Poster: 932

Increased progression to liver disease and death in HIV/HCV- compared to HIV/HBV-co-infected patients.

Colette Smit1, Luuk Gras1, Ard van Sighem1,Thomas Ruys2, Joep Lange2, Frank de Wolf1,3

1 HIV Monitoring Foundation, Amsterdam, The Netherlands, 2 Center for Infection and Immunity (CINIMA), Academic Medical Centre of the University of Amsterdam, Amsterdam, The Netherlands, 3 Department of Infectious Diseases Epidemiology, Imperial College School of Medicine, London, United Kingdom

HIV Monitoring Foundation
Meibergdreef 9
1105 AZ Amsterdam, The Netherlands
Phone/Fax: 31-20-5664172/566 91 89
Email: colette.smit@amc.uva.nl

1. Background

Hepatitis B (HBV) and C (HCV) are associated with liver fibrosis, cirrhosis and hepato cellular carcinoma (HCC) and progression is accelerated in the presence of HIV. We studied differences in liver disease progression between HCV and HBV co-infected HIV-positive patients.

2. Methods

All HIV-1 infected patients were participants in the Netherlands ATHENA national observational HIV cohort, and at least 18 years old at time of the HIV diagnosis. Patients who had not been tested for both HBV and HCV were excluded from the analysis. Patients positive for HBs-Ag were defined as HBV-co-infected. Patients positive for HCV antibodies or HCV-RNA were defined as HCV-co-infected. Liver disease was defined as having liver fibrosis, cirrhosis or HCC.

The effect of HBV and/or HCV co-infection on the time to liver disease and mortality was assessed using Cox proportional hazards models, for those patients who initiated HAART. Follow up time was the date of HAART initiation to that of liver disease, death, last contact or closure of the database (1 July 2006).

Data on liver disease was systematically collected from January 1 2001 onwards, left entry was used when HAART initiation was before January 1 2001. Kaplan Meier estimates of the probability of liver disease or death was used to compare the time from HAART initiation until death, stratified by co-infection. Patients were divided into 4 groups. 1) HIV with HBV-co-infection, 2) HIV with HCV-co-infected, 3) HIV infection only, and 4) the patients with HIV, HBV and HCV-co-infection.

Table 1: Baseline characteristics

	total	No co-infection	HBV co-infection	HCV co-infection	Double infection
Patients screened for HBV and HCV	9190/12257 (75%)	-	-	-	-
Patients	9190	7515 (82%)	670 (7%)	891 (10%)	114 (2%)
Male gender	7130(78%)	5812 (77%)	571 (85%)	654 (73%)	93 (82%)
Age (median,IQR)	38 (32-45)	37 (31-45)	37 (32-43)	38 (33-43)	38 (33-44)
Transmission category:					
MSM	4783 (52%)	4151 (87%)	421 (9%)	190 (4%)	21 (0.4%)
Heterosexual	3084 (34%)	2718 (88%)	197 (6%)	152 (5%)	127 (1%)
IDU	481 (5%)	40 (6%)	3 (1%)	390 (81%)	58 (12%)
other	842 (9%)	616 (73%)	49 (6%)	159 (19%)	18 (2%)
Deaths	683(7%)	452(6%)	51(8%)	153(17%)	27(24%)
Liver disease	110 (1%)	20 (0.3%)	36 (5%)	49 (6%)	5 (4%)

3. Results

Of the 12,257 HIV-infected patients in the ATHENA cohort, 9190 (75%) were tested for both HBV and HCV. The prevalence of the co-infections is shown in table 1. Amongst patients tested for both HBV and HCV co-infection, 82% was infected with HIV only, 7% of the tested patients were HBV-co-infected and 10% had a HCV-co-infection. Men who have sex with men (MSM) and patients infected with HIV heterosexually had more often an HIV infection only. A majority of the patients infected with HIV by injecting drug use (IDU) was co-infected with HCV (81%) and 12% of the IDU was co-infected with HBV and HCV.

Morbidity

Among the co-infected patients, 24 developed liver fibrosis, 63 liver cirrhoses and 3 HCC between 2001 and 2006. Of the HBV- or HCV- co-infected patients, and 1430 (85%) initiated HAART. Time to liver disease was associated with hepatitis co-infection (p<0.001, log-rank test), but did not differ significantly between HBV and HCV co-infected patients. The adjusted risk of liver disease was 1.34 (95% confidence interval (CI): 0.58-3.10) in HIV/HCV-co-infected patients compared to HIV/HBV-infected patients. Compared to patients with HIV only, the risk of progression to liver disease was 18 and 20 times higher in HBV- and HCV co-infected patients, respectively. Those co-infected with both HBV and HCV had the highest risk of developing liver disease (table 2).

Mortality

231(14%) of the patients died during follow up. The probability of dying was not the same for all patients. 5 years after HAART initiation all-cause mortality was highest amongst those with an HIV/HCV-co-infection (16%(CI:14-20)), mortality among the double co-infected patients was somewhat lower 14% (8-23). 5 years after HAART, 7 %(5-10) of the HBV- and 2% (1-2) of the non-co-infected died.

Table 2: Hazard ratios (HR) of time to liver-related disease or death.

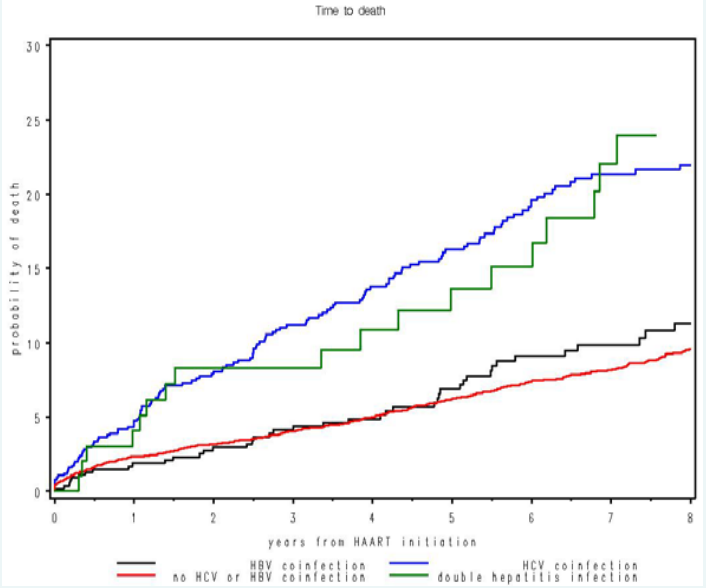
Co-infection	Morbidity Adjusted HR (95% CI)	Mortality Adjusted HR (95% CI)
HBV-co-infection	1	1
HCV-co-infection	1.34 (0.58-3.10)	1.65 (0.94-2.92)
Double co-infection	1.36 (0.35-5.25)	2.14 (1.00-4.57)
Non- co-infected	1	1
HBC-co-infection	17.79 (7.24-43.75)	1.03 (0.67-1.58)
HCV-co-infection	20.65 (8.19-52.01)	1.68 (1.17-2.43)
Double co-infection	21.70 (5.32-88.48)	2.11 (1.15-3.90)

Adjusted for age, gender, transmission category, baseline CD4 cell counts and HIV RNA levels

Mortality continued

As shown by the figure: HCV-co-infected patients and double co-infected patients died significantly faster compared to HBV-co-infected patients (p logrank test<0.0001), time to death did not differ between HBV and non-co-infected patients (p=0.40), but did differ between HCV- and non-co-infected patients (p<0.001).

Those with a HIV/HBV/HCV-co-infection had a significantly increased risk of dying compared to HBV-co-infected patients, while a non-significantly increased risk was observed among HCV-co-infected patients. Compared to the non-co-infected patients, HCV- and double co-infected patients were at significant increased risk of dying. Risk of dying did not differ between HBV-co-infected patients and the non-co-infected patients (table 2).



4. Conclusions

Since 10% of the HIV infected population is HCV-co-infected, and HAART treated HIV/HCV-co-infected patients have a faster progression to hepatitis related liver disease and death compared to HIV/HBV-co-infected patients, more attention should be paid to the HCV screening of HIV-infected patients, and all HIV/HCV-co-infected patients should be evaluated for HCV combination therapy.