Management of Hepatitis C Virus in HIV-Infected Patients in the Era of Direct-Acting Antivirals

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(See the Major Article by Fierer et al on pages 873–9.)

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Hepatitis C virus (HCV) is a blood-borne pathogen most efficiently transmitted through direct blood-to-blood contact. Injection drug use is the principal route of HCV transmission in developed countries [1]. Although sexual transmission of HCV is uncommon among heterosexual couples in monogamous relationships [2], accumulating evidence suggests that among specific high-risk groups, sexual transmission may be a major route for HCV acquisition. Because HCV and human immunodeficiency virus (HIV) can be transmitted by similar mechanisms, HCV infection is relatively common in HIV-infected patients. In the last decade, an increased incidence of acute HCV infection among HIV-positive men who have sex with men (MSM), attributed to sexual exposure, has been documented worldwide [3, 4]. Incidence rates of acute HCV among HIV-infected MSM in the United States range from 0.21 to 0.51 cases per 100 person-years with most cases attributed to injection drug use and high-risk sexual practices [5, 6]. The increasing burden of acute HCV among MSM underscores the urgent need for prevention of HCV transmission among those who remain unexposed as well as evaluation and possibly treatment among those already infected. At the same time, this epidemic provides an opportunity to study early phases of HCV infection that have not been well characterized.

HIV/HCV-coinfected patients have been shown to have accelerated liver disease compared to those infected only with HCV, and liver-related complications have become a primary cause of hospitalizations and death in HIV-infected individuals in developed countries [7, 8]. HCV treatment efficacy during the chronic phase of the infection is also reduced in HIV/HCV-coinfected patients when pegylated interferon (peg-IFN) and ribavirin (RBV) are used. Sustained virologic response (SVR) to peg-IFN/RBV is achieved in up to 50% of patients monoinfected with HCV genotype 1, the genotype that is most difficult to treat [9, 10], and by only 14%–29% of those coinfected with HIV [11, 12]. The approval of the first 2 direct-acting antivirals (DAAs) in 2011, telaprevir (TVR) and boceprevir (BOC), began a new era in the treatment of hepatitis C. Both of these agents are NS3/4A protease inhibitors and were approved only for treatment of HCV genotype 1–monoinfected patients. TVR or BOC, when used in combination with peg-IFN and RBV, achieved SVR rates of ≥70% [13–16].

Uptake of DAA treatment in HCV/HIV-coinfected individuals has lagged, at least in the United States, largely because their use in this population has not yet been approved by the US Food and Drug Administration. Some concerns also exist regarding potential drug–drug interactions between DAAs and certain antiretrovirals as well as overlapping medication toxicity. The initial phase 2 pilot studies that evaluated triple therapy in coinfected patients reported significant improvement over treatment with peg-IFN and RBV. The addition of a DAA to peg-IFN/RBV therapy increased SVR rates from 45% to 74%, in the case of TVR [17], and from 29% to 63% in the case of BOC [18]. More recently, an IFN-sparing 24-week regimen comprised of the NS5B polymerase inhibitor sofosbuvir used in combination with RBV has been studied in HIV/HCV-coinfected patients. Among genotype 1–infected individuals who were also infected with HIV, SVR rates of 76% were achieved...
in individuals on diverse antiretroviral regimens, and patients suffered minimal side effects [19]. Similar results have been described with use of the second-generation HCV protease inhibitors simeprevir [20] and faldaprevir [21] in combination with peg-IFN and RBV. Although all of these studies are limited by small numbers of previously untreated patients, they suggest that new treatment options for HCV infection will have similar efficacies in monoinfected and coinfected patient populations.

Our knowledge of the early phases of hepatitis C infection is limited, as acute hepatitis is rarely diagnosed due to its largely asymptomatic nature. Even less is known about treatment of acute HCV infection. Despite the difficulty of identifying this subgroup of patients, cohort studies have illustrated that treatment of acute hepatitis C results in response rates far superior to those obtained during chronic infection [22–24]. Ninety percent or more of acute monoinfected patients treated with peg-IFN with or without RBV obtain an SVR [25], while in the context of HIV coinfection, successful treatment responses with peg-IFN and RBV range from 53% to 83% regardless of genotype [26]. Treatment duration in acute monoinfected patients with peg-IFN/RBV is typically 24 weeks, but some coinfected patients with slow HCV RNA declines require ≥48 weeks of treatment.

In the current issue of Clinical Infectious Diseases, Fierer et al describe treatment of acute HCV infection in a cohort of 19 HIV/HCV-coinfected patients over a 15-month period [26]. All patients were MSM identified through a network of HIV providers in the New York City area. Considering the difficulties of identifying acute hepatitis C infections, the assembly of this cohort is a tremendous accomplishment.

In the study by Fierer et al, all patients were infected with HCV genotype 1 and all had viremia detected within 6 months of their referral. Patients were treated with a triple therapy regimen of TVR, peg-IFN, and RBV for a total duration of 12 weeks and achieved an SVR rate of 84%. This was a significant improvement compared to the control group, comprised of 48 patients treated with peg-IFN/RBV for 24–48 weeks, which achieved an SVR rate of 62%. This manuscript describes one of the very few studies that utilized triple therapy in HIV/HCV-coinfected patients, and it is the first one performed in the context of acute HCV infection. Although the study was performed in a relatively small number of patients, the reported results are very promising and suggest that treatment of HIV/HCV-coinfected patients with an HCV regimen that includes a DAA could shorten treatment duration if delivered during the acute phase of the infection. The data also confirm previous reports that suggest similar HCV treatment efficacy in regimens that contain DAAs, whether delivered in monoinfected or coinfected patient populations. Further extrapolation of the results suggests that use of triple therapy in coinfected patients might be equally efficacious whether utilized during the acute or chronic phase. Studies in larger numbers of coinfected patients in both acute and chronic phases of the infection, using different durations and types of treatment, will be necessary to determine optimal HCV management practices in these patients.

In light of the increased HCV morbidity in HIV-infected patients, the pending approval of new DAAs that result in increased efficacy with reduced side effects, improved dosing intervals, and fewer drug–drug interactions holds great promise among this population. The astounding efficacy results encountered with the new generation of DAAs are revolutionizing the current HCV treatment paradigm in which significant divisions exist among patient populations—that is, acute vs chronic, coinfection vs monoinfection. Several studies performed to date, including the work by Fierer et al, provide further evidence for the homogenization of patient subgroups in regard to therapeutic responses in HCV infection.

Note

Potential conflicts of interest. All authors: No reported conflicts.

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References

12. Torriani FJ, Rodriguez-Torres M, Rockstroh JK, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection in


