

HIV-HCV Coinfection

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Abstract: Human immunodeficiency virus and hepatitis C virus are global health concerns. Due to shared routes of transmission, coinfection is common. Since the introduction of highly active antiretroviral therapy in the mid-1990s and the associated marked reduction in HIV-related mortality, the incidence of liver-related mortality in coinfecting patients has risen significantly. This rise has led to increased research into the evaluation and management of the coinfecting patient. This article reviews the epidemiology and evaluation of the coinfecting patient and outlines the principles necessary for successful management of this challenging patient population.

Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) are global health concerns. Due to shared routes of transmission, coinfection with HIV and HCV is common and represents an emerging area of clinical importance and research with regard to evaluation and optimal management. The seroprevalence of HCV among HIV-infected individuals is approximately 15–30%,^{1,2} which translates to more than 200,000–300,000 coinfecting individuals in the United States. However, the risk of coinfection is dependent on the individual risk factors for acquiring infection. Factors such as intravenous drug use and receipt of blood product transfusions, especially in hemophiliacs, carry much higher prevalence rates for coinfection—91% and 71% respectively—than risk factors such as sexual transmission.³ Although both HIV and HCV are single-stranded RNA viruses with worldwide distribution that can result in chronic, subclinical infection, they differ with regard to several important characteristics. Both viruses have several subtypes and, in the case of HCV, the specific genotype has a significant impact on response to treatment. Although both viruses are transmitted parenterally, their transmission rates differ in that there is a higher prevalence of sexual transmission in HIV, whereas parenteral transmission is more common than sexual transmission in HCV.

The rate of mortality related to HIV has dropped precipitously over the past decade with the introduction of highly active antiretroviral therapy (HAART).⁴ Following the introduction of HAART, there has been a sharp increase in the number of deaths due to end-stage liver disease among the HIV-HCV coinfecting population.^{5,6} This has led to the increased awareness of HCV among

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HIV healthcare providers and the emergence of data on both the natural history of HCV in the setting of HIV infection and the impact of HCV on HIV prognosis. Efficacy of HCV treatment has significantly improved in the last decade, with response rates exceeding 50–60% in patients with HCV alone. Although clinical trials of HCV therapy in coinfecting patients have lagged behind, results of several recent large trials have led to the approval of HCV therapy in this population. Given the complexities of both HIV and HCV and the unique disease burden of coinfection, a discussion of the evaluation and nuances of management of HCV/HIV is warranted.

Natural History

Impact of HIV on HCV Disease Progression

With the increasing use of HAART in the management of HIV and the subsequent decreasing morbidity and mortality from opportunistic infections, greater attention is being paid to the natural history of HCV among coinfecting individuals, both in histologic and virologic terms. Prior to a diagnosis of HCV coinfection, early reports on liver histology in HIV-infected individuals are limited to patients with either unexplained fever associated with hepatomegaly and/or abnormal liver enzymes.^{7–11} In the absence of hepatitis B virus (HBV), mycobacterium, or cytomegalovirus infections, the most common findings have been nonspecific steatosis and granuloma¹² when typical features of chronic hepatitis C are not present.

Several reports published both prior to^{13–17} and following the institution of HAART^{18–24} have described hepatic histology in patients with HCV-HIV coinfection. These reports included living and autopsy specimens from coinfecting patients, as well as HIV-negative/HCV-positive patient samples for comparison. Overall, most studies show that histologic severity appears worse in those with HIV-HCV coinfection, particularly in patients with low CD4 counts and a history of alcohol abuse. In a meta-analysis of four studies performed by Graham and colleagues,²⁵ the relative risk in coinfecting patients for developing histologic cirrhosis was 2.07 (95% confidence interval [CI], 1.40–3.07) when compared to HCV monoinfected patients. The great variability in these data, however, is demonstrated by noting that two of these studies did not reach statistical significance for this outcome. However, a limitation of most of these trials was the inclusion of only patients with elevated liver chemistries or obvious signs of liver disease. This is an important point as almost half of patients with HIV-HCV coinfection have normal alanine aminotransferase (ALT) levels at the time of biopsy^{26,27} compared to 20–30% in HCV monoinfected individuals.^{28,29} In a recent study that included patients with and without abnormal

ALT, the histologic spectrum of liver disease was similar in coinfecting patients and HCV-only controls.²⁶

When coinfecting patients were stratified by normal or abnormal ALT, no significant differences were seen in CD4 count, hepatic activity index (HAI), or its inflammation or fibrosis components. In particular, the prevalence of advanced fibrosis (bridging fibrosis or cirrhosis) in those with normal ALT levels was 26%, highlighting the importance of liver biopsy in this subset of coinfecting individuals. Similar observations were made in a study of coinfecting patients drawn from an HIV clinic, where no differences in severe hepatic fibrosis or necroinflammatory activity were seen in patients receiving HAART for an average of 3 years, or in a review of coinfecting patients undergoing a prospective study of HCV treatment with combination therapy.^{30,31} A limitation in all of these studies is that histologic conclusions were determined from single biopsy samples versus paired samples, which may have provided more accurate information regarding the natural history of the disease.

Impact of Antiretroviral Therapy on the Natural History and Histologic Spectrum of HCV

There are emerging data on the impact of specific antiretroviral agents on HCV in coinfecting patients. In a retrospective analysis, Benhamou and colleagues¹⁹ observed that along with young age at infection, heavy alcohol consumption, and a high CD4 count, patients whose HAART regimen did not contain a protease inhibitor (PI) had higher inflammation and fibrosis scores when compared to those who took a PI as part of their HAART regimen. In contrast, a recent study found no significant differences in the spectrum of liver disease in patients whose HAART regimen contained a PI when compared to those whose regimen did not.³² These discordant results may have been due to the populations studied, patient demographics and alcohol use, and the dynamic changes that have occurred in anti-HIV therapy. In the French study by Benhamou and colleagues,¹⁹ non-nucleoside reverse transcriptase inhibitors (NNRTIs) were not given in the PI-treatment group and of those 119 patients not taking a PI, 76 (66%) were on nucleoside reverse transcriptase inhibitor (NRTIs) alone, 40 (33%) were on no antiretroviral medications, and only 3 patients were taking both NRTIs and NNRTIs. Furthermore, patients on a PI had a lower CD4 count compared to patients not on a PI (mean 286 vs 399 cell/mm³; $P=.001$). Therefore, it is unclear whether the use of PIs themselves or the lower CD4 count accounted for less histologic damage observed, as no patients with cirrhosis had CD4 levels measuring less than 200 cells/mm³.³² In a retrospective analysis of

690 coinfecting patients, no significant differences in the proportion with severe fibrosis (approximately 25%) were observed between those on an NNRTI, a PI, or both.³³ Therefore, specific PI or NNRTI use may not be associated with obvious histologic benefit or obvious histologic worsening of HCV disease.

Impact of HCV on HIV Disease Progression

The effect of HCV on the natural history of HIV is not clear. Some studies have suggested an increased progression to AIDS in coinfecting patients, as well as a decrease in survival from the time of diagnosis of HIV and AIDS.³⁴⁻³⁶ In contrast, a study by Sulkowski and coworkers,³⁷ found no difference in progression to AIDS or death over a 2-year period after adjustments were made for therapy with HAART. In a more recent study of 970 HIV-positive subjects in the HIV Atlanta Veterans Affairs Cohort Study (HAVACS), Anderson and colleagues³⁶ found no difference in CD4 cell recovery after initiating HAART when comparing patients coinfecting with HCV and those with HIV alone. Although coinfecting patients were 2.5 times more likely to die during follow-up, as measured from the time of HIV diagnosis, after controlling for other covariates patients on HAART were 75% less likely to die than those who had not received HAART. The increased mortality in coinfecting patients may be explained in part by a lower use of HAART in these individuals. The discordant results regarding the effect of HCV on HIV progression or response to HIV therapy are reflected in recommendations from recent panel sessions of the HCV-HIV International Panel.^{38,39}

HAART Hepatotoxicity

The risk of hepatotoxicity is increased in HIV patients coinfecting with chronic viral hepatitis. Although most reports have focused on severe grade 3 (5–10 × upper limit normal [ULN]) and grade 4 (>10 × ULN) elevations in liver enzymes, more mild-to-moderate (1.25–5 × ULN) elevations are seen frequently in patients on HAART. The proposed mechanisms for each class of antiretroviral agent are shown in Table 1.⁴⁰⁻⁴² NRTIs inhibit mitochondrial DNA, which can result in lactic acidosis and hepatic steatosis.^{43,44} This may be problematic, particularly with administration of didanosine coupled with combination therapy for HCV including ribavirin. The overall incidence of severe hepatotoxicity associated with NNRTIs is 8–10%⁴⁵ and may be increased when combined with a PI.⁴⁶ HCV or HBV coinfection increased the relative risk several fold. The use of PIs has also been associated with severe hepatotoxicity, especially with the use of higher-dose ritonavir in some,⁴⁷ but not all, studies.^{48,49} As with

Table 1. Hepatotoxicity and Highly Active Antiretroviral Therapy (HAART)

Class	Mechanism	Manifestation
NRTI	Decreased mitochondrial DNA polymerase- γ	Lactic acidosis, steatosis
NNRTI	Immune hypersensitivity	Lactic acidosis, steatosis, eosinophilic hepatic injury
PI	Possible inhibition of retinoic acid binding protein, direct cytopathic effect (RTV), decreased UDP-glucuronide transfer (IDV, ATV)	Hepatocellular injury, steatosis, increased unconjugated bilirubin
HAART	Possible immune constitution	Hepatocellular injury

ATV = atazanavir; IDV = indinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RTV = ritonavir; UDP=undegraded protein.

NNRTIs, coinfection was associated with an increased risk of PI-induced hepatotoxicity.⁵⁰ As a consequence, coinfecting patients are more likely to discontinue HAART.⁵¹ The key points on natural history and epidemiology of coinfection are summarized in Table 2.

Evaluation of the Coinfecting Patient

Evaluation of the coinfecting patient follows that of the HCV mono-infected patient, with a few exceptions (Figure 1). All HIV patients should be tested for HCV antibodies. HIV patients with elevated transaminases and negative HCV antibodies should be tested for HCV RNA with a polymerase chain reaction assay, given the possibility of false-negative antibodies in the coinfecting patient, particularly those with low CD4 (<100 cells/mm³) counts.⁵² In those patients with elevated liver enzymes and persistently undetectable HCV RNA, other causes of hepatitis should be excluded. In those with detectable HCV RNA, HCV genotype, HIV viral load, and CD4 counts should be determined. As with HCV mono-infected patients, HBV serologies should be obtained in order to rule out the possibility of triple infection.

The following steps in evaluation will help to determine whether to proceed with treatment of the coinfecting patient as discussed below. In those with detectable HCV RNA, the next step is to determine the amount of liver damage. Traditionally, liver biopsy has been used as a key diagnostic tool in assessing the degree of liver inflam-

Table 2. Key Points in the Natural History and Epidemiology of HIV-HCV Coinfection

- Shared modes of transmission explain high rates of HIV-HCV coinfection, particularly in high-risk behaviors such as intravenous drug use
- Decrease in morbidity and mortality from HIV is paralleled by an increase in mortality from liver disease in HIV-HCV coinfecting patients
- Although controversial, study results trend toward an increase in the rate of fibrosis in coinfecting patients compared to HCV mono-infected patients, and, therefore, consideration should be given to treatment of HCV disease in these patients
- The effect of coinfection on progression of HIV disease remains inconclusive, but does not warrant withholding treatment for HCV in these patients
- HCV coinfection increases risk of severe hepatotoxicity associated with highly active antiretroviral therapies, which limits HIV therapy

HCV = hepatitis C virus.

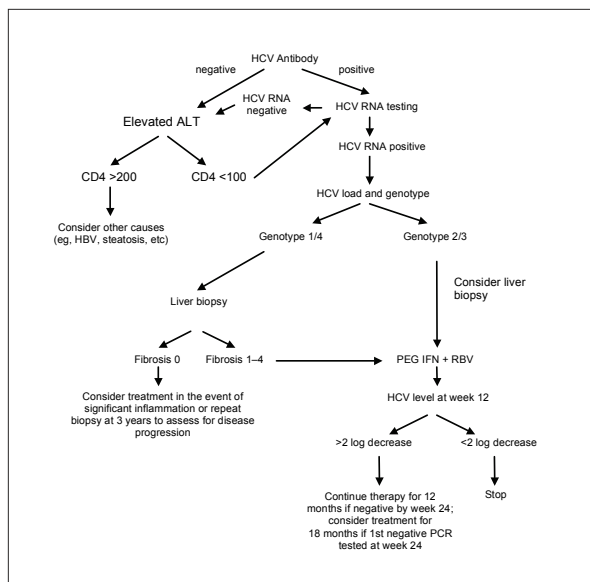


Figure 1. Algorithm for evaluating and treating hepatitis C virus (HCV) in patients coinfecting with HIV.

ALT = alanine aminotransferase; HBV = hepatitis B virus; PCR = polymerase chain reaction; PEG IFN = pegylated interferon; RBV = ribavirin.

mation and fibrosis in chronic liver disease.⁵³ Reviewing histologic patterns can provide information regarding the possibility of hepatotoxicity in the case of HAART or other comorbid conditions such as hepatic steatosis,⁵⁴ which may be more prevalent in patients with HIV. Understanding the stage and grade of the liver damage provides useful information in determining prognosis in chronic hepatitis C. A favorable prognosis is given in the absence of both moderate-to-significant inflammation and fibrosis.^{55,56} However, given the faster progression of fibrosis in those with coinfection, even those with mild disease can be considered for therapy. As with any invasive procedure, however, liver biopsy carries significant risks, which include bleeding, pain, bowel or lung perforation, sampling error, financial cost of the procedure, and anxiety to both patient and physician.

Because of concerns regarding risks that are associated with liver biopsy, there has been an attempt to identify other, noninvasive tests or surrogate markers that might be able to predict liver histology. Single tests, such as measurement of serum aminotransferases (aspartate aminotransferase [AST] and ALT), prothrombin time, albumin, or bilirubin, are not sensitive enough to accurately predict the degree of fibrosis. New noninvasive models using single surrogate tests or panels of tests have been studied.⁵⁷⁻⁶² However, their use is limited by restricted availability, high costs, and the fact that almost half of patients fall outside the cut-off ranges, leading to inconclusive results.

Few studies have addressed noninvasive markers of hepatic fibrosis in coinfecting patients.⁵³ Myers and colleagues⁶³ studied the use of an index incorporating age, sex, α -2 macroglobulin, apolipoprotein-A1, haptoglobin, bilirubin, and γ -glutamyl-transpeptidase (GGT) in 130 coinfecting patients from a single French center. They found an area under the receiver-operating curve (AUROC) of this index to detect METAVIR score F2–F4 fibrosis (septal fibrosis–cirrhosis) of 0.856. Using a range of 0–1, cut-off values of greater than 0.6 had a positive predictive value of 86%, whereas a score of less than 0.2 had a negative predictive value of 93%. These thresholds could reduce the need for liver biopsy in this cohort by 55% with an accuracy of 89%. The use of the AST-to-platelet ratio index (APRI) was assessed in 119 coinfecting patients in a single US site and found an AUROC of 0.82.⁶⁴ An APRI of less than 0.5 had a sensitivity of 87%, whereas a value greater than 1.5 had a specificity of 96% for predicting the presence or absence of bridging fibrosis or cirrhosis. They report that using these cut-offs would avoid liver biopsy in 35% of patients.

More recently, Kelleher and colleagues⁶⁵ examined the role of fibrosis markers, including hyaluronic acid (HA) and YKL-40, in a cohort of 95 HIV-HCV coinfecting patients

randomly selected from the Johns Hopkins HIV Clinic in identifying those with little-to-mild (Ishak fibrosis score 0–2) versus those with moderate-to-severe (Ishak fibrosis score 3–6) fibrosis. They report that those with moderate-to-severe fibrosis had higher HA levels and an index that measures serum HA, albumin, and AST (SHASTA Index), had an AUROC of 0.878 compared to 0.71 for APRI. This index performed well at the extreme cutoffs (<0.3 and >0.8). However, only 26 patients had Ishak fibrosis scores of 3 or higher and the index performed poorly in those with SHASTA scores between 0.3 and 0.8. Consequently, only 42% of patients could be correctly classified and a liver biopsy would still be required in the majority.

In an attempt to develop a simple model of readily available tests that would help to differentiate mild-to-moderate from advanced fibrosis in HIV-HCV coinfecting patients, Sterling and associates⁶⁶ retrospectively analyzed 832 of the patients enrolled in a study of HCV treatment of coinfecting patients. In a multiple logistic regression analysis in a training set of 555 patients, age, AST level, international normalized ratio (INR), and platelet count were found to be independent predictors of fibrosis (C-index 0.708). A novel index using these factors, with the replacement of INR with ALT level, was developed, known as the FIB-4 index: $\text{age (y)} \times \text{AST (U/L)} / \text{platelet count (10}^9\text{/L)} \times [\text{ALT (U/L)}] \times 0.5$. Index values ranged from 0.2 to 10 with an AUROC of 0.76. When applied to a validation set of 277 patients, the index performed well (AUROC=0.765) and, importantly, was applicable to 70% of the population, with an accuracy of 87%. However, before these models replace biopsy, they need to be validated in other cohorts including those with normal ALT. The key points in evaluating coinfecting patients are summarized in Table 3.

Treatment of HCV in the Coinfecting Patient

Treatment of HCV in HIV-HCV coinfecting patients should be contemplated in all patients with detectable HCV RNA, with careful consideration of each individual patient. As in HCV mono-infected patients, patients with a history of liver decompensation, such as portal hypertensive gastrointestinal bleeding, hepatic encephalopathy, or ascites, a history of severe neuropsychiatric conditions, or patients with persistent heavy use of alcohol or other substance abuse issues should not be considered for treatment at this time, outside of clinical trials. Recommending professional psychiatric management and detoxification programs if necessary is advisable, with the possibility of treatment in the future. With specific regard to the coinfecting patient, careful attention should be paid to CD4 counts. Given limited success in achieving a positive response,

Table 3. Key Points in the Evaluation of the HIV-HCV Coinfecting Patient

- Test all HIV patients for HCV, regardless of LFTs
- Liver biopsy should be considered, particularly in the setting of normal LFTs and lack of signs of clinical liver disease
- Development of noninvasive testing shows promise for accurate alternative methods of assessment, particularly in patients with increased risk of complication from liver biopsy

HCV = hepatitis C virus; LFT = liver function test.

treatment of HCV is currently not recommended in patients with a CD4 count of less than 200 cells/mm³.³⁸ Rather, initiation of antiretroviral therapy is suggested, as well as prophylactic therapy for opportunistic infections. However, treatment can be considered despite a CD4 count of less than 200 cells/mm³ in those with an undetectable HIV RNA. As per current panel recommendations, treatment should be considered in those patients with a CD4 count of >350 cells/mm³, low levels of HIV RNA (<50,000 copies/mL), and none of the other contraindications stated above with regard to liver decompensation, active substance abuse, or psychiatric comorbidities. Patients with normal serum aminotransferases should still be considered for treatment if the liver biopsy indicates a significant degree of inflammation or fibrosis. The goals of HCV therapy in the setting of HIV mirror those of treatment in the HCV mono-infected patient, including virologic eradication and histologic improvement with prevention of progression to cirrhosis. In this setting, treatment of HCV may also help to reduce the risk of hepatotoxicity associated with HAART.⁶⁷ As in the setting of the mono-infected HCV patient, the current optimal treatment regimen is with pegylated interferon (PEG-IFN) and ribavirin. Current recommendations are based on recent randomized trials that have evaluated the use of either PEG-IFN alfa-2a or -2b with ribavirin versus combination treatment using standard interferon (Table 4). The AIDS Pegasys Ribavirin International Coinfection Trial (APRICOT)⁶⁸ and the AIDS Clinical Trials Group (ACTG) A5071⁶⁹ studies both compared PEG-IFN alfa-2a plus ribavirin to standard IFN plus ribavirin. The APRICOT study included an arm to evaluate PEG-IFN monotherapy. Results from this study demonstrated a significantly higher sustained viral response (SVR; HCV RNA <50 IU/mL, at 24 weeks following treatment for 48 weeks) among all genotypes among those patients receiving PEG-IFN plus ribavirin versus those receiving standard IFN combination therapy (40% vs 12%; odds

Table 4. Recent HIV-HCV Treatment Trials

Study	N	Treatment Regimen	SVR, %		
			All	GT1	Non-GT1
ACTG A5071 ⁶⁹	133	PEG-IFN alfa-2a (180 mcg) + RBV (600 mg - >1 g)	27	14	73
		IFN alfa-2a (6 MIU - >3 MIU) + RBV (600 mg - >1 g)	12	6	33
APRICOT ⁶⁸	868	PEG-IFN alfa-2a (180 mcg) + RBV (800 mg)	40	29	62
		IFN alfa-2a (3 MIU) + RBV (800 mg)	12	7	20
		PEG-IFN alfa-2a (180 mcg) + RBV placebo	20	14	36
RIBAVIC ⁷⁰	412	PEG-IFN alfa-2b (1.5 mcg/kg) + RBV (800 mg)	27	17	44
		IFN alfa-2b (3 MIU) + RBV (800 mg)	20	6	33
Laguno ⁷¹	95	PEG-IFN alfa-2b (1.5 mcg/kg) + RBV (800-1,200 mg)	44	38	53
		IFN alfa-2b (3 MIU) + RBV (800-1,200 mg)	21	7	47

ACTG = AIDS Clinical Trials Group; APRICOT = AIDS Pegasys Ribavirin International Coinfection trial; GT1 = genotype 1; HCV = hepatitis C virus; PEG-IFN = pegylated interferon; LRVB = ribavirin; SVR = sustained virologic response.

ratio [OR], 5.40; 97.5% CI, 3.20-9.12; $P < .001$) and versus those receiving PEG-IFN monotherapy (40% vs. 20%; OR, 2.89; 97.5% CI, 1.83-4.58; $P < .001$). As seen in the HCV monoinfected population, higher SVRs were achieved with HCV genotype 2 or 3 compared to genotype 1, in all three treatment arms. In addition, patients with HCV genotype 1 with high HCV RNA levels (>800,000 IU/mL) had lower response rates in all three treatment arms compared to those with low HCV RNA levels (<800,000 IU/mL).⁶⁸ Similar results were seen in ACTG A5071, a two-armed study that used a step-wise dosing of ribavirin in the PEG-IFN combination arm as well as a dose reduction from 6 MIU to 3 MIU in the standard IFN arm.⁶⁹ Significantly higher SVR was seen in patients receiving PEG-IFN compared to standard IFN (18% vs. 8%, $P = .03$), with only 14% of genotype 1 patients achieving an SVR with PEG-IFN compared to 73% of patients with genotype 2 or 3 ($P < .001$). Interestingly, a detectable HIV RNA level at entry into the study was found to be a predictor of SVR in multivariate analysis (OR, 3.55; 95% CI, 1.19-10.6; $P = .023$). Both the French RIBAVIC study⁷⁰ and the Spanish study by Laguno and colleagues⁷¹ evaluated combination therapy

with PEG-IFN alfa-2b and ribavirin compared to combination therapy using standard IFN. In general, both the French and Spanish groups demonstrated significantly higher SVRs in all patients treated with PEG-IFN and in non-HCV genotype 1 groups (Table 4).

With regard to safety, all four of the studies demonstrated known adverse effects from IFN-based therapy, similar to those seen in treatment of HCV mono-infection, including neutropenia, thrombocytopenia, anemia, influenza-like syndrome, and psychiatric disturbances. Only the APRICOT study showed a significantly higher withdrawal rate due to adverse affects in the PEG-IFN group compared to the standard IFN group (14% vs 12%, respectively; $P < .001$).⁶⁸ Also, hepatic decompensation and liver-related deaths did occur in some patients who entered the trial with mild hepatic decompensation.

With regard to the safety of using antiretroviral therapy during treatment for HCV, data from the APRICOT study suggest that ribavirin does not appear to alter the metabolism of lamivudine, stavudine, or zidovudine and that these drugs would theoretically be safe for use during treatment of HCV.⁶⁸ Regarding toxicity of nucleoside analogs, particularly didanosine, of greatest concern in the

setting of treatment for HCV are mitochondrial toxicities that are manifested by pancreatitis and hyperlactatemia. Furthermore, hepatic decompensation has been observed in patients with advanced fibrosis who were receiving concomitant didanosine and ribavirin.³⁸ Didanosine should, therefore, be discontinued prior to the initiation of ribavirin.

Key trials of PEG-IFN and ribavirin combination therapy in HCV monoinfected patients identified the predictive value of an early virologic response (EVR) (decrease of 2 log or more in the HCV RNA level by week 12).⁷²⁻⁷⁴ This measure is now used routinely in decision making regarding treatment strategy for these patients. Trials of coinfecting patients with PEG-IFN-based combination therapy confirm the importance of determining the EVR and its role in managing HCV treatment in the coinfecting patient. In the APRICOT study, 71% of patients demonstrated an EVR. Of these, 56% went on to have an SVR.⁶⁸ Of the 29% of patients who had no early virologic response, only 2% went on to have an SVR. None of the patients who failed to achieve an EVR in the PEG-IFN monotherapy arm and the standard IFN arm went on to have an SVR. A negative predictive value of 100% for no EVR at week 12 was also seen in results from the ACTG A5071 trial.⁶⁹

As in treatment of HCV monoinfection, the development of adverse effects should not elicit an immediate cessation of therapy. Rather, various supportive measures can be initiated such as epoetin in the case of anemia, antidepressants for psychiatric symptoms, and dose reductions of ribavirin. In attempting to achieve virologic clearance, optimizing dose of medication and maintaining duration of therapy are critical. Key points in the treatment of the coinfecting patient are summarized in Table 5.

Conclusions

Since it was first recognized that HCV is a significant cause of morbidity and mortality in those living with HIV, there have been significant advances in our understanding of the impact of HIV on HCV disease progression. Although the data on HCV negatively affecting HIV disease progression is mixed, patients with HCV coinfection are at increased risk of HAART hepatotoxicity, which may lead to antiretroviral discontinuation. Consequently, all HIV patients should be screened for HCV and evaluated for disease severity and considered for therapy. Liver biopsy remains the gold standard for determining histologic severity. However, noninvasive models, which have been proposed, may replace biopsy in some, but not all, patients. Several recently published trials have definitively shown that PEG-IFN combined with ribavirin therapy is superior to standard IFN combination therapy with

Table 5. Key Points in the Treatment of the HIV-HCV Coinfecting Patient

- Follow general guidelines for HCV monoinfection when screening HIV-HCV coinfecting patients for treatment
- Studies have confirmed that combination therapy with pegylated interferon and ribavirin are associated with higher rates of sustained virologic response and should be considered first-line therapy in the absence of contraindications
- Genotypes 2 and 3 and lower HCV RNA levels are associated with more favorable response to treatment in coinfecting patients, though rates of response are still lower than in HCV monoinfected patients
- Guidelines regarding monitoring of viral response, such as the predictive value of early virologic response, are similar to that for treatment of HCV monoinfection
- Careful attention should be paid to the development of adverse effects and supportive care should be provided where possible in order to continue treatment
- Simultaneous treatment of HIV with didanosine and combination HCV therapy with interferon is strongly discouraged due to significant interactions

HCV = hepatitis C virus.

acceptable, albeit lower sustained response rates when compared to patients with HCV infection alone. Trials using higher doses of ribavirin are planned, which should narrow this gap. The optimal duration of therapy in those coinfecting is not clear and results of ongoing trials comparing 48 weeks to 72 weeks of therapy are anxiously awaited. We have learned to use extreme caution in patients with decompensated liver disease and to avoid coadministration of didanosine and ribavirin. However, with attention to detail, experienced providers can get most patients through therapy. There have been significant advances in the care of HIV patients coinfecting with HCV, which provide optimism in this challenging patient population.

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