

HBsAg Quantification as Surrogate of Hepatitis Delta Virus (HDV) Replication in HIV Co-Infected Patients

Jose Martínez-Alarcón¹, Julie Sheldon^{1,3}, Marcelle Bottecchia^{*1,3}, Antonio Madejón^{2,3}, Carlos Toro¹, Pilar Ríos^{1,3}, Javier García-Samaniego^{2,3} and Vincent Soriano¹

¹Infectious Diseases Department and ²Hepatology Unit, Hospital Carlos III, Madrid. ³Ciber of Liver Diseases, Madrid, Spain
email: mbottecchia@globo.com



Background

Hepatitis Delta virus (HDV) is a human virus that is associated with co-infection/super-infection of hepatitis B virus (HBV) carriers. HDV has a unique replication process and uses the host cellular polymerase. The HBsAg is essential in the HDV lifecycle and its quantification could be useful in the management of chronic HDV patients. Recent reports have highlighted that long-term, suppressive anti-HBV therapy may reduce HDV viremia and improve liver damage. Although this is likely due to a reduction in HBsAg expression needed for HDV particles assembly, this hypothesis has not yet been demonstrated.

Results

A total of 16 HIV patients with chronic hepatitis delta were included in the study. A significant correlation was found between serum HDV-RNA and HBsAg levels ($r=0.557$, $p<0.0001$), but not between HBV-DNA and HBsAg ($r=-0.083$, $p<0.392$). Moreover, 10 patients showed a simultaneous decrease in both serum HDV-RNA and HBsAg levels following initiation of therapy. Baseline HDV-RNA and HBsAg were 7.7 log copies/ml and 15750 IU/ml, respectively, and after a median of 6.1 years of HAART-containing active anti-HBV drugs dropped to 5.6 log copies/ml and 2878 IU/ml, respectively. For the remaining 6 patients there was no significant change in serum HBsAg and HDV-RNA levels despite successful anti-HBV treatment, as shown by undetectable serum HBV-DNA.

Table 2. Follow-up of 14 hepatitis delta patients under anti-HBV therapy.

Parameters	Baseline	End of follow-up	p
CD4 counts, median (IQR) [cells/ μ L]	360 (159.5-470.5)	362 (262.5-761)	0.753
Plasma HIV-RNA, median (IQR) [log ₁₀ copies/mL]	1.7 (1.7-4.3)	1.7 (1.7-2.9)	0.735
Serum HBV-DNA, median (IQR) [log ₁₀ IU/mL]	1.1 (1.1-4.6)	1.1 (1.1-1.1)	0.116
Serum HDV-RNA, median (IQR) [log ₁₀ copies/mL]	7 (6.2-7.8)	5.8 (2-6.3)	0.011
Serum HBsAg, median (IQR) [IU/mL]	6899 (1792.5-20085.5)	4428 (406-6885)	0.424
Serum ALT, median (IQR) [IU/mL]	98 (66.5-147)	63.5 (32.8-110.8)	0.03
Serum AST, median (IQR) [IU/mL]	87 (59.5-102)	60 (35-90.3)	0.033

Methods

A longitudinal study was carried out in all HIV patients with chronic hepatitis delta following HAART containing lamivudine, tenofovir and/or emtricitabine attended our hospital. HBV and HIV serological assays were analyzed by enzyme immunoassay using AxSym systems (Abbott) and HDV serology by Radim EIA (Radim Diagnostics). Serum HDV-RNA was quantified as described by le Gal et al. (J Clin Microbiol 2005) and serum HBV-DNA was quantified using Roche Cobas TaqMan (Roche). HBsAg was quantified by ELISA using Monolisa HBsAg Ultra (BioRad) and an NIBSC standard.

Table 1. Baseline characteristics of 16 HIV-infected patients with chronic hepatitis delta under HAART.

Variables	Values
Male sex, n (%)	13 (81.3)
Age, median years (IQR)	33 (29.3-35.5)
Risk group, n (%)	
Intravenous drug use	13 (81.3)
Heterosexual	1 (6.3)
Horizontal	1 (6.3)
Unknown	1 (6.3)
HBeAg positive, n (%)	4 (24)
Anti-IgM Delta, n (%)	8 (50)
HBV genotype, n (%)	
A	3 (18.8)
D	5 (31.3)
Unknown	8 (50)
Anti-HCV Ab positive, n (%)	15 (93.8)
HCV-RNA positive, n (%)	3 (18.8)
Median years on anti-HBV antiretrovirals or follow-up (IQR)	6.1 (4.7-8.7)

Conclusions

There is a good correlation between serum HDV-RNA and HBsAg levels in most HIV-infected patients with chronic hepatitis delta receiving HAART-containing active anti-HBV drugs. This is one of the first evidences of indirect activity of anti-HBV nucleos(t)ide analogs against HDV. Quantification of HBsAg could be a useful surrogate tool for monitoring HDV replication in patients undergoing anti-HBV therapy. The lack of correlation between serum HBV-DNA and HBsAg levels may be due to high levels of circulating HDV particles trapping HBsAg.