Drugs used to treat heart failure and high blood pressure may help decrease obesity

June 17 2013

A type of drug normally used to treat heart failure and high blood pressure helped prevent weight gain and other complications related to a high-fat diet in an animal study. The results were presented today at The Endocrine Society's 95th Annual Meeting in San Francisco.

Weight gain, especially around the waist, and high blood pressure, combine with other abnormalities to form a cluster of diseases known as metabolic syndrome, which increases the risk of heart disease, diabetes and other serious illnesses. With obesity rates climbing in developed countries throughout the world, medical researchers are trying to find new drugs to prevent metabolic syndrome from occurring.

One new and promising approach involves blocking the action of aldosterone and glucocorticoids, hormones synthesized in the adrenal cortex of mammals. These hormones are capable of activating the mineralocorticoid receptors (MRs). MRs are ligand-activated transcription factors that play a key role in many physiological and pathological processes occurring in several tissues and organs, including kidney, heart and adipose tissue.

Drugs that prevent MRs from reacting to their ligands are known as MR antagonists. In this study, investigators examined, in mice fed a high-fat diet, the effects of drospirenone and spironolactone, two MR antagonists currently used in clinical practice that have been previously shown to modulate adipocyte differentiation in vitro.

They found that the drugs had several benefits, including helping to prevent weight gain and to increase the number of energy-burning fat cells. Animals that received MR antagonists combined with a high-fat diet exhibited more brown fat cells interspersed within white fat tissue, compared to untreated controls. The so-called good kind of fat, brown fat cells actually burn energy to help prevent weight gain, while white fat does the opposite, storing energy as more fat cells.

In order to evaluate the expansion of brown adipose tissue, the investigators also used special imaging tests to measure the percentage of water in fat cells which, at high levels, indicates the presence of brown fat.

In addition, these MR antagonists were effective in reducing the high levels of blood glucose related to impaired glucose tolerance, which can be a precursor to diabetes.

"These data open new unexpected applications of MR antagonists in the treatment of obesity and its metabolic complications, since their use in animal models reverses the metabolic dysfunction induced by a high-fat diet, promoting the activation of brown-like fat in classical white fat depots," said study lead author Andrea Armani, Ph.D., a post-doctoral fellow in obesity research. "Indeed, MR antagonism has promise as a novel approach to treat metabolic syndrome."

The study was coordinated by Massimiliano Caprio, MD, PhD, at the IRCCS San Raffaele Pisana Research Center in Rome, Italy. Previous research by Dr. Caprio's laboratory showed that blocking MR expression in human and animal precursor fat cells prevented them from developing further. These findings led the investigators to design the current study to examine the effects of MR antagonists on adipose tissue and glucose metabolism under obesogenic conditions.

The IRCCS San Raffaele Pisana (Ricerca Corrente); the University of Rome; and the Italian Ministry of Foreign Affairs supported the study.

Provided by The Endocrine Society