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ORIGINAL ARTICLE

Metabolic syndrome in children and adolescents with phenylketonuria☆,☆☆

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KEYWORDS
Phenylketonuria;
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Diet

Abstract
Objective: This study aimed to identify markers of metabolic syndrome (MS) in patients with phenylketonuria (PKU).
Methods: This was a cross-sectional study consisting of 58 PKU patients (ages of 4-15 years): 29 patients with excess weight, and 29 with normal weight. The biochemical variables assessed were phenylalanine (phe), total cholesterol, HDL-c, triglycerides, glucose, and basal insulin. The patients had Homeostasis Model Assessment (HOMA) and waist circumference assessed.
Results: No inter-group difference was found for phe. Overweight patients had higher levels of triglycerides, basal insulin, and HOMA, but lower concentrations of HDL-cholesterol, when compared to the eutrophic patients. Total cholesterol/HDL-c was significantly higher in the overweight group. A positive correlation between basal insulin level and HOMA with waist circumference was found only in the overweight group.
Conclusion: The results of this study suggest that patients with PKU and excess weight are potentially vulnerable to the development of metabolic syndrome. Therefore, it is necessary to conduct clinical and laboratory monitoring, aiming to prevent metabolic changes, as well as excessive weight gain and its consequences, particularly cardiovascular risk.

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☆☆ Study conducted at Núcleo de Ações e Pesquisa em Apoio Diagnóstico (NUPAD), Hospital das Clínicas, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil.
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PALAVRAS-CHAVE
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Dieta

Síndrome metabólica em crianças e adolescentes com fenilcetonúria

Resumo

Objetivo: Determinar marcadores bioquímicos da síndrome metabólica em pacientes com PKU.
Métodos: Foram avaliados dois grupos de pacientes com PKU, 4 a 15 anos de idade, com excesso de peso (29) e eutróficos (29). As variáveis bioquímicas avaliadas foram a fenilalanina (phe), colesterol total, HDL-c, triglicérides, glicose e insulina basal. Foi determinado o HOMA e mensurada a circunferência da cintura.
Resultados: As concentrações de phe, de colesterol total e de glicose foram equivalentes entre os grupos. Os pacientes com excesso de peso apresentaram maiores concentrações de triglicérides, de insulina basal, maiores valores da determinação do HOMA, menores concentrações de HDL colesterol e valores mais elevados da relação do colesterol total/HDL-c. Houve correlação positiva entre a dosagem de insulina basal e do HOMA com a circunferência da cintura nos pacientes do grupo com excesso de peso.
Conclusões: Os resultados deste estudo sugerem que pacientes com PKU e excesso de peso são potencialmente vulneráveis ao desenvolvimento da síndrome metabólica. Há, portanto, necessidade de acompanhamento clínico-laboratorial que previna as alterações metabólicas, o ganho excessivo de peso e as suas consequências, em especial o risco cardiovascular.

Introduction

Phenylketonuria (PKU), an inborn error of amino acid metabolism characterized by the loss or reduction in the activity of hydroxylase phenylalanine (phe) enzyme, leads to elevated blood levels of phe and its metabolites, resulting in neurological damage that culminates in irreversible mental retardation.[1,2] Disease control is accomplished by prescribing a diet free of animal protein and with restricted vegetable protein consumption. Due to the diet characteristics, some researchers have associated PKU to a tendency of excessive weight gain and metabolic syndrome (MS).[3–6] Conversely, excess weight and metabolic alterations associated with it have been associated to increased cardiovascular risk, which has prompted researchers worldwide to consider the importance of early identification and damage prevention in at-risk populations.[7–11]

Due to the particularities of their diet, PKU patients can be considered a vulnerable group to metabolic abnormalities and excess weight. Protein restriction favors – and even stimulates – the consumption of carbohydrate-rich foods (especially simple carbohydrate) and lipids, in particular, increasing the risk of weight gain.

MS would be present in this population due to both the diet and the disease itself. The detection of parameters that identify the presence of MS may prevent the emergence of other diseases in these patients, for instance, diabetes and cardiovascular disease. The International Diabetes Federation (IDF) considers the measurement of waist circumference (WC), associated with the measurements of HDL cholesterol (HDL-c), triglycerides (TG), and glucose to be parameters for the identification of MS. The latter would be defined by WC measurements > 90th percentile, associated with at least two of the following findings: high levels of TG, reduced HDL-c, and increase in blood pressure and fasting glucose.[11]

This study sought to determine some markers of MS in patients with PKU treated at the Special Genetics Department of Hospital das Clínicas, Universidade Federal de Minas Gerais (SEG-HC-UFMG), to identify risks and to promote better clinical and laboratory control of the disease and the adoption of special protocols for preventing cardiovascular damage.

Methods

A study of case series involving 58 children and adolescents with PKU, aged 4 to 15 years was conducted. Data collection was performed between October of 2008 and November of 2009. Patients were selected, scheduled, and submitted to clinical and laboratory assessment.

The study was approved by the Ethics Committee of the Universidade Federal de Minas Gerais (COEP-UFMG). An informed consent was signed by a parent, legal guardian, and/or PKU patient older than 6 years old, after due explanations.

The groups were defined according to the body mass index (BMI) calculated according to the formula: BMI = weight (kg)/height^2 (m). The value obtained was assessed using the growth curves of the World Health Organization (WHO) for children aged 0-5 years (2006) and 5-19 years (2007), considering as cutoffs for overweight and obesity BMI > 85th percentile and > 97th percentile, respectively. The groups were constituted as follows: 29 patients with normal weight and 29 with excess weight.

Measures of waist circumference were analyzed in accordance with the percentile suggested by MacCarthy et al.[7]

As for the laboratory tests, patients underwent a 10-hour fast, with a maximum of 14 hours of fasting. Serum concentrations of fasting phe, total cholesterol (TC), HDL-c,