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Antiretroviral Therapy in Chronic Liver Disease: Focus on HIV/HCV Coinfection – Statements of the First Italian Consensus Workshop

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Abstract

Hepatitis C virus (HCV) and HIV share common transmission routes and HCV coinfection is frequent in persons living with HIV. Liver enzyme elevation following the initiation of antiretroviral therapy is frequently seen in HIV-infected patients with chronic liver disease, particularly those with chronic hepatitis C. This complication may lead to treatment discontinuation, complicating HIV therapeutic management. Multiple factors influence the risk of liver toxicity under antiretroviral therapy, including the specific drug in use (e.g. use of full doses of ritonavir), and environmental factors (e.g. alcohol abuse). However a beneficial effect of antiretroviral therapy on liver disease has been supported by some studies. Despite increasing knowledge of HCV/HIV coinfection, there is no clear consensus on how to treat HIV in HCV-coinfected patients An Italian group of experts were invited to discuss in detail the current risks and implications of antiretroviral treatment in HIV-infected persons with chronic hepatitis C, and their main conclusions are summarized in this consensus document. **(AIDS Reviews 2005;7:161-7)**

Key words

HIV. Hepatitis. ART. Liver. Hepatotoxicity.

Introduction

Several million people in the world are coinfected with HCV and HIV. The prevalence of HCV coinfection in Europeans living with HIV is estimated to be 33%, with a north to south gradient[1]. In Italy and Spain it is estimated that 50% of HIV-infected persons are also coinfected by HCV[2,3]. Antiretroviral therapy (ART) has led to dramatic improvements in the HIV morbidity and mortality[4]. However, ART has been associated with serious hepatic toxicities and interferences with anti-HCV treatment[4]. On the other hand, a beneficial effect of ART on liver disease has been supported by some studies[5]. Despite increasing knowledge of HCV/HIV coinfection[5], there is no clear consensus on how to treat HIV in HCV-coinfected patients[6]. This encouraged the organization of a consensus workshop of Italian HIV-treating physicians in order to review the current knowledge of treatment of HIV disease in HCV-coinfected persons, with a view to developing these consensus statements according to the method of a nominal group meeting.

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Table 1. Modified Infectious Diseases Society of America scoring system for consensus recommendations

Strength of recommendation	Quality of evidence
A. Good	I. Properly randomized controlled trials
B. Moderate	II. Other published studies
C. Poor	III. Expert opinion

From Soriano, et al.[4]

Statements and recommendations were graded for their strength and quality using a system based on the one adopted by the Infectious Diseases Society of America (IDSA) (Table 1). An organizing committee drafted four groups of questions to be addressed to the participants, and asked four experts in the field to prepare a draft of the consensus statements, grading the quality of each evidence after a careful review of the literature. The latter was obtained by searching the Ovid databases (including AIDSLINE and MEDLINE) from January 1st, 1993 to February 20th, 2005, using the following key words: hepatitis C, HCV, HIV, liver diseases, drug toxicity, antiviral therapy, therapy, interferon, and vaccination. These key words were exploded and appropriate search combinations were performed. References were manually scanned for relevant articles published prior to 1993. A selection of the literature was provided for all those who attended the workshop.

In a two-day workshop, after two lectures held by experts in the field, the four experts presented their statements, and after a plenary discussion the four groups of statements were reviewed and reformulated by a working group of 10 to 15 HIV-treating physicians. On the second day the new statements were presented in a plenary session by a tutor from each group, modified if necessary after a plenary discussion, and then voted on by all participants using a televoting system. All the participants voted on their degree of agreement with the statement and the strength of the recommendation. Participants ranked their agreement on a scale of 1 (complete disagreement) to 9 (complete agreement). They ranked the strength of the recommendation on a scale of 1 to 9: (1-3 insufficient C; 4-6 moderate B; 7-9 strong A). Median scores and ranges were calculated for each voting session and agreement between participants was calculated according to the distribution of the ranking. Statements were accepted only when all the ranking of agreement was between 7 and 9, otherwise they were reformulated and voted on again. This report summarizes the main conclusions and recommendations of the consensus workshop.

When to start treatment for HIV, HCV or both?

HIV-induced immune deficiency causes a progressive worsening of chronic hepatitis C acceleration, its evolution towards cirrhosis, and possibly increased risk of hepatocellular carcinoma (HCC)[5-7]. Therefore, all HIV/HCV coinfected persons should be evaluated for the treatment of both infections (AII).

There are no contraindications for antiretroviral therapy in patients with HCV infection; a beneficial effect of ART on the evolution of liver disease has been reported[5,6,8]. ART-related liver injury, though more frequent in coinfected persons, has a low incidence[9-13] and should not be considered as a limiting factor (AII).

In subjects naive for both anti-HIV and anti-HIV treatments it is advisable not to start both therapies at the same time (AIII).

ART-naive patients

In subjects naive for both therapies, indications for treatment vary with the clinical scenario, which should take into consideration the degree of HIV-induced immune deficiency. In all patients with CD4 counts ≥ 500/μl, anti-HCV treatment – when indicated – should be strongly encouraged before ART[4,6] is implemented (AI).

In patients with CD4 counts of 350-500, anti-HCV treatment should be taken into consideration before starting ART, after a careful evaluation of the evolution of HIV disease. Early ART introduction before starting anti-HCV treatment could improve immune function in patients with rapidly progressing HIV disease and thereby increase the efficacy and tolerability of the postponed anti-HCV treatment (BII).

In patients with CD4 counts of 200-350, it would be better to start with ART (AII). In patients with CD4 counts < 200 and/or symptomatic HIV disease, it is

mandatory to start ART first (AI). In drug-naive patients with CD4 counts > 350 and with absolute contraindications for anti-HCV treatment, starting ART earlier could be taken into consideration (BII).

Higher CD4 counts were predictors of sustained virologic response after anti-HCV treatment only in earlier studies performed with interferon (IFN) monotherapy[14]. In investigator-driven multicenter studies, the high rate of withdrawal unrelated to adverse events was the main factor limiting sustained response[15-17]. A significant reduction in CD4 absolute counts was observed during anti-HCV treatment[15-19]. For these reasons, starting anti-HCV treatment with the highest possible CD4 count will make both the patient and the treating physician more comfortable with concurrent HIV management.

Although there is still no clear-cut evidence, many studies have shown an inverse relationship between CD4 nadir and accelerated progression of hepatitis C towards cirrhosis. Therefore, in patients with contraindications to anti-HCV treatment, maintenance of CD4 counts > 350 seems to be an alternative option[8;19,20].

Patients on ART

When indicated, anti-HCV treatment is recommended in patients with CD4 counts > 350 with stable virologic and immunologic response (AII). In patients with CD4 counts of 200-350 with stable immune and virologic response, anti-HCV treatment could be taken into consideration. A CD4 count > 200 was an inclusion criterion in most randomized controlled trials (RCT) on anti-HCV treatment in HIV-seropositive patients published in 2004[15,16,18,19]. In asymptomatic patients with HIV-RNA < 5000 copies/ml and with CD4 counts < 200/ml, anti-HCV treatment could not be excluded in the presence of advanced or rapidly progressing liver disease (BII). A small group of patients with these characteristics was in fact included in the APRICOT study, and did not show a significantly lower response[19].

Drug addiction and psychiatric disturbances

Patients undergoing treatment with opioid agonists due to opioid dependency can be treated for both infections. Social and psychological support is strongly recommended for such persons. Treatment of active drugs users should be taken into consideration on a case-by-case basis (BII). Mild or moderate psychiatric disease is not an absolute contraindication to anti-HCV treatment, but adequate social and psychiatric support should be guaranteed (BII). Severe depression is an absolute contraindication to anti-HCV treatment (AI).

How to start in noncirrhotic patients – Drug hepatotoxicity and drug interactions

The definition of hepatotoxicity of ART in the current literature is heterogeneous and its pathogenesis multifactorial[8-13]. All the etiologic factors have still not been completely identified and each of them plays a different role in the single patient (BII). The use of certain antiretrovirals, although not absolutely contraindicated, is still pending.

Although in most cases drug-induced hypertransaminasemia is subclinical and self-limiting, the use of nevirapine could increase the risk of ART hepatotoxicity, especially in females with CD4 counts > 250/ml during the first few weeks of treatment[10]. In these circumstances, the drug should be used very cautiously with a strict follow-up (AII), which is also needed for coinfected patients taking efavirenz (BII).

The use of protease inhibitors (PI) boosted by a low dose of ritonavir (< 200 mg/day) does not appear to be related to a risk higher than that associated with the use of unboosted PI[22] (BII).

The following antiretrovirals should be used with caution or avoided in patients in whom pegylated interferon (PEG-IFN) and ribavirin are prescribed for the treatment of chronic hepatitis C[6]:

– Didanosine (ddI): should be avoided (AII).

– Zidovudine (ZDV): should be avoided due to the risk of anemia and neutropenia, which are related to its interaction with ribavirin and PEG-IFN, respectively (BII).

– Stavudine (d4T): contraindicated, especially in combination with didanosine due to an increased risk of lactic acidosis and pancreatitis (A2).

– Efavirenz (EFV): should be avoided in patients with a history of or current psychiatric disorders, but without contraindication to IFN, because of the risk of a positive interaction with IFN's psychiatric side effects (CIII).

Which counseling?

Alcohol

Alcohol abuse increases HCV replication, accelerates liver fibrogenesis[23] and decreases the efficacy of and adherence to ART[24]. For these reasons, alcohol consumption should be assessed with reproducible and validated instruments in all HIV/HCV coinfected patients. Psychological, social and medical support is

always useful, and sometimes necessary, in limiting or, better, stopping alcohol consumption (AIII).

Recreational Drugs

Counseling is required to achieve the withdrawal of recreational drugs used intravenously and other psychotropic substances. Opiate agonist therapy (managed by a multidisciplinary team) may be considered an intermediate tool for achieving abstinence and reduction of harm related to parenteral exposure (AII).

Sexual and parenteral risk behaviors

In patients with HIV/HCV coinfection, counseling should explain what behaviors contribute to the risk of acquiring A, B and Delta hepatitis virus infection and transmitting HIV and HCV (including vertical transmission). Non-immune HIV/HCV coinfected patients should undergo anti-HAV and anti-HBV vaccinations[6]. These vaccinations, without specific contraindications in those HIV seropositive, could be proposed for all patients, since the chances of response are greatly reduced in the presence of CD4 counts < 200/ml (AII).

Candidates for anti-HCV treatment

HIV/HCV coinfected patients should be informed that the risk of progression towards cirrhosis is higher than in HCV monoinfection (AII).

It is necessary to inform all patients of the actual degree of efficacy of anti-HCV treatments, their side effects, the potential benefits of such treatments not only on liver disease but also on HIV management (i.e. reduction of ART hepatotoxicity), and the need to obtain and maintain optimal adherence once anti-HCV treatment is started (BII).

Patients receiving ART and anti-HCV treatment

Due to the increased risk of pancreatitis and lactic acidosis[15,25,26] in patients on NRTI (particularly didanosine and stavudine), it is advisable to inform the subjects of the symptoms potentially related to hyperlactatemia/lactic acidosis (abdominal pain, fever, malaise, nausea, vomiting, weight loss, progression of lipoatrophy) (AII).

Patients taking zidovudine and ribavirin should be informed of the increased risk of anemia (AI), and those taking efavirenz and IFN of the increased risk of neuropsychiatric side effects (CIII).

What monitoring?

Initial Evaluation

Anti-HCV reactivity should be assessed in all HIV-infected persons. Serum HCV-RNA should be assessed in all patients with anti-HCV seroreactivity (AI). Since all HIV/HCV coinfected patients are potential candidates for anti-HCV treatment, an adequate work-up should be pursued.

History

Data to help assess the duration of HCV infection (time of first drug injection, tattooing and piercing, history of surgical procedures, transfusion of blood or blood derivatives, history of jaundice, etc.) and behavior and comorbidities likely to worsen the course of hepatitis C (use of recreational drugs, past and present alcohol consumption, history of familial metabolic disturbances, history of metabolic or autoimmune diseases, etc.) should be obtained from all HIV/HCV coinfected patients. It is also useful to obtain details of any previous episodes of depression or other psychiatric conditions (AIII).

Lab and imaging

The following data should be obtained from all HIV/HCV coinfected patients: HCV genotype, HBsAg reactivity (if positive, HBeAg, HBeAb, HBcAb-IgM, anti-HDV and HBV-DNA reactivity should be assessed), anti-HBc and anti-HBs, anti-HAV IgG reactivity, total and fractionated bilirubin, coagulation tests, albumin, blood glucose, cholesterol, triglycerides, complete blood counts, ALT/AST, γ-GT, ALP, CK, LDH, amylase and AFP. An abdominal US examination must be performed to evaluate the presence of signs of cirrhosis, ascites and/or portal hypertension, and liver nodules (AII). In patients with known or suspected cirrhosis, an esophagogastroduodenoscopy (EGD) should be performed to identify esophageal or gastric varices, or hypertensive gastropathy (AII).

Liver Biopsy

Liver biopsy, even taking into account sampling error, is currently still the gold standard for evaluating the grading of necroinflammatory activity and fibrosis[27]. Even in the absence of adequate data on HIV/HCV coinfected patients, fibrosis staging is the

best way to assess patient prognosis and obtain information that is crucial for deciding whether or when to start anti-HCV treatment[4,6]. In the absence of contraindications, liver biopsy could be recommended for HIV/HCV coinfected patients who are candidates for anti-HCV treatment. The decision to perform a liver biopsy should be taken on a case-by-case basis after an accurate evaluation of the risks and benefits[4]. A histologic evaluation of liver fibrosis seems more important in patients infected by HCV genotypes 1 and 4, which are more resistant to treatment[4,6,15-19], and could be crucial for patients with contraindications to anti-HCV treatment (AII). The refusal of a patient to undergo a liver biopsy should not compromise their chances of being treated.

Noninvasive tests for fibrosis assessment (i.e. serum biomarkers or elastography) are under evaluation in HCV-monoinfected patient populations[28,29] and have still not been fully evaluated in patients with HIV coinfection[30]. Therefore, these tests should currently be used only in clinical studies (CIII).

Follow-up

Details of the use of alcohol, recreational and non-recreational drugs, and dietary supplements should be obtained at each appointment (AIII). AST/ALT should be measured at least every three months/quarterly, albumin, PT and bilirubin at least annually. Data from the upper abdomen, US examination and AFP measurement should be obtained at least every 24 months (AIII). In patients with cirrhosis and/or porto-central bridging fibrosis, regular screening for HCC should be established, with upper liver US examination and AFP measurement at least every six months (AIII). Shorter intervals could be taken into consideration on a case-by-case basis (BIII). The same patients should undergo EGD every 24 months if the previous examination did not show esophageal varices, and every 12 months in patients with small (F1) varices (AI).

Patients on ART alone

Considering the significantly increased risk of hepatotoxicity in HIV/HCV coinfected persons, it is useful to plan evaluation liver tests (AST, ALT, ALP, γGT, bilirubin) every two weeks and if a rash occurs in the first three months (early hepatotoxicity), and every two to three months thereafter (late hepatotoxicity) (AII).

Patients assuming ART and anti-HCV treatment

Considering the increased risk of pancreatitis and lactic acidosis in patients taking NRTI (especially stavudine and didanosine), it is advisable to monitor levels of lactic acid and serum amylase monthly (BII). Complete blood counts should also be monitored at least once a month in patients taking zidovudine together with IFN and ribavirin (BII).

How can tolerability be improved?

ART should be withdrawn in the presence of grade IV hepatotoxicity (according to ACTG scale), especially if the patient reports hepatitis-related symptoms such as weakness, anorexia or jaundice (AII). ART interruption should be considered in the presence of grade III hepatotoxicity and repeatedly increased levels of lactate (BII), in all other cases of clinical and laboratory signs of liver failure (AII), and in patients with a Child-Turcotte-Pugh score of more than 6 (AIII).

In patients with HIV/HCV/HBV coinfection and a positive HBV-DNA serum assay, associations of NRTI with anti-HBV activity should be used as NRTI backbone (i.e. tenofovir + lamivudine or emtricitabine) in order to suppress HBV replication[6] and reduce ART hepatotoxicity (AIII).

What treatment for cirrhotics?

Liver dysfunction may be associated with higher plasma levels of NNRTI and PI in subjects with advanced liver disease, and with increased susceptibility to pharmacologic interactions[30]. Unfavorable pharmacologic interactions should be considered carefully in subjects with both HIV and liver dysfunction[30].

Therapeutic drug monitoring could be indicated in patients with severe liver dysfunction. However, the application of therapeutic drug monitoring (TDM) in routine clinical practice is still not supported by a complete knowledge of antiretroviral pharmacology and needs to be validated in controlled studies. At the current state of the art, TDM should be adopted on a case-by-case basis with the support of an expert in the field, and the following issues should be taken into consideration:

– Selection of patients with the highest probability of altered metabolic profile on the basis of the severity of the liver disease (cirrhosis) and of the given drug (BII).

– Knowledge of a relationship between dose, plasma concentrations and toxicity for the drug to be monitored (i.e. efavirenz or indinavir) (BI).

– Possibility of adjusting the dose in individual cases on the basis of specific patterns of resistance mutations and the inhibitory quotient of drugs to be monitored (BII).

Occurrence of a significant worsening of liver function calls for a new evaluation of pharmacokinetic parameters (CIII). The use of simplified assays (e.g. ELISA) is still not sufficiently validated (BII).

References

1. Rockstroh J, Mocroft A, Soriano V, et al. Influence of hepatitis C on HIV disease progression and response to antiretroviral therapy. J Infect Dis 2005;192:992-1002.
2. Del Romero J, Clavo P, García S, et al. Prevalence of HCV infection among two groups with HIV risk behaviors in Madrid (Spain). XIII IAS Conf. Durban, South Africa; 2000.
3. De Luca A, Bugarini R, Lepri A. Coinfection with hepatitis viruses and outcome of initial antiretroviral regimens in previously naive HIV-infected subjects. Arch Intern Med 2002;162:2125-32.
4. Soriano V, Puoti M, Sulkowski M, et al. Care of patients with hepatitis C and HIV coinfection: updated recommendations from the HIV-HCV International Panel. AIDS 2003;17:1-12.
5. Qurishi N, Kreuzberg C, Luchters G, et al. Effect of antiretroviral therapy on liver-related mortality in patients with HIV and HCV coinfection. Lancet 2003;362:1708-13.
6. Alberti A, Clumeck N, Collins S, et al. Short statement of the first European consensus conference on the treatment of chronic hepatitis B and C in HIV-coinfected patients. J Hepatology 2005;42:615-24.
7. Puoti M, Bruno R, Soriano V, et al. HCC in HIV-infected patients: epidemiological features, clinical presentation and outcome. AIDS 2004;18:2285-93.
8. Braitstein P, Palepua A, Dieterich D, Benhamou Y, Montaner J. Special considerations in the initiation and management of antiretroviral therapy in individuals coinfected with HIV and hepatitis C. AIDS 2004;18:2221-34.
9. Sulkowski M. Drug-induced liver injury associated with antiretroviral therapy that includes HIV-1 protease inhibitors. Clin Inf Dis 2004;38 (suppl 2):90-7.
10. Dieterich D, Robinson P, Love J, Stern J. Drug-induced liver injury associated with the use of NNRTI. Clin Infect Dis 2004;38 (suppl 2):80-9.
11. Montaner J, Coté H, Harris M, et al. Nucleoside-related mitochondrial toxicity among HIV-infected patients receiving antiretroviral therapy: insights from the evaluation of venous lactic acid and peripheral blood mitochondrial DNA. Clin Infect Dis 2004;38 (suppl 2):73-9.
12. Pol S, Lebray P, Vallet-Pichard A. HIV infection and hepatic enzymes abnormalities intricacies of the pathogenic mechanisms. Clin Infect Dis 2004;38 (suppl 2):65-72.
13. Sabin C. Pitfalls of assessing hepatotoxicity in trials and observational cohorts. Clin Infect Dis 2004;38 (suppl 2):56-64.
14. Soriano V, Garcia-Samaniego J, Bravo R, et al. IFN-α for the treatment of chronic hepatitis C in patients infected with HIV. Clin Infect Dis 1996;23:585-91.
15. Carrat F, Bani-Sadr F, Pol S, et al. PEG-IFNα-2b vs. standard IFNα-2b, plus ribavirin, for chronic hepatitis C in HIV-infected patients: a randomized controlled trial. JAMA 2004;292:2839-48.
16. Cargnel A, Angeli E, Mainini A, et al. Open, randomized, multicenter Italian trial on PEG-IFN plus ribavirin versus PEG-IFN monotherapy for chronic hepatitis C in HIV-coinfected patients on HAART. Antivir Ther 2005;10:309-17.
17. Brau N, Rodriguez-Torres M, Prokupek D, et al. Treatment of chronic hepatitis C in HIV/HCV coinfection with IFNα-2b full-course *vs.* 16-week delayed ribavirin. Hepatology 2004;39:989-98.
18. Chung R, Andersen J, Volberding P, et al. PEG-IFNα-2a plus ribavirin *versus* IFNα-2a plus ribavirin for chronic hepatitis C in HIV-coinfected persons. N Engl J Med 2004;351:451-9.
19. Torriani F, Rodriguez-Torres M, Rockstroh J, et al. PEG-IFNα-2a plus ribavirin for chronic HCV infection in HIV-infected patients. N Engl J Med 2004;351:438-50.
20. Puoti M, Bonacini M, Spinetti A, et al. Liver fibrosis progression is related to CD4 cell depletion in patients coinfected with HCV and HIV. J Infect Dis 2001;183:134-7.
21. Benhamou Y, Di Martino V, Bochet M, et al. Factors affecting liver fibrosis in HIV and HCV coinfected patients: impact of protease inhibitor therapy. Hepatology 2001;34:283-7.
22. Sulkowski M, Mehta S, Chaisson R, Thomas D, Moore R. Hepatotoxicity associated with PI-based antiretroviral regimens with or without concurrent ritonavir. AIDS 2004;18:2277-84.
23. Peters M, Terrault N. Alcohol use and hepatitis C. Hepatology 2002;36:220-5.
24. Samet J, Horton N, Meli S, Freedberg K, Palepu A. Alcohol consumption and antiretroviral adherence among HIV-infected persons with alcohol problems. Alcohol Clin Exp Res 2004; 28:572-7.
25. Moreno A, Quereda C, Moreno L, et al. High rate of didanosine-related mitochondrial toxicity in HIV/HCV-coinfected patients receiving ribavirin. Antivir Ther 2004;9:133-8.
26. Mauss S, Valenti W, DePamphilis J, et al. Risk factors for hepatic decompensation in patients with HIV/HCV coinfection and liver cirrhosis during IFN-based therapy AIDS 2004;18:F21-5.
27. Dienstag J. The role of liver biopsy in chronic hepatitis C. Hepatology 2002;36 (Suppl);152-60.
28. Imbert-Bismut F, Ratziu V, Pieroni L, et al. Biochemical markers of liver fibrosis in patients with HCV infection: a prospective study. Lancet 2001;357:1069-75.
29. Castera L, Vergniol J, Foucher J, et al. Prospective comparison of transient elastography, Fibrotest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. Gastroenterology 2005;128:343-50.
30. Myers R, Benhamou Y, Imbert-Bismut F, et al. Serum biochemical markers accurately predict liver fibrosis in HIV and HCV coinfected patients. AIDS 2003;17:721-5.
31. Wyles D, Gerber J. Antiretroviral drug pharmacokinetics in hepatitis with hepatic dysfunction. Clin Infect Dis 2005;40:174-81.

Appendix

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