

Liver vitamin D receptor, CYP2R1 and CYP27A1 expression related to progression of metabolic and viral chronic liver damage

Simone Carotti¹, Ilaria Barchetta², Umberto Vespasiani-Gentilucci³, Andrea Onetti-Muda⁴, Antonio Picardi², M.G. Cavallo² and Sergio Morini¹

¹ Laboratory of Microscopic and Ultrastructural Anatomy, University Campus Bio-Medico, Rome, Italy

² Department of Internal Medicine and Medical Specialties, Sapienza University of Rome, Italy

³ Clinical Medicine and Hepatology Unit, University Campus Bio-Medico, Rome, Italy

⁴ Department of Anatomical Pathology, University Campus Bio-Medico, Rome, Italy

Background and aim: Low serum 25(OH)vitamin D3 levels were associated with the presence and prognosis of liver diseases [1]. The biological effects of 1,25(OH)₂ vitamin D3 are mediated by the vitamin D receptor (VDR) and VDR has been widely detected in liver, but its expression in the course of liver disease has never been investigated [2]. We aimed to evaluate the hepatic expression of VDR and vitamin D 25-hydroxylases in patients with chronic hepatitis C (CHC) or non-alcoholic steatohepatitis (NASH) and its relationship with liver histology and serum 25(OH) vitamin D3 levels.

Methods: Patients affected by CHC or NASH who had undergone liver biopsy and subjects without liver disease were included. Expression of VDR, CYP2R1 and CYP27A1 was evaluated by immunohistochemistry.

Results: In CHC subjects, fibrosis stage was associated with low hepatic CYP27A1 expression, whereas in patients with VDR-negative inflammatory cells and low VDR expression on hepatocytes, the portal inflammation was significantly higher ($p < 0.009$ and $p < 0.03$). In NASH patients, VDR expression on cholangiocytes was inversely correlated with steatosis severity ($p < 0.02$), lobular inflammation ($p < 0.01$) and NAS score ($p < 0.03$).

Conclusions: The liver of patients with viral and metabolic chronic liver disease expresses VDR in a manner inversely proportional to the severity of histological lesions and a role of the vitamin D/VDR system in the progression of chronic liver damage is suggested.

References

- [1] Barchetta I et al. (2011) Strong association between non alcoholic fatty liver disease (NAFLD) and low 25(OH) vitamin D levels in an adult population with normal serum liver enzymes. *BMC Med.* 12;9(1):85.
- [2] Gascon-Barre M et al. (2003). The normal liver harbours the vitamin D nuclear receptor in non-parenchymal and biliary epithelial cells. *Hepatology* 37:1034-1042.

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