

Mayo Clinic seeks new therapies for alcoholic hepatitis

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A new study from Mayo Clinic finds the use of the drug therapy etanercept ineffective in treating alcoholic hepatitis, an acute inflammation of the liver caused by excessive consumption of alcohol. The results of the study are published in the December issue of *Gastroenterology*.

Alcoholic hepatitis is a major cause of morbidity and mortality worldwide. Severe alcohol-related liver disease carries a poor prognosis. Several research studies have worked to find a successful treatment for alcoholic hepatitis, but no consensus has been reached on the most effective treatment regimen.

"Alcohol usage has long been associated with serious liver diseases such as hepatitis," says Vijay Shah, M.D., a Mayo Clinic hepatologist and lead researcher on the study. "The relationship between drinking and alcoholic hepatitis is complex. Not all heavy drinkers develop alcoholic hepatitis, and the disease can sometimes occur in people who drink only moderately. Though damage from alcoholic hepatitis often can be reversed if patients stop drinking, the disease can progress to cirrhosis and liver failure."

In this placebo-controlled clinical trial, Mayo researchers collaborated with seven other medical centers to enroll 48 patients with moderate to severe alcoholic hepatitis. Patients were either given a placebo or etanercept, a compound which blocks the effects of toxic cytokines. Etanercept is approved for treatment of inflammatory arthritis and is

under investigation for effectiveness in treating other inflammatory conditions. Research results found a significantly higher rate of six-month mortality in patients with moderate to severe alcoholic hepatitis who received etanercept. The six-month mortality rate was more than double that of the placebo group. The major cause was an increased rate of infections.

"Etanercept therapy showed promise in our animal models, but was not effective in treatment of patients with alcoholic hepatitis. A few possible causes of increased late mortality rate may relate to impaired liver regeneration, and another is the effects of etanercept on immune function," says Dr. Shah.

Liver disease complications from alcohol are typically severe and difficult to treat, which further emphasizes the importance of not drinking too much.

"Despite awareness of hepatitis C and non-alcoholic fatty liver syndrome, our recent studies show that alcoholic liver disease is still the major cause of liver disease and liver-related death," says Dr. Shah. "Our Mayo Clinic research team will continue to examine other avenues of treatment for alcoholic hepatitis patients -- including examining other anti-inflammatory proteins for study purposes."

Complete abstinence from alcohol is the single most important treatment for alcoholic hepatitis. It's the only way to reverse liver damage or, in more advanced cases, to reduce the chance that the disease will become worse. Without abstinence, the majority of people with alcoholic hepatitis eventually develop cirrhosis and die, says Dr. Shah.

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