

Infection with multiple HCV genotypes is associated with faster HIV disease progression

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Background

The effect of Hepatitis C virus (HCV) on HIV remains controversial. Discordant results from different studies may be due to HCV genetic heterogeneity. Among haemophilic men HCV genotype 1 appears to be associated with faster HIV progression. The effect of infection with type 4, a genotype on the rise among injecting drug users (IDU), and the effect of infection with concurrent multiple HCV types has not been studied. Therefore, we investigated HIV disease progression in HIV-HCV co-infected IDU for whom the HCV genotype was known early in HIV infection. Their interval of HIV seroconversion was known, so bias by unknown duration of HIV infection was not present.

Objective

To study the impact HCV genotype on HIV disease progression in injecting drug users with known interval of HIV seroconversion and for who HCV genotype was determined early in HIV infection.

Methods

126 IDU coinfected with HIV and HCV, and receiving no treatment for HCV were studied. These HIV seroconverters originated from cohorts in 7 European countries. HCV genotype was determined using an RT-PCR targeting the core region of the HCV genome (104 IDU) by the line probe assay protocol (22 IDU). The HCV genotype was determined early in HIV infection (median 1.4 years following HIV seroconversion, IQR: 0.7-3.3). The effect of HCV genotype on HIV disease progression (both clinical and immunological progression) was assessed in a Cox proportional hazards model. Clinical progression was defined as progression to AIDS or pre-AIDS death. Immunological progression was defined as progression to a CD4+ T-cell count of 200 cells/ μ l.

Results

The median duration of follow-up was 7.3 years (IQR: 4.6-10.12 years). The majority of the HCV infections were genotypes 1 (60 IDU, 47.6%) and 3 (43 IDU, 34.1%). 16 IDU (13%) harbored genotype 4, and concurrent multiple infections (6 IDU, 5%) consisted of HCV genotypes 1b+3a, 1b+4 or 3a+4. In the pre-HAART era, IDU infected with concurrent multiple HCV types showed a significantly elevated risk of clinical (HR:6.92, see table 1a) and immunological (HR:4.38, see

table 1b) progression, compared to IDU infected with HCV genotype 3. Immunological progression was also significantly increased among IDU infected with HCV genotype 1 (HR 2.02 in the total study period, HR:3.92 in the pre-HAART era, see table 1b). In individuals infected with only one (sub) type, neither subtype 1b nor type 4 was associated with increased HIV progression compared to genotype 3, ruling out the possibility that a specific subtype was singly responsible for the increased risk associated with multiple genotypes. Median CD4+ counts at the date of HCV sampling were lower in IDU with multiple HCV genotypes (233/ μ l IQR:201-738) than in others (500/ μ l IQR:308-720), although time since seroconversion did not differ. This finding may reflect a detrimental impact of multiple genotype infections on HIV disease progression, but conversely it might reflect a greater susceptibility to multiple genotype infections among faster HIV progressors, or a faster outgrowth to detectable levels of multiple HCV genotypes among this group that were either acquired early in HIV infection or even prior to HIV infection.

Table 1a. Hazard ratios for progression to AIDS or pre-AIDS death of a natural cause by hepatitis C virus genotype

Hepatitis C Genotype	Total study period				Pre- Haart era			
	Person years (No. Cases)	Adjusted HR (CI)	p-value	Overall p-value	Person years (No. cases)	Adjusted ¹ HR (CI)	p-value	Overall p-value
Genotype 3	404 (14)	1		0.35	233 (6)	1		0.06
Genotype 1	310 (10)	1.14 (0.50-2.60)	0.75		185 (6)	0.95 (0.30-2.99)	0.95	
Genotype 4	120 (4)	0.83 (0.25-2.78)	0.77		71 (1)	0.52 (0.07-4.74)	0.56	
Multiple genotypes	31 (2)	3.42 (0.82-14.32)	0.09		21 (2)	6.92 (1.43-33.45)	0.02	

¹Adjusted for: age at HIV seroconversion, geographic region (northern, central and southern Europe) and setting of follow-up (hospital vs non-hospital-based).

Table 1b. Hazard ratios for progression to a CD4+ T-cell count of 200/ μ l by hepatitis C virus genotype

Hepatitis C Genotype	Total study period				Pre- Haart era			
	Person years (No. Cases)	Adjusted HR (CI)	p-value	Overall p-value	Person years (No. cases)	Adjusted ¹ HR (CI)	p-value	Overall p-value
Genotype 3	231 (27)	1		0.04	146 (18)	1		0.02
Genotype 1	226 (16)	2.02 (1.04-3.92)	0.04		145 (6)	3.92 (1.51-10.20)	<0.01	
Genotype 4	89 (4)	0.66 (0.22-2.00)	0.47		57 (2)	1.01 (0.20-5.14)	0.99	
Multiple genotypes	30 (5)	2.74 (0.95-7.90)	0.06		22 (3)	4.38 (1.04-18.40)	0.04	

¹Adjusted for: age at HIV seroconversion, geographic region (northern, central and southern Europe) and setting of follow-up (hospital vs non-hospital-based).

Conclusions

HIV progression differs by HCV genotype and is especially faster in individuals infected with concurrent multiple HCV genotypes. The effect of HCV genotype on HIV progression appears to have been much greater in the pre-HAART era, suggesting that the effectiveness of HAART may diminish the effect of HCV genotype on HIV disease progression.