Preclinical muscular dystrophy data shows promise

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Cedars-Sinai Heart Institute researchers have found that an experimental compound may help stem the debilitating effects of muscular dystrophy by restoring normal blood flow to muscles affected by the genetic disorder.

The researchers studied HCT 1026, a new type of molecule in which nitric oxide is chemically attached to a standard anti-inflammatory agent, in a preclinical model of muscular dystrophy. Results suggest HCT 1026 may be beneficial for the treatment of Duchenne muscular dystrophy, which begins in early childhood, and Becker muscular dystrophy, which often occurs later in adulthood.

Preliminary results were presented in April 2012 at the Experimental Biology meeting and now the full study is published in the Public Library of Science (*PLOS ONE*) and is available online.

Both forms of muscular dystrophy are caused by problems with a protein called dystrophin, which helps maintain healthy muscles. If patients have less dystrophin protein or if their body manufactures dystrophin protein that does not function correctly, their muscles cannot work properly and eventually become permanently damaged. As diseased muscles weaken over time, patients gradually can lose their ability to walk, sit or use their muscles in other ways. There is no cure now for either form of the disease.

"There is an urgent unmet need for effective therapeutic options for this

devastating disease," said Ronald G. Victor, MD, director of the Cedars-Sinai Center for Hypertension in the Cedars-Sinai Heart Institute and the Burns and Allen Chair in Cardiology Research. "If we can improve blood flow in muscular dystrophy patients, we may be able to preserve some muscle function over a longer period of time."

HCT 1026 dramatically improved blood flow in muscles used during exercise by dystrophin-deficient laboratory mice who share the same genetic defect as humans, Cedars-Sinai researchers found. The compound may have accomplished this by delivering nitric oxide, a key molecule involved in many physiological functions and found at reduced levels in dystrophic muscles.

The compound fully restored blood flow to affected muscles within the first month of treatment, and the impact was completely sustained for three months without any noticeable adverse side effects.

Authors of the study said the results represent a step in the quest to find an effective treatment for muscular dystrophy that will reduce muscle wasting as well as slow the progression of the disease.

"Based on our previous work, we think the ability of HCT 1026 to release nitric oxide is the key to restoring muscle blood flow in dystrophin-deficient mice," said Gail Thomas, PhD, a lead author of the Cedars-Sinai study. "HCT 1026 is an interesting prototype which allowed us to investigate the potential of this family of molecules in muscular dystrophies. While we do not expect these nitric oxide-donating compounds to cure the disease, our hope is that the improved blood flow could reduce muscle fatigue and injury, allowing patients to be more active while slowing down the loss of vital muscle."

Provided by Cedars-Sinai Medical Center