Journal of Infection (2015) 71, 571—577

BIA
British Infection Association

www.elsevierhealth.com/journals/jinf

Hepatitis C virus reinfection after sustained virological response in HIV-infected patients with chronic hepatitis C

Juan A. Pineda [a,*], Rocio Núñez-Torres [a], Francisco Téllez [b], María Mancebo [a,c], Federico García [d], Nicolás Merchante [a,c], Montserrat Pérez-Pérez [b], Karin Neukam [a,c], Juan Macías [a,c], Luis M. Real [a,c], on behalf of the HEPAVIR Group of The Andalusian Society of Infectious Diseases (SAEI)

[a] *Unidad Clínica de Enfermedades Infecciosas y Microbiología, Hospital Universitario de Valme, Avda. de Bellavista s/n, 41014 Sevilla, Spain*
[b] *Unidad Clínica de Enfermedades Infecciosas y Microbiología, Hospital La Línea, AGS Campo de Gibraltar, Avda. Menéndez Pelayo 103, 11300 La Línea de la Concepción, Cádiz, Spain*
[c] *Instituto de Biomedicina de Sevilla (IBiS), Campus Universitario Virgen del Rocío, Avda. Manuel Siurot s/n, 41013 Sevilla, Spain*
[d] *Servicio de Microbiología, Complejo Hospitalario Universitario de Granada, Centro San Cecilio-PTS, C. Dr. Oloriz, 18012 Granada, Spain*

Accepted 15 July 2015
Available online 23 July 2015

KEYWORDS
Hepatitis C virus;
HIV;
Reinfection;
Parenteral drug use;
Direct acting antivirals

Summary *Objectives:* To assess the incidence of hepatitis C virus (HCV) reinfections after therapy-induced clearance in HIV-coinfected patients with prior chronic hepatitis C.
Methods: Eighty-four HIV-infected subjects, who had previously achieved sustained virological response (SVR) after being treated of chronic hepatitis C, were analyzed. In all of them, at least yearly HCV RNA determinations were carried out during a median (range) of 34 (12—146) months.
Results: Seventy-two (86%) subjects had been people who inject drugs (PWID), of whom 11 (15%) continued to use snorted or injected drugs during the follow-up. Four (4.76%) patients showed HCV reinfection (incidence 1.21 [95% confidence interval: 0.3—3.09] cases per 100 person-years). These patients maintained risk factors for HCV infection. In three cases, HCV genotype switched. Phylogenetic analysis of the remaining case suggested reinfection from his sexual partner.

* Corresponding author. Tel.: +34 955015684; fax: +34 955015795.
E-mail address: japineda@telefonica.net (J.A. Pineda).

http://dx.doi.org/10.1016/j.jinf.2015.07.006

Conclusion: The incidence of HCV reinfection in the overall population of HIV-coinfected patients who achieved SVR after being treated against chronic hepatitis C is low. A low frequency of risk behavior is the main factor accounting for this modest rate of reinfection. The possibility of reinfection should not be considered a reason against treatment of HCV infection with direct acting antivirals in PWID.

Introduction

Hepatitis C virus (HCV) reinfection may occur after spontaneous or treatment-induced clearance of a prior episode of HCV infection.[1,2] HCV reinfections are a major problem in the field of HCV infection. Indeed, the emergence of HCV reinfection episodes raises questions on the durability and effectiveness of immune response against HCV, and, consequently on the potential efficacy of vaccines against HCV. Thus, understanding the mechanisms underlying clearance of and reinfections with HCV is critical to improve our knowledge on the susceptibility to HCV infection and for vaccine design.[1,3] In addition, the chance of reinfections has led some clinicians to be reluctant to treat hepatitis C in specific settings where reinfections might be particularly common, such as in people who inject drugs (PWID).[4] However, in many PWID are treated against chronic hepatitis C when they have stopped using injected drugs or are under opiate substitution therapy, and in these cases the incidence of reinfection could be completely different. Indeed, in our area, as in others, most of these people either permanently stop using opiates and cocaine or, in case of relapse, they use smoked crack and or heroin.[5]

After spontaneous clearance, the reported rates of HCV reinfection in PWID have been extremely variable, ranging from 0.8 to 24.6 per 100 person-years,[2,6–11] which has been explained on the basis of differences in risk behaviors for infection between populations. However, these studies included few or no HIV-coinfected subject. In HIV-infected men who have sex with men (MSM), HCV reinfections are particularly common. Thus, rates of reinfections of 9.6 per 100 person-years in patients who had reached sustained virological response (SVR) after therapy and 4.5 per 100 person-years in those who spontaneously cleared HCV have been described,[12] although higher figures have also been reported.[13] In some case series, up to one fourth of patients who cleared HCV after an episode of acute hepatitis C suffered from a reinfection.[14] However, data on the frequency of HCV reinfections in HIV-coinfected PWID, particularly in the setting of subjects who attained SVR after therapy for chronic hepatitis C are scarce. Obtaining information on this issue is critical, as the cost of the newer therapies against HCV require prioritizing potential candidates according to the likelihood of achieving definitive cure of hepatitis C in specific subsets.

The objective of the present study was to assess the incidence and main features of HCV reinfections after therapy-induced clearance in a HIV-coinfected population, mainly made up of PWID.

Methods

Patients and follow-up

From a cohort of HIV/HCV-coinfected patients who received treatment against chronic hepatitis C in two Spanish hospitals and who were prospectively followed from 2001 to 2013, those fulfilling the following criteria were selected for this retrospective analysis: i) Having attained SVR, as defined as undetectable plasma HCV RNA 24 weeks after therapy completion, and, ii) having at least yearly subsequent plasma HCV RNA determinations or plasma samples frozen at −80 °C which enabled such determinations. All patients underwent clinical evaluations at least every six months during the follow-up. In every visit, routine laboratory determinations, including liver function tests were performed.

Definition criteria

When a patient, after developing SVR, tested positive for plasma HCV RNA, a definite diagnosis of reinfection was established if the HCV genotype detected in such an episode was different than the one found in the prior infection. In case the first and the second genotype were the same, the diagnosis of reinfection was done according to the phylogenetic analysis of the strains at the first and at the second episode.

Laboratory procedures

HCV RNA was screened by means of COBAS® AmpliPrep/COBAS® TaqMan® HCV Qualitative Test, v2.0 (Roche Diagnostic Systems Inc, Pleasanton, CA, USA) with a limit of detection of 15 UI/ml. When positive, quantification was carried out by COBAS® AmpliPrep/COBAS® TaqMan® HCV Quantitative Test, v2.0 (Roche Diagnostic Systems Inc, Pleasanton, CA, USA).

For HCV genotyping, the core region was amplified by nested PCR as previously described[15,16] except for genotype 3a, which was amplified by semi-nested PCR with the same conditions. The primers used for genotype 3a were: 5′-GTCTGCGGAACCGGTGAGTA[17] and 5′-GGAGGTCTCGTAGACCGTGCA,[15] as forward primers for the first and second PCR rounds, respectively, and 5′-TGTCACTGGGGGTCCAGCAC, as reverse primer for both rounds. The PCR products were bi-directionally sequenced using standard capillary electrophoresis techniques.

To determine genetic relatedness between HCV strains, phylogenetic trees were built. With this purpose,