NIH study to test treatment for fatty liver disease in children

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With the launch of a new clinical trial supported by the National Institutes of Health, researchers are working to determine whether treating children diagnosed with the most severe form of fatty liver disease with a drug called cysteamine will help improve the liver.

The trial, called Cysteamine Bitartrate Delayed-Release for the Treatment of Nonalcoholic Fatty Liver Disease in Children (CyNCh),will enroll 160 boys and girls ages 8 to 17 with nonalcoholic fatty liver disease (NAFLD). The participants will receive cysteamine or placebo by mouth twice a day for a year. There are no weight cutoffs or percentiles for the children participating in CyNCh. However, more than 90 percent of the children are expected to be overweight or obese. Participants need a baseline biopsy that confirms severe NAFLD to be eligible for the study. Children with poorly managed diabetes, heart disease, and other chronic liver diseases will be excluded.

NAFLD covers a range of severity from simple liver disease without injury, called steatosis, to the more concerning nonalcoholic steatohepatitis, or NASH, which includes fat accumulation, inflammation, and liver injury. Most children with fatty liver disease are overweight and resistant to insulin, a hormone that regulates energy. The only way to distinguish NASH from other forms of fatty liver disease is with a liver biopsy.

"We did not see fatty liver disease in children until recently," said Edward Doo, M.D., NASH Clinical Research Network project scientist

and director of the Liver Diseases Program at NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), which is funding the study in collaboration with Raptor Pharmaceutical of Novato, Calif., which makes the drug and will provide it to the trial. "Fatty liver disease affects about 17 percent of children in the United States. This rise in the number of children with NAFLD most likely mirrors the increase in obesity, which affects more than 16 percent of American children and teens," Dr. Doo said.

Results from a small pilot study using cysteamine in 11 children with NASH suggest that it improves liver enzymes by reducing toxins that can damage the liver. Cysteamine is approved to treat cystinosis, a genetic disease that causes the amino acid cystine to accumulate in the kidneys, liver, eyes, brain, and white blood cells. Modest weight loss through diet and physical activity may help some children with fatty liver disease, but it is a treatment option that seldom helps people meet their goals. "We know that following a weight loss plan for many children and adults can be daunting, especially if they have limited access to healthy food options that are low in fat, added sugars, and calories, and infrequent opportunities for physical activity," said Joel E. Lavine, M.D., Ph.D., a CyNCh principal investigator and professor of pediatrics at Columbia University, New York City. "Hopefully, this trial will move us closer to finding a safe and effective treatment that helps children with fatty liver disease."

NAFLD can be a precursor to NASH, which may progress to cirrhosis, liver failure and liver cancer. NAFLD may also increase a patient’s risk of developing heart disease. A healthy liver helps the body remove harmful chemicals from the blood, fight infection and digest food. If too much scar tissue forms, the liver could fail. Then a liver transplant is required. "We are concerned that the disease may advance as children become adults and increase their risk for cirrhosis, liver failure, liver transplantation, and death as adults," said Stephen P. James, M.D.,

director of the NIDDK's Digestive Diseases and Nutrition Division. "This multicenter, double-blind trial offers researchers and NIDDK an opportunity to rigorously assess how safe and effective cysteamine is in treating children with NASH, as well as to reveal new avenues worthy of scientific study."

The following clinical centers are conducting the CyNCh trial:

- Children's Memorial Hospital, Chicago
- Cincinnati Children's Hospital Medical Center
- Columbia University, New York City
- Indiana University, Indianapolis
- Mount Sinai Medical Center, New York City
- St. Louis University
- Texas Children's Hospital, Houston
- University of California, San Diego
- University of California, San Francisco
- University of Washington, Seattle

For more information:

- NIDDK's NASH Clinical Research Network: jhuccs1.us/nash/open/centers/centers.htm
- NIDDK's Action Plan for Liver Disease Research: www.liverplan.niddk.nih.gov
- National Digestive Diseases Information Clearinghouse: digestive.niddk.nih.gov
- Weight-control Information Network: www.win.niddk.nih.gov
- ClinicalTrials.gov: www.clinicaltrials.gov