Two-day results predict ultimate response to therapy in chronic hepatitis C

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A new study suggests that previously noted low rates of successful hepatitis C virus (HCV) therapy in African Americans are in large part due to very early differences in the antiviral activity induced by interferon. The study is published in the April 15 issue of the *Journal of Infectious Diseases*, now available online.

More than 3 million Americans are infected with HCV, and in some countries more than 10 percent of the population is infected. Chronic HCV infection is the leading cause of liver failure worldwide. Response to standard therapy with peginterferon and ribavirin varies widely. Those infected with one strain of the virus—genotype 1—are the least likely to have a successful response to therapy, known as a sustained virological response (SVR). About one-half of patients infected with genotype 1 do not achieve SVR.

Studies have shown that African Americans have consistently lower rates of SVR to interferon-based therapy, compared to Caucasian Americans. A recent study of those with chronic genotype 1 HCV infection found that only 28 percent of African American patients attained SVR, compared with 52 percent in Caucasian Americans. This new study shows that the variation in therapy responsiveness between African Americans and Caucasian Americans can be partly explained by differences in viral response noted as early as one to two days after the first dose of peginterferon.

The study, conducted by a collaborative group of eight medical centers throughout the United States, monitored 341 patients with chronic HCV, genotype 1, who underwent therapy with peginterferon and ribavirin for at least 24 weeks. It focused on response rates to interferon therapy within the first 28 days of therapy, noting viral factors such as HCV RNA levels and host factors such as race, gender, and weight.

Results showed that HCV RNA levels decreased in almost all patients, and that the degree and pattern of decrease, as expected, was different between African and Caucasian Americans. Most important was the new finding that these differences were statistically significant by day 2 of treatment, and that this early viral kinetic measurement was a reliable predictor of ultimate SVR rates. After 28 days of treatment, 22 percent of Caucasian Americans, but only 12 percent of African Americans, were HCV RNA negative.

These findings are particularly important because they point toward the presence of some block or defect in the immediate antiviral response of those who do not respond to therapy. As the authors summarize, "The underlying cause of virological non-response and the reasons why it is more common among African Americans than Caucasian Americans are not clear. [But] the current analyses demonstrated that these differences are fundamentally biologic and become apparent within 24 to 48 hours of starting therapy." As a next step, future research should focus on these host biologic factors that are induced by interferon in an attempt to improve therapy response rates.

In an accompanying editorial, Andrew W. Tai, MD, PhD, and Raymond T. Chung, MD, of Massachusetts General Hospital agree that the findings will prove vital for future research into HCV, remarking, "[this study] demonstrates that the low rates of SVR in African American patients in response to IFN-based therapy appear to result, in large part, from impaired early viral kinetics. Further studies are necessary to uncover the relevant mechanisms that underlie this defect in IFN signaling… with the hope that such mechanisms can be manipulated to restore interferon responsiveness in the otherwise nonresponsive host."

Source: Infectious Diseases Society of America