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Drug trial shows dramatic reduction in hidden heart disease

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(PhysOrg.com) -- A Harvard-led study shows that the risk of heart attack and stroke among subjects with “silent heart disease” — and normal cholesterol levels — can be dramatically reduced by the use of an already widely prescribed class of drugs.

The international study, led by researchers at Harvard Medical School (HMS) and Brigham and Women’s Hospital, was designed to test the ability of statins — among the most widely prescribed drugs in the world — to help people at risk of heart attack and stroke who don’t have those ailments’ classic symptoms. About half of all heart attacks and strokes today occur among those who don’t meet medical standards for treatment.

“That’s what this study is all about,” said Paul Ridker, the Eugene Braunwald Professor of Medicine at HMS and Brigham and Women’s Hospital, who led the study. “It’s about the guy who goes running and does not come back, and the doctor and the spouse are shocked because this is someone who was thin and seemingly in good health and with a good cholesterol level.”

The study screened subjects for possible hidden heart attack and stroke risk using a different measure from the cholesterol levels commonly used today. Researchers used levels of “high sensitivity C-reactive protein,” (hsCRP), which previous studies have shown are an indicator of inflammation and heart disease risk, even among those otherwise considered healthy.

The study was funded by the drug company Astra-Zeneca, the maker of the statin used in the trial, rosuvastatin, marketed under the name Crestor. Astra-Zeneca had no access to unblinded trial data and played no role in the study's analysis or interpretation, according to Brigham and Women's Hospital.

The enormous study involved 17,802 subjects in 26 countries who had high C-reactive protein levels. It excluded subjects with high LDL or "bad" cholesterol levels, as well as those with a host of other medical conditions that might indicate elevated heart attack or stroke risk. Older subjects were selected, with men ages 50 or older and women 60 or older.

The study divided the subjects into two groups, with half receiving rosuvastatin and the rest receiving a placebo. The results were so dramatic — nearly a 50 percent reduction in the risk of heart attack, stroke, and heart-related death — among the statin group that an independent data and safety monitoring board voted in March to end the study early, after less than two years.

The study's results have drawn an enormous amount of attention since they were announced yesterday at the 2008 Scientific Sessions of the American Heart Association in New Orleans and published in the New England Journal of Medicine.

Associate Professor of Medicine and Associate Professor of Biostatistics Robert Glynn, the statistician involved in the study, estimated that if the trial's screening and treatment procedures were broadened to the entire country, 250,000 heart attacks, strokes, revascularization surgeries, and cardiac deaths could be avoided in the United States over five years.

While some have hailed the trial as a watershed in the detection and treatment of hidden heart disease, others have counseled caution. In an

editorial that accompanied the study article in the New England Journal of Medicine, Mark Hlatky, a professor at Stanford University, said that the investigation will doubtless cause a reassessment of the use of statins as a preventive measure, but cautioned that safety and cost need to be considered before a major expansion in statin use takes place.

The study showed similar results among several different groups, including men, women, and people of different ethnicities and nationalities. Results for specific conditions showed that the risk of heart attack was 54 percent lower in the group taking the statin, the risk of stroke 48 percent lower, the risk of needing angioplasty or bypass surgery was 46 percent lower, and the risk of deaths from all causes was 20 percent lower. The results were roughly two times the effect doctors expect when they prescribe statins for those who have high cholesterol levels.

“Our results are relevant for patient care and the prevention of heart attack and stroke,” Ridker said. “Physicians can no longer assume that patients are at low risk for heart disease simply because they have low cholesterol. We have confirmed that patients with increased hsCRP are at high risk even if cholesterol levels are low, and we now have evidence that a simple and safe therapy cuts that risk and saves lives.”

Provided by Harvard University