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Pancreatic hormone linked with severe heart disease in obese and diabetic patients

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Severe heart damage in people who are obese and diabetic is linked with a pancreatic hormone called amylin, UC Davis researchers have found.

In the failing hearts of patients who were obese and diabetic, the scientists discovered strings of proteins, small fibers and plaques made of amylin, the hormone that produces the feeling of being full after eating. They also showed in an animal model that amylin accumulation in the heart leads to heart muscle destruction and failure.

Published in the February 17 issue of the journal Circulation Research, the study also found amylin buildup in overweight patients who are not obese, suggesting the potentially dangerous accumulations may start before a diabetes diagnosis.

Heart failure is the number-one killer in obese and diabetic populations. Controlling the circulation of amylin hormone in the blood might lessen or prevent disabilities and deaths from heart disease, the scientists said.

"Amylin appears to be a stealth killer," said Florin Despa, an assistant professor of pharmacology at UC Davis and senior author of the study. "There is only one amylin protein for every 100 insulin proteins in the blood, so it has been under the radar until recently."

In healthy people, amylin circulates in the blood together with insulin --the hormone that controls carbohydrate and fat metabolism -- and principally regulates gastric fluxes and the sensation of satiety.

In studies of both normal and failing donated hearts of people undergoing heart-transplant surgery, the researchers found little or no amylin accumulation in lean people. But a quite different picture emerged from examinations of heart tissue of obese and type 2 diabetic patients. In failing hearts of these patients, they found extensive accumulation of amylin in strings of 10 to 20 proteins called oligomers. They detected a smaller but still abnormal buildup in nonfailing hearts from patients who were overweight but not obese.

Using genetically engineered rats that secrete human amylin in the same proportion as it is found in obese people, the researchers determined that amylin oligomers attach to membranes of myocytes -- the heart-muscle cells that control heart beats. This made the membranes more porous to calcium, which changed myocyte contractility, altered the expression of vital proteins and, eventually, caused heart muscle cells to die.

"The significantly altered cardiac myocyte structure and function in the rats, along with the high levels of oligomers in the human heart tissue, strongly suggest that amylin is a major contributor to heart failure in obese and diabetic patients," Despa said.

Despa thinks that the link between cardiac amylin accumulation and heart disease has been overlooked because amylin circulates in relatively small amounts in blood, and because animals, including rats, that are often used in most studies of diabetic cardiac dysfunction do not normally express the form of amylin that aggregates and builds up in tissues.

The scientists now hope to find ways to curb amylin buildup in the heart before it has the chance to destroy muscle tissue.

"Drugs that block amylin from forming into toxic oligomers could significantly reduce the chances of heart failure," Despa said.

For the research, amylin protein accumulation was detected in human and rat heart tissues and cell cultures using immunohistochemistry, immunofluorescence and Western blot. Heart dysfunction in the rats was identified by studying the physiological performance of isolated myocytes and by measuring the expression of tell-tale proteins that deform cardiac muscle. The researchers used echocardiography and measurements of blood flow to assess heart tissue structure and performance and changes in myocardium contractions.

Provided by University of California - Davis