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Nutritional assessment in neonatal and prepubertal children with a history of extrauterine growth restriction

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ABSTRACT

Background: Nutritional deficit during perinatal stage may induce significant alterations in adipose tissue and increase the risk of obesity, metabolic syndrome and cardiovascular disease in children with a history of extrauterine growth restriction (EUGR).
Aims: To describe the nutritional status in neonatal and prepubertal with a history of EUGR and establish an association between EUGR and later conditions.
Study design: Descriptive, analytical, observational case–control study.
Subjects: The study included a sample of 38 prepubertal children with a history of EUGR, and 123 gender-and-age matched controls.
Outcome measures: The EUGR group was asked to answer a food frequency questionnaire. Analysis of body composition in both groups included anthropometric measurements, assessment of blood pressure and biochemical markers.
Results: Newborns with EUGR received parenteral feeding with a standard nutritional regime and long-chain fatty acid support for 41 ± 23 days; enteral feeding with a special formula for premature infants was initiated at 7 ± 11 days of life. At the prepubertal stage, daily fiber and fatty acid intake in children who had experienced EUGR in the neonatal stage was below the recommended intake. In the EUGR group, the intake of vegetables, fruits and olive oil was below dietary recommendations, while the intake of butchery, fatty meats, pastries and snacks was above the recommendations for the Spanish population.
Conclusions: Appropriate nutrition education strategies should be developed for children with a history of EUGR to prevent later associated pathologies, as neonatal nutritional support and feeding during childhood are associated with an increase in diseases in this risk group.

1. Introduction

Intrauterine life and the early postnatal period may program adipose tissue and metabolic pathways, which might be associated with alterations even in early life [1]. Accelerated catch-up growth induces fat accumulation during renutrition. An increase in nutritional intake may remodel adipose tissue and body composition. This situation is occasionally associated with a higher risk of cardiovascular disease (CVD) and other related conditions such as metabolic syndrome (MS), obesity, type 2 diabetes, hypertension and dyslipidemia [2,3].

The use of fortified breast milk, special formulas for premature newborns and special amino acid formulas has improved postnatal growth and neurological development in some neonates [4,5]. Some authors have recommended to provide early aggressive feeding to premature neonates and infants with growth impairment so that their nutrition intake exceeds their needs, in order to compensate the catabolic state of the first days of life and improve later growth [6,7]. The type of nutritional regime in these patients has been associated with an increase in fat mass and visceral adipose tissue, and with changes in the adipocyte, as compared to healthy full-term neonates with adequate growth for gestational age (GA) [4]. However, the long-term metabolic, endocrine and cardiovascular outcomes of nutritional deficit and overfeeding in newborns with very low birth weight are still unknown [7].

In the last two decades, the increased survival in premature newborns with very low birth weight has resulted in an increase in the incidence of pathology such as extrauterine growth restriction (EUGR). Although in-hospital nutrition management has improved in recent years, nutritional support in neonates with EUGR may not be adequate in time or in content [5]. EUGR occurs in preterm newborns who develop a serious nutrition deficit in the first weeks of life and experience slow growth [8]. Although, there is no consensus on the definition of EUGR, a preterm newborn is considered to have EUGR when he has a body weight below the 10th percentile (p) [9] or the p3 [10] at discharge from the Neonatal Intensive Care Unit. Other studies assess growth independently of the time of discharge [11], or at 36 weeks' corrected GA [12].

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Nutrition in early life is crucial, as it has an influence both on the infant's growth and body development, and on the prevention of later conditions in adulthood [13]. Intrauterine growth restriction (IUGR) may induce alterations in fetal adipose tissue development and endocrine sensitivity with serious long-term effects. IUGR has been associated with central obesity and with an increase in the risk of later diseases in adulthood. Such alterations might be caused by a hormonal programming that would induce metabolic and body composition alterations. In fact, both birth weight and postnatal growth are positively associated with later body composition [14].

It has been observed that a deficient nutritional status in the perinatal period followed by a rapid weight gain and an accelerated catch-up growth may induce important alterations in the adipose tissue and increase the risk of later diseases in adulthood [14]. Though scarce literature has been published on EUGR, this condition might cause alterations in the adipocyte, as some nutritional strategies – such as feeding the neonate with special hypercaloric formulas – together with the influence of certain environmental conditions, may induce an accelerated postnatal weight gain causing body fat accumulation and non-linear growth in the newborn [15]. Consequently, the provision of nutritional support to neonates with EUGR should be reviewed, and the nutritional status of these patients during childhood should be monitored to prevent the occurrence of metabolic diseases later in life.

The aims of this study were threefold: a) to review the neonatal data of premature newborns with EUGR, in terms of the nutritional support provided and weight gain; b) to thoroughly describe the nutritional status of these children when they reach the prepubertal stage; c) and to establish a potential association between EUGR and the risk of later diseases.

2. Methods

2.1. Study population

Participants were assigned to two groups; the EUGR group included 38 Caucasian male and female subjects meeting the following eligibility criteria: a history of prematurity, birth date between 1996 and 2008, birth weight $\leq$1500 g and above p10, meeting EUGR characteristics as defined in this study (body weight after birth below p3 at 36 week's corrected GA and at discharge from Neonatal Intensive Care Unit) and free of any disease unrelated to prematurity and EUGR. Clinical records of 86 eligible newborns were obtained, though only 55 subjects presented EUGR at 36 week's corrected GA and at discharge from the hospital. Consent was obtained from 44 subjects; six subjects were discharged, as they exhibited a Tanner $>$I.

The control group included 123 healthy age-and-sex matched children at prepubertal stage born at full term between 1996 and 2008, birth weight adequate for GA (2500–3500 g, 38–42 weeks), free of basal disease (including perinatal stage), attended at an outpatient hospital unit on suspicion of disease, requiring a blood test. All analyses showed that the controls were free of any disease.

2.2. Methods

A descriptive, analytical, observational case–control study. We used Spanish percentile charts for age, sex and corrected GA [16] in the selection of the EUGR group. Neonatal clinical records were collected and reviewed. Neonates with EUGR had received parenteral nutrition according to their maturity state and clinical evolution; parenteral nutrition included carbohydrates, proteins, amino acids, oligoelements, vitamins, and long-chain fatty acids in amounts established at the Neonatal Intensive Care Unit. Neonates received enteral feeding – initially trophic and then full-feeding – by a special formula for premature neonates. None of the neonates had been breast-fed. Medical records were reviewed to examine the duration of parenteral feeding, day of initiation of enteral feeding, day with maximum weight loss, maximum weight loss rate and days needed to regain birth weight.

Personal and family health records of all participants were documented in the prepubertal stage. Anthropometry and a complete physical examination were conducted, blood pressure (BP) was measured and Tanner staging was performed [17]. All infants were at prepubertal stage I. This stage was confirmed by sexual hormone test. Blood count and biochemical parameters were assessed in all participants, who were asked about their life habits and educational environment. The children were asked to answer a food frequency questionnaire to assess their nutritional state.

2.3. Anthropometry and blood pressure

Anthropometric parameters were weight, crown-to-heel height, and head and chest circumference at birth. Neonatal weight was assessed at 36 weeks' GA and at discharge. In the prepubertal stage, weight and height were measured in all participants according to standard protocols with a Health Scale® Ade Rgt-200, stadiometer with children barefoot and in minimal clothing. Body mass index (BMI) was measured as the ratio of the weight and the square of the height (kg/m^2). We estimated the z-score for weight, height and BMI of all participants. Growth was assessed using growth percentile charts for the Spanish child population [18]. Waist circumference was measured midway between the lowest rib and the high point of the iliac crest with a measuring tape at the end of expiration. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured with a digital random-zero sphygmomanometer (Dinamap V-100), with subjects resting supine for $\geq$5 min and placing a pediatric cuff around the left arm. All measurements were performed twice by the same observer.

2.4. Nutritional assessment

A standard questionnaire designed by the Nutritional Institute of the University of Granada [19] was realized to obtain information about food frequency intake and to collect information on food habits in both groups at prepubertal age. The questionnaire was done by a pediatric nutrition specialist (the same in all the children), asking directly to the parents. The daily energy intake and dietary macronutrient composition analyzed in both groups were estimated by a computer program, which performed an approximation of the data collected from the standardized questionnaire and the Spanish food composition chart [20]. Dietary composition was analyzed by food groups and portions in EUGR children. The information obtained from the food frequency questionnaire was compared against the charts included in the Guide of Healthy Food Habits designed by the Spanish Society of Community Nutrition (SENC) [21]. A standardized questionnaire [22] was employed to collect information on physical activity among participants, EUGR children and controls.

2.5. Sample collection and biochemical analysis

An intravenous catheter was inserted into a median cubital vein to collect blood samples after 12 h fasting. Blood samples were analyzed within 2 h after collection. We determined serum concentrations of the biochemical markers glucose, urea and creatinine, ions, albumin, total protein, calcium, total cholesterol, high density lipoprotein cholesterol (HDLc), low density lipoprotein cholesterol (LDLc), triglycerides (TG), apolipoprotein A-1 (Apo A-1), apolipoprotein B (Apo B), iron, ferritin and insulin by spectrophotometry in an autoanalyzer Architect c16000 (Abbott Diagnostics®). We analyzed sex hormones, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol and testosterone. Blood count measured concentrations of platelets and red and white blood cells. Special attention was given to hemoglobin and hematocrit using an Advia 120 Hematology System