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ORIGINAL ARTICLE

Hypercholesterolemia – A disease with expression since childhood☆

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Abstract
Introduction: Hypercholesterolemia results from an alteration, genetic or acquired, in lipoprotein metabolism. Evidence that hypercholesterolemia is associated with the atherosclerotic process from childhood justifies the screening of high-risk children and initiation of therapy at preschool ages.
Objective: To assess children referred for pediatric consultations due to hypercholesterolemia.
Methods: Children and adolescents referred for pediatric consultations with a diagnosis of hypercholesterolemia were enrolled. Information on family history and clinical, anthropometric and biochemical parameters was recorded and, when appropriate, molecular study was performed.
Results: A total of 168 children were assessed. Forty-six presented a familial hypercholesterolemia phenotype and in 22 of these, a mutation in the low-density lipoprotein (LDL) receptor gene was identified. The lipid profile of the group with mutations showed significantly higher values of total and non-high-density lipoprotein (HDL) cholesterol compared to the group without mutations (total cholesterol 316.5±75.9 mg/dl vs. 260.9±42.0 mg/dl; non-HDL cholesterol 268.3±72.6 mg/dl vs. 203.5±43.9 mg/dl; $p<0.05$). Of the total, 55 were prescribed pharmacological therapy and the others underwent diet and exercise interventions only. A greater reduction in LDL cholesterol was observed in individuals under pharmacological therapy compared to those prescribed diet and exercise only (30.3% vs. 18.1%). Drug side effects were insignificant.

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Conclusion: It is possible to maintain a normal lipid profile in most individuals with familial hypercholesterolemia in order to reduce the risk of early onset of atherosclerosis, which is associated with serious cardiovascular complications from childhood.

PALAVRAS-CHAVE
Perfil lipídico;
Hipercolesterolemia familiar;
Estudo molecular;
Terapêutica farmacológica;
Doença cardiovascular

Hipercolesterolemia – uma patologia com expressão desde a idade pediátrica

Resumo
Introdução: A hipercolesterolemia resulta de uma alteração do metabolismo das lipoproteínas e pode ter uma origem ambiental ou genética, como é o caso da hipercolesterolemia familiar. A evidência de que a hipercolesterolemia se associa ao processo aterosclerótico desde a idade pediátrica justifica o rastreio obrigatório em todas as crianças de risco e a instituição de terapêutica individualizada desde a idade pré-escolar.
Objetivo: Avaliar as crianças referenciadas por hipercolesterolemia à consulta de Pediatria.
Método: Foram incluídas as crianças e adolescentes referenciados à consulta de Pediatria por hipercolesterolemia. Procedeu-se à avaliação da história familiar e de parâmetros antropométricos, clínicos e bioquímicos e, quando justificado, ao estudo molecular.
Resultados: Foram avaliadas 168 crianças. Apresentavam fenótipo de hipercolesterolemia familiar 46 crianças e, em 22 destas, foi identificada uma mutação no gene do recetor das lipoproteínas de baixa densidade. O perfil lipídico revelou valores significativamente superiores de colesterol total e colesterol n-HDL no grupo com mutação relativamente ao sem mutação (colesterol total 316,5 ± 75,9 mg/dL *versus* 260,9 ± 42,0 mg/dL; colesterol n-HDL 268,3 ± 72,6 mg/dL *versus* 203,5 ± 43,9 mg/dL; $p < 0,05$). Do total das crianças, 55 efetuaram terapêutica farmacológica, as restantes apenas intervenção comportamental. Registou-se maior redução do c-LDL nos indivíduos com intervenção farmacológica relativamente aos sujeitos apenas a alterações comportamentais (30,3 *versus* 18,1%). Os efeitos laterais dos fármacos foram desprezíveis.
Conclusão: É possível manter um perfil lipídico sustentado em valores normais na maioria dos indivíduos com hipercolesterolemia familiar, de forma a reduzir o risco de evolução precoce do processo aterosclerótico, comprovadamente associado a graves complicações cardiovasculares logo desde a idade pediátrica.

Introduction

Cardiovascular disease is the leading cause of mortality and morbidity in developed countries.[1,2]

Studies such as PDAY (Pathobiological Determinants of Atherosclerosis in Youth) and the Bogalusa Heart Study have shown that the atherosclerotic process begins in childhood, and that both genetic and environmental factors, particularly diet and exercise, play a role.[2–6]

The principal risk factors for cardiovascular disease in adulthood are high low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), hypertension, type 1 and 2 diabetes, smoking and obesity.[1–3] Many of these factors are manifested in childhood, which justifies intervention at early ages for cardiovascular disease prevention.[1–3]

Hypercholesterolemia results from alterations in lipoprotein metabolism that lead to high total cholesterol, LDL-C or triglycerides, and/or low HDL-C. Most children with dyslipidemia have an idiopathic form (polygenic, risk factor-associated or multifactorial), whereas a minority will have monogenic forms, such as familial hypercholesterolemia (FH) or secondary dyslipidemias.

FH is an autosomal dominant disease, with a prevalence of 1/500 in European populations, that results from a mutation in one of three genes: *LDLR*, *APOB* and *PCSK9*. It is characterized by high plasma levels of LDL-C, which is deposited in arteries, leading to premature development of atherosclerosis and cardiovascular disease.[8] Serum lipid and lipoprotein levels increase progressively during infancy, approaching adult levels by the age of two. Levels subsequently decrease during puberty, only to rise again to adult values.[2,7] This has implications for hypercholesterolemia screening, and it is recommended that high-risk children be screened after the age of two.[2]

Evidence that hypercholesterolemia is associated with the atherosclerotic process from childhood and is accompanied by increased prevalence of cardiovascular risk factors, particularly obesity and metabolic syndrome, justifies screening for dyslipidemia in children and initiation of therapy at preschool ages.[3,9]