Hepatitis C treatment reduces the virus but liver damage continues

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Treating patients who have chronic hepatitis C and advanced liver disease with long-term pegylated interferon significantly decreased their liver enzymes, viral levels and liver inflammation, but the treatment did not slow or prevent the progression of serious liver disease, a study finds.

These findings come from the clinical trial, Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis (HALT-C) and are reported in the Dec. 4 issue of the *New England Journal of Medicine*. HALT-C was funded by the National Institutes of Health (NIH) with additional support from Hoffmann-La Roche Inc.

"The results from HALT- C show without question that maintenance therapy with peginterferon does not prevent progression of liver disease among patients who have failed prior treatments," said James Everhart, M.D., project scientist for HALT-C in the Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the principal sponsor of HALT-C at NIH. "These findings heighten the incentive to develop more effective drugs for patients with severe liver disease due to hepatitis C."

Peginterferon therapy for up to 48 weeks is standard for chronic hepatitis C. But patients who do not have a sustained response to initial therapy have been given the drug over a longer time based on studies showing that this approach suppresses viral and enzyme levels, even if the virus is not completely eliminated. However, it was not known if long-term therapy would improve important clinical outcomes such as liver damage and death.

HALT-C, a randomized multicenter trial of 1,050 patients with chronic hepatitis C who had failed prior treatment to eradicate the infection, tested whether long-term treatment with peginterferon alfa-2a would reduce the development of cirrhosis, liver cancer, or liver failure. The 517 patients randomized to the treatment arm received 90 micrograms of peginterferon in weekly injections for 3.5 years. The 533 patients in the control arm underwent the same follow-up and care as the treated patients including liver biopsies, quarterly clinic visits and blood tests. All patients had advanced liver fibrosis, a gradual scarring of the liver that puts patients at risk for progressive liver disease and liver failure.

The outcomes studied in HALT-C were death, liver cancer, or liver failure, and for those who did not have cirrhosis initially, the development of cirrhosis. At the end of the study, 34.1 percent of the treated group and 33.8 percent of the control group had experienced at least one outcome. Patients in the treated group had significantly lower blood levels of the hepatitis C virus and improvement in liver inflammation. However, there was no major difference in rates of any of the primary outcomes between the groups.

Among treated patients, 17 percent stopped peginterferon after 18 months and 30 percent stopped the drug after two years. Infections, musculoskeletal or digestive problems were the most common reasons for stopping the drug.

According to HALT-C study chair and principal investigator Adrian M. Di Bisceglie, M.D., professor of internal medicine at Saint Louis University School of Medicine in Missouri, looking into how maintenance therapy works in non-responders is an important step. "Patients should not receive interferon as maintenance therapy for chronic hepatitis C. However, we can build on what was learned in HALT-C to identify better treatments that may delay or prevent liver damage in patients with advanced disease," he said.

The hepatitis C virus infects more than 100 million persons worldwide and as many as 4 million in the United States. Hepatitis C ranks with alcohol abuse as the most common cause of chronic liver disease

and leads to about 1,000 liver transplants in the United States each year. The best current antiviral therapy of pegylated interferon given by injection in combination with oral ribavirin for about 6 months to a year eliminates the virus in about 50 percent of infected patients.

Source: National Institute of Diabetes and Digestive and Kidney Diseases