Hepatotoxicity of Antiretroviral Drugs Is Reduced after Successful Treatment of Chronic Hepatitis C in HIV-Infected Patients

Pablo Labarga, Vicente Soriano, Maria Eugenia Vispo, Javier Pinilla, Luz Martin-Carbonero, Carol Castellares, Rebeca Casado, Ivana Maida, Pilar García-Gascó, and Pablo Barreiro

1Department of Infectious Diseases, Hospital Carlos III, Madrid, and 2HIV Unit, Hospital San Millán, Logroño, Spain

Background. The risk of liver toxicity during antiretroviral drug use in human immunodeficiency virus (HIV)–positive patients increases in the presence of chronic hepatitis C virus (HCV) infection. It is unknown whether sustained HCV clearance after interferon (IFN)–based therapy might reduce this complication.

Methods. The incidence of severe elevations in liver enzyme levels during antiretroviral therapy was retrospectively analyzed in a group of HIV/HCV-coinfected patients after completion of a full course of IFN-based therapy. Hepatic events were recorded according to the achievement of a sustained virological response (SVR), and the presence of advanced liver fibrosis was assessed by transient elastometry.

Results. A total of 132 HIV/HCV-coinfected patients were analyzed (66% men; mean age, 38 years). Overall, 33% achieved an SVR and 40% had advanced liver fibrosis after IFN therapy. A total of 49 episodes of liver toxicity occurred during a mean of 35 months of follow-up (9.7% per year) after IFN therapy. The yearly incidence of hepatic events was greater in patients who did not achieve an SVR than in those who did (12.9% vs. 3.1%; P < .001) and in patients with advanced liver fibrosis than in those without it (14.4% vs. 7.6%; P = .003). Drugs involved in hepatic events were dideoxynucleoside analogues (namely, didanosine and stavudine; 40%) nevirapine (30%), efavirenz (11%), and protease inhibitors (PIs; 8%). In logistic regression analysis, lack of an SVR (odds ratio [OR], 6.13 [95% confidence interval {CI}, 1.83–37.45]; P = .003) and the use of dideoxynucleosides (OR, 3.59 [95% CI, 1.23–10.42]; P = .02) were independent predictors of hepatotoxicity after IFN therapy. Conversely, regimens containing PIs (OR, 0.07 [95% CI, 0.02–0.30]; P < .01) or efavirenz (OR, 0.13 [95% CI, 0.04–0.44]; P = .001) were associated with a diminished risk of hepatic events.

Conclusion. Sustained HCV clearance after IFN-based therapy reduces the risk of liver toxicity during antiretroviral therapy, which should further encourage the treatment of chronic hepatitis C in HIV-coinfected patients. In this population, prescription of PIs or efavirenz decreases and use of dideoxynucleoside analogues increases the risk of hepatotoxicity.

Hepatic events are at present one of the main causes of morbidity and mortality in HIV-infected patients [1, 2]. Almost all antiretroviral drugs currently in use may cause elevations in liver enzyme levels, although the mechanisms involved vary widely [3]. Chronic hepatitis C is particularly frequent in this population [4] and enhances the risk of drug-related hepatotoxicity by 3 times [5]. The extent of liver fibrosis in HIV-infected patients with chronic hepatitis C seems to be an important determinant of the risk of hepatotoxic events during antiretroviral use [6], and it is well established that the progression of liver fibrosis is accelerated in HIV/hepatitis C virus (HCV)-coinfected patients [7–10].

The administration of interferon (IFN)-based therapy may eradicate HCV infection in a substantial number of patients [11–15], and this virological success is generally associated with improvements in liver histology [16–18] and a better clinical prognosis in the long run [19]. However, at present, it remains unclear whether sustained clearance of HCV after any IFN treatment...
based therapy could improve the hepatic tolerance of antiretroviral drugs in HIV/HCV-coinfected patients.

PATIENTS AND METHODS

Study population. All patients with HIV/HCV coinfection who had received a full course of IFN-based therapy since 1992 at 2 large Spanish HIV clinics were identified. Those who subsequently were exposed to antiretroviral therapy were selected for the present study. All subjects were invited to undergo liver fibrosis staging by use of transient elastometry between September 2004 and September 2006. Patients with chronic hepatitis B or other liver illnesses (hemochromatosis, Wilson disease, autoimmune hepatitis, α-1-antitrypsin deficiency, etc.) were excluded. Alcohol abuse was recorded regularly by patient interview and was defined as an average daily consumption >50 g for ≥2 years, either currently or in the past.

Patients could have been treated with any anti-HCV treatment modality, including subcutaneous IFN-α (3 × 10^6–10 × 10^6 U 3 times/week), with or without oral ribavirin (RBV; 800–1200 mg/day), or subcutaneous pegylated (peg) IFN-α (2a, 180 μg/week; 2b, 1.5 μg/kg/week) plus oral RBV. Overall, patients infected with HCV genotype 2 or 3 had completed at least 6 months of treatment, whereas patients infected with HCV genotype 1 or 4 had completed 12 months of treatment. Dose adjustments for either IFN (or pegIFN) or RBV were made in accordance with standard recommendations. Data on the use of growth factors were not available in this patient population. Subjects who interrupted therapy prematurely for any reason or who received further treatment thereafter because of initial treatment failure were not included in the study.

Clinical outcome, antiretroviral therapy, and main laboratory parameters (transaminase levels, CD4 cell counts, plasma HIV RNA and serum HCV RNA loads, etc.) were recorded retrospectively after the completion of IFN-based therapy in samples obtained every 3 months until the last visit. All patients underwent hepatic elastometry examination by a single well-trained technician at least 6 months after the completion of IFN-based therapy. Episodes of liver toxicity during the study period were registered according to the following criteria: grade 3–4 elevations in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) level (>5-fold above the upper limit of normal [ULN] [20] or >3.5-fold increases over baseline values if already elevated) or any interruption of antiretrovirals due to symptomatic elevations in transaminase levels, regardless the grade (ULN, 40 IU/L for both).

The serum HCV RNA load was measured using a commercial real-time polymerase chain reaction (PCR) assay (COBAS TaqMan), which has a lower limit of detection of 10 IU/mL. HCV genotypes were assessed using a commercial reverse-hybridization method (InnoLiPA HCV II; Innogenetics). Patients were considered as having achieved a sustained virological response (SVR) after anti-HCV therapy if HCV RNA remained undetectable in serum for 6 months after treatment withdrawal and thereafter. Individuals with HCV RNA detectable in serum after the end of anti-HCV therapy were considered to have had no SVR. In both responders and nonresponders, serum HCV

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>SVR</th>
<th>No SVR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, no. (%)</td>
<td>132</td>
<td>43 (33)</td>
<td>89 (67)</td>
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</tr>
<tr>
<td>Age, mean ± SD, years</td>
<td>38 ± 5</td>
<td>38 ± 5</td>
<td>38 ± 5</td>
<td>.4</td>
</tr>
<tr>
<td>Male sex, no. (%)</td>
<td>87 (66)</td>
<td>28 (65)</td>
<td>59 (66)</td>
<td>.8</td>
</tr>
<tr>
<td>Alcohol abuse, no. (%)</td>
<td>14 (11)</td>
<td>4 (9)</td>
<td>10 (12)</td>
<td>.7</td>
</tr>
<tr>
<td>CD4 cell count, mean ± SD, cells/μL</td>
<td>613 ± 289</td>
<td>620 ± 271</td>
<td>610 ± 300</td>
<td>.9</td>
</tr>
<tr>
<td>HCV RNA load before IFN therapy, mean ± SD, log IU/mL</td>
<td>5.1 ± 1.9</td>
<td>4.8 ± 2.1</td>
<td>5.3 ± 1.7</td>
<td>.6</td>
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<tr>
<td>HCV genotype 3, no. (%)</td>
<td>39 (30)</td>
<td>26 (61)</td>
<td>13 (15)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ALT/AST after IFN therapy, mean ± SD, IU/L</td>
<td>54 ± 43/51 ± 39</td>
<td>25 ± 10/28 ± 12</td>
<td>68 ± 46/63 ± 43</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Advanced liver fibrosis, no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before IFN therapy</td>
<td>29 (69)</td>
<td>8 (57)</td>
<td>21 (75)</td>
<td>.2</td>
</tr>
<tr>
<td>After IFN therapy</td>
<td>53 (40)</td>
<td>6 (14)</td>
<td>47 (53)</td>
<td>.001</td>
</tr>
<tr>
<td>Duration of HAART exposure, mean ± SD, months</td>
<td>19.3 ± 10.9</td>
<td>21.6 ± 10.5</td>
<td>18.2 ± 10.9</td>
<td>.1</td>
</tr>
</tbody>
</table>

NOTE. HAART, highly active antiretroviral therapy; IFN, interferon; SVR, sustained virological response.

a More than 24 weeks after the end of IFN therapy.
b Assessed using liver biopsy.
c Assessed using FibroScan.
d From the initiation of HAART to the time of liver toxicity or at the last follow-up visit.
Table 2. Comparison of HIV/hepatitis C virus (HCV)–coinfected patients with and without hepatic events using antiretroviral therapy.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hepatic events</th>
<th></th>
<th>OR (95% CI) P, multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Patients, no. (%)</td>
<td>37 (28)</td>
<td>95 (72)</td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD, years</td>
<td>37 ± 5</td>
<td>39 ± 5</td>
<td>.1</td>
</tr>
<tr>
<td>Male sex, no. (%)</td>
<td>26 (69)</td>
<td>61 (64)</td>
<td>.3</td>
</tr>
<tr>
<td>Alcohol abuse, no. (%)</td>
<td>2 (7)</td>
<td>12 (13)</td>
<td>.4</td>
</tr>
<tr>
<td>CD4 cell count, mean ± SD, cells/μL</td>
<td>665 ± 362</td>
<td>584 ± 233</td>
<td>.2</td>
</tr>
<tr>
<td>HCV RNA load before IFN therapy, mean ± SD, log IU/mL</td>
<td>5.6 ± 1.5</td>
<td>4.8 ± 2.2</td>
<td>.2</td>
</tr>
<tr>
<td>HCV genotype 3, no. (%)</td>
<td>6 (16.7)</td>
<td>33 (34.5)</td>
<td>.06</td>
</tr>
<tr>
<td>ALT/AST after IFN therapy, mean ± SD IU/L²</td>
<td>61 ± 50/54</td>
<td>51 ± 41/50</td>
<td>.3/6</td>
</tr>
<tr>
<td>ALT/AST at the time of liver toxicity, mean ± SD, IU/L</td>
<td>212 ± 192/162</td>
<td>133 ± 125</td>
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<tr>
<td>Antiretrovirals used at the end of follow-up, no. (%)³</td>
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<tr>
<td>Dydeoxynucleosides</td>
<td>15 (40)</td>
<td>20 (21)</td>
<td>.02</td>
</tr>
<tr>
<td>Protease inhibitors</td>
<td>3 (8)</td>
<td>36 (38)</td>
<td>.001</td>
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<tr>
<td>Nevirapine</td>
<td>11 (30)</td>
<td>12 (13)</td>
<td>.02</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>4 (11)</td>
<td>29 (31)</td>
<td>.01</td>
</tr>
<tr>
<td>Triple-nucleoside analogues³</td>
<td>8 (22)</td>
<td>21 (22)</td>
<td>.9</td>
</tr>
<tr>
<td>Advanced liver fibrosis, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before IFN therapy</td>
<td>4 (80)</td>
<td>25 (68)</td>
<td>.6</td>
</tr>
<tr>
<td>After IFN therapy</td>
<td>24 (65)</td>
<td>29 (31)</td>
<td>.003</td>
</tr>
<tr>
<td>Liver stiffness after IFN therapy, mean ± SD, kPa</td>
<td>13.9 ± 10.2</td>
<td>8.6 ± 4.1</td>
<td>.001</td>
</tr>
<tr>
<td>Lack of SVR, no. (%)</td>
<td>32 (89)</td>
<td>56 (59)</td>
<td>.001</td>
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<tr>
<td>Episodes of liver toxicity, mean ± SD, no.</td>
<td>1.43 ± 0.83</td>
<td>0</td>
<td>.65</td>
</tr>
<tr>
<td>Total follow-up, mean ± SD, months³</td>
<td>33 ± 38</td>
<td>29 ± 25</td>
<td>.65</td>
</tr>
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</table>

**NOTE.** IFN, interferon; SVR, sustained virological response.

² More than 24 weeks after the end of IFN therapy.
³ At the time of liver toxicity or at the last follow-up visit.
⁴ Without dydeoxynucleosides.
⁵ Assessed using liver biopsy.
⁶ Assessed using FibroScan.

RNA loads were measured at least once yearly during the posttherapy follow-up.

**Assessment of liver fibrosis.** Liver stiffness was measured using transient elastometry (FibroScan; EchoSens). Briefly, the hepatic region of each patient was explored with an ultrasound transducer that was placed in the right intercostal spaces. When the echography window showed the characteristic image of liver tissue, the vibration of the ultrasound probe emitted an elastic shear wave. The speed of propagation of this vibration through the liver parenchyma was calculated using ultrasound scanning. On the basis of physical principles, the stiffer the liver, the faster the vibration would pass through the organ. Previous studies have shown that the area under the receiver operating characteristic curve for advanced liver fibrosis—bridging fibrosis to overt cirrhosis (Metavir score of F3–F4)—is 97% when elastometry renders liver stiffness values >9.5 kPa [21]. Patients with median elastometric measures ≥9.5 kPa were considered to not have advanced liver fibrosis (Metavir score of F0–F2). Information regarding baseline hepatic histology was available for all patients who underwent a liver biopsy before IFN-based therapy.

**Statistical analyses.** Descriptive values are expressed as percentages or means ± SDs. The association of multiple variables with hepatic events was explored by splitting the population into SVR and non-SVR after the response to IFN-based therapy or into current liver fibrosis stage (having or not having advanced liver fibrosis). Comparisons were made using the χ² test for proportions and parametric or nonparametric tests for continuous variables, as needed. Crude incidence rates were calculated as the proportion of hepatic events per the total number of patients in each particular group; mean time in follow-up was considered for the calculation of per-year incidence rates. Kaplan-Meier and log rank tests were used for survival analyses. Finally, all variables included in the univariate analyses with P ≤ .05 were used in logistic regression analysis. All data were recorded and analyzed using the SPSS software package (version 13.0; SPSS).
Figure 1. Incidence of severe liver toxicity during antiretroviral drug use in HIV/hepatitis C virus (HCV)–coinfected patients after interferon-based therapy. The influence of sustained HCV clearance is shown.

**RESULTS**

**Study population.** A total of 132 HIV/HCV-coinfected patients were recruited into the study. The main characteristics of the study population are recorded in table 1. Most subjects were men (66%), and the mean age was 38 years. A relatively small proportion were alcohol abusers (11%), and most had been infected by HCV genotype 1 (58%) or 3 (30%). Most had slightly elevated liver enzyme levels before HCV therapy, and 69% had advanced liver fibrosis at baseline, as assessed by liver biopsy. However, after receiving a full course of IFN-based therapy, the proportion of patients with advanced liver fibrosis as estimated using FibroScan was lower (40%), particularly among patients who achieved an SVR (14%). Liver fibrosis assessment using FibroScan was made a median of 27 months (interquartile range [IQR], 17–41 months) after ending treatment for chronic hepatitis C; this lag was comparable between responders (25 months) and nonresponders (29 months).

All patients had completed a full course of IFN-based therapy for chronic hepatitis C, and treatment resulted in an SVR in 43 (33%) of them. The remaining 89 patients (67%) had a relapse of HCV RNA in serum after IFN-based therapy and were considered to have no SVR. The proportion of patients receiving suboptimal anti-HCV therapy (namely, standard IFN with or without ribavirin) was greater among patients without an SVR than among those achieving an SVR (13.5% vs. 4.6%; *P* < .01). None of these patients were treated again thereafter.

The mean duration of exposure to antiretroviral therapy during the follow-up period was 19.3 ± 10.9 months in the overall population and was comparable between patients who achieved an SVR (21.6 ± 10.5 months) and those who did not (18.2 ± 10.9 months).

**Hepatic events.** A median of 7.7 (IQR, 4.2–11.1) different ALT/AST determinations were made during the follow-up period in the study population, without significant differences between patients who achieved an SVR (6.1; IQR, 3.4–10.9) and those who did not (8.7; IQR, 4.8–11.1). Episodes of liver toxicity during antiretroviral use were observed in 37 patients (28%) (table 2). Among these, 10 patients (27%) had symptomatic liver reactions with transaminase levels not achieving grade 3–4 severity. Overall, a total of 49 different hepatic events were recorded, and 7 patients had >1 episode during follow-up. The overall incidence of hepatotoxicity in the study population was 9.7 episodes/100 patient-years (95% confidence interval [CI], 7.2–12.4 episodes/100 patient-years). Exposure to highly active antiretroviral therapy lasted 12.7 ± 7.8 months in patients with hepatic events and 21.7 ± 10.9 months in the rest of the patients (*P* < .001).

The rate of hepatotoxicity was 9.3% in patients who achieved an SVR (3.1% [95% CI, 0.1%–6.1%] per year), compared with 37.5% in patients who did not achieve an SVR (12.9% [95% CI, 8.9%–17.1%] per year) (*P* < .001). Figure 1 shows the Kaplan-Meier curves for hepatic events according to HCV clearance after IFN therapy in the study population. The proportion of patients having grade 3–4 elevations in ALT level was also greater among patients with no SVR (27.3%) than in those who achieved an SVR (6.9%) (*P* = .007).

Current liver fibrosis as assessed by FibroScan was significantly associated with episodes of liver toxicity during antiretroviral use. Hepatic events occurred in 54% (14.4% [95% CI,
10.3%–18.3% per year) and 23% (7.6% [95% CI, 3.6%–11.6%] per year) of patients with and without advanced liver fibrosis, respectively ($P = .003$). Figure 2 shows the Kaplan-Meier curves for hepatotoxicity according to liver stiffness in the study population. The results of liver biopsy before IFN-based therapy were available for only 42 patients, 29 (69%) of whom presented with advanced liver fibrosis (Metavir score of F3–F4). The probability of hepatic events was 2 times higher in patients with advanced liver fibrosis according to baseline biopsy results (13.8%), compared with that in patients with a lesser extent of hepatic fibrosis (7.7%), but the difference did not reach statistical significance ($P = .2$).

**Factors associated with hepatotoxicity.** The main characteristics of patients who had episodes of liver toxicity while using antiretrovirals are depicted in table 2. They had demographic characteristics and immune status similar to those of patients who did not have antiretroviral-related liver toxicity events.

Antiretrovirals prescribed at the end of follow-up (when elevations in liver enzyme levels occurred in patients with hepatotoxicity or at the time of collection of the last sample available from patients remaining free of hepatic episodes) were examined in detail. Patients who developed hepatotoxicity, compared with those who did not, more frequently received regimens containing dideoxynucleoside analogues (namely, didanosine and stavudine [40% vs. 21%; $P = .02$]) or nevirapine (30% vs. 13%; $P = .02$). Conversely, patients without episodes of liver toxicity were more frequently treated with protease inhibitors (PIs; 38% vs. 8%; $P = .001$) or efavirenz (31% vs. 11%; $P = .01$). Exposure to triple-nucleoside regimens (mainly Trizivir) was equally frequent among patients with and without hepatic events (22% each).

As shown in the logistic regression analysis, lack of an SVR (odds ratio [OR], 6.13 [95% CI, 1.83–37.45]; $P = .003$) and receipt of dideoxynucleosides (OR, 3.59 [95% CI, 1.23–10.42]; $P = .02$) were the only independent predictors of hepatotoxicity in the study population. Conversely, the use of antiretroviral regimens containing PIs (OR, 0.07 [95% CI, 0.02–0.30]; $P<.01$) or efavirenz (OR, 0.13 [95% CI, 0.04–0.44]; $P = .001$) was associated with a reduced risk of elevations in liver enzyme levels (table 2).

![Figure 2](https://academic.oup.com/jid/article-abstract/196/5/670/837107)

**Figure 2.** Incidence of severe liver toxicity during antiretroviral drug use in HIV/hepatitis C virus (HCV)–coinfected patients after anti-HCV therapy. The influence of liver fibrosis stage is shown.

The possible contribution of HCV genotype 3 to the risk of liver toxicity during antiretroviral use was analyzed in 89 patients who were not cured of chronic hepatitis C. The rate of hepatic events in patients with relapse was 14% of those infected with HCV genotype 3 and 16% of those infected with other HCV genotypes ($P = .8$).

**DISCUSSION**

The presence of underlying chronic hepatitis C significantly increases the risk of elevations in liver enzyme levels during antiretroviral therapy [22–24]. This complication frequently leads to changes in antiretroviral drug regimen or even to treatment discontinuation [25], which is an important interference of HCV in the management of HIV infection. In this regard, the results of the present study are largely relevant. We demonstrate that the risk of antiretroviral-associated hepatic events in coinfected patients who had eliminated HCV after a course of anti-HCV therapy was significantly diminished, compared
with that in patients who did not clear the virus (9.3% vs. 37.5%). Moreover, the former group showed rates of antiretroviral-related hepatotoxicity comparable to those in patients who never had chronic viral hepatitis (8.3%) [26], which suggests that no residual risk persists in coinfectected patients after having cleared HCV using IFN-based therapy.

Our results are somewhat in agreement with those of a prior pilot study conducted in HIV/HCV-coinfected patients in Italy [27]. In that study, the risk of severe liver toxicity during antiretroviral therapy decreased by 10% in patients treated for chronic hepatitis C during the preceding 2 years, and this benefit was recognized even in subjects who did not achieve an SVR. Interruption of subsequent antiretroviral therapy because of hepatic events was 5-fold higher in a control group of coinfectected patients not treated for HCV infection [27]. However, the impact of other variables, such as liver fibrosis stage and antiretroviral treatment modality, was not assessed or could not be investigated appropriately in that study.

Patients who developed hepatic events during antiretroviral therapy in our study presented more-advanced liver fibrosis than did patients who tolerated the medication well. However, this association lost statistical significance in the regression analysis. This fact is noteworthy and highlights the notion that ongoing liver injury and dysfunction caused by active HCV replication, rather than liver fibrosis itself, may be the main determinant of the poorer tolerance of antiretroviral drugs in coinfectected patients.

The only single study that so far has shown a direct relationship between liver fibrosis staging in chronic hepatitis C and the risk of antiretroviral-associated liver toxicity specifically acknowledged a higher risk of hepatotoxicity during nonnucleoside analogue use [10]. In our study, patients with hepatic events were more frequently receiving dideoxynucleoside analogues or nevirapine. The hepatotoxic potential of these drugs has been highlighted in previous studies [28–31]. However, in our series, only the use of dideoxynucleosides remained associated with hepatotoxicity in the multivariate analysis. The deleterious influence of nevirapine, however, might have been underestimated because of its less-frequent use in subjects with chronic hepatitis C, at least in the 2 clinics participating in this study. On the other hand, because nevirapine had been frequently prescribed along with dideoxynucleosides in this patient population, the greater impact of the latter might have hidden any independent contribution of nevirapine to hepatotoxicity in our analyses.

In agreement with previous reports, triple-nucleoside regimens not containing dideoxynucleoside analogues [32, 33], efavirenz [23, 34, 35], or PIs [36, 37] resulted in a diminished risk of antiretroviral-related hepatic events in our study. These results were confirmed in the multivariate analysis and therefore support the hypothesis that the assessment of liver fibrosis using noninvasive tools, such as hepatic elastometry, might help optimize antiretroviral therapy in HIV/HCV-coinfected patients. When possible, safer antiretroviral drugs should be preferred in subjects with advanced hepatic fibrosis [38].

The retrospective nature of this study is a limitation when interpreting the results. However, the objective definition of the main end points (hepatic episodes of drug-related toxicity and sustained HCV clearance) and the fact that liver fibrosis could be assessed in the whole population, thanks to the use of a noninvasive tool such as elastometry, make the analyses more robust. A further limitation of this study was that the evolution of liver enzyme levels before hepatitis C treatment was not considered; this information would have permitted us to determine whether patients who did and did not achieve an SVR were homogeneous in terms of liver tolerance to antiretrovirals before IFN-based therapy was instituted.

In conclusion, successful treatment of chronic hepatitis C, besides preventing the development of end-stage liver disease, may reduce the risk of subsequent liver toxicity during antiretroviral therapy in HIV/HCV-coinfected patients. This fact represents a further argument for prioritizing the treatment of chronic hepatitis C in this population.

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