

Diabetes Newsletter



1600 North Second Street

September 1, 2009

Volume 18, Issue 9

Considerable Risk of Cardiovascular Events May Linger Despite Achieving Target LDL Cholesterol Levels with Statins in Patients with Metabolic Syndrome

LDL Particle Concentration More Closely Related to Risk of Cardiovascular Events than is LDL Cholesterol

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Jul 29, 2009

DiabetesHealth Professional Online, Issue 212, August 4, 2009

May 5 - Ann Arbor, MI - In the first study of the effects of statins on the concentrations of both low-density lipoprotein cholesterol (LDL-C; known as the "bad" cholesterol) and low-density lipoprotein particles (LDL-P) in patients with metabolic syndrome, it was shown that even though the statins lowered the concentrations of LDL-C to target levels, the patients retained considerable residual risk for cardiovascular events because LDL-P concentrations were not reduced to a similar extent. A pre-print version of the study in *Diabetes Care* is available online at <http://dx.doi.org/10.2337/dc08-1681>, and the final version will be available in print in the June 2009 issue, as well as online at the same URL. "LDL cholesterol is not an accurate biomarker for cardiovascular risk in patients with metabolic syndrome," according to Robert S. Rosenson, M.D., of the University of Michigan, Ann Arbor, and first author of the study. "The findings of the study suggest that patients with metabolic syndrome should be treated to targets based on LDL-P rather than LDL-C in order to better manage cardiovascular risk."

"There is a real danger to patients when LDL cholesterol is equated with LDL," said James D. Otvos, Ph.D., of LipoScience, Inc., in Raleigh, North Carolina, and second author of the new study. "A lot of people are treated 'successfully' with potent statins and reach their LDL cholesterol goal, but are nowhere near their LDL particle goal."

Although up to 80 percent of patients achieved desired levels of LDL-C (less than 2.59 mmol/l or 100 mg/dl) with statins, LDL-P levels were reduced to target (less than 1000 nmol/l) in only 27 percent of patients with metabolic syndrome.

The results of the study take on added significance given the increasing prevalence of metabolic syndrome. Estimates suggest that metabolic syndrome now affects as many as 47 million adults in the U.S. The condition is characterized by having three out of these five risk factors: excessive abdominal fat, high triglyceride levels, low HDL-C, elevated blood pressure, and elevated fasting blood sugar.

Why Discordant Results with LDL-C and LDL-P?

Although statins have been shown in studies of patients at risk for cardiovascular disease to lower LDL-C and LDL-P, several studies in the last few years showed that LDL-C was reduced to a greater degree than was LDL-P. But in patients with metabolic syndrome, the discordance is particularly

striking and potentially dangerous.

"As the number of metabolic traits increases in patients with metabolic syndrome, LDL-C *doesn't* increase," explains Dr. Rosenson. "As people become more insulin-resistant, LDL-C *doesn't* increase. In fact, LDL-C isn't even part of the definition of metabolic syndrome."

"However, the number of LDL particles *increases* linearly as the number of metabolic factors increases, or as the insulin resistance worsens. And as study after study has shown, increased LDL particle concentration means increased cardiovascular risk." For these people, it becomes critical to treat with agents that reduce LDL particles to target levels as well as lower LDL-C levels. Being content with just a reduction in LDL-C is being lulled into a false sense of security. "The patient is still at significant residual risk of a cardiovascular event," adds Dr. Rosenson.

"In addition," explains Dr. Otvos, "as statins work in the body, they may lower the amount of cholesterol in some LDL particles - replacing it with triglyceride. This accounts for a removal of cholesterol from the LDL particles without affecting either the number of LDL particles or their size. The statins work by inducing both a compositional change and a concentration change of LDL. These two elements combined lead to a greater cholesterol reduction than particle number reduction. The bottom line: the patient is still at risk for a cardiovascular event if LDL-P has not been lowered sufficiently," summarizes Dr. Otvos.

The findings of this study are in alignment with the suggestion of the American Diabetes Association (ADA)/ American College of Cardiology (ACC) Foundation Consensus Statement of April, 2008, that patients with the greatest cardiometabolic risk be treated to more aggressive lipoprotein goals.

What's the Answer?

Would patients benefit from combined treatment rather than statin monotherapy, which seems to be insufficient? Dr. Rosenson elaborates, "The validity of a combination approach versus statin monotherapy is actually the emphasis of three large-scale clinical trials, two of which are being sponsored by the National Institutes of Health - the ACCORD (Action to Control Cardiovascular Risk in Diabetes) and the AIM HIGH (Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides and Impact on Global Health Outcomes) trial, and the third is the HPS (Heart Protection Study) - THRIVE funded by the National Health Service in the U.K. They are exploring whether two drugs are better than one in patients at high cardiometabolic risk who may or may not have diabetes."

References

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"Jim was diagnosed with diabetes, and his doctor says he needs to keep active, so I hide his TV remote three times a week."

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Due to a death in the family, I was not able to do the support groups in August. The September support groups will be on new products and medication. I will plan on doing this support group in Windsor during October.



"The dietician said he should watch what he eats!"

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Clinton Support Group

TOPIC

New diabetes products and medication

DATE

Thursday,
September 10, 2009

TIME

10:30—11:30 a.m.

PLACE

GVMH Hospital Classroom A & B
(Note change of classroom. This classroom is on the ground floor of the hospital)

Presented By:

Jamie Ketterman, RN, BSN, CDE

Warsaw Support Group

TOPIC

New diabetes products and medication

DATE

Tuesday,
September 8, 2009

TIME

11:30 am—12:30 p.m.

PLACE

Warsaw GVMH Medical Clinic Wellness Center

Presented By:

Jamie Ketterman, RN, BSN, CDE