Decrease in Serial Prevalence of Coinfection with Hepatitis C Virus among HIV-Infected Patients in Spain, 1997–2006

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The prevalence of injection drug use decreased from 67.3% in 1997 to 14.5% in 2006 among Spanish patients infected with human immunodeficiency virus (HIV). A parallel decrease in the prevalence of coinfection with hepatitis C virus was observed, from 73.8% in 1997 to 19.8% in 2006. This steady decrease in the prevalence of coinfection among Spanish patients was caused by a change in transmission routes of HIV infection.

Injection drug use (IDU) contributed to a rapid spread of both human immunodeficiency virus (HIV) infection and hepatitis C virus (HCV) infection in the Spanish population during the 1980s. IDUs still constitute the group with the greatest burden of disease [1]. Nevertheless, the prevalence of both reported IDU and new HIV infection due to IDU has decreased in Spain during the past decade [2, 3]. To our knowledge, the impact of IDU and new HIV infection due to IDU has decreased in Spain during the past decade [2, 3].

RESULTS

Coinfection with HIV and HCV was observed in 2142 of the 5042 patients (42.5% overall prevalence). The whole population provide reliable data on serial prevalence. The aims of this study are to describe changes in the serial prevalence of HCV coinfection in patients infected with HIV who are naïve to highly active antiretroviral therapy (HAART) and who initiated care in Spanish institutions during a 10-year period (1997–2006) and to assess whether the association between risk factors and HCV coinfection has changed over time.

MATERIALS AND METHODS

We collected data from 5042 HIV-infected HAART-naive patients who were seen for the first time at 1 of the participating institutions and who had at least 1 HCV test. These patients were included in 1 of 2 different cohorts of the Spanish AIDS Research Network, a retrospective cohort (CoRIS-MD) and a prospective one (CoRIS), which are described elsewhere [4, 5]. Thus, patients included in CoRIS-MD were incorporated at any time from 1 January 1997 through 30 June 2003 (n = 2519) and patients in CoRIS were incorporated at any time from 1 January 2004 through 31 December 2006 (n = 2523).

For the purposes of this study, we considered the following common variables in both cohorts: decade of birth, age at cohort entry, sex, year of entry into each cohort, transmission category, and HCV serological status. HCV status was considered to be the outcome variable in association analyses. No information was collected on HCV RNA level.

The descriptive analysis of baseline characteristics was performed using frequency distributions. We calculated HCV prevalence for each cohort-year to determine the serial HIV-HCV coinfection prevalence for the study period. The Mantel-Haenszel method was used to estimate odds ratios (ORs) of crude prevalence in univariate analyses. 1998 was considered to be the baseline year of cohort entry; we anticipated that patients who entered the study in 1997 may contribute to biased estimates of the prevalence because of the free-of-charge availability of HAART in Spain beginning in mid-1996. Because of the same reasoning, data for 1997 were removed from the logistic regression analysis, and the calendar time was split into 3-year periods. Logistic regression was performed to estimate ORs adjusted by those variables that had shown association in crude analysis. Statistical analyses were performed using Stata software, version 10 (Stata).
Our study has some limitations. We decided to eliminate data from 1997 from logistic analyses to avoid possible selection bias. We also found an interaction between the decade of birth and HCV prevalence. The OR for <1950 was 1.00, the OR for 1950–1959 was 3.92 (95% CI, 2.18–7.03), the OR for 1960–1969 was 5.52 (95% CI, 3.19–9.58), and the OR for 1970–1979 was 2.51 (95% CI, 1.42–4.43).

DISCUSSION

Our results show a steady, significant decrease in the serial prevalence of coinfection with HIV and HCV during a 10-year period that was driven by a change in HIV transmission patterns, largely because of reduction of IDU, as previously stated by the Spanish Ministry of Health [6]. The size of this study also allowed us to identify a cohort effect (decade of birth) on coinfection with HIV and HCV that, to our knowledge, had not been previously documented, although a similar cohort effect was described with regard to AIDS and IDU [7].

We found an interaction between calendar period and transmission patterns. Although no time trend in HCV coinfection was observed among patients who engaged in IDU, a steady decrease in the serial prevalence of HCV infection was seen in both the heterosexual and the MSM categories. The observed decreasing trend in coinfection with HIV and HCV by year of entry in the cohort was led by changes in HIV transmission patterns. A steady reduction in the prevalence of HCV infection among HIV-infected patients with non-IDU behavior could be explained by a reduction of exposure. Because the overall prevalence of HCV infection was reduced by a decrease in IDU and an increase of hygienic measures, there was also reduced probability of having sexual intercourse with a person coinfected with HIV and HCV. Consequently, the decrease in the proportion of IDU could explain the steady decrease in other categories.

It is important to note that, in other European studies, an increase in the prevalence of HCV infection among MSM has been reported [8, 9]; however, the importance of IDU in the HIV epidemic in those countries is minimal, compared with that in Spain. Therefore, it is also likely that certain misclassification may be taking place and that anecdotal episodes of IDU in heterosexual persons and in MSMs back in the 1980s were not identified.

Although age initially appeared to be associated with coinfection, this effect waned if we considered transmission route and decade of birth. Being born during the 1960s also allowed for exposure to IDU and unprotected sexual intercourse during the late 1980s and early 1990s, when both HIV and HCV infection were poorly known by the general population. Because we considered patients included from 1997 through 2006, our patients were likely to have been exposed during those periods.

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Figure 1. Parallel decrease in the prevalence of injection drug use (IDU) and coinfection with human immunodeficiency virus (HIV) and hepatitis C virus (HCV) in the cohorts of the Spanish AIDS Research Network (CoRIS and CoRIS-MD). Dotted line, serial prevalence of IDU; solid line, overall serial prevalence of coinfection with HIV and HCV.

Biases caused by changes in treatment-seeking patterns subsequent to HAART introduction, free of charge, in 1996. The results of descriptive and crude analyses confirmed this possibility. Another limitation was related to the joint analysis of 2 different cohorts with slightly different inclusion criteria.

In summary, the change in HIV transmission practices from IDU to unprotected sex has resulted in a significant decrease in the serial prevalence of HCV infection in the overall HIV-infected population. This observation is important not only from an epidemiologic point of view but also from a clinical perspective. At present, end-stage liver disease secondary to coinfection with HCV is a leading cause of death among HIV-infected patients. Furthermore, anti-HCV treatment and liver transplantation are expensive resources that are becoming commonly used in these patients. The decrease in coinfection with HIV and HCV that we have documented may have a positive impact on these important aspects of clinical care.

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Hospital Son Dureta (Palma de Mallorca). Melchor Riera and Javier Murillas.

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Acknowledgments


Potential conflicts of interest. All authors: no conflicts.

References