SOUTHWESTERN NEWS

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TWO CHOLESTEROL-LOWERING STATIN DRUGS REDUCE ANOTHER MARKER OF CORONARY-ARTERY DISEASE

DALLAS – Dec. 13, 2001 – Two out of three statins, powerful drugs lauded for dramatically lowering low-density lipoproteins (LDL) – the bad cholesterol – have been found to significantly decrease another risk factor for coronary-artery disease, researchers at UT Southwestern Medical Center at Dallas reported.

In the first head-to-head comparison of the effect of three commonly prescribed statins on remnant lipoprotein (RLP) cholesterol levels, the researchers reported in today's issue of *Arteriosclerosis, Thrombosis and Vascular Biology* that atorvastatin (Lipitor) and simvastatin (Zocor) significantly reduced RLP levels. Pravastatin (Pravachol), the third drug used in the study, had no significant effect on RLP levels.

Remnant lipoproteins, particles that circulate in the bloodstream much like LDL cholesterol, promote plaque formation in the arteries and subsequently are independent risk factors of coronary-artery disease.

"Given that RLPs are atherogenic and promote plaque formation, it is not unreasonable to attribute part of the benefit of statins in reducing cardiovascular events to the reduction in RLP levels," said Dr. Ishwarlal Jialal, professor of pathology and internal medicine at UT Southwestern and senior author of the study. "It's clinically proven that statins lower LDL and reduce cardiovascular events. Results from this study provide evidence of another mechanism by which statins are beneficial."

Twenty-two patients with combined hyperlipidemia (LDL levels greater than 130 milligrams per deciliter and triglyceride levels between 160 and 600 mg/dL) randomly received 40 mg of pravastatin, 20 mg of simvastatin and 10 mg of atorvastatin for six weeks per medication. A three-week washout period followed the administration of each drug.

"The RLP levels were tested using a novel assay that utilizes a gel containing specific

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antibodies," said Dr. Sridevi Devaraj, assistant professor of pathology. "The antibodies bind to HDL and LDL, as well as large chylomicrons (triglyceride-rich lipoproteins synthesized by the intestine from dietary fat) and most very-low-density lipoproteins, leaving the RLP, which is measured using a sensitive cholesterol assay."

The assay was recently approved by the Food and Drug Administration for assessing coronary-artery disease risk.

The median reduction in RLP levels was 6 percent with simvastatin and 25.9 percent with atorvastatin, but only 2.9 percent with pravastatin

As expected, Jialal said, LDL cholesterol levels were significantly lowered with all three statins.

"Statins are clearly the drug of choice for people with high cholesterol, but statins also are a drug of choice for patients with combined hyperlipidemia," said Jialal.

Researchers are increasingly investigating risk factors other than the classic factors of coronary-artery disease: high cholesterol, high blood pressure, diabetes and smoking, Jialal said.

"The common factors are not present in 50 percent of individuals who have heart attacks, and the majority of patients with coronary-artery disease have only mildly elevated cholesterol levels and frequently have other lipoprotein abnormalities such as increased RLP cholesterol," Jialal said.

In a report published in *Circulation* earlier this year, the investigators showed that all three statins lowered a relatively new risk marker for cardiovascular disease called C-reactive protein in these patients.

Other UT Southwestern researchers on the current study were Beverley Adams-Huet, faculty associate in internal medicine, and Dr. David Balis, assistant professor of internal medicine. Dr. David Stein, from the Albert Einstein College of Medicine of Yeshiva University, was first author of the study.

The study was funded by the National Institutes of Health, Merck & Co. and Pfizer.

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