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****Combined-drug therapy packs one-two punch against moderately high serum cholesterol

DALLAS -- Two drugs are better than one at bringing moderately high cholesterol levels under control.

Researchers at The University of Texas Health Science Center at Dallas tested a program of treatment that included lovastatin (formerly mevinolin) and colestipol hydrochloride on patients whose total cholesterol levels were in the 250 to 350 milligram per deciliter range, well above the 200 mg/dL considered safe for middle-aged adults. The combination provided a one-two punch that lowered blood levels of total cholesterol 36 percent and low density lipoproteins (LDL) 48 percent while increasing high density lipoproteins (HDL) 17 percent.

"The best news for people at risk for heart attack is that the LDL, which is the primary cause of atherosclerosis, is lowered so significantly while the HDL cholesterol increases, showing that cholesterol is being cleared from the blood efficiently," said Dr. Gloria Lena Vega, an instructor of biochemistry at the health science center. LDL causes atherosclerosis by depositing cholesterol in the fatty plaques that clog arteries.

The impressive changes occur because the two drugs act in different ways to clear cholesterol from the blood. Lovastatin inhibits the production of cholesterol within cells, forcing them to pull the cholesterol they need from LDL particles circulating in the blood. On the other hand, colestipol "pulls cholesterol from the body" by binding bile acids, which have a significant cholesterol component, before being excreted from the body.

The therapy was tested on patients with moderate primary hypercholesterolemia. They had elevated serum cholesterol levels in the range of 250 to 350 mg/dL with no apparent genetic cause. The group had been screened to eliminate patients with familial hypercholesterolemia, which is genetically linked. About 15 percent of all middle-aged Americans and 35 percent of patients with coronary heart disease have cholesterol levels exceeding 245 mg/dL. Most of these have primary moderate hypercholesterolemia like the group in the study. Only one in 500 people has the more severe condition, heterozygous familial hypercholesterolemia.

"Although most patients with moderate hypercholesterolemia are at increased risk for coronary heart disease, a maximum effort to lower LDL by means of drugs is not always indicated," said Dr. Scott Grundy, professor of internal medicine and biochemistry at UTHSCD and director of its Center for Human Nutrition. "Careful attention to diet, sometime combined with one medication, is often able to bring cholesterol within a safe range.

(More)

"However, we think the two-drug treatment is appropriate in certain cases. For example, patients who have undergone coronary artery bypass surgery and have cholesterol levels of 250-350 mg/dL could develop new blockage in their grafts and in other arteries. They could benefit from the treatment. Another group is cigarette smokers with hypercholesterolemia. Their risk for coronary heart disease is six to 10 times the average."

Vega and Grundy collaborated in the clinical investigation, conducted on 10 patients at the Dallas Veterans Administration Medical Center and the NIH-funded General Clinical Research Center at Parkland Memorial Hospital in Dallas. Each patient was hospitalized for two periods of seven to eight weeks while undergoing LDL turnover studies. The first hospitalization was a control period, and the second tested combined-drug therapy.

The patients were fed a diet consisting of 40 percent of calories as fat, 45 percent as carbohydrate and 15 percent as protein -- equivalent to a "typical" American diet. After a week for stabilizing the metabolism, a blood sample was drawn and the LDL component was isolated. The LDL was tagged with a marker and reinjected, which allowed the researchers to follow the breakdown and elimination of LDL by testing subsequent blood samples by radioimmunoassay.

Dosages of 20 milligrams of Lovastatin twice daily and 10 grams of colestipol hydrochloride twice daily resulted in a 36 percent decreased in total serum cholesterol, a 48 percent decrease in LDL cholesterol and a 17 percent increase in HDL.

According to Vega and Grundy's report of the research in the Jan. 2, 1987, Journal of the American Medical Association, the reduction in LDL cholesterol level was due to three factors: a 27 percent decrease in the production of LDL, a 20 percent increase in the breakdown of LDL and a 15 percent depletion of cholesterol in LDL particles.

Seven of the patients had previously been tested on lovastatin alone. These patients showed a 53 percent drop in LDL cholesterol with combined drug therapy versus a 34 percent drop on lovastatin only. This indicates that using moderate dosages of lovastatin and colestipol together may achieve satisfactory results without risking possible side effects with larger dosages of either.

The researchers concluded that the combination therapy may provide one means for preventing progression of atherosclerosis in high-risk patients. "Once again, I want to point out that this treatment is not indicated for everyone," says Grundy. "Patients with elevated cholesterol levels can't ignore other risk factors like smoking. They can't neglect to eat prudently. They shouldn't ignore their responsibilities to themselves and rely on medication to do the job."

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Note: The University of Texas Health Science Center at Dallas comprises Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences and the School of Allied Health Sciences.