New enzyme-replacement therapy shows promise for genetic lipid disease treatment

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Of the more than 50 known lysosomal storage diseases (LSDs)-rare inherited metabolic disorders-only seven can be treated with approved enzyme-replacement therapies. Lysosomal acid lipase deficiency (LALD) is an LSD that causes fatty liver disease and cirrhosis. There is no treatment for the disease, which afflicts 1- 40,000 - 1 in 300,000 people across the world. In this week's *New England Journal of Medicine*, researchers report results of a trial showing the efficacy of a new enzyme-replacement therapy for LALD. In an accompanying editorial, Daniel J. Rader, MD, chair of the department of Genetics in the Perelman School of Medicine at the University of Pennsylvania, notes that this first-ever hepatocyte-targeting therapy will be pivotal in treating this disease.

In a phase 3 trial in patients with lysosomal acid lipase deficiency, researchers evaluated the safety and effectiveness of the hepatocyte-targeting enzyme-replacement therapy for LALD, known as sebelipase alfa. The therapy works by administering enzymes that specifically target hepatocytes, cells that make up nearly 80 percent of the liver. These enzymes are taken up by the hepatocytes, directed to the lysosomes, and replace the missing lysosomal acid lipase enzymes. With 66 patients involved in the 20-week trial, researchers found that treatment with sebelipase alfa resulted in reduced disease-related liver and blood cholesterol abnormalities, such as cirrhosis, hepatomegaly, and liver fibrosis. More, patients experienced lower cholesterol levels, and reduced liver fat content and size with continued treatment.

"LALD is an underdiagnosed disease with serious medical consequences," Rader said. "Sebelipase alfa could be a game-changer in the treatment of this disease. However, to effectively treat patients, physicians need to think of diagnosing this disorder and initiating this therapy, once available, as early as possible."

Rader also notes that while a larger, longer-term study is needed to prove that this treatment will prevent serious liver consequences, he says "sebelipase alfa has shown great potential for effectively treating and managing this underappreciated genetic lipid disorder."

Provided by University of Pennsylvania School of Medicine