Age and Prediction of Sustained Virological Response to Hepatitis C Virus (HCV) Infection Treatment Based on 28-Day Decrease in HCV RNA Levels

To the Editor—Several virus and host characteristics, such as different viral genotypes or race, may affect the efficacy of treatment for chronic hepatitis C virus (HCV) hepatitis [1, 2].

Hoofnagle et al [3] observed that the chance of obtaining a sustained virological response (SVR) in 341 patients infected with HCV genotype 1 who underwent treatment with pegylated interferon α-2a and ribavirin was directly related to the 28-day decrease in HCV RNA level. However, the authors found that, after adjustment for 28-day response, SVR rates remained poorer among African American patients than among white patients.

We have previously shown that being aged ≥40 years has a detrimental effect on SVR in patients infected with HCV genotypes 1 or 4 [4]. Thus, we repeated the analysis of Hoofnagle et al [3] in a hospital-based cohort of adult patients to evaluate the effect of age as a predictor of SVR, taking into account the 28-day decrease in HCV RNA level. Our analysis focused on the 62 adult Italian patients (age, 25–75 years) infected with HCV genotype 1 or 4 who started a regimen of pegylated interferon α-2 and ribavirin during the period 2001–2007 and who had a measurement of HCV load on treatment day 28.

Overall, patients aged <40 years experienced higher rates of SVR than did those aged ≥40 years (84.2% vs 30.2%). On the basis of the 28-day decrease in the HCV RNA level, we grouped patients as follows: 25 patients with a decrease <1 log_{10} IU/mL, 18 patients with a decrease of 1–3 log_{10} IU/mL, and 19 with a decrease ≥3 log_{10} IU/mL. Patients aged <40 years experienced SVR rates of 60%, 83.3%, and 100%, respectively, which were higher than the rates observed in patients aged ≥40 years (15%, 25%, and 63.6%, respectively; adjusted relative risk, 0.44; 95% confidence interval, 0.29–0.67; P <.001).

We then determined the probability of SVR in patients aged <40 years and in those aged ≥40 years on the basis of the level of decrease in the HCV RNA load by using a multivariable logistic regression model with sex, age, and 28-day decrease in the HCV RNA level as covariates. As shown in Figure 1, younger patients experienced higher SVR rates than did older patients over the range of 28-day decreases, although this effect tended to be reduced in patient groups with the greatest HCV RNA decreases.

Similar to the findings of Hoofnagle et al [3], who analyzed differences in response to combination treatment according to race, we observed that, although the 28-day decrease in HCV RNA level was significantly greater in younger than in older patients, this effect did not completely account for the age-related disparity in the rates of SVR. Age-specific differences in the interactions between virus and host immune response may explain different rates of SVR in different age groups. Our findings may be relevant to those countries, such as the United States, Italy, or Japan [5–7], where the prevalence of chronic HCV infection is increasing with age, to better define the optimal treatment in patients aged ≥40 years.

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Reply to Antonucci et al

To the Editor—Antonucci et al [1] report that younger age (<40 years) was a strong risk factor for a higher rate of sustained virological response (SVR) to pegylated interferon and ribavirin therapy for chronic hepatitis C in a cohort of 62 Italian patients infected with genotypes 1 or 4. The association of younger age with a higher rate of response to combination therapy for hepatitis C was reported in several large treatment trials. Thus, in the initial, large registration trials for pegylated interferon alfa-2a [2] and alfa-2b [3] with ribavirin, younger age was associated with a higher response rate, which was highly significant (P < .001) even after controlling for other factors. In contrast, among the 341 patients with hepatitis C virus (HCV) genotype 1 infection included in our secondary analysis of the Virahep-C trial [4, 5], the SVR rate among patients aged <40 years was similar to that in older patients (47% vs 44%; P = .76). While there were only 30 subjects aged <40 years in the Virahep-C trial, the sample was certainly large enough to capture the degree of difference reported by Antonucci and colleagues (84% vs 30%), suggesting that confounding variables may have accounted for the marked differences (such as genotype, viral level, race, hepatic fibrosis, insulin sensitivity, and compliance). In a recent study of a 48-week course of pegylated interferon and ribavirin treatment in children [6], the SVR rate in the genotype 1–infected group was 47%—a rate similar to that in the adult population of the Virahep-C trial.

Finally, the figure provided by Antonucci et al [1] suggests that, even with a decrease in the HCV RNA level of <1 log10 IU/mL during the first 28 days of therapy, younger patients should be expected to have an SVR rate >60%, which seems unlikely. Thus, patients aged <40 years may have a somewhat higher rate of response to combination therapy for HCV infection than do older subjects, but the degree of difference reported by Antonucci and colleagues is probably greater than can be expected.

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Is onerous Regulation Responsible for Adenovirus Outbreaks?

To the Editor—I read with interest the reports of the adenovirus 14 outbreaks and am intrigued by its appearance in the post–adenovirus vaccination era in the military, which began in 1996 [1–3]. The fact that prior evidence of immunity to adenovirus 7 protected against severe adenovirus 14 disease suggests the possibility that the lack of immunity to adenovirus 7 may play a role in adenovirus 14 disease [1].

Wyeth Laboratories, the manufacturer of the adenovirus 4 and adenovirus 7 vaccines used in the past, delivered its last lots of vaccine in 1996 and ceased production of the adenovirus vaccine. The company cited regulations promulgated by the government as influencing their decision [4]. With the continued burden of adenovirus infection in the military, the second-

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