OP-2 IN VITRO CHARACTERIZATION OF HEPATITIS B VIRUS REPLICATION AND VIRAL ANTIGEN EXPRESSION AMONG GENOTYPES

Mercedes Elizalde[1], Micaela Martinez[1], Micaela Speroni[1], Luciana Tadey[2], Mammana Lilia[2], Bouzas Belen[2], Mojsiejczuk Laura[3], Campos Rodolfo[3], Diego Flichman[1]

[1] *Instituto de Investigaciones Biomédicas en Retrovirus y Sida, Buenos Aires, Argentina*
[2] *Unidad de Virología, Hospital de Infecciosas "Francisco J. Muñiz", Buenos Aires, Argentina*
[3] *Cátedra de Virología de la Facultad de Farmacia y Bioquímica de la Universidad de Buenos Aires, Buenos Aires, Argentina*

Background: Hepatitis B virus (HBV) has been classified into 10 genotypes (A-I) and numerous subgenotypes (SGTs). There is growing evidence that HBV genotypes (GTs) influence clinical outcomes, HBeAg seroconversion rates, severity of liver disease, and response to interferon therapy. However, there is a paucity of data regarding their distinctive biological characteristics, in particular for GTF, the most prevalent in Latin America.

Aim: To investigate the impact of HBV genotypes on HBV-DNA levels and viral antigen expression.

Materials and Methods: Full-length HBV genomes representing GTs A-D and SGTs F1b and F4 were transfected in Huh7 cell line. Secreted HBeAg and intra and extracellular HBsAg were quantified by EIA. HBV-DNA was analyzed by real-time PCR.

Results: Marked differences were observed in HBV replicative capacity as well as HBeAg and HBsAg antigen expression across genotypes (Table 1). GTC secreted significantly higher levels of HBeAg in relation to the other GTs. GTD showed lower HBsAg extracellular levels than all other GTs, while GTA showed the highest HBsAg intracellular levels. Finally, SGTs F1b and F4 showed significantly lower HBV-DNA levels. Regarding the ratio of extra and intracellular HBsAg, GTs A and D showed the lower ratios compared to SGTs F1b and F4, while SGTs F1b and F4 showed the highest HBsAg/HBV-DNA ratio.

Discussion: This study provides new insights into the impact of HBV genotypes on HBV antigen expression and HBV-DNA levels. The uneven expression of antigens, as well as their intracellular accumulation, could be associated with the role of genotypes in pathogenesis. Likewise, the extracellular levels of HBsAg and the replication rate might have implications in immunopathogenesis as well as in the exhaustion of the host's immune system. The virus-cell interaction in different genotypes deserves further study to understand its role in the pathogenesis of HBV infection.

Genotype	A	B	C	D	F1b	F4	P<0.001
HBeAg (S/Co)	17.5±1.3	ND	38.2±6.9	9.2±1.2	2.3±0.1	3.6±0.1	A vs F1b/F4 and C vs D, F1b and F4.
HBsAg							
Extracellular (IU/ml)	82.7±6.6	83.7±8.7	37.2±6.6	6.5±0.6	62.3±2.2	41.7±2.0	D vs all GTs.
Intracellular (IU/ml)	32.8±1.6	17.6±3.1	4.5±0.3	4.6±0.4	2.7±0.3	2.6±0.2	A vs C,D,F1b and F4.
Extra/intracellular	2.5	4.8	8.3	1.4	23.3	16.2	A and D vs C, F1b and F4.
HBV-DNA (10^4 copies/ml)	39.1±0.8	45.9±1.3	43.0±2.1	56.9±4.7	34.7±0.1	30.5±2.1	F1b / F4 vs A, B and D.
HBsAg/HBV-DNA	14.8	10.0	11.4	1.7	25.2	21.7	F1b / F4 vs A, B, C and D; D vs A, B and C.

https://doi.org/10.1016/j.aohep.2021.100517

OP-3 LONG-TERM RIFAXIMIN IS SAFE AND ITS RELATED TO LESS FREQUENCY OF COMPLICATIONS LIKE VARICEAL BLEEDING IN CIRRHOTIC PATIENTS

Fátima Higuera-de-la-Tijera[1], Karen Soto-Martínez[1,2], Victor H. Fúnez-Madrid[1], José L. Pérez-Hernández[1], Graciela Alexanderson-Rosas[3], Alfredo Servín Caamaño[3]

[1] *Gastroenterology and Hepatology Department, "Hospital General de México Dr. Eduardo Liceaga", Mexico City, Mexico*
[2] *Superior School of Medicine, "Instituto Politécnico Nacional", México City, Mexico*
[3] *Internal Medicine Department, "Hospital General de México Dr. Eduardo Liceaga", Mexico City, Mexico*

Introduction: Is well established that rifaximin (RFX) is effective as secondary prophylaxis in patients with a previous episode of hepatic encephalopathy (EH); but recently, some studies have found that RFX is related to a lower frequency of other complications.

Aim: To evaluate the clinical effect of long-term prescription of RFX (more than 6 months) in cirrhotic patients, and also the possible adverse effects.

Methods: A case-control study nested in a cohort which included cirrhotic patients taking secondary prophylaxis with RFX because of history of a previous EH episode. From this cohort we abstracted two different groups, cases were those who continue taking RFX for more than 6 months, controls were those who suspended RFX before the first three months because of medical indication or by their own decision and therefore they did not continue the medication for long-term. The two groups were match by age, gender, decompensation of cirrhosis (Child-Pugh B/C), history in the last year of at least an episode of variceal bleeding (VB), infections, EH, ascites, also was considered the previous use of beta-blockers and diuretics in patients with ascites. Adherence to therapy was mandatory, it was evaluated through the simplified medication adherence questionnaire (SMAQ) in all patients.

Statistical analysis: Categorical variables were compared with X2 or Fisher's exact test, odds ratios and 95% confidence intervals were also calculated. Quantitative variables were compared with Student's t test. A $p<0.05$ value was considered significant. Considering the difference in incidence regarding the development of complications between the groups, we also calculate the number needed to treat (NNT) to prevent one event.

Results: A total of 139 cirrhotic patients who met the selection criteria were identified, of them, 58 were identified as cases taking long-term RFX (41.7%), and were matched with 81 controls without RFX (58.3%). The median time taking RFX was 8.5 months (range= 6-18). The mean dose identified in the medical prescriptions was 400 mg twice or thrice in day. Basal characteristics were similar in both groups (see Table). Patients taking long-term RFX had significant lower frequency of recurrence of EH (adjusted OR=0.2, 95%CI 0.1-0.4; p=0.003; NNT=3.4); and also regard the development of VB (adjusted OR=0.2, 95%CI= 0.068-0.6; p<0.0001; NNT= 4.8); despite no statistical difference, also there was a tendency to a less frequency of severe bacterial infections: RFX 1.7% vs. without RFX 8.6% (NNT= 14.5). There were no adverse effects related to the RFX prescription, neither multidrug resistant bacterial infections were documented.

Conclusions: Long-term use of RFX (more than 6 months) was associated with significant less development of VB, less recurrence of EH, and there was a tendency to a less frequency of severe bacterial infections. Mechanisms that could explain our findings are the modulation of intestinal microbiota, reduction of bacterial translocation, reduction of the inflammatory process and secondary regulation of the portal pressure, all of them possible mediated primarily or secondarily by RFX action.