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Hepatitis C in African Americans

The advances of the last decade in our understanding of hepatitis C virus (HCV) infection have led to significant improvements in treatment responses. However, data has also emerged that HCV may behave differently in certain populations of patients and particularly in African Americans. This article will review our current understanding of this issue and discuss ongoing research projects and future directions.

One of the initial reasons for concern about HCV in African Americans was the disparity in prevalence. The NHANES III survey has been our best source for epidemiologic data about HCV. A report using these data estimated that 1.8% (3.9 million) of the U.S. population had a positive HCV antibody test but found this rate was higher in blacks than among whites (3.2% versus 1.5%).¹ The study also found that 74% of these people had chronic infection, and again the rate of viremia was higher in blacks than whites (86% versus 68%). Black men had higher rates of infection, and the highest prevalence rate was 9.8% among black males ages 40 to 49 years. After adjusting for socioeconomic status and high-risk behaviors, race was not a risk factor for HCV infection.

Although the prevalence of HCV is greater in African Americans, natural history data has suggested a more favorable outcome for African Americans. A

recent study examined the progression of HCV in African Americans.² African Americans were more likely to be infected with genotype 1 virus (88%) than were non-African Americans (67%). HCV RNA levels were similar, but liver enzymes (ALT) were lower in African Americans. African Americans had less inflammation and fibrosis in their liver biopsies, and there was a trend toward less cirrhosis (22% versus 30%). The authors theorized that these findings might be explained by a difference in the immune response of African Americans, and further research is investigating this question.

Although the improvements in response rates with current therapeutic regimens have been encouraging, reports have also emerged during the last several years that the response rate is lower in African Americans. The initial report by Reddy and colleagues detailed the experience of patients treated with unmodified interferon alfa-2b and interferon alfacon-1 (also known as consensus interferon).³ In this group, only 1 of 40 black patients (2%) had a sustained virologic response. Several other reports then followed with similarly dismal response rates. A report by McHutchison and colleagues challenged these findings and reported the experience with treatment with unmodified interferon alfa-2b and ribavirin.⁴ In this analysis, the overall response rate was lower among black patients at 11%. However, they also observed a

higher proportion of genotype 1 infection in the black patients. When they looked at genotype 1 patients who received unmodified interferon alfa-2b and ribavirin, the sustained virologic response rates were similar with 22% for white and 23% for black patients. These data suggested that genotype and not race was the critical predictor of a response.

With these conflicting results and growing concern regarding HCV in African Americans, the National Institutes of Health sponsored a workshop in December 1999 to review previous work and plan future research in this area. One clear finding was the underrepresentation of African Americans in HCV treatment trials. Even in the more recent trials with the pegylated interferon alfa regimens, enrollment of black patients has been extremely low. As a result, NIDDK launched the VIRAHEP-C Study (Viral Resistance to Antiviral Therapy of Chronic Hepatitis C). This study is being conducted at eight medical centers in the United States and will examine the treatment responses of African Americans but will also examine the immune response, virologic kinetics, and genetic factors to better understand the reason for any disparity in treatment response. For more information about this study, go to: <http://www.edc.gsp.h.pitt.edu/virahepc/index.html>

In addition to VIRAHEP-C, other studies are currently examining treatment issues for African

Americans with HCV infection. Our group is currently completing a study of 100 African American and 100 non-Hispanic white patients with HCV infection. The enrollment was balanced for genotype, and 98% of patients in each group were genotype 1. All patients received 48 weeks of pegylated interferon alfa-2b and ribavirin. To date, we have reported our preliminary results.⁵

Americans have lower neutrophil counts at baseline. Treatment with interferon alfa regimens lowers the neutrophil counts, and there has been concern that this would lead to an increased risk of infection. In an early report from the WIN-R trial, they found that African American patients did have lower baseline neutrophil counts, but the neutrophil counts during treatment were similar for African

their liver biopsy. For patients who are recommended treatment, I remind them that none of the large trials have been published at this time, and we should wait to see their final results before making formal recommendations. Nevertheless, many patients are aware of the literature suggesting a lower response for African Americans in addition to the preliminary findings of the current trials.

References:

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Other studies have also improved the enrollment of African Americans and will add to the knowledge in this field. The WIN-R trial has more than 4000 patients, and almost 10% are African American.

After 12 weeks of therapy, 58% of Non-Hispanic Whites had no evidence of HCV RNA versus 28% of African Americans. This difference was highly statistically significant. Patients are currently completing the follow-up phase, and we anticipate final results later this year. A similar study by Dr. Lennox Jeffers and his group at the University of Miami is treating 78 African Americans and 28 Caucasians with pegylated interferon alfa-2a and ribavirin. Their 12-week data also showed a disparity in virologic response with 28% in the African Americans and 50% in the Caucasians.⁶ This study should also have final results later this year.

Other studies have also improved the enrollment of African Americans and will add to the knowledge in this field. The WIN-R trial has more than 4000 patients, and almost 10% are African American. This study is ongoing, and the treatment regimen is pegylated interferon alfa-2b and weight-based ribavirin. This study has already provided valuable information regarding treatment of HCV in African Americans. African

Americans and whites.⁷ A recent report from Soza and colleagues also confirmed that black race was associated with this baseline neutropenia.⁸ However, neutrophil count decreases were similar in different racial groups, and the infections reported during treatment did not occur in patients with neutropenia. With concerns about risk of infection, current recommendations include an absolute neutrophil count greater than 1500. Using the NHANES III data, these authors also found that 12% of blacks versus 1.5% of non-Hispanic whites had this level of neutropenia. With so many patients potentially being excluded from therapy and possibly decreased concerns about the risk of infection with neutropenia, future studies should include treatment of African Americans with lower neutrophil counts.

Significant research is ongoing among African Americans with HCV infection. However, what should we tell African American patients who are currently considering therapy? As with patients of all races and ethnic groups, I do not recommend treatment for patients with early stage disease on

I also remind all patients that we will evaluate their virologic response at 12 weeks. Recent work has shown that patients are much more likely to respond to treatment if they have negative HCV RNA or at least a two-log reduction from their baseline HCV RNA.⁹ Although this predictor has not been replicated in African Americans, I find this a reasonable recommendation to my patients. For the patients who do not respond to treatment or elect to not receive pegylated interferon-a and ribavirin, I also make them aware of the large number of therapies in various stages of development for HCV. For interested patients, I encouraged them to consider participating in one of these clinical trials. If we find that African Americans in particular respond well to one of these new therapies, this may provide even greater breakthroughs in our understanding of the pathogenesis of HCV. With the amount of research focused on HCV, I encourage optimism for my patients.