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The Influence of Protease Inhibitors on the Evolution of Hepatitis C in Patients with HIV and HCV Co-Infection

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Abstract

Prevalence of hepatitis C in HIV infected patients is much higher than in the general population. There is the possibility of viral clearance HCV, in some patients co-infected HIV and HCV, in the phase of immune reconstruction after antiretroviral treatment (ART). There are patients' anti-HCV positive who initially did not show HCV viral load detected and after the start of ART becomes HCV viral load detectable. There are studies that described that immune restoration with increase in CD4+ and CD8+ T cells, from ART, was important in control of HCV viremia. Has been proposed hypothesis that direct or indirect effect of ART on HCV replication play a role in spontaneous resolution of HCV infection. We evaluated the co-infected patients with HIV and HCV under combined antiretroviral treatment, containing PI boosted with ritonavir in terms of immunological and virological status (for both infection) and also liver disease. Patients were evaluated for liver damage by non-invasive methods. We have shown that a small percentage of patients have severe liver damage. We demonstrated the negative role of HCV on immunological status and in liver fibrosis in co-infected patients. A high proportion of these HIV and HCV co-infected patients had no detectable viremia, higher than other studies published.

Keywords: protease inhibitors, HCV, HIV, co-infection, non invasive liver fibrosis test, seroclearance

1. Introduction

Approximate 1/3 of HIV infected patients are also infected with hepatitis C virus (HCV) due to shared routes of transmission.

The clinical implications of this crossroad are important and challenging issues regarding the evaluation and management of the co-infected patient.

Patients with HIV and HCV infection have higher risk for developing cirrhosis, hepatic decompensation, increased rates of end-stage liver diseases, hepatocellular carcinoma and shortened lifespan after hepatic decompensation.

2. Virology

There are similarities by virological point of view for these two viruses: HIV and HCV. 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. HCV is a *flavivirus*, which does not replicate through a DNA-intermediate, as retroviruses do. This allows the possibility of eradication of HCV. HIV viral production rates are approximate 10^{10} virions per day with half life less than 6 hours and this production is even greater for HCV with production of 10^{12} virions per day and average virions half-life 27 hours [1]. Details of the HCV replicative process are still not well known.

In chronic mono-infection with hepatitis C virus or HIV is maintained a viral load relatively stable as a “set point” over long periods of time. Virus specific T-cell responses play a role in the control of virus during chronic HCV.

In co-infection HIV and HCV, HCV RNA levels increase after HIV seroconversion, and continue to increase over time, different from HCV mono-infection. Quantitative loss of memory lymphocytes that occurs in HIV infection could potentially be responsible for the elevated HCV RNA levels, observed in co-infected patients [2]. In combined infection, HCV viral load is related with level of immunosuppression (inversely correlated with CD4 counts), and can increase with heavy alcohol use and transient with the antiretroviral therapy initiation [3]. HIV by himself can increase HCV replication due to gp120 protein (HIV envelope protein) through engagement of cellular co-receptors of HIV (ie, CXCR4 or CCR5) [4].

In addition to quantitative changes of T-cells, HIV may induce qualitative defects in immune responses through alteration of cytokine secretion profiles, and/or dendritic cell function. Innate effectors, such as natural killer (NK) cells and natural killer T (NKT) cells, also mediate antiviral defenses. Disruption of NK cell function such as increased activation or decreased cytokine secretion induced by HIV-1 could also be responsible for the development of chronic HCV [5, 6].

HIV replicates in CD4+ T-cells as well in many cell types. There are controversial data regarding HCV replicates in extrahepatic sites, a study suggests peripheral blood mononuclear cells (PBMCs) [7]. Some studies have suggested that HCV RNA replication in PBMCs may occur in patients with HIV/HCV co-infection, but not in those with HCV alone [8]. The mechanism for the relapse of HCV viral load after HIV treatment discontinuation can be HCV replication in dendritic cells or PBMCs [9].

The higher rates of perinatal HCV transmission in co-infected patients can be explained by the fact that HCV has been isolated from the cervico-vaginal lavage fluid in HIV HCV positive women (not in HCV positive alone) [10].

After introduction of directly acting agents against HCV (DAA) it was demonstrated the potential drug resistance for HCV parallels as in HIV, resistance mutation to specific polymerase and protease HCV inhibitors [11].

3. Epidemiology

Since both infections have similar routes of transmission, co-infection HIV and HCV is common. The prevalence of co-infection varies by geographic areas, across risk groups, by route of transmission. Also the sequence of infection depends by transmission route.

HCV infection is transmitted by **percutaneous route** with highest rates in people who inject drugs (PWID) and hemophiliacs. The risk of **post-transfusion** HCV infection deeply decreases. Injection drug use is the most important route of HCV transmission, approximately 80% of HIV persons with history of injection

drug use are infected with HCV, and they usually acquire HCV before HIV infection while men who have sex with men (MSM) typically are infected with HIV before HCV infection [12].

HIV is much easily transmissible via **sexual intercourse** than HCV. In heterosexual partners the prevalence of HCV co-infection is estimated as 4% in persons whose main HIV exposure risk is heterosexual sex with multiple partners. Globally, is estimated a 6.4% of HCV/HIV co-infection prevalence among MSM, with variations depending on the geographic region [13]. In MSM, HCV acquisition is associated with unprotected anal intercourse, group sex, fisting and recreational drugs [14]. HCV transmission may be increased by mucosal injury and/or concomitant other sexually transmitted diseases [15]. Ongoing HCV transmission is occurring in MSM with declining after DAAs but high rate of reinfection.

Regarding **perinatal** transmission of HCV, vertical transmission of HCV seems to be facilitated by HIV co-infection. Maternal co-infection increases the risk of vertical HCV transmission to their infants with about 2.82 fold more than for women who are infected with HCV alone [16].

There are rare reported cases of acquisition HIV and HCV via percutaneous exposure in **health care workers**.

4. Pathophysiology

Patients with co-infection HIV/HCV have higher rates of liver fibrosis progression compared with patients with HCV alone.

In patients with HIV, liver fibrosis progression is linked to weak cellular immune responses to HCV antigens. The cellular immune response to viral infection is linked to CD8+ T-cell responses and in HIV infection there is a decreases number of CD4 cells, functional impairment of CD4 and CD8 cells and a down-regulation of a co-stimulatory molecule necessary for lymphocyte activation CD28. These observations explain the link between liver progression and advanced immunosuppression.

Also, liver progression can be determined by chronic immune activation through increased levels of pro-inflammatory cytokines, secondary to HIV infection. Kupffer cell depletion is associated with CD4 cell decline and may be related to development of fibrosis [17].

In HCV related liver fibrosis, activated hepatic stellate cells (HSCs) mediate collagen formation. There levels were associated with T cell immune activation and increased gene expression of interleukin-15. In HIV/HCV patients IL-15 play a pathogenic role in mediating liver fibrosis [18].

In normal hepatocytes apoptosis is mediated by tumor necrosis factor-related apoptosis-inducing ligand (TRAIL). Glycoproteins of HIV (gp120) through upregulation of TRAIL-mediated apoptosis triggered to hepatocytes death [19].

HCV-associated proinflammatory cytokines may contribute to liver fibrosis progression and these may have a damaging effect on HIV disease [18].

In acute HCV infection, patients with HIV, especially those with low CD4 counts, have lower rates of spontaneous virologic clearance.

In co-infected patients there is a much more rapid rate of progression to cirrhosis than in HCV alone [20]. The prevalence of extensive liver fibrosis was higher in coinfecting patients [21]. Non-invasive assessments of liver fibrosis can be used more frequently and these also suggested more rapid fibrosis progression in coinfection but this can be related with the degree of HIV-immunosuppression.

In coinfection, as in mono-infection, some patients clinical characteristics: older age, diabetes, alcohol consumption, diabetes, obesity, elevated liver enzymes, have been associated with fibrosis progression [22].

5. Effect of antiretroviral treatment (ART) on HCV progression

There are studies that suggested a decline in liver-related mortality associated with a potent ART introduction which also slows the rates of fibrosis progression, due to immune reconstruction [23]. A cross-sectional study demonstrated a lower necroinflammatory activity on liver biopsy in HIV viral suppressed ART patients and another study showed an increased risk of fibrosis progression in those patients with ART interruption [24, 25]. There is a decrease in AIDS and non-AIDS related morbidity and mortality in HIV patients with early ART initiation and this approach is important especially in HIV/HCV patients. There is evidence that use of ART partially restores T-cell responses to core HCV peptides. Successful response to ART among HIV/HCV patients is associated with increased cellular immune responses to HCV infection, long-term reduction in HCV RNA levels and with HCV clearance [26].

Drug induced liver injury (DILI) is more common in HIV/HCV coinfection following ART. Even liver toxicity is more common in patients with chronic viral hepatitis the benefit of ART exceeds the risk of liver injury. Some studies found an increased risk not for all ART regimens, only for some antiretroviral agents, such as ritonavir or nevirapine [27, 28].

The role of particular drug or antiretroviral class in liver progression rates is questionable, there are conflicting data. In a retrospective analysis, the authors observed that along with young age at infection, heavy alcohol use, and a low CD4 count, patients whose ART 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 ART regimen [29]. In another retrospective analysis of coinfecting patients, no significant differences in the proportion of severe fibrosis (approximately 25%) were observed between those on a non-nucleoside reverse transcriptase inhibitors (NNRTI), a PI, or both [30]. Therefore, specific PI or NNRTI use may not be associated with evident histological benefit or obvious histological worsening of HCV disease.

There are conflicting studies regarding the role of HCV in clinical progression of HIV disease. Some studies have suggested that co-infected patients have an increased progression to AIDS, as well as a decrease in survival from the time of diagnosis of HIV and AIDS [31, 32].

6. Treatment of chronic hepatitis C virus infection in the patient with HIV

The goal of HCV antiviral treatment is to cure the infection, characterized by achievement of a sustained virological response (SVR) defined as an undetectable HCV RNA at week 12 to 24 after the end of treatment. Thus, an effective cure is associated with substantial reduction in liver-related mortality and morbidity and reduced incidence of hepatocellular carcinoma.

HIV/HCV coinfecting patients had lower response rates to HCV treatment with peginterferon and ribavirin regimens compared with individuals without HIV. They have comparable SVR rates with DAA-regimens as HCV-monoinfecting patients. Eradication of HCV infection may reduce the antiretrovirus-associated DILI.

The decision of optimal regimen and timing vary based upon: genotype, the stage of liver disease, prior treatment history, drug interaction and some medical and social priorities.

Because of the more rapid progression of liver fibrosis in the settings of HIV infection, coinfecting patients should be prioritized for HCV antiviral therapy and

another reason to prioritize HCV treatment is cirrhosis and bridging fibrosis. With highly effective interferon-free regimens (DAA), curative all-oral treatment is possible also for those patients with coinfection. There is a low incidence of adverse events and high efficacy and that means that almost all patients can benefit from HCV treatment.

All HIV patients should be evaluated for chronic HCV infection using a third generation enzyme immunoassay. Patients found to be HCV positive should undergo quantitative HCV RNA testing to confirm the presence of viremia. HIV patients who are found to be HCV seronegative but if they are with advanced immunosuppression (CD4 counts < 100 cells/mm³), risk factors for HCV acquisition or elevated liver enzymes should undergo HCV-RNA testing.

Evaluation for coinfecting patients for HCV treatment, by the point of view of HCV infection, is similar to those mono-infected. Prior to treatment evaluation should focus on these factors: HCV genotype, viral resistance testing for certain populations, history of prior treatment, assessment of liver fibrosis stage using noninvasive tests for fibrosis or liver biopsy, history, physical and basic laboratory tests, evaluation for conditions that might affect the therapy.

6.1 Management of antiretroviral treatment in coinfecting patients

Timing of HCV therapy in relation to ART initiation in ART-naïve patients is important and that it will be discussed below. For special population, such as those with decompensate liver diseases, the treatment should be established only in specialized center with expertise in managing HIV/HCV coinfection.

For HIV/HCV coinfecting patients whom are considered to receive HCV treatment, the appropriate antiretroviral treatment regimen used should not have serious drug interaction with HCV antiviral agents. Another management issue in coinfecting patients is the timing of antiretroviral therapy initiation or regimen switch. It is not recommended an ART interruption to allow HCV antiviral therapy [33].

In ART-naïve HIV/HCV patients is preferable to start ART first and begin HCV treatment later. HIV/HCV patients should be initiated on ART for HIV disease without taking into account their CD4 cell count [34]. In selection of ART regimen should be taken into account the potential drug–drug interactions with HCV antivirals. It is recommended to initiate ART approximately 4 to 6 weeks before starting HCV therapy for two reasons: initiation of ART first allows assessment of tolerability and adverse effects of ART alone and the second reasons is an improved HCV outcome, by suppression HIV viral load by ART treatment through restoration of immune response or other effects [35].

In ART-experienced HIV/HCV patients, who achieved HIV viral suppression on an ART well tolerate regimen, should continue the regimen, if it does not have significant drug interactions with the HCV treatment selected. A regimen switch may be necessary if ART regimen components cannot be used with HCV antiviral drugs. In failure to suppress HIV or adverse effects or intolerance to an ART regimen, the regimen switch should be indicated. In this case should be taken into account in selection of a new ART regimen potential drug interaction with HCV-antivirals, in addition to all specific recommendations that appeared in the choice of ART regimen in treatment-experienced patients. In ART regimen switches, prior antiretroviral history drugs and resistance profiles should be studied, to ensure that the new regimen is active, with two or three fully active antiretroviral drugs. The treatment should be initiated after 4 to 6 weeks after ART regimen switch by the same reasons as in ART-naïve patients. Additionally, HIV RNA should be determined at 4 to 6 weeks after the switch to ensure that the new regimen maintains HIV viral suppression. If it is wished to switch back, the new ART regimen to the original ART

regimen, following completion of HCV treatment, this should be delayed until at least two weeks after completion of HCV treatment, to ensure clearance of the HCV antivirals [34].

6.2 HCV regimen selection in coinfecting patients

The efficacy of DAA regimens among HIV/HCV coinfecting patients it seems to be comparable to that in HCV mono-infected patients, the regimen selection decisions are similar for these two groups.

The HCV selection regimen is based on genotype, prior HCV treatment, the stage of liver fibrosis and in rare cases by the presence of baseline NS5A inhibitor resistance associated substitutions. In co-infected patients, the HCV regimen drug interaction with HIV antiretroviral is the major consideration in selection of HCV regimen.

The regimen options for coinfecting patients with a particular genotype are the same as those for HCV mono-infected patients with the same genotype. Potential drug interactions with antiretroviral regimen is the major consideration factor that decide between the several regimens available for a specific genotype. There are regimens that have been studied in coinfecting patients.

6.2.1 Genotype 1 HCV infection

- Elbasvir-grazoprevir- high efficacy of this regimen in HIV/HCV patients. Analysis in mono-infected patients has suggested an association between lower SVR rates and pre-existing variations in the genotype's 1 NS5A inhibitor sequence. In genotype-1a infected patients is recommended testing for these resistance-associated substitution, and, if present, adding ribavirin and extended to 16 weeks the duration of treatment [35, 36].
- Sofosbuvir- velpatasvir- is a highly effective pangenotypic regimen, for 12 weeks, the SVR rates are high regardless cirrhosis or treatment history [37].
 - Sofosbuvir-velpatasvir-voxilaprevir, a regimen reserved for patients who failed on certain DAA-regimen, can be used also for 8 weeks in naïve patients, has not been studied in coinfecting patients but is thought to be the same efficient as in mono-infected patients
- Glecaprevir-pibrentasvir, is also a potent effective pangenotypic regimen, with high efficiency in coinfecting patients treatment for 8 or 12 weeks [38].
- Ledipasvir-sofosbuvir- is highly effective in several studies in coinfecting patients treatment naïve or experienced, for 12 weeks, with high SVR overall even in patients with cirrhosis or prior treatment failure [39].
- Ombitasvir- paritaprevir- ritonavir plus dasabuvir- this regimen with or without ribavirin is highly effective for coinfecting patients with genotype1, given for 12 to 24 weeks (depending on the infection subtype and the presence of cirrhosis) [40].
- Simeprevir and sofosbuvir – effective in HIV/HCV patients with cirrhosis who had failed to a prior regimen, given 16 or 24 weeks. (telaprevir plus peginterferon and ribavirin) [41]. The SVR rates in real-life are higher in patients without these negative predictors of response.

- Daclatasvir combinations
 - Daclatasvir plus sofosbuvir is highly effective for genotype 1, 12 weeks of treatment in naïve or experienced- coinfecting patients. For these regimens, allowed ART agents included darunavir, atazanavir, or lovinavir, each ritonavir-boosted, efavirenz, rilpivirine, raltegravir and dolutegravir. When it is used with specific asntiretrovirals, the dose adjustment of daclatasvir is needed.
 - Daclatasvir plus asunaprevir is available in Japan for genotype 1b infection.

6.2.2 Genotype 2 infection: highly effective options, formally evaluated for coinfecting patients

- Sofosbuvir-velpatasvir 12 weeks [37].
- Glecaprevir-pibrentasvir 8 weeks in non-cirrhosis patients, 12 weeks for patients with compensated cirrhosis [38]. The choice between them depends on drug interaction.
- Sofosbuvir- velpatasvir-voxilaprevir – reserved for patients who previously failed on an certain DAA regimen, 8 weeks treatment, has not been studied for HIV/HCV patients

Administration and dosing of these regimens in coinfecting patients are similar to mono-infection.

6.2.3 Genotype 3 infection

- Glecaprevir-pibrentasvir for 8 to 16 weeks depending on treatment history and presence of cirrhosis
- Sofosbuvir-velpatasvir with or without ribavirin for 12 weeks.
- Daclatasvir plus sofosbuvir
- Sofosbuvir- velpatasvir-voxilaprevir – reserved for patients who previously failed on an certain DAA regimen,, has not been studied for HIV/HCV patients

The choice between them depends on drug interaction. The studies are in a limited number of coinfecting patients [37, 38].

6.2.4 Genotype 4, 5 and 6 infection

Studies in limited numbers of coinfecting patients have demonstrated good efficacy with various regimens as those recommended for HCV-mono-infected patients.

- Ledipasvir-sofosbuvir
- Elbasvir-grazoprevir
- Glecaprevir-pibrentasvir

6.3 Potential drug interaction with ART

When assessing a HIV/HCV patient for HCV treatment there some important drug interactions to be considered.

- ribavirin. The interaction between it and antiretroviral agents include direct interaction but also a combination that potentiate adverse effects (with atazanavir- containing ART, patients may develop jaundice).
- sofosbuvir. Have few drug interactions with antiretroviral agents. In clinical studies was used in combination with tenofovir disoproxil fumarate- emtricitabine (TDF-EMT), efavirenz, darunavir or atazanavir boosted with ritonavir, raltegravir and rilpivirine, without any evidence of decreased efficacy or adverse events.
- ledipasvir- sofosbuvir. It is available only as a fixed-dose combination. Co-administration with tenofovir disoproxil fumarate (TDF), increased levels of tenofovir. Co-administration with tenofovir alafenamide (TAF) does not elevate plasma levels of tenofovir, that's why we can switch patients from TDF to TAF containing regimen when planning a treatment with ledipasvir- sofosbuvir. There are specific options for different TDF-containing antiretrovirals in combination with ledipasvir-sofosbuvir.
- sofosbuvir –velpatasvir is only available in fixed-dose combination. There are no evidence of interaction or adverse events in combination with abacavir, atazanavir, darunavir, ritonavir, cobicistat, elvitegravir, raltegravir, lamivudine, emtricitabine, TAF, rilpivirine.
- glecaprevir-pibrentasvir is available in fixed-dose combination. It was used in studies in combination with tenofovir, abacavir, lamivudine, emtricitabine, raltegravir, dolutegravir, elvitegravir with cobicistat and rilpivirine without clinical relevant interactions.
- elbasvir-grazoprevir- is available in fixed-dose combination. Both are primarily metabolized through CYP3A metabolism, thus, coadministration with several antiretrovirals is not advised. It can be used in combination with tenofovir, lamivudine, abacavir, emtricitabine, rilpivirine and dolutegravir, raltegravir.
- Ombitasvir-paritaprevir-ritonavir plus dasabuvir. Drug –interactions are expected since all of these agents are substrates and inhibitors of major metabolic enzymes. It was used safely with TDF-FTC and raltegravir, or in combination with atazanavir, when ritonavir boosting was served by ritonavir contained in HCV regimen.
- voxilaprevir, is available in fixed-dose combination pills with sofosbuvir and velpatasvir. Voxilaprevir is a substrate and inhibitor of P-glycoprotein, slowly metabolized by CYP3A4. Coadministration with several antiretrovirals is not advised.
- daclatasvir is metabolized by CYP3A, thus inducers or inhibitors of these enzyme are expected to modify daclatasvir concentration.
- simeprevir is oxidatively metabolized by CYP3A. Inducers or inhibitors of CYP3A are expected to modify simeprevir concentration.

Patients should be monitored for side effects and adherence, viral loads responses on therapy and also depending on ART regimen all the tests needed for evaluate side effects or toxicity.

7. Personal contribution

In our hospital, we are treating patients with HIV infection for about 20 years, with a history of long-term antiretroviral regimens which include protease inhibitors (PI). The newly regimens for HCV treatment with direct-acting antivirals contains protease inhibitors (PI) and ritonavir for HCV infection, like in HIV infection.

In our clinic there are 4.33% patients HIV/HCV coinfectd, this incidence is similar to HCV in general population in Romania. In a previous study using noninvasive methods FibroScan (transient elastography) we demonstrated that 84.6% of HIV patients had mild or no fibrosis, 15.4% had moderate–severe fibrosis, and no cirrhosis [42]. We also demonstrated the concordance between noninvasive fibrosis evaluation methods Fibroscan, APRI and FIB-4 score for HIV [43, 44] and in literature these are used in coinfectd HIV/HCV patients monitoring.

We evaluated the patients HIV/HCV coinfectd under combined antiretroviral treatment containing PI boosted with ritonavir in terms of immunological and virological status (for both HIV and HCV infection) and also liver disease. Patients were evaluated for liver damage by non-invasive methods, APRI score and FIB-4.

By immunological HIV status 64.5% have $CD4 \geq 500$ cells/mm³, 29.03% have $CD4 = 200-499$ cells/mm³, and 6.45% $CD4 \leq 200$ cells/mm³. HIV viral load was <40 copies/ml in 70% of cases, 11% presented less than 100 copies/ml, and 19% of patients, noncompliant to ART treatment, with detectable HIV viral load.

Using APRI score 69% of HIV/HCV patients have APRI < 0.5, representing mild or no fibrosis, 24% moderate or severe fibrosis and 7%, APRI > 1.5 corresponding to cirrhosis. The same results are when we used FIB-4 score: 77% no/mild fibrosis, (FIB4 < 1.45), 16% moderate/severe fibrosis, 7% cirrhosis (FIB-4 > 3.25. We have shown that a small percentage of patients have severe liver damage but significantly higher in HIV HCV co-infection than in mono HIV infected persons (**Table 1**).

In another study on these cohort 34% of coinfectd patients have undetectable HCV viral load without any HCV regimen only the same exposure to PI, (ritonavir-boosted lopinavir majority or other PI) [45]. This seroclearance can be explained by immune reconstruction induced by antiretroviral treatment or by direct antiviral effect of PIs on HCV infection.

A high proportion of these HIV/HCV co-infectd patients had no detectable viremia, higher than other studies published which may be explained by the fact that these patients have had HCV clearance, spontaneous or induced by the antiretroviral therapy.

Infection	Non-invasive liver fibrosis tests	Fibrosis		
		No/mild (%)	Moderate/severe (%)	Cirrhosis (%)
HIV	APRI	84.6	15.4	0
	FIB-4	82.0	18.0	0
HIV/HCV	APRI	69	24	7
	FIB-4	77	16	7

Table 1.
Liver fibrosis.

The immunological and virological HIV status of these undetectable HCV viral load patients was better than in those with detectable HCV viral load. There are also differences regarding PI regimens and duration between these two groups. We have limited experience on DAA treatment in HIV/HCV coinfecting patients.

8. Conclusion

With the growing availability and diversity of direct-acting antiviral combination regimens for HCV treatment, a curative treatment will be possible for majority patients, even those with HIV.

The sustained virologic response rates in coinfecting patients treated with DAA are similar with mono-infected patients, with almost the same regimens. These are associated with substantial reductions in liver-related morbidity and mortality. A testing algorithm based on primary care screening (e.g. with APRI, FIB-4) followed by referral for specialty confirmatory testing (e.g. transient elastography) would best fit most practice models.

There are some management issues in HIV/HCV coinfection regarding appropriate antiretroviral regimens and drug interactions with HCV treatment.

With these DAA regimens, as in HIV pre-exposure prophylaxis (PrEP), maybe we can limit the extension of HCV infections in some risk group of HIV patients.

Conflict of interest

“The authors declare no conflict of interest.”

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