MICRORNA PROFILE IN HIV-HBV COINFECTION

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Introduction After the successful exploit of the interaction between hepatitis C virus and the liver enriched miR-122, that conducted to the development of the first anti-miR drug-Miravirsen, an antisense oligonucleotide that sequesters mature miR-122, there is a considerable interest in the role of miRNA in viral diseases. miR-34a was shown to be involved in HBV related liver fibrosis and development of hepatocellular carcinoma, a key regulator of tumor suppression genep53 and a promoter of HIV replication.The aim of this study was to investigate the possible relation between miR-34a expression and HBV progression in a HIV-HBV coinfected cohort.

Methods Expression levels of miR-34a were measured by quantitative real-time PCR (Life Technologies - TaqMan® MicroRNA Assays) and levels found in HIV patients were normalized against those in age- matched healthy subjects. The correlation between miR-34a levels and the participants' HBV status, liver fibrosis and cytolysis were evaluated.

Results 237 HIV positive participants (47.7% males, median age 24 years) were included. 64.6% (n=153) were anti-HBc positive, out of which52.3% (n=80) were HBsAg positive with16.3% (n=13) HBeAg positive patients. 31.4%(n=48) patients had HBV recovery markers (anti-HBc and anti-HBs positive) and 16.3% (n=25)maintained isolated anti-HBc antibodies.Only 12.5% (n=10) chronic HBsAg carriers had significant liver fibrosis (APRI>1).

21.3% (n=17) patients had high (>1000 copies/ml) HBV plasma viral load, out of which 82.4% (n=14) were infected with genotype A and 52.9% (n=9) patients had Lamivudine resistance mutations. No difference in miRNA expression was found between HIV monoinfected and HIV-HBV coinfected study participants.Patients with HBsAg had significant higher miR-34a expression than those with resolved HBV infection (median miR-34a expression 0.31 vs 0.08, p=0.05). Among chronic HBsAg carriers an upregulated expression of miR-34a was present in patients with liver fibrosis (0.87 vs 0.22, p=0.02) as well as in those with hepatic cytolysis (0.48 vs. 0.14, p=0.01).

In HBsAg carriers, miR-34a was overexpressed in patients with detectable HIV viral load (0.40 vs. 0.22, p=0.05), immunosuppression (1.20 vs. 0.40, p=0.05) andhigh CD4 Nadir cell number (p=0.04).

Conclusion miR-34a expression seems to be a correlated with parameters of active HBV infection and hepatocellular injury and can constitute a marker for the progression of liver disease, as well as a potential therapeutic target.