used for assessing body composition is the dual-energy X-ray absorptiometry. It is based on the model of the three compartments and, through direct and indirect measurements, determines the body fat, lean mass and bone mass in the body. Reference values have been established for healthy children, taking body composition data from birth to 16 years of age. In this way, useful comparative indices can be provided.[7,8]

The aim of this study is to assess the changes that occur in the body composition of a group of SGA children over 3 years of treatment with GH in order to test the hypothesis that this causes changes in it, determining a reduction in metabolic risk, inherent to these patients.

Materials and methods

Study design and participants

This is a prospective longitudinal study with a cohort of 28 children born at the University Hospital of Zaragoza between 1995 and 2009, diagnosed with SGA.

At the beginning of the indication of treatment at our hospital (2008), patients who at the age of 4 had not experienced a catch-up growth were selected. GH treatment was approved for them. Since then, the inclusion of all patients has been consecutive.

A 3-year follow-up was carried out, period during which sample data were compared over this time. Complete follow-up has been achieved by 75% of the sample, finding the remaining 25% in earlier stages of treatment, as their inclusion in the sample took place later.

Patients included fulfilled the criteria required by the Advisory Committee for Human Growth Hormone of the Ministry of Health, Social Services and Equality for SGA children:

– Birth length and/or weight below 2 SD of reference standards (tables and graphs 2008 Carrascosa et al.[9]).
– Length from 4 years of age below −2.3 SD below the reference standards (tables and graphs Andrea Prader Centre of the Government of Aragon, Ferrández et al.[10]).
– Not having experienced catch-up growth at 4 years of age taking into account the growth rate of previous years.
– Having previously ruled out any medical condition or treatment that could cause a growth disorder, including GH deficiency.

Exclusion criteria were as follows:

– Non-compliance with auxological inclusion criteria.
– Certain potentially non-beneficiary syndromic symptoms.
– Diabetes mellitus and other potentially serious carbohydrate metabolism disorders.

Procedure

The following variables were studied before starting treatment with GH and the 3-year follow-up:

– *Anthropometric and clinical variables*: weight (SD, according to the charts of the Spanish longitudinal growth study, 1978–2000[10]); height (SD, according to the Spanish longitudinal growth study, 1978–2000[10]); body mass index (BMI) as SD and waist circumference in cm.
– *Metabolic risk laboratory variables:* blood glucose (mg/dl), HDL/total cholesterol ratio, insulinemia (mU/ml) and HOMA index[11] according to the *American Diabetes Association* 2011[12] criteria (blood glucose [mg/l] × insulinemia [mU/ml] / 22.5).
– *Body composition variables:* all patients have undergone annual examinations of body composition with densitometer model HOLOGIC2003-ExplorerTM, collecting data on the following variables:
  (a) *Total body composition*: fat mass and lean mass (in grams and percentage). Fat mass/fat mass + lean mass (FM/FM + LM) ratio has been calculated, as well as the lean mass/fat mass + lean mass ratio (LM/FM + LM) to assess changes in body composition and analyze the relationship between the two variables and their changes over time.
  (b) *R1 abdominal region composition*: R1 abdominal region extends from the end of the last rib to the anterior superior iliac spine. The deposit of fat in this area is directly related to an increased metabolic risk. We analyzed the previously mentioned variables specifically in this area.
  (c) *Bone mineral density (BMD)*: full-body data was obtained, allowing to perform a bone mineralization estimate (total BMD). An estimate of the mean BMD of the vertebral