

Hepatitis C

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Liver Steatosis

Steatosis, or fatty liver, is a type of progressive liver damage sometimes seen in people with hepatitis C, especially those with genotype 3. Three recent articles shed further light on the condition.

In the March 2004 issue of *Gut*, L. Castera and colleagues from France reported on the relationship between steatosis and HCV clearance after antiviral treatment. The study included 151 subjects who had paired (before and after treatment) liver biopsies (37 with HCV genotype 3; 114 with non-3 genotypes). None were obese or heavy alcohol users. Twenty-five patients (16.5%) achieved a sustained virological response (SVR). Post-treatment biopsies showed

improved steatosis in 36% of subjects, worsened steatosis in 13%, and stable steatosis in 51%. Steatosis improvement was seen significantly more often in patients who achieved SVR (64%) compared with nonresponders (31%). The responder/ nonresponder difference was significant in patients with genotype 3 (91% versus 19%), but not in those with non-3 genotypes (43% versus 34%). Among the 25 subjects who achieved SVR, steatosis improvement occurred significantly more often in genotype 3 patients (91%) than in those with other genotypes (43%). Among the nonresponders, steatosis improvement did not differ by genotype. In a multivariate analysis, improved steatosis was independently associated with SVR, initial steatosis severity, genotype 3 HCV, and body mass index of 25 or greater (a BMI over 25 is considered "overweight," and a BMI over 30 is considered "obese"). In conclusion, pa-

Continued on page 2

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Continued from page 1

tients with genotype 3 HCV who achieved SVR showed significant improvement in steatosis, suggesting that genotype is an important factor in steatosis pathogenesis.

In the same issue of *Gut*, L. Rubbia-Brandt and a group of international colleagues confirmed that genotype affects steatosis. The researchers performed a multivariable logistic regression analysis on data from 755 patients with chronic hepatitis C, 178 of whom had genotype 3. Liver biopsies revealed that 315 had steatosis and 605 had fibrosis (of whom 187 had progressed to cirrhosis). In this study, steatosis was independently associated with presence of fibrosis, genotype 3 HCV, ongoing heavy alcohol use, and older age. Fibrosis was independently associated with presence of steatosis, past heavy alcohol use, Metavir activity score (degree of liver damage), older age, and body mass index, but not with genotype. When patients were separated based on genotype, steatosis was associated with ongoing heavy alcohol use and older age only in people with

non-3 genotypes, and was associated with Metavir score only in genotype 3 patients. Similarly, fibrosis was associated with steatosis only in those with genotype 3, and was only associated with past heavy alcohol use in those with non-3 genotypes. The researchers concluded that “steatosis influences chronic hepatitis C progression in a genotype specific way,” and suggested that patients with genotype 3 HCV and histologically confirmed steatosis should receive antiviral treatment.

Finally, in the March 2004 issue of the *Journal of Hepatology*, Heather Patton and colleagues from the Scripps Clinic reported on the impact of steatosis on liver disease progression and treatment response in patients with chronic hepatitis C. The researchers evaluated liver biopsies from 574 patients, and found that steatosis severity was associated with body mass index, HCV genotype 3, older age, and longer duration of infection. Among those with genotype 3, higher HCV viral load was associated with more severe steatosis. In people with

genotype 1, fibrosis with associated with steatosis severity. Also in the genotype 1 group, patients with less severe pre-treatment steatosis were more likely to achieve SVR. Indeed, genotype 1 patients who achieved an early virological response were more likely to have grade 0 (minimal or no) steatosis compared with early nonresponders. As in Castera’s study, steatosis improved markedly in genotype 3 patients who achieved SVR. The researchers concluded that “steatosis is an important cofactor in hepatitis C as it is associated with fibrosis and reduces the likelihood of achieving early and sustained virologic response in genotype 1 infected patients.”

Body Weight and Liver Disease

In the March 2004 issue of *Hepatology*, Saverio Stranges from the State University of New York at Buffalo and colleagues looked at the association between body weight, body fat distribution, and liver enzyme levels. Recent research has shown that in addition to increasing the

Continued on page 3

Continued from page 2

risk of insulin resistance and cardiovascular disease, abdominal (or central) fat accumulation is also a risk factor for liver steatosis. The researchers analyzed data from 2,074 subjects without known liver disease. Using multiple linear regression models, they found that abdominal fat accumulation was a better predictor of elevated ALT and GGT (two liver enzymes) than body mass index in both men and women. The authors concluded that central fat accumulation (that is, having a “pot belly,” or an “apple” versus a “pear” shape) is associated with elevated liver enzyme levels independent of body weight, and suggest this may be due to unrecognized steatosis.

In the March 2004 issue of *Gut*, I. Hickman and colleagues from Australia reported that modest weight loss and increased physical activity led to decreased ALT, improved fasting insulin levels, and better quality of life in overweight patients with chronic liver disease. The study looked at 31 participants who completed a 15-month diet and exercise program. At the

end of the program, 21 patients (68%) achieved and maintained a reduction in body weight. ALT improvements were correlated with the amount of weight lost. Among patients who maintained their weight loss at 15 months, ALT levels remained significantly below baseline values, while those who regained their lost weight had ALT levels similar to baseline. These results are not surprising, since obesity is associated with steatosis and fibrosis progression in people with chronic hepatitis C and other types of liver disease. Those who lost weight also had improved fasting serum insulin levels and reported a significantly better quality of life. The researchers concluded that “[t]reatment of overweight patients should form an important component of the management of those with chronic liver disease.”

HCV Rates Among Veterans

In the March 2004 issue of the *Journal of Clinical Gastroenterology*, Kevin Sloan and colleagues confirmed that hepatitis C prevalence

is higher among U.S. veterans in the Northwest compared with the population as a whole. It is estimated that among the general population, about 1.8% are infected with HCV. Past studies of veterans have found prevalence rates between 1.7% and 3.5%. In this study, researchers conducted a retrospective review of medical records from nearly 38,000 patients tested for HCV between October 1994 and December 2000 at eight Veterans Administration Medical Centers in the Northwest Network. Based on their results, the authors estimated that 11.4% of veterans in the region are HCV positive, with a lower bound of 4.0% and an upper bound of 19.5%. This rate is higher than the 8-10% seen in a national sample of all veterans who received blood tests throughout the Veterans Healthcare Administration on a single day in 1999. However, the researchers noted that changes in testing practices (that is, increased testing of a broader range of patients) makes it difficult to make comparisons with rates from past studies.

