Hormone that controls iron levels may be target for atherosclerosis treatment

16 November 2011

Researchers at Emory University School of Medicine have identified hepcidin, a hormone that regulates iron levels in the body, as a potential target for treating atherosclerosis.

Suppressing hepcidin is a way to reduce the iron levels inside the white blood cells found in arterial plaques. Reducing iron levels pushes those cells to clean up harmful cholesterol in a process called "reverse cholesterol transport," interfering with atherosclerosis, researchers have found.

The data is being presented Wednesday, Nov. 16 by Aloke Finn, MD, assistant professor of medicine (cardiology) and colleague Omar Saeed at the American Heart Association Scientific Sessions meeting in Orlando. Charles Hong, MD, PhD, from Vanderbilt University and collaborators from CVPath Institute contributed to the research.

When mice modeling atherosclerosis are given a compound that reduces hepcidin levels, they have smaller atherosclerotic plaques and less fat in their plaques, as well as reduced foam cell formation. Foam cells are white blood cells that accumulate cholesterol and are signs of atherosclerosis, which can lead eventually to heart attacks and strokes.

The compound LDN 193189 reduces hepcidin levels by blocking its production. LDN 193189 is also being investigated as a treatment for inflammatory bowel disease and for anemia related to critical illness.

Finn is also presenting research on how hemoglobin, the iron-containing protein that allows red blood cells to carry oxygen, affects macrophages.

Finn and his colleagues used isolated human cells and a rabbit model of atherosclerosis to show that macrophages respond to hemoglobin by increasing production of proteins that transport cholesterol and pump iron out.

In the context of atherosclerosis, iron is toxic because it amplifies the action of reactive oxygen species, leading to more inflammation and more foam cells. Previous research has shown that hemorrhage within atherosclerotic plaques, leading to the release of hemoglobin from red blood cells, is linked to enlargement of the plaque's necrotic core - a sign of "vulnerable plaque."

"We were led to the hepcidin research by our work on macrophages," Finn says. "We discovered a different type of macrophages that detoxify iron. They take it up and spit it out again with an iron transport protein."

"Hemorrhage is bad, but as bad at it is, these macrophages seem to protect against the toxic effects of iron. Giving macrophages hemoglobin encourages them to behave in this detox mode," he says.

More information: More information on the abstracts is available here:

Hepcidin
bit.ly/uM7JWU

Hemoglobin
bit.ly/rN4dNx

Provided by Emory University