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Liz Highleyman

Obesity Has a Negative Impact on HCV Progression

Data continues to accumulate indicating that obesity promotes HCV progression and liver fibrosis and renders interferon therapy less effective. For example, Canadian researchers reported in the September issue of *Hepatology* that obese patients (body mass index [BMI] greater than 30 kg/m²) had about an 80% lower chance of a sustained response to therapy compared with normal or moderately overweight patients. And in the October issue of *Gastroenterology*, another research team reported that hospitalization or death due to cirrhosis was more likely among obese individuals.

Now, Ke-Qin Hu, MD, from the University of California at Irvine and colleagues report in the January 2004 issue of the *Journal of Hepatology* that hepatic steatosis (fatty liver) is more common in obese or overweight people and is associated with progression of liver fibrosis. The authors reviewed medical charts from 324 patients at a U.S. university medical center and a regional Veterans Administration medical center. They found that patients who were either obese (BMI at least 30 kg/m²) or moderately overweight (BMI at least 25 kg/m²) were at higher risk for hepatic steatosis. They also found that steatosis—especially advanced (grade II or III) steatosis—was significantly associated with persistently elevated ALT levels, advanced (stage III or IV) fibrosis, and higher histological activity index (HAI) scores. The authors concluded that being overweight or obese is as an independent risk factor for hepatic steatosis in patients with chronic HCV, and that steatosis accelerates activity and progression of chronic hepatitis C.

It is unclear how increased fat accelerates liver fibrosis, but recent research provides some clues. In the December 2003 issue of the same journal, Ingrid Hickman from the University of Queensland in Brisbane and colleagues measured serum levels of insulin, C-peptide, and leptin (a hormone produced by fat cells that helps promote normal insulin activity) in 160 HCV patients and 45 uninfected control subjects matched for age, sex, and body weight; the HCV patients also underwent liver biopsies. Consistent with previous research, patients with HCV genotype 3 had more severe steatosis than those with genotype 1. Among subjects with

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either genotype, overweight patients had significantly more steatosis and higher insulin and leptin levels. In the overweight HCV patients, an increase in serum insulin was correlated with increasing fibrosis, leading the authors to suggest that elevated circulating insulin “may be a factor responsible for the association between [body mass index] and fibrosis in patients with HCV.”

Another study in the same issue suggests that blood glucose abnormalities themselves, rather than excess body weight, may trigger fibrosis progression. Vlad Ratziu, MD, from Hôpital Pitié Salpêtrière in Paris and colleagues analyzed 710 patients with chronic HCV. When analyzing various factors separately, both elevated serum glucose (blood sugar) and higher BMI were associated with increased fibrosis. However, in a multivariate analysis (which corrects for confounding associations), age at infection, duration of infection, serum glucose, and alcohol intake were independently associated with increased fibrosis, but body mass was not. The authors concluded that, “High serum glucose is an independent co-factor of fibrosis in chronic hepatitis C with a higher pro-fibrogenic impact than overweight.”

Hepatocellular Carcinoma on the Rise

Hepatocellular carcinoma is a type of liver cancer that can occur in people with advanced hepatitis C or B. Because HCV progresses slowly, many people infected years or even decades ago are only now coming down with liver cancer and other serious long-term consequences of chronic hepatitis. In the November 18, 2003 issue of the *Annals of Internal Medicine*, Hashem El-Serag, MD, MPH, of the Houston Veterans Affairs Medical Center and Baylor College of Medicine, and colleagues reported that hepatocellular carcinoma is increasing rapidly in the U.S. The authors conducted a retrospective analysis of data from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) registries, which represent about 10% of the U.S. population. Between 1975 and 1998, the overall age-adjusted incidence rate of hepatocellular carcinoma doubled from 1.4 cases per 100,000 persons in 1975–1977 to 3.0 cases per 100,000 persons in 1996–1998. In 1995–1998 alone, the rate increased 25%. Rates rose for men and women, all ethnic groups, and most age groups over 40, but the increase was greatest among white men aged 45–54. The authors concluded that their results likely reflect a true increase in the incidence of hepatocellular carcinoma, rather than changes in diagnostic practices or changing demographic features of the general population. “This is an alarming increase in a highly lethal cancer,” said Dr. El-Serag. “We think that hepatitis C virus infections, acquired two to three decades earlier [e.g., in the 1960s and 1970s], are partially responsible for this increase in liver cancer.”

Clues about HCV/HBV Coinfection

While in recent years considerable attention has focused on HCV/HIV infection, and is increasingly turning to HBV/HIV coinfection, very little is known about dual infection with HCV and HBV. However, since the two viruses are spread in similar ways, it is likely that

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HCV/HBV coinfection is more common than generally recognized. In the February issue of the *Journal of Medical Virology* (published online in December 2003), Takeshi Tanaka of Tokyo Metropolitan Komagome Hospital and colleagues reported on the incidence and significance of low-level HBV infection in patients with HCV-associated liver disease. The authors collected blood samples from 93 HCV-infected subjects without detectable HBV surface antigen (HBsAg) and 220 healthy, uninfected volunteers. Using a PCR test for HBV DNA, they determined that 34.4% of the HCV-infected patients had HBV genetic material in their blood—despite having no evidence of HBsAg—compared with just 1.8% of the uninfected volunteers. The researchers also reported that hepatocellular carcinoma was more common in HCV/HBV coinfecting patients than in those with HCV alone, and that the hepatitis C and B viruses were distributed differently in the liver tissues of coinfecting patients than in those with either virus alone. The results suggest that low-level HBV infection is common in people with HCV, and points to the need for more research on this form of coinfection.

