UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: LaKisha Ladson
214-648-3404
lakisha.ladson@utsouthwestern.edu

Medication effective for acute liver failure in early stages of disease, UT Southwestern doctors find

DALLAS – Oct. 8, 2009 – The antidote for acute liver failure caused by acetaminophen poisoning also can treat acute liver failure due to most other causes if given before severe injury occurs, UT Southwestern Medical Center researchers and their colleagues at 21 other institutions have found.

Acute liver failure occurs when cells in the liver die quickly, resulting in toxins being released into the bloodstream and brain. Patients often end up in a hepatic coma as a result of toxins not being cleared by the failing liver. Known causes of acute liver failure include autoimmune hepatitis, drug-induced liver injury, hepatitis A and B, and acetaminophen poisoning.

In a study published in the September issue of *Gastroenterology*, researchers found that acute liver failure patients in early stages of hepatic comas, when treated with the medicine N-acetylcysteine (NAC), were nearly 2.5 times more likely to survive than those treated only with a placebo.

"NAC is safe, easy to administer, doesn't require intensive care and can be given in community hospitals," said Dr. William M. Lee, professor of internal medicine at UT Southwestern and lead author of the study. "NAC is an excellent treatment for non-acetaminophen acute liver failure if the disease is caught early."

Acute liver failure affects about 2,000 people annually in the U.S., and 50 percent of those cases are caused by acetaminophen poisoning. Until this study, liver transplantation was the only treatment if the failure was from non-acetaminophen causes.

To test NAC's use in non-acetaminophen cases, researchers at 22 sites randomly assigned non-acetaminophen acute liver failure patients by the level of their coma, with those with mild to moderate coma in one group, and patients with more severe coma in the other group. Beginning in 1999 and continuing for eight years, 173 patients received either NAC or a placebo for 72 hours. Doctors recorded patient survival three weeks after they were placed on treatment.

Researchers found that 52 percent of acute liver failure patients in mild to moderate comas survived when treated with NAC, compared to just 30 percent of those treated with only a placebo. In

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patients experiencing more severe coma, treatment with NAC did not result in a significant difference in survival rates.

"That makes sense because patients with advanced comas typically die or get a transplant within a few days," said Dr. Lee, principal investigator of the Acute Liver Failure Study Group, a national consortium of liver centers formed in 1997 to increase research into the rare disease.

"This study establishes NAC as a treatment for non-acetaminophen acute liver failure patients in mild to moderate coma and provides the first glimmer of hope that something can help these direly ill patients," Dr. Lee said.

He said he will continue to study NAC as a therapy for acute liver failure not caused by acetaminophen poisoning to determine optimal dosing and duration.

Other UT Southwestern researchers involved in the study included Dr. Linda Hynan, professor of clinical sciences and psychiatry; Dr. Anne Larson, associate professor of internal medicine; and Dr. Joan Reisch, professor of clinical sciences and family and community medicine. Other Acute Liver Failure Group investigators involved in the study were from the University of California, Davis; the University of Michigan; Virginia Commonwealth University; University of California, San Francisco; Baylor University Medical Center; University of Nebraska; and the National Institute of Diabetes and Digestive and Kidney Diseases.

The study was funded in part by the National Institutes of Health, the Food and Drug Administration, and the Northwestern Medical Foundation. The N-acetylcysteine used was supplied by Apothecon/Geneva Pharmaceuticals, a division of Bristol Myers Squibb and Cumberland Pharmaceuticals.

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