

News

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****Fewer heart attacks for diabetics
goal of new cholesterol-lowering therapy

DALLAS -- "Most people who develop diabetes by the age of 50 have coronary heart disease by the time they are 60," says Dr. Scott Grundy. "We hope to be able to do something about that."

Grundy, director of the Center for Human Nutrition at The University of Texas Southwestern Medical Center at Dallas, and Dr. Abhimanyu Garg, a research associate at the center, hope they can give Caucasian Type II diabetics a lower risk of developing coronary heart disease by making their metabolisms simulate those of Pima Indians.

"Pima Indians have a high incidence of Type II, or non-insulin dependent diabetes. (It develops in late middle-age, particularly in obese people.) The Indians, however, rarely die of heart attacks, and we believe it is because they have below-average cholesterol levels and their arteries are less likely to clog up with cholesterol-laden plaques," said Garg.

"On the other hand, Caucasian Type II diabetics are likely to have average or slightly above average cholesterol levels. If we lower their cholesterol to the level of Pima Indians, might we help them avoid heart attacks, too? It's a challenging concept," he said.

There has been no chance to test the theory adequately in the past. Although the drugs gemfibrozil and niacin, which lower cholesterol in non-diabetics, were tested, they were not extensively studied because it appeared there might be problems in using them in the presence of diabetes.

Now a different type of cholesterol-lowering drug, lovastatin, is available. It speeds up the clearance of low density lipoprotein cholesterol (LDL) from the blood by stimulating the production of LDL receptors to pull the "bad" LDL out of the bloodstream and into cells. LDL receptors also help clear very low density lipoproteins (VLDL), which are heavily laden with triglycerides.

Garg and Grundy worked with 16 patients at the Dallas Veterans Administration Medical Center and the General Clinical Research Center at UT Southwestern. Most of them had developed diabetes after the age of 40. Nine of the patients were

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taking an oral medication, glyburide, to control their diabetes, and the other seven received insulin shots daily.

The patients were put on diets that conformed with recommendations of the American Diabetic Association: 50 percent carbohydrate, 35 percent fat and 15 percent protein, with 300 mg. of cholesterol daily. At the beginning of the study, patients were hospitalized for five days to stabilize their glucose and weight. Blood samples were taken to analyze lipids and lipoproteins, glucose and other elements related to the diabetes. Then each person was given either 20 mg. of lovastatin twice daily or a placebo in a double-blind randomized manner. After 28 days they were hospitalized and the blood tests repeated. Finally, each person changed to the other medication and continued for 28 days longer before being tested again.

Blood lipids declined dramatically while the patients received lovastatin. Total cholesterol and low density lipoprotein (LDL) fell 26 percent. Tri-glycerides and very-low-density lipoprotein (VLDL) fell by 31 and 42 percent respectively.

The average total cholesterol of a patient in the study after receiving lovastatin was in the range of 170 milligrams per deciliter. It was well below the 200 mg/dl threshold considered safe for adults over 30 and was in line with the average total cholesterol of the Pima Indians (180 mg/dl). The study was reported in the New England Journal of Medicine January 14, 1988.

Garg believes that reducing the cholesterol level of diabetics to 180 or less will lower the risk of their having heart disease to that of the general population. At present, diabetics are at least twice as likely to develop coronary heart disease. Now that an effective medication has been found, the concept can be put to the test with long-term trials.

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NOTE: The University of Texas Southwestern Medical Center at Dallas comprises Southwestern Medical School, Southwestern School of Biomedical Research and Southwestern Allied Health Sciences School.