Integrating Treatment for Hepatitis C Virus Infection into an HIV Clinic

Kathleen A. Clanon, Juergen Johannes Mueller, and Michael Harank

Alameda County Medical Center, Oakland, California

In the United States, one-third of human immunodeficiency virus (HIV)–infected patients are also coinfected with hepatitis C virus (HCV). Of 228 coinfected patients whose charts were reviewed in our 2000 study, only 2 had received therapy with interferon. To address low rates of treatment, in 2001 we implemented a program to shift the primary responsibility for oversight of care for HCV-infected patients from the liver clinic to HIV primary care clinicians and to provide education and support regarding adherence to patients. Critical elements of the program include education of HIV clinicians with regard to treatment for HCV infection, establishment of a coinfection clinic in the HIV clinic, assignment of a full-time Registered Nurse for monitoring and support of patients undergoing treatment for HCV infection, and development of a weekly peer group for the coinfected patients. Preliminary treatment results for patients in the program suggest that this approach has promise for improving outcomes of treatment among coinfected patients.

HCV AND HIV COINFECTION

In the United States, 150,000–300,000 people are infected with both HIV and hepatitis C virus (HCV), representing 15%–30% of all HIV-infected persons and 5%–10% of HCV-infected persons [1, 2]. Some estimates of coinfec-
tion are even higher (>75%) among selected at-risk populations, such as injection drug users [1, 3]. As overall HIV-related mortality has declined, liver disease has be-
come an increasingly significant cause of morbidity and death among HIV-infected patients [4–6]. In 1999, >50% of the mortality among HIV-infected patients in the United States [4] was due to liver failure, and the primary cause of liver failure in this population is HCV-related decompensation [4–7].

Treatment of HCV infection has improved markedly during the last few years, first with the introduction of combination therapy with ribavirin and IFN-α and now with the availability of pegylated IFN [8, 9]. However, treatment for coinfected patients has lagged behind, in terms of both numbers treated and success rate for those who undergo treatment [2, 10, 11]. Immunologic impairment associated with HIV disease is likely the primary cause of the poorer treatment outcomes seen in the coinfected group, and optimal management of HIV disease is the only available strategy to address that issue [12]. However, improvements can likely be made in the access to and support for therapy for HCV in-
fec tion among coinfected patients. Adherence to dif-
ficult treatment regimens is a focus of research and resources in sites offering care for HIV-infected persons, and this experience can be used to address the chal-

ASSESSING COMMUNITY-BASED COINFECTION CARE

In 2000, the quality management advisory body of a publicly funded HIV care consortium in Alameda County, California, identified increasing numbers of liver disease–related deaths among network patients as a critical quality care issue. Anecdotal concerns about care for HCV-infected patients and disagreement about
the appropriate standard of care among coinfected patients also surfaced in the community providers’ HIV Journal Club. Finally, a local testing initiative for HCV among high-risk injection drug users had resulted in increased concern and questions about the infection from the local organized patient groups. These concerns resulted in a cooperative project among local providers of care for HIV-infected patients to review the state of care for HCV-HIV–coinfected patients, identify probable causes for any deficiencies, and develop an interim community standard of care based on local experts’ best assessment of the current data.

Funds were identified from local government and pharmaceutical companies to do the community assessment, which was conceived in 3 parts: a chart review, focus groups with patients, and interviews with health-care providers. At the same time, an advisory group, which included HCV experts and practitioners who treat HIV-infected patients, was brought together to develop a local community consensus about appropriate workup and treatment algorithms for coinfected patients.

**Chart review results.** The chart review was done in late 2000 and included 929 patients in care with the network or one of its community partners (S. O’Brien, personal communication). HCV coinfection was present in 228 patients (25% of the total). Four HCV quality-of-care indicators were reviewed. Screening for HCV in the HIV-infected population was nearly 100%; however, counseling regarding cessation of alcohol abuse was rarely documented, only 12% of patients had received vaccinations against hepatitis A virus (HAV) and hepatitis B virus (HBV), and only 2 patients had ever received treatment with IFN for HCV infection. Similar deficits were identified at a multisite Department of Veterans Affairs study in 2002 [10].

In 36% of charts reviewed, the reasons for not pursuing therapy with IFN and ribavirin could not be identified from chart notes. Providers’ assessment of active substance abuse (16%) or a history of noncompliance with visits or treatment (12%) were the 2 most frequently identified reasons.

**Provider interviews and patient focus group.** Both providers who treat HIV-infected patients and gastrointestinal or liver specialists were interviewed to identify common concerns about and/or barriers to care for HCV-infected patients. Providers of care for HIV-infected patients reported knowledge deficits about HCV and fear about complications of treatment with IFN and ribavirin. Providers of care for HCV-infected patients identified lack of experience with and data about treatment for coinfected patients, as well as pessimism about treatment outcome, as reasons not to recommend treatment for HCV infection to patients coinfected with HIV [13]. In addition, the clinicians perceived liver biopsies as being dangerous, as a result of earlier publications [14, 15] (not supported by later data) that suggested higher mortality rates in HIV-positive patients.

Costs of work-up and treatment were identified by both sets of providers as a barrier to care. Although patient assistance programs through pharmaceutical companies exist, they require significant staff knowledge and time to be used successfully (authors’ unpublished data). Availability of liver consultation for uninsured and Medicaid patients was extremely limited (3 h twice a month at the already overburdened local public hospital), resulting in many months’ delay in getting expert consultation. Communication between primary care and liver clinics was paper based, slow, and too unreliable to allow for coordination and monitoring of a complex treatment regimen.

Barriers identified in patient focus groups held in April 2001 included lack of knowledge about HCV and fear of side effects of treatment for HCV infection. Some patients were concerned that self-injecting IFN might trigger relapse of injection drug use. Patients in 1 group were asked to evaluate some possible treatment support models, which were drawn from the experience of a local successful treatment program for HCV monoinfection (D. L. Sylvestre, personal communication). They believed that availability of injections in the doctor’s office, nursing advice for management of adverse effects, and peer support from people who had had treatment were desirable components of a program of treatment for HCV infection.

**DESIGN OF THE NEW PROGRAM**

On the basis of the information gathered in the assessment phase and consultation with Dr. Diana Sylvestre, a local expert in treatment for HCV infection, a 3-pronged approach to reducing barriers to care was implemented, including education of clinicians, integration of gastrointestinal expert care into the HIV primary care site, and the hiring and training of a nurse specialist in HCV.

**Clinician education.** Clinician knowledge deficits were addressed in 3 venues. Three Journal Clubs were held, with joint attendance by liver specialists and providers who treat HIV-infected patients, in which data regarding coinfection were reviewed and a protocol about who should be treated was developed. “Mini-residencies” were arranged with a local clinic that treats a high volume of HCV-infected patients, in which HIV clinicians spent time in a monoinfection clinic, reviewed patient management models, and saw first-hand how clinical and social problems were addressed. Regular case conferences were begun in which liver and HIV specialists shared information about patient treatment in the course of discussing individual patients. The outcome of this education program has been a successful transition of primary responsibility for
overseeing treatment with IFN and ribavirin from the liver specialists to the HIV primary care clinicians.

Integration of liver and HIV clinics. We noted that, within the program’s institution, referrals from HIV clinic to liver clinic had a dismal completion rate, with <10% of referred patients keeping appointments (authors’ unpublished data). This problem was addressed in 2001, when a monthly coinfection session was established in the HIV clinic. The nursing and support staff resources of the HIV clinic were engaged to get patients and laboratory results to this special coinfection session. More than 70% of the patients scheduled for the coinfection clinic are seen.

HCV nurse specialist. The experience of the coinfection clinic demonstrated the complexity of treating coinfected patients and highlighted the critical role of a single dedicated case manager or nurse in counseling and following the patients as they considered, decided on, and then began treatment. Because the HIV clinicians were new to treatment for HCV infection and because the resource of the liver specialist was limited, we hired and cross-trained an HCV/HIV nurse specialist to act as the coordinating staff member. The nurse who was hired was experienced in HIV care. A mini-residency was arranged for him with the local HCV clinic so that he could have hands-on experience with treatment for HCV infection. He was then assigned responsibility for developing a counseling protocol covering the basics of HCV and its treatment, establishing a program of vaccination against HAV and HBV for coinfected patients, establishing and running the weekly support and education group, and providing preteaching about side effects and support for their mitigation for those undergoing therapy with IFN and ribavirin.

Addressing systemic barriers. Both patients and providers were reluctant to pursue liver biopsy, and we debated its necessity. Our review of the literature suggested that it was important [11] and safe [16], particularly for patients infected with HCV genotype 1. Availability of the procedure at our county hospital was poor, with a wait of many months. In 2003, our gastrointestinal specialists agreed to do biopsies in the HIV clinic, with use of portable ultrasound guidance and recovery in the treatment area of the clinic. HIV clinic nurses were trained in procedures of care during recovery for patients after biopsy. To date, we have done 20 biopsies with no complications, good rates of showing up for the procedure, and good patient reports of the experience.

EXPERIENCE WITH THE PROGRAM TO DATE

Counseling and education. The cohort of patients with coinfection were initially counseled by the HCV nurse with regard to nonmedication aspects of management of HCV infection, including cessation of alcohol and drug use, diet, vaccination against HAV and HBV, and avoidance of hepatotoxic medications. The need for pretreatment biopsies was discussed with them in detail. The options and potential complications of treatment with IFN and ribavirin were also addressed, and any questions were answered. Most patients were initially hesitant about starting treatment. During the counseling and education process, patients were screened for absolute contraindications to treatment for HCV infection. Once willing and appropriate candidates were identified, they were referred to the coinfection clinic and simultaneously enrolled in the newly established weekly education and support group.

Peer support and education group. The support group started in February 2002 with 15 members. Weekly meetings are 2 h long and include an education session, followed by participants’ exchanges of experiences. In the initial meetings, monoinfected and coinfected patients from outside the site who had already undergone therapy were recruited to act as mentors and sources of information. Initial topics included lengthy discussions about expected adverse effects and possible interventions to treat them. Patients became quite knowledgeable and participated more and more with pointed questions, brought in their own researched information, and began to seriously consider treatment. Once the first patient started and did well on the medications without any serious adverse effects, more patients were willing to start, in a positive “snowball effect” mediated through the exchange of experiences in the support group. Within 4 months, 6 patients were undergoing treatment.

Treatment results and lessons learned. The number of patients who have been treated through the program and who have been followed for at least 6 months after treatment is still small, so treatment outcomes may be biased. Since the program began, 15 patients have started treatment with ribavirin and IFN at the project site, 6 discontinued treatment before finishing therapy, and 7 are evaluable for sustained virological response (at least 6 months after completion of therapy). Thirteen are infected with HCV genotype 1; the rate of sustained virological response is 40% in this population, for which rates of 20% have been reported in the literature. Patients infected with HCV genotypes 2 and 3 (2 total) cleared HCV as expected. In summary, of our initial 12 patients, 6 discontinued treatment for various reasons (1 of them, infected with HCV genotype 1, nevertheless achieved sustained virological response after 27 weeks of therapy). The patients who completed therapy all achieved sustained virological response. Long-term follow-up information is available for only 2 patients, who are free of HCV after 18 months.

Since initiation of the program, experience has highlighted several clinical “pearls” that have guided evolution of our program treatment protocols. First, aggressive management of adverse effects and maintaining maximum doses of IFN and ribavirin throughout the treatment course is the strategy most likely to result in sustained virological response. This has been
demonstrated among monoinfected patients [17]. The literature suggests, not surprisingly, that cytopenias are common among coinfected patients undergoing therapy [8]. We have adjusted our protocol to start treatment with epoetin-α when hemoglobin levels decrease to <10 g/dL and now often start treatment with epoetin before commencing therapy for HCV infection [18]. This strategy has allowed us to avoid reduction of ribavirin doses for our later-treated patients. Other expected complications, including neutropenia and depression, we also treat aggressively. All patients with a history of depression or a moderately high depression score on a standard screening test (Centers for Epidemiologic Studies depression scale) are treated with selective serotonin reuptake inhibitors before treatment for HCV infection is started [19].

Next, water is the best tool for management of symptoms. Patients are instructed to drink at least 3 L of water daily, which reduces pain, fatigue, and headaches and obviates the need for supplementary pain medications for almost all patients.

Finally, patients’ CD4 cell counts invariably decrease during treatment for HCV infection and persist at low levels for 1–6 months after therapy is stopped. Like others, we have seen no morbidity associated with this decrease [20], but it is upsetting to patients, and counseling about this issue before starting therapy has become part of our pretreatment educational checklist.

Of interest, we noted that for patients not undergoing HAART but with detectable HIV loads, the HIV loads almost invariably became undetectable during treatment for HCV infection. The anti-HIV effect of ribavirin plus IFN might be considered an additional benefit of treatment for HCV infection [21].

**SUMMARY**

HCV coinfection affects a large percentage of patients with HIV and is a significant and growing cause of morbidity and mortality. HIV-infected patients, particularly those who are uninsured, may experience difficulties in gaining access to or following through with care for HCV infection in the specialty referral model. In this example, barriers to care for HCV-infected patients who were attending the HIV clinic, supervised by the HIV primary clinicians, were assessed, and a program was developed to address them. Additional resources were made available, in the form of hands-on educational experiences for the HIV clinicians in care for HCV-infected patients, as well as time the gastrointestinal clinicians spent on additional teaching and holding conferences regarding cases while the HIV clinicians were gaining experience with treatment for HCV infection. Most costly, and most valuable, has been the assignment of a full-time registered nurse to manage cases and monitor the patients who are considering, moving toward, and undergoing therapy.

The program described here has resulted in promising early results of treatment for HCV infection, suggesting that aggressive medical and social support of patients during therapy for HCV infection may have an effect on rates of sustained virological response reported among coinfected patients. As results of large cohort studies become available, understanding how patients were supported during treatment may give clues to how we can maximize results for our HIV-HCV–coinfected patients.

**Acknowledgments**

**Financial support.** K.A.C.: Federal Health Resources Services Administration Ryan White Comprehensive AIDS Resources Emergency Act program, including titles III, IV, and part F; Alameda County Medical Center. J.J.M.: Alameda County Medical Center; M.H.: unrestricted grant from Roche Pharmaceuticals.

**Potential conflicts of interest.** K.A.C.: consultant to Roche Pharmaceuticals and Gilead Sciences; speakers’ bureau for Merck and Pfizer; J.J.M. and M.H.: speakers’ bureau for Roche Pharmaceuticals.

**References**