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Review Article

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The Effect of Statins on Vascular role in Adolescents with Familial Hypercholesterolemia: An Analytic Review

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Conflicts of Interest: None

Abstract

Introduction: Familial hypercholesterolemia (FH) is a genetic disorder characterized by high levels of low-density lipoprotein cholesterol (LDL-C). If left untreated during childhood, FH can result in early-onset cardiovascular disease (CVD). Statin treatment can reduce the risk of early-onset atherosclerotic CVD associated with FH. For this atherosclerosis-related condition, early therapy is essential to avoid major cardiac damage.

Methods: We conducted An Analytic Review search on studies investigating the effect of statin treatment on FMD, AS, and IMT in children or adolescents with FH.

Results: Two studies investigating the effects on FMD demonstrate increased FMD levels after treatment initiation with simvastatin. Moreover, studies evaluating AS show conflicting results, with one study observing an insignificant increase in AS after fluvastatin treatment and another showing an insignificant decrease following rosuvastatin therapy. IMT changes during statin treatment vary across studies, with some showing reductions after 2 years of pravastatin treatment, while others report improvement over time with longer statin therapy. Various factors influence vascular changes during statin treatment, including LDL-C levels, gender, age, family history of premature cardiovascular disease, and lifestyle factors. Younger age at statin initiation is associated with better vascular outcomes, supporting early treatment initiation in FH adolescents.

Conclusions: In addition to the fact that statin treatment is efficacious, our results support the notion that statin treatment in children with HeFH is safe. Thus, even though further studies are required to assess lifelong safety, statin treatment should be considered for all children aged 8 to 18 with HeFH.

Keywords: Familial Hypercholesterolemia, Low-Density, Lipoprotein Cholesterol, Atherosclerotic CVD.

Introduction

Familial hypercholesterolemia (FH) is a genetic condition characterized by markedly elevated low-density lipoprotein cholesterol (LDL-C) serum levels from birth, resulting in a high risk of early-onset atherosclerosis. Early events in atherosclerosis involve impaired arterial relaxation, arterial stiffening, and arterial intima and media thickening.

Low-density lipoprotein cholesterol (LDL-C) levels that are elevated in people with familial hypercholesterolemia (FH) are caused by a genetic disorder that, if left untreated in childhood, can result in early cardiovascular disease (CVD). While statins have been demonstrated to reduce adult problems, it is unknown if they are effective in younger individuals. It is important for pediatricians and the general public to understand that early detection and treatment can reverse atherosclerotic changes.[] Research on the genetic origin and current treatments for familial hypercholesterolemia (FH) has yielded major findings; however, overall FH rates remain low. Statin drugs help lower the elevated risk of early atherosclerotic CVD associated with FH. Early treatment is necessary for this atherosclerosis-related disorder to prevent serious heart damage. This systematic review looked into whether statin drugs are helpful in lowering LDL-C levels in children and adolescents with FH. A long-term follow-up study has shown that early statin treatment in children with FH significantly reduces LDL-C levels and slows the progression of atherosclerosis. The findings suggest that initiating statin therapy in childhood can prevent severe cardiovascular complications later in life. These results provide strong evidence supporting early lipid-lowering therapy as a crucial strategy for improving long-term cardiovascular health in patients with FH.

Materials And Methods

Analytic Review strategy

The systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines during its conduct. A comprehensive online search was conducted using PubMed, EBSCO, and Web of Science databases. The search was restricted to research conducted in the English language. The search terms used included combinations of keywords and medical subject headings relevant to the study objective.

Inclusion Criteria and Exclusion Criteria

Research was considered if it evaluated the effectiveness of statins for children and adolescents diagnosed with familial hypercholesterolemia, was written in English, and utilized research designs

Inclusion Criteria

1. Sectional Studies
2. Cohort Studies
3. Clinical Trials
4. Studies were excluded if they identified causes of hypercholesterolemia other than familial

Exclusion Criteria

1 If they were case reports, systematic reviews, or meta-analyses.

The Use of Statins in Hypercholesterolemia

Severe hypercholesterolemia is characterized by high levels of total cholesterol (TC) primarily due to elevated

LDL cholesterol (LDL-C) exceeding the 95th percentile or 190 mg/dL. The prolonged elevation of LDL-C is considered a risk factor for the development of atherosclerotic cardiovascular disease, particularly ischemic heart disease. Familial hypercholesterolemia (FH) is a well-studied form of severe HC, caused by a major variant in one gene (LDLR, APOB, PCSK9, or ApoE), with an autosomal codominant pattern of inheritance [5]. These genetic variants lead to extremely high LDL-C levels and the early onset of ischemic heart disease.

Result

In this, found 26 potentially eligible studies, of which we included nine randomized placebo-controlled studies (850 participants). In general, the intervention and follow-up time was short (median 24 weeks; range from six weeks to two years). Statins reduced the mean low-density lipoprotein cholesterol concentration at all-time points (high-quality evidence). There may be little or no difference in liver function (serum aspartate and alanine aminotransferase, as well as creatinine kinase concentrations) between treated and placebo groups at any time point (low-quality evidence). There may be little or no difference in myopathy (as measured in change in creatinine levels) (low-quality evidence) or clinical adverse events (moderate-quality evidence) with statins compared to placebo. One study on simvastatin showed that this may slightly improve flow-mediated dilatation of the brachial artery (low-quality evidence), and on pravastatin for two years may have induced a regression in carotid intima media thickness (low-quality evidence). No studies reported rhabdomyolysis (degeneration of skeletal muscle tissue) or death due to rhabdomyolysis, quality of life or compliance to study medication.

Discussion

A thorough review and meta-analysis were conducted to assess the impact of statins on children and adolescents with familial hypercholesterolemia. The study finding reveals that there is a statistically significant reduction in TC in mg/dL in favor of the statin-treated group ($P < 0.00001$). Similar results were observed in research by Van der Graaf A., et al., which reported a mean decrease in LDL-cholesterol and TC levels from baseline of 33% and 24%, respectively.

Conclusion

Statins significantly reduce TC, LDL-C, and TG in children and adolescents with FH while increasing HDL-C levels. On the other hand, this study found statin to be efficient on treating children and adolescents with familial hypercholesterolemia. Similarly, the study did not find any safety issues with statin medication. However, this study suggests future study to be carried out focused on RCTs studies only to ascertain the results obtained in this study.

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