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Executive Summary

Familial Hypercholesterolemia: Screening, diagnosis and management of pediatric and adult patients

Clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia

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Abstract: The familial hypercholesterolemias (FH) are a group of genetic defects resulting in severe elevations of blood cholesterol levels and increased risk of premature coronary heart disease. FH is among the most commonly occurring congenital metabolic disorders. FH is a treatable disease. Aggressive lipid lowering is necessary to achieve the target LDL cholesterol reduction of at least 50% or more. Even greater target LDL cholesterol reductions may be necessary for FH patients who have other CHD risk factors. Despite the prevalence of this disease and the availability of effective treatment options, FH is both underdiagnosed and undertreated, particularly among children. Deficiencies in the diagnosis and treatment of FH indicate the need for greatly increased awareness and understanding of this disease, both on the part of the public and of healthcare practitioners. This document provides recommendations for the screening, diagnosis and treatment of FH in pediatric and adult patients developed by the National Lipid Association Expert Panel on Familial Hypercholesterolemia. This report goes beyond previously published guidelines by providing specific clinical guidance for the primary care clinician and lipid specialist with the goal of improving care of patients with FH and reducing their elevated risk for CHD.

Background and rationale

The familial hypercholesterolemias (FH) are a group of genetic defects resulting in severe elevations of blood cholesterol levels. Although the term FH has, in the past, been used to refer specifically to LDL receptor (LDLR) defects, this document will use a broader definition to reflect discoveries of defects in the genes for apolipoprotein (Apo) B, proprotein convertase subtilisin/kexin type 9 (PCSK9), and possibly others yet to be described, which produce severe hypercholesterolemia and increased risk of premature coronary heart disease (CHD). Total cholesterol concentrations in heterozygous FH patients (genetic defect inherited from one parent) are typically in the range of 350 to 550 mg/dL and in homozygotes (genetic defects inherited from both parents) range from 650 to 1000 mg/dL. FH is among the most commonly occurring congenital metabolic disorders. The heterozygous form occurs in approximately 1 in 300 to 500 people in many populations, although this ratio is much higher in certain populations in the U.S. The homozygous form is quite rare, occurring in approximately 1 out of every 1,000,000 individuals. Because FH is due to a genetic defect or defects, hypercholesterolemia is present from childhood, leading to early development of CHD. Of particular concern are FH homozygotes, in whom the severity of hypercholesterolemia usually results in severe atherosclerosis and even cardiovascular disease during childhood and adolescence.

FH is a treatable disease. Aggressive lipid lowering is necessary to achieve the target LDL cholesterol reduction of at least 50% or more. Even greater target LDL cholesterol reductions may be necessary for FH patients who have other CHD risk factors. In addition to diet and lifestyle modifications, safe and effective medical therapies are available, including statins and other lipid-lowering drugs, and LDL apheresis, (a method of removing LDL and other Apo B particles from the blood). Despite the prevalence of this disease and the availability of effective treatment options, FH is both underdiagnosed and undertreated, particularly among children. Some estimates suggest that approximately 20% of patients are diagnosed and, of those, only a small minority receive appropriate treatment.

Deficiencies in the diagnosis and treatment of FH indicate the need for greatly increased awareness and understanding of this disease, both on the part of the public and of healthcare practitioners. Central to that education is comprehension of the importance of universal screening during childhood and cascade lipid screening of family members of known FH patients. This document provides recommendations for the screening, diagnosis and treatment of FH in pediatric and adult patients (including women of childbearing potential and during pregnancy) developed by the National Lipid Association Expert Panel on Familial Hypercholesterolemia. This report goes beyond previously published guidelines by providing specific clinical guidance for the primary care clinician and lipid specialist with the goal of improving care of patients with FH and reducing their elevated risk for CHD. The rationale and supporting evidence for these recommendations are published separately in a supplement,[1–5] but are not intended to be a comprehensive examination of the published literature.

1. Definition, prevalence, genetics, diagnosis and screening

1.1 Definition of familial hypercholesterolemias

1.1.1 The FH are a group of inherited genetic defects resulting in severely elevated serum cholesterol concentrations.

1.1.2 For purposes of this document, FH will refer to the autosomal dominant forms of severe hypercholesterolemia unless otherwise specified. However, causes of inherited high cholesterol are not restricted to autosomal dominant FH.

1.2 Prevalence of FH and associated risk

1.2.1 The prevalence of FH is 1 in 300 to 500 in many populations, making FH among the most common of serious genetic disorders.