New treatment significantly reduces cardiovascular events when combined with statins

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Statins are the most commonly used treatment for cardiovascular disease. Despite reducing certain risk factors, if triglyceride levels remain high with use of statins, there is still a significant risk for heart attack, stroke or other ischemic events.

In a study in the current edition of the New England Journal of Medicine, researchers at Baylor College of Medicine who are a part of the Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT) have shown that a particular treatment significantly reduced cardiovascular events, including cardiovascular death, in patients who continue to have high triglyceride levels on statin therapy. These findings could lead to a more effective and life-saving treatment option when used with other combinations of drugs to treat cardiovascular disease.

REDUCE-IT researchers are studying icosapent ethyl, a highly purified eicosapentaenoic acid (EPA) ethyl ester, which is an omega-3 fatty acid purified from fish oil. The main goal of the study is

to determine whether treatment with this drug reduces ischemic events in statin-treated patients with hypertriglyceridemia.

"For the last three decades, we have focused on drugs that lower cholesterol to reduce cardiovascular events. Recent genetic studies have shown that triglycerides play an important role in heart disease, but we have not had outcome studies to test if adding another therapy to a statin would help individuals with high triglycerides and heart disease or diabetes," said Dr. Christie Ballantyne, professor of medicine and chief of the sections of cardiology and cardiovascular research at Baylor.

The multicenter, double-blind study followed more than 8,000 participants, some for up to six years. Some were given a 4 gram daily dosage of icosapent ethyl ester while others were given a placebo. All participants were being treated with statins and had a triglyceride level of greater than or equal to 135 mg/dL and less than 500 mg/dL with established cardiovascular disease or diabetes and other risk factors. Triglyceride levels are considered healthy when they are less than 100 mg/dL.

The study was focused on clinical endpoints. The primary endpoint showed a 25 percent reduction in cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization or unstable angina, and the secondary endpoint showed a 26 percent reduction in cardiovascular death, nonfatal myocardial infarction or nonfatal stroke.

"Our group has been studying omega 3 fatty acids for over 20 years and have been working on EPA for almost a decade. These results support the previous finding of a Japanese study, Japan EPA

Lipid Intervention Study, which showed that EPA reduced cardiovascular events by 19 percent in individuals with high cholesterol on a low-dose of statin. However, low doses of a mixture of EPA and docosahexaenoic acid, another omega-3 fatty acid, have not shown benefit in reducing cardiovascular events."

The next step will be to understand what mechanisms are at play that help in the reduction of ischemic events when treated with EPA as this agent is known to have many biological activities in addition to the effects on lipids.

More information: Deepak L. Bhatt et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia, *New England Journal of Medicine* (2018). DOI: 10.1056/NEJMoa1812792

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