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A new controversy: early statin use in children with hypercholesterolemia?

Evidence gathered in the adult population over the past 15 years endorses the efficacy of statins regarding both lipid lowering and primary and secondary prevention for coronary artery disease. **Interestingly, contrary to the wealth of statin trial data in adults, relatively little is known about the effects of these agents in hyperlipidemic children and adolescents.¹ A recent study² in children with familial hypercholesterolemia (FH) showed that statin treatment started at an early age resulted in a reduction of carotid artery intima thickness on follow-up.** These results, suggesting that children as young as 8 with high cholesterol levels should be put on statins to reduce their risk of heart disease, have triggered a debate on both sides of the Atlantic.^{1,3} The present article briefly summarizes currently available data in relation to this important issue.

The Rodenburg study

This double-blind, randomized, controlled trial in 214 children with FH (aged 8 to 18.5 years) comparing pravastatin versus placebo was conducted by the University of Amsterdam, and funded by Bristol-Myers Squibb.² The main objective of the trial was to assess the efficacy and safety of statins in children. Children aged <14 years in the treatment arm received 20 mg pravastatin, and children ≥14 years, 40 mg. The trial lasted 2 years, and the investigators assessed changes in carotid intima-media thickness, cholesterol and triglyceride levels, as well as adverse events. Total cholesterol was reduced by pravastatin by 22.5%, LDL-cholesterol by 29.2%, and triglycerides by 1.9%. HDL-cholesterol increased from baseline by 3.1%.

The study showed that the younger the subjects were started on statin therapy, the smaller the progression of carotid intima-media thickness at follow-up. Of importance, no serious adverse events were reported.²

Statin treatment in children and adolescents with familial hypercholesterolemia (FH)

The results of the study by Rodenburg et al² suggest that pharmacological lipid-lowering treatment given at an early age can slow down the progression of atherosclerosis. Prior to these findings, the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee, Council of Cardiovascular Disease in the Young,

recommended the use of lipid-lowering drug therapy in boys >10 years of age and after the onset of menses in girls.⁴ Whilst in the UK only children with FH are offered statin treatment for hypercholesterolemia, very recently, the American Association of Paediatricians (AAP) has suggested that children as young as 8 with a very high cholesterol level, plus risk factors such as obesity or a family history of cardiovascular disease might benefit from taking statins.⁵ The committee recommends starting a child on statins if, despite lifestyle measures, LDL cholesterol remains ≥190 mg/dL, or if it is >160 mg/dL in children with a positive family history of premature heart disease or two additional risk factors; or if it is >130 mg/dL in children with diabetes.⁵

Questions awaiting answers

Many questions have emerged in relation to the new recommendations by AAP.^{1,3} We do not know whether these children with FH will develop atherosclerosis, although it is likely they will do so. People opposing the AAP recommendation argue that there are no outcome data with statin use in this age group, and statins have side effects. An important consideration is the vital role of cholesterol in the synthesis of important hormones and neurological development. As stated by de Ferranti and Ludwig³: "At 8 years of age, a child's brain and other organ systems remain in dynamic stages of growth and development, raising concern that long-term pharmacotherapy initiated at this age may adversely affect the central nervous system, immune function, hormones, energy metabolism, or other systems in unanticipated ways." **Implementing the new recommendation is problematic at present, in the absence of robust data regarding whether these drugs remain safe over such long periods of time, and if such early treatment will truly prevent more coronary events or strokes than if the cholesterol-lowering drugs were initiated at a later age.** Another interesting argument is that, as seen with other pharmacological interventions, these children will not make an effort to change their proatherogenic lifestyle, as they will place big expectations on the medication.

In conclusion, the gauntlet has been thrown, and action is now urgently required in the form of well-designed studies that can provide a definitive answer to such an important question.

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