P271

Vitamin D pathway polymorphisms impact on HBV interferon treatment outcomes in a cohort of HBeAg negative patients.

Jessica Cusato, Lucio Boglione, Amedeo De Nicolo', Chiara Simona Cardellino, Rosaria Imbornone, Giuseppe Cariti, Giovanni Di Perri and Antonio D'Avolio.

1. Department of Medical Sciences, Unit of Infectious Diseases, University of Turin, Amedeo di Savoia Hospital, 10149, Turin, Italy.

Author info:
Jessica Cusato
Jessica.cusato@gmail.com
website: www.tdm-torino.org

Stampa a cura della S.C. Relazioni Esterne ASL TO 2

BACKGROUND

To date 350 million people are chronically infected by Hepatitis B virus (HBV) worldwide (1). Vitamin D (VD) deficiency has been related to chronic liver diseases, hepatic fibrosis progression and treatment poor response (2). Variability on genes involved in VD network could play a role in response to HBV infection, since this is known to be a key immunomodulator: *CYP27B1* VD activator enzyme single nucleotide polymorphism (SNP), together with *IL28B* ones, are considered pharmacogenetics predicting factors of HBV treatment outcomes (3). For these reasons, this work aimed to investigate the role of other VD signaling gene SNPs in HBV-treatment with peg-interferon (peg-IFN).

OBJECTIVES

Our aim was to investigate the role of other VD signaling gene SNPs in HBV-treatment with peg-interferon (peg-IFN).

MATERIALS AND METHODS

We retrospectively enrolled 173 HBeAg-negative infected adult patients treated for 48 weeks with peg-IFN α-2a. We evaluated virological and serological response according to SNPs on following genes: CYP27A1 (VD precursor production enzyme), CYP24A1 (VD inactivating enzyme), VDR (VD receptor) and VDBP (VD binding protein, transporter), determined by real-time PCR.

	UNIVARIATA	MULTIVARIATA
	p;OR (IC 95%)	*p;OR (IC 95%)*
Metavir	0,55; 0.99 (0.97; 1.02)	**0.032; 0.056 (0,005;0,106)**
Sesso	0,45; 0.77 (0.38; 1.53)	
BMI	0,40; 1.05 (0.94; 1.17)	
Genotipo Virale	**0,001; 0,70(0.56; 0.87)**	**0.006; 0.69; (0.53; 0.90)**
CYP27B1 +2838 TT	**<0.001; 3.25 (1.68;6.30)**	0.81; 0.77; (0.10; 6.22)
CYP27B1 -1260 GT/TT	**<0.001; 0.28 (0.15;0.54)**	**<0.001; 0.18 (0.08; 0.42)**
CYP24A1 rs2248359 CC	0.63; 1.18 (0.60; 2.33)	
CYP24A1 rs927650 CT/TT	0.63; 1.87 (0.97;3.60)	0.42; 1.44, (0.60; 3.47)
CYP24A1 rs2585428	0.92; 0.98 (0.63;1.52)	
VDR ApaI AA	**0.086; 0.56 (0.29;1.09)**	0.74; 0.87; (0.37; 2.02)
VDR TaqI CC	0.47; 1.17 (0.76;1.80)	
VDR FokI TC/CC	0.70; 0.83 (0.33; 2.13)	
VDR BsmI AA	0.41; 1.20 (0.78; 1.83)	
VDR Cdx2 AG/GG	0.63; 1.10 (0.74; 1.64)	
VDBP rs7041 TG/GG	0.36; 1.11 (0.68;2.88)	
CYP27A1 rs4674343	**0.007; 3.03 (1.36;6.67)**	**0.064; 2.29; (0.94; 5.57)**
IL28B rs12979860 CC	**<0.001; 4.78 (2.73;8.37)**	**<0.001; 6.90; (3.46; 13.75)**
IL28B rs12980275 AA	**<0.001; 3.78 (2.22;6.44)**	0.77, 0.81; (0.20; 3.32)
IL28B rs8099917 TT	**0.001; 0.29 (0.14;0.62)**	0.18; 0.49; (0.27; 1.39)

Table 1. Factors, in univariate and multivariate analyses, able to predict the virological outcome.

RESULTS

HBV-DNA drop at 3 months of therapy was influenced by *VDR ApaI AA* (p=0.001) and *VDR Cdx2 AG/GG* (p<0.001) genotypes, whereas HBV-DNA drop at 6 months of therapy was significant associated with *CYP24A1 rs927650 CT/TT* (p=0.023), *VDR ApaI AA* (p=0.009) and *VDR Cdx2 AG/GG* (p<0.001) genotypes. Related to HBsAg clearance, significant influences of *VDR ApaI CA/AA* (p=0.023) and *VDBP TG/GG* (p=0.009), and *VDR Cdx2 AG/GG* (p<0.001) and *VDBP TG/GG* (p=0.009) were respectively highlighted at 3 and 6 months of treatment. In logistic regression analysis, concerning virological outcome, *CYP27A1 rs4674343 GG* genotype remained in the final model (Table 1), together with already known ones (*IL28B* and *CYP27B1* SNP, metavir score and HBV viral genotype), but with a "border-line" statistical significance (p=0.064, OR 2.29; IC 95% 0.94-5.57); related to serological response, we confirmed *IL28B* and *CYP27B1* SNPs, metavir and HBV viral genotype role.

CONCLUSIONS

Pharmacogenetic evaluation could become an important tool for therapy individualization. Our work provides a new overview of VD pathway pharmacogenetics in HBV field, but further studies are required to confirm this findings on a large cohort of patients.

REFERENCES

1. Dupinay, (2013) Hepatology, 2013. 58(5): p. 1610-20.
2. Kitson (2014). doi: 10.1016/j.jhep.2014.08.004.
3. Boglione (2015) J.of Viral Hepatitis, 22, 318-327.

In collaboration with CoQua Lab srl
Web Site: www.coqualab.it
Mail: info@coqualab.it