Two drugs may stabilize plaques in atherosclerosis

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Two drugs that a Wake Forest University School of Medicine research team has been investigating for lupus for several years may stabilize atherosclerotic plaque in the walls of arteries and help avert heart attacks and strokes.

Nilamadhab Mishra, M.D., and colleagues reported at the American College of Rheumatology meeting in Washington that the two drugs – TSA (trichostatin A) and SAHA (suberoylanilide hydroxamic acid) – decreased cholesterol deposits in the walls of arteries.

The two drugs are part of a class of drugs called histone deacetylase inhibitors, or HDIs, which work by multiple mechanisms, one of which is anti-inflammatory: they decreased inflammatory proteins produced by macrophages, a type of white blood cell. These inflammatory proteins can make the atherosclerotic plaque unstable. Mishra said. The macrophages were taken from normal mice and the experiments were done in a laboratory setting.

After the macrophages were treated with either TSA or SAHA, the researchers also measured dramatic decreases in LDL and total cholesterol in the macrophages.

And the drugs prevented macrophages from turning into foam cells inside arterial walls, which is a key component of the buildup of plaque that leads to a narrowing of the arteries and increases the risk of heart attacks and strokes.

With the growing understanding that atherosclerosis, also known as hardening of the arteries, is in part an inflammatory disease, Mishra noted that doctors might be able to take advantage of the anti-inflammatory effects of TSA and SAHA.

Mishra, a rheumatologist, is looking for new ways to treat atherosclerosis because, he said, "Premature accelerated atherosclerosis is one of the leading causes of death and disability in lupus."

He added, "There is great enthusiasm to develop drugs that can stabilize atherosclerotic plaque and reduce acute coronary events."

SAHA already is being tested as an anticancer drug, and TSA is an antifungal antibiotic also being tested against cancer.

The research is part of a larger project, supported by a $1,793,750 grant from the National Institutes of Health, to further develop the HDI class of drugs for the treatment and prevention of atherosclerosis, Mishra said.

"Despite the success of lipid-lowering drugs for the prevention of coronary artery disease and myocardial infarction (heart attacks), atherosclerosis remains the most common cause of disease-related death in the Western world and in developing countries," he said.

Source: Wake Forest University Baptist Medical Center