

Hepatitis C

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Treatment of Patients with Mild Liver Damage

Many experts believe that HCV positive individuals with histologically mild liver disease will not benefit greatly from therapy, and current guidelines recommend against treating patients with minimal liver damage as determined by biopsy. But according to a study from the U.K. published in the January 2005 *Journal of Viral Hepatitis*, treatment may be indicated for people with mild disease and HCV genotypes other than 1. In this randomized multicenter trial, treatment-naive patients with histologically mild hepatitis C received either no therapy or three-times-weekly standard interferon plus daily ribavirin for 48

weeks. One-third of participants (32 out of 98) achieved sustained virological response (SVR); by genotype, the SVR rates were 18% for genotype 1 and 49% for non-1 genotypes. As seen in most studies, no patients who did not experience at least a 2-log drop in HCV RNA by week 12 went on to achieve SVR. Using the SF-36 questionnaire, treated subjects reported improved quality of life 24 weeks after the end of therapy. The authors concluded that the high response rate and good outcomes among people with non-1 HCV genotypes suggest that this group should be offered treatment regardless of histological stage. For those with genotype 1, the low SVR rate is likely to be outweighed by side effects, and therapy should thus be reserved for those

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with biopsies showing liver disease progression. However, SVR rates would be expected to be higher for genotype 1 patients using pegylated interferon plus ribavirin (as high as 50% in some trials), so this type of study should be repeated using the newer, more effective form of the drug.

SSRIs to Prevent Depression During Interferon Therapy

Depression related to interferon is a treatment-limiting side effect for many patients with hepatitis C. But as reported in the January 2005 *Journal of Viral Hepatitis*, preventive use of selective serotonin re-uptake inhibitors (SSRIs), a class of antidepressant, can enable many to succeed with therapy. M.R. Kraus and colleagues studied patients who were retreated with pegylated interferon plus ribavirin after previous unsuccessful therapy attempts. Eight subjects who had developed major depression during their prior treatment were given prophylactic (preventive) SSRIs, while 9 were retreated without preventive antidepressants. The Hospital Anxiety and Depression Scale was used to assess mood before, during, and

after therapy. All patients who received prophylactic SSRIs completed HCV therapy, and the researchers determined that depression scores were significantly lower in this group. Subjects who did not receive preventive SSRIs experienced depression levels similar to those during their first course of HCV treatment. "SSRI prophylaxis is safe and efficacious," the authors concluded, "and should be considered, if antiviral re-therapy is indicated."

HCV Genotype and HIV Disease Progression

It is well known that HCV genotype 1 is less responsive to interferon-based therapy. Research increasingly suggests that it may also contribute to worsened progression of both hepatitis C and HIV disease. Studies have shown that HCV/HIV coinfection is associated with more rapid liver disease progression, but its effect on the course of HIV disease remains controversial, with recent studies yielding conflicting data. One possible reason for this disparity may be that the effect of HCV on HIV disease progression varies by genotype.

In the January 1, 2005 *Journal of Infectious Diseases*, T.W. Yoo and colleagues reported on a study looking at the relationship between genotype and HCV viral load, HIV viral load, CD4 cell count, and clinical disease progression. The analysis included 333 hemophiliac children and adolescents, 207 of them HCV/HIV coinfecting and 126 with HCV alone. After seven years of follow-up, the researchers found that mean HCV RNA levels were higher among genotype 1 patients compared to those with other HCV genotypes, in both the coinfecting and HCV-monoinfecting groups. In addition, coinfecting subjects with genotype 1 had significantly lower absolute CD4 cell counts and CD4 percentages and were at increased risk for HIV disease progression than coinfecting individuals with non-1 genotypes. HCV genotype was not, however, associated with differences in HIV viral load. "The present study has demonstrated that HCV genotype has an effect on HCV replication in both individuals infected with HCV only and individuals coinfecting with HIV-1 and HCV," the authors concluded, recom-

mending further studies be conducted to elucidate the mechanism behind these observations.

Looking at another recent study, L. van Asten and colleagues reported in the November 19, 2004 issue of *AIDS* that concurrent infection with more than one HCV genotype is also associated with more rapid HIV disease progression. This research team analyzed data from 126 HIV/HCV-coinfected injection drug users from seven European countries (68% male, average age at HIV seroconversion 27 years). Genotype 1 was most common (48%), followed by genotype 3 (34%), genotype 4 (13%), and genotype 2 (1%); 5% were infected with more than one genotype. After a median follow-up of about seven years, subjects with HCV genotype 1 and those with multiple HCV genotypes experienced more rapid immunological progression to a CD4 cell count of 200 cells/mm³ or fewer (that is, an AIDS diagnosis). Further breaking down the results, the researchers determined that worsened immunological decline was linked to HCV genotype 1a but not 1b.

Also, those with multiple HCV genotypes experienced slightly faster clinical progression to AIDS, but no significant differences in clinical progression were seen when comparing subjects with genotypes 1, 3, or 4 alone. The authors concluded that, "HIV disease progression differs by HCV genotype and is especially faster in individuals whose HCV infection involves more than one HCV genotype." Because the observed differences in immunological decline and clinical HIV disease progression were more pronounced when looking only at data from before the advent of highly active antiretroviral HIV therapy (HAART), they added that effective anti-HIV therapy "may diminish the effect of HCV genotype on HIV disease progression."

High Hepatitis C Rates in U.S. Veterans

U.S. veterans have a hepatitis C infection rate more than twice as high as that of the general population, according to a report in the January 2005 issue of *Hepatology*. In a study of nearly 1,300 patients at Department of Veterans Af-

fairs medical centers, the prevalence of hepatitis C virus (HCV) infection was estimated at 5.4%. Nearly one-third of participants responding to the researchers' survey reported at least one traditional risk factor. Among those who tested HCV antibody positive, 78% had either received a blood transfusion or injected drugs. Tattoos and incarceration^{3/4}but not direct military-related exposures^{3/4}were also linked to higher HCV rates.

