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Statins for children with familial hypercholesteremia: effective and safe in the short term, long-term safety remains unknown

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Question

Are statins effective and safe to treat children with familial hypercholesterolemia?

Context

Familial hypercholesterolemia is a common inherited metabolic disease in which the blood choles-terol level is high. It is an autosomal dominant disorder in which heterozygotes, so-called carriers, are affected and homozygotes have severe disease. The average worldwide prevalence of heterozygous familial hypercholesterolemia is at least 1 per 500, but according to more recent data could be closer to 1 per 250. Coronary atherosclerosis and its clinical complications often occur at an earlier age than usual, especially in men.

Lifelong therapies, started in childhood, are therefore needed to reduce the risk of vascular disease. In children with the disease, diet has been the cornerstone of treatment. The addition of lipid-lowering medication has provided significant improvement in treatment, but anion exchange resins, such as cholestyramine and colestipol, are poorly tolerated due to their unpleasant taste and treatment plans are not followed. Statins seem to be safe and well-tolerated in children, but their long-term safety in this age group remains unknown. This Cochrane review therefore assessed the efficacy and safety of statins.

Criteria for study selection

The Cochrane review included studies comparing statins to placebo or diet alone in children and adolescents up to 18 years old. The participants had to be diagnosed with heterozygous familial hy-percholesterolemia based on genetic testing or clinical criteria (level of serum total cholesterol is higher than age-adjusted upper limit and at least one parent has hypercholesterolemia). The main outcomes of interest were change in carotid intima-media thickness, change in serum LDL cholester-ol-level and change in measures of growth and maturation, e.g. age of puberty onset.

Summary of the results

The review identified nine randomised controlled trials with a total of 1177 participants. The studies compared different statin treatments with placebo. Both the intervention and follow-up was rather short and ranged from six weeks to two years with a median of 24 weeks.

Statins reduced the mean LDL cholesterol concentration at all time points (6 studies, 669 partici-pants, high-certainty evidence). The mean change in serum LDL cholesterol level in the placebo groups ranged from a 5% increase to a 4% decrease , whereas in the statin groups the LDL cholesterol decreased with a mean of 32% (95%CI*: 35% lower to 29% lower). Despite some concerns regarding risk of bias and heterogeneity across studies, the review authors consider this to be high-certainty evidence given the effect size. The effect of statins on puberty was measured by the change in Tanner stage. There may be little or no difference between treatment with statins or placebo on this measure of growth and maturation (placebo: 636 per 1000 vs statins: 604 per 1000 (95%CI 489 to 750); 1 study, 211 participants, low-certainty evidence). There may be little or no difference in liver func-tion, measured as proportion of participants with changed aspartate aminotransferase or alanine aminotransferase levels (7 studies, up to 924 participants, low-certainty evidence). Statins may also make little or no difference on myopathy, measured as change in serum creatine kinase (6 studies, up to 669 participants, low-certainty evidence), or adverse events (control: 399 per 1000 vs statins: 402 per 1000 (95%CI 323-502); 2 studies, 276 participants, moderate-certainty evidence). One study on simvastatin showed that it may slightly improve flow-mediated dilatation of the brachial artery (1 study, 50 participants, low-certainty evidence). One study showed that pravastatin may induce a regression of the carotid intima-media thickness at 2 years (1 study, 211 participants; low-certainty evidence). No studies reported on rhabdomyolysis or death due to rhabdomyolysis, quality of life or compliance with the treatment.

Conclusion

Statins are an effective lipid-lowering therapy in children with familial hypercholesterolemia. Statin treatment seems to be safe in the short term but longer-term safety still remains unknown.

Implications for practice

Children receiving statins for familial hypercholesterolemia should be carefully monitored by their paediatrician.

REFERENCE:

Vuorio A, Kuoppala J, Kovanen PT, Humphries SE, Tonstad S, Wiegman A, Drogari E, Ramaswami U. Statins for children with familial hypercholesterolemia. Cochrane Database of Systematic Reviews 2019, Issue 11. Art. No.: CD006401. DOI: 10.1002/14651858.CD006401.pub5.

Access the full text of these reviews via the Cebam Digital Library for Health (www.cebam.be/nl/cdlh or www.cebam.be/fr/cdlh)

^ **CI:** confidence interval