

Hepatitis C Virus and Human Immunodeficiency Virus Coinfection in an Urban Population: Low Eligibility for Interferon Treatment

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One hundred eighty human immunodeficiency virus (HIV)– and hepatitis C virus (HCV)–coinfected patients were prospectively evaluated for suitability for interferon and ribavirin therapy. Of the 149 patients with chronic HCV infection who completed the evaluation, 44 (30%) were eligible for treatment and 105 (70%) were ineligible, with the main barriers being missed clinic visits, active psychiatric illness, active drug or alcohol use, decompensated liver disease, or medical illness.

Coinfection with hepatitis C virus (HCV) and HIV is increasingly recognized as a public health problem in the United States [1]. About 30% of HIV-infected patients are coinfecting with HCV, with the highest prevalence in injection drug users [2–4]. HIV is a risk factor for accelerated HCV disease, and liver disease has emerged as a major cause of mortality and morbidity in coinfecting patients [5, 6]. Combination therapy with pegylated IFN and ribavirin is the current standard of care for chronic HCV infection, with sustained response rates of ~50%, and early data suggest that responses are similar among HIV-coinfecting patients [7–9].

For current therapies to have a major impact on HCV-related morbidity, a substantial proportion of the infected population will need to undergo treatment. Recent data for patients in-

fecting with HCV alone suggest that only a small proportion are eligible for treatment, and no data are available for HIV-coinfecting persons [10]. The objectives of this study were therefore to prospectively evaluate coinfecting patients' suitability for HCV therapy with IFN and ribavirin and to identify barriers to treatment among this population.

Methods. About 1250 HIV-infected patients receive primary care at Boston Medical Center, of whom ~55% are HCV-coinfecting [4]. A designated consult clinic, staffed by infectious disease and hepatology specialists, was established to evaluate coinfecting patients for HCV treatment. Patients were referred by their primary care providers and underwent a standardized evaluation, comprising patient history, physical examination, and laboratory tests, which included determination of HCV RNA level, complete blood count, measurement of serum creatinine level, random blood sugar test, liver function tests, and coagulation studies. If HCV RNA was detectable, genotype was determined and a liver ultrasound was obtained. Patients without absolute contraindications for treatment were encouraged to undergo liver biopsy for disease staging; however, this was not required.

Baseline eligibility criteria for HCV treatment were detectable serum HCV RNA and elevated serum aminotransferase levels within the previous 12 months. Exclusion criteria included nonadherence (missing >3 clinic appointments), ongoing alcohol or drug use (other than marijuana) in the preceding 6 months, active psychiatric illness (defined as symptomatic psychosis or depression or a suicide attempt within the previous year), active medical illness (defined as ongoing illness that is a contraindication to IFN therapy or is associated with a life expectancy of <3 years), decompensated liver disease (defined as a Child Pugh score of >7), advanced HIV disease (defined as a CD4 cell count of <100 cells/mm³ regardless of HIV load or count of 100–200 cells/mm³ with HIV load of >10,000 copies/mL), neutrophil count of <1.5 × 10⁹ cells/L, and platelet count of <75 × 10⁹ cells/L.

Patients who were not treatment candidates were reevaluated after 6 months, and their treatment eligibility reassessed. All patients received a comprehensive education program during their initial clinic visits, and onsite addiction counseling was available, with referral to methadone and drug rehabilitation programs. Psychiatric consultation was obtained for all patients with a history of, or symptoms suggestive of, ongoing psychiatric illness. Each patient's eligibility for HCV therapy was evaluated jointly by the attending infectious disease and hepatology staff by use of the above criteria. Institutional review board

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approval for this study was obtained from Boston University School of Medicine, and guidelines for human experimentation of the US Department of Health and Human Services and Boston University School of Medicine were followed. Statistical analysis was done with the χ^2 test for categorical data and Student's *t* test for continuous data.

Results. From 1 January 2000 to 1 February 2002, 180 HCV- and HIV-coinfected patients were referred for evaluation; 173 completed the evaluation and are included in this study. The demographics and laboratory values for the study patients are shown in table 1. Twenty-four patients (14%) had undetectable HCV RNA and were considered to have inactive HCV infection. Of the 149 patients with chronic HCV infection, 44 (29%) were considered to be eligible for HCV therapy (table 1). Fifty-five patients (37%) underwent liver biopsy, 23 of whom were subsequently considered to be ineligible for HCV therapy because of intercurrent medical issues, psychiatric ill-

ness, relapsed drug or alcohol use, or failure to follow up in clinic. Twelve otherwise eligible patients refused liver biopsy, 3 of whom subsequently commenced treatment. The eligible patients were significantly more likely to have CD4 cell counts of >200 cells/mm³ and HIV loads of <50 copies/mL and to be infected with HCV genotype other than 1; however, there were no other differences in laboratory values or demographics (table 1).

Of the 44 chronically infected patients who were assessed as appropriate for HCV therapy, 28 (64%) decided not to proceed. Reasons for not starting treatment were potential side effects for 9 patients (8 of whom had minimal fibrosis on liver biopsy), unstable social circumstances for 3 patients, concerns about ability to work for 3 patients, and worry about relapse of injection drug use for 2 patients. One patient's wife became pregnant, and 1 patient died of an unrelated cause. Six patients did not return to the clinic after discussing therapy, and 3 patients

Table 1. Demographics and laboratory results for 173 hepatitis C virus (HCV)- and HIV-coinfected patients, categorized by IFN treatment eligibility.

Variable	Total (<i>n</i> = 173)	Treatment-ineligible (<i>n</i> = 105 [61%])	Treatment-eligible (<i>n</i> = 44 [25%])	HCV RNA-negative (<i>n</i> = 24 [14%])
Demographic characteristics				
Age, years	43.6 ± 7.1	43.3 ± 6.8	44.8 ± 7.3	43.0 ± 8.0
Sex				
Male	132 (76)	83 (79)	34 (77)	15 (63)
Female	41 (24)	22 (21)	10 (23)	9 (37)
Race				
White	59 (34)	40 (38)	12 (27)	7 (29)
African-American	69 (40)	41 (39)	20 (45)	8 (33)
Hispanic	45 (26)	24 (23)	12 (27)	9 (38)
Risk factor				
Injection drug use	153 (88)	96 (91)	38 (86)	18 (75)
Other ^a	20 (12)	9 (9)	6 (14)	6 (25)
Laboratory values				
ALT level >40 U/L	125 (72)	80 (76)	35 (80)	10 (42)
CD4 cell count >200 cells/mm ³	139 (80)	78 (74)	43 (98) ^b	18 (75)
HIV RNA level <50 copies/mL	76 (44)	43 (41)	27 (61) ^b	6 (25)
HCV RNA level >2 million IU	45/135 (33)	31/91 (34)	14/44 (32)	
HCV genotype				
1	93/122 (76)	64/78 (82)	29/44 (66) ^b	
2, 3, or 4	29/122 (24)	14/78 (18)	15/44 (34)	
Liver biopsy results (METAVIR score)				
F1 (minimal fibrosis)	12/55 (22)	4/23 (17)	8/32 (25)	
F2 (few septae)	20/55 (36)	6/23 (26)	14/32 (44)	
F3 (many septae)	13/55 (24)	8/23 (35)	5/32 (16)	
F4 (cirrhosis)	10/55 (18)	5/23 (22)	5/32 (16)	

NOTE. Data are mean ± SD, no. (%) of patients, or no. of patients/total no. (%), as appropriate. ALT, alanine aminotransferase.

^a Homosexual, heterosexual, transfusion, and unknown risk factor for HCV acquisition.

^b *P* < .05 by χ^2 analysis, comparing eligible and ineligible groups.

relocated. Sixteen patients (36%) commenced HCV treatment, 8 (50%) of whom were infected with genotypes 2, 3, or 4, compared with a 24% prevalence of these genotypes overall.

One hundred five patients (70%) were considered to be ineligible for HCV therapy. The major barriers included nonadherence with medical visits for 24 patients (23%), active psychiatric disease for 22 patients (21%), drug or alcohol use in the previous 6 months for 24 patients (23%), decompensated liver disease for 13 patients (12%), advanced HIV disease for 14 patients (13%), and medical comorbidities for 8 patients (8%). The latter group included poorly controlled diabetes, cardiac disease, anemia, Hodgkin's disease, and end-stage renal disease.

Discussion. Despite having a designated clinic and standardized evaluation, only 44 (30%) of 149 coinfecting patients with chronic HCV infection were eligible for HCV therapy. Of the eligible patients, only 16 (36%) embarked on treatment. These data underscore the challenges that exist in treating HCV disease in an urban population of HCV- and HIV-coinfecting patients. Of interest, 14% of the patients referred were HCV RNA-negative, similar to the general population [10].

This study was designed to assess eligibility for HCV treatment on the basis of a standardized clinical evaluation in which a liver biopsy was not required. Although the eligibility criteria used in this study may be criticized as overly stringent, we sought to minimize provider subjectivity. Eligible patients decided to proceed with treatment on the basis of risks of therapy and the perceived risks of disease progression, incorporating liver biopsy results if available. That the 8 eligible patients with histologically mild disease chose to defer therapy indicates the utility of liver histology in balancing the treatment risks and benefits.

About 70% of the coinfecting patients had contraindications for HCV therapy. Primary barriers to treatment included nonadherence with clinic visits, active psychiatric disease, and substance use. In addition, a significant proportion of those eligible for treatment were reluctant to proceed. These barriers persisted despite ongoing education regarding the seriousness of HCV disease and access to a designated psychiatrist and substance abuse programs. Decompensated liver disease was seen in 13% at presentation, reinforcing the prevalence of liver-related morbidity in HCV- and HIV-coinfecting patients [6]. Because the majority of coinfecting patients have a history of injection drug use, we believe that our results are generalizable to other urban populations with injection drug use as a risk factor [3]. Interestingly, our findings are remarkably similar to the results of Falck-Ytter et al. [10], who reported that only 28% of urban patients with HCV infection alone were eligible for HCV therapy.

Our study may have overestimated the proportion of eligible patients among all inner-city coinfecting persons, because primary care physicians tended to refer patients they perceived

as good candidates, thus introducing referral bias. However, the proportion of patients with severe liver disease may also be an overestimate, because patients with severe liver disease were also more likely to have been referred. The fact that the majority of these patients had well-controlled HIV disease, evidenced by the fact that >40% had an undetectable HIV load, reinforces that fact that even for those patients adhering to HIV treatments, embarking on HCV treatment may pose a significant challenge. Patients with non-HCV genotype 1 disease were more likely to commence treatment, indicating that the poor response and longer duration of therapy in HCV genotype 1-infected patients are also perceived as being significant barriers.

Our data highlight the numerous barriers to HCV treatment in this inner-city minority population. Of the ineligible patients, one-third had medical problems, whereas the remaining two-thirds had psychiatric or behavioral problems, including poor compliance and ongoing substance abuse, that excluded them. Strategies to improve the proportion of coinfecting patients eligible for HCV treatment will therefore need to concentrate on substance abuse treatment, optimizing psychiatric care, and improving the possibility of compliance by linking HCV treatment and methadone use with programs to supervise and administer IFN. Earlier referral for HCV evaluation and treatment, before the development of severe liver disease, or to HIV- or HAART-related complications will also be required. In addition, the relative success in treating patients with non-HCV genotype 1 disease suggests that to achieve higher treatment rates, IFN treatment must be perceived as both efficacious and tolerable. Addressing the barriers to IFN therapy among coinfecting patients is necessary if the recent advances in HCV treatment are to be replicated in the HIV- and HCV-coinfecting population.

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