

Benefit of achieving low-density lipoprotein-cholesterol levels

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ABSTRACT

Reduced Low-Density Lipoprotein Cholesterol (LDL-C) with statin medication is one of the most important strategies for preventing and treating Atherosclerotic Cardiovascular Disease (ASCVD). With a drop in LDL-C, the risk of Coronary Artery Disease (CAD) diminishes, although there is no accepted level at which the risk becomes minor. The current practice guidelines for primary CAD prevention advocate calcula-

calculating ASCVD risk rather than starting statin medication at a specific cholesterol level. Patients with known CAD or who come with Acute Coronary Syndromes (ACS) should take a high-dose statin regardless of their baseline LDL-C values. However, the ideal LDL-C level for secondary CAD prevention is unknown. Statins have pleiotropic effects, such as decreasing inflammation and stabilizing atherosclerotic plaques, in addition to lowering LDL-C.

Key Words: *Lipoprotein-cholesterol; Cardiovascular disease; Acute coronary syndromes*

INTRODUCTION

The level of LDL-C reduction correlates closely with the risk of ischemia events, according to recent findings from clinical trials. Patients with LDL-C less than 40 mg/dL had a decreased risk of adverse cardiac events than those with LDL-C greater than 60 mg/dL in the PROVE IT-TIMI22 study. Similarly, the Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) trial found that individuals with LDL-C 50 mg/dL had a decreased risk of ischemic events than patients with LDL-C > 50 mg/dL, with no side effects. The Improved Reduction of Outcomes: Vytorin Efficacy International Experiment (IMPROVE-IT TIMI 40) trial recently added to the growing body of evidence showing reaching very low LDL-C correlates with better cardiac outcomes. 144 patients with acute coronary syndrome were treated with simvastatin and ezetimibe or simvastatin alone and followed for 7 years in the IMPROVE-IT trial, which was a double-blind, randomized, placebo-controlled experiment. The primary outcome was mortality from cardiac causes, a significant coronary event (non-fatal myocardial infarction, documented unstable angina requiring hospitalization, coronary revascularization happening at least 30 days after randomization), or a non-fatal stroke. The average LDL-C in the simvastatin-ezetimibe group was 53.7 mg/dL at the end of the study, compared to 69.5 mg/dL in the simvastatin immunotherapy group. Patients who took simvastatin-ezetimibe had a lower rate of the primary end point than those who received simvastatin alone. Furthermore, there was no significant difference between the two groups in the incidence of medication-related side effects. Intensive lipid lowering medication with a combination of simvastatin and ezetimibe was found to be effective in all subgroups. Patients in the simvastatin/ezetimibe arm had lower total cholesterol, Non-High-Density Lipoprotein (HDL) cholesterol, and triglycerides after a year of treatme-

nt than those in the simvastatin immunotherapy arm. In addition, simvastatin/ezetimibe significantly reduced high-sensitivity C-Reactive Protein (hs-CRP), an inflammatory marker and predictor of adverse vascular events, when compared to simvastatin alone. Furthermore, a higher proportion of patients on simvastatin/ezetimibe met the dual goal of an LDL-C level less than 70 mg/dL and an hs-CRP level less than 2 mg/L, which was linked to better clinical outcomes.

In summary, the IMPROVE-IT study is the first randomized trial to show that adding a non-statin LDL-C reducing drug to statin therapy results in a net clinical benefit. This shows that additional non-statin lipid-lowering treatments, such as PCSK9 inhibition, may have a promising role in decreasing LDL-C and improving cardiac outcomes. Furthermore, this study demonstrates that lowering LDL-C levels to dangerously low levels is both safe and beneficial. In today's practice, physicians should use a high-intensity statin, either alone or in conjunction with ezetimibe, to achieve very low LDL-C values in patients at higher risk of cardiac events. More information about PCSK9 inhibitors' role in lowering cardiovascular risk will come from ongoing PCSK9 inhibitor outcome trials.

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