No Clear Evidence for Ultra-Low Cholesterol Targets

There is no scientifically valid evidence to support the ultra-low LDL target of 70 milligrams/deciliter for very high-risk patients. Further, they suggest that the evidence previously cited to support an LDL goal of less than 100mg/dL for high risk patients also has major flaws.

Americans have been trying to get their cholesterol levels down for decades, ever since studies showed a strong link between high cholesterol and heart disease. But in recent years, experts have suggested that some people should aim even lower, recently recommending very low levels of the type of cholesterol called low-density lipoprotein for some high-risk people — even if it means they had to take multiple medications to get there.

Ina new paper in the October Annals of Internal Medicine, a team of researchers from the VA Ann Arbor Healthcare System and the University of Michigan, show that the current studies do not support treating cholesterol levels to below and LDL of 70 or even less then 100mg/dL.

After performing an exhaustive review of existing research on LDL cholesterol and heart health, they conclude that there is no scientifically valid evidence to support the ultra-low LDL target of 70 milligrams/deciliter for very high-risk patients that has been advocated by some members of the federal government's National Cholesterol Education Program. Further, they suggest that the evidence previously cited to support an LDL goal of less than 100mg/dL for high risk patients also has major flaws.

That evidence may come someday, but until that day, it may be better for society to concentrate less on cholesterol and more on getting people with multiple heart disease risk factors on medications called statins — regardless of their cholesterol levels. Statins are great at lowering a person's LDL cholesterol, but it is not yet clear if lowering cholesterol is the main reason that statins prevent heart attacks and save lives. A focus on statin therapy may provide more public benefit than focusing on getting high-risk patients' levels as low as they can go using multiple drugs.

"Our review suggests that we in the medical community have misunderstood the scientific evidence on whether very low LDL is important, or whether adequate doses of statins are what is really important," says lead author Rodney Hayward, M.D., director of the VA Center for Health Services Research and Development and professor of internal medicine at the U-M Medical School. "Current practice guidelines and recommendations often focus on getting LDL as low as possible, but the literature to date doesn't demonstrate that low LDL is what is truly important – but it does show that statins save lives in high cardiac risk patients regardless of a person's LDL level."

In fact, Hayward and his colleagues say, it may be that the other effects of statin drugs help reduce the risk of heart disease and heart attacks as much or more than the drugs' LDL-lowering power does. Statins inhibit inflammation and clotting, as well as reduce cholesterol, attributes that can be important for preventing heart attacks.

People who have survived a heart attack or have risk factors that put them at high risk of future heart problems should probably be on a moderate or high dose of a statin and stay on it no matter what happens to their exact LDL level, Hayward says.
However, the benefits and safety of using multiple medications to get LDL levels low is open to debate, and is not supported by valid clinical evidence, he adds. Still, many physicians recommend using statins in combination with medications such as niacin, gemfibrozil, fenofibrate and newer drugs to try to bring LDL levels down to low levels.

"Going beyond statin therapy is becoming more common, but when you do that you are also going beyond the current evidence," Hayward says. "Neither the benefit nor the long-term safety of using multiple medicines to lower LDL cholesterol has been studied to date. There is a temptation to believe that lower cholesterol is always good, but recently two treatments that improve cholesterol profiles, hormone replacement therapy and muraglitazar, were found to actually harm people. We would never have known this if we hadn't insisted on scientifically rigorous assessments of these treatments."

For the new paper, the authors examined every study cited by the NCEP panel in their 2004 report that led to the current ultra-low recommendations, and other studies that assessed the relationship between LDL cholesterol and cardiovascular outcomes in patients with LDL under 130 mg/dL. They also contacted more than 20 experts from around the world and none could identify any valid clinical evidence supporting that achieving a low LDL level was important independent of statin therapy.

The problem is not solely a lack of studies, but how past studies have been analyzed, says Hayward. Many studies have looked at associations between LDL and outcomes, but such studies didn't distinguish between whether the LDL level achieved was important or whether the statin dose given was important. They also didn't assess whether patients actually took their statins regularly — a crucial factor — and often didn't consider whether the accuracy of the blood test that measures LDL is adequate to guide patient therapy.

"This is an ongoing problem in the medical literature," says Hayward. "We do randomized controlled trials well, but when it comes to analyzing subgroups or a treatment's mechanism of action, we often get the science all wrong. We need to do better, and in this paper we have tried to lay out a better statistical approach to analyzing treatment goals and clinical trials in the future, including those examining LDL cholesterol."

Also, almost all the published clinical trials on this topic were designed to see how well a statin did against a placebo, or how well patients did on different doses of statins. None were based on getting patients to a specific LDL target using multi-drug therapy and seeing how they did once they were there.

In fact, he says, the evidence strongly suggests that a high dose of a statin produces the same benefit in a person who has an LDL level of 100 mg/dL as it does in a person with an LDL level of 200 mg/dL if the two have the same overall heart attack risk. High-risk individuals are defined by

NCEP as those who have survived a heart attack or who have clogged arteries or diabetes or multiple heart disease risk factors such as high blood pressure, smoking and a strong family history of heart disease.

The distinction between concentrating on LDL versus concentrating on statins is not a minor issue, the authors suggest. The paper notes that compared to simply treating all high CV-risk patients with statins, titrating cholesterol therapy to recommended LDL goals entails considerably greater complexity, frequent use of multi-drug therapy and greater societal and patient out-of-pocket costs, which can result in increased patient burden and lower adherence to all treatments.

“Pharmaceutical companies, which pay for most drug studies, have a natural and understandable interest in wanting to sell their medications to as many people as possible, but the scientific community has a public and moral responsibility of guarding the scientific integrity of the evidence,” Dr. Hayward notes. “In this instance, our analyses suggest that we should have done a better job.”

Until more evidence is available, the authors emphasize the importance of getting more people to modify their diet, exercise more, understand their overall risk of heart disease, and take a statin if their risk is high. “Statins are lifesaving medicines when used in high-risk patients. They can reduce the risk of heart attacks and strokes by 30 percent to 35 percent and the risk of dying by 20 percent to 25 percent, and we need to work harder to help people at risk take them and afford them,” says Hayward. “We do not have many instances where medicines can save lives and money, but this may be one of those instances.”

Individuals who know their cholesterol levels can assess their heart risk using the NCEP online http://hp2010.nhlbihin.net/atpiii/calculator.asp
October 2006 Annals of Internal Medicine online

==

Get your Free Trial Issue to Diabetes Health magazine today! Living with diabetes can be difficult, but Diabetes Health magazine is here to help! Each supportive issue contains expert advice, gripping features, research updates, product comparison charts and low-fat and lower-carb recipes you'll actually want to make. Make your life a little easier. Subscribe today and instantly receive 6 FREE health guides.
https://www.diabeteshealth.com/customerservices/subscribe.html?affiliate=dic&code=M5DHDIC

This article came from
http://www.diabetesincontrol.com/index.php?option=com_content&view-article&id=4206

Please visit Diabetes In Control for the most current news in Diabetes care.
www.diabetesincontrol.com