Hepatitis C virus interference via hepcidin synthesis

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Iron overload, a common feature of chronic liver disorders, has been linked with oxidative DNA damage, insulin resistance and liver steatosis, and with triggering of hepatic stellate cells thus inducing liver fibrosis. Recently, a key iron regulatory hormone, hepcidin, was discovered. This hormone has been found to suppress intestinal absorption of iron through its binding to ferroportin. Hepcidin is synthesized in the liver from its precursor protein, prohepcidin.

A research article to be published on April 14, 2010 in the World Journal of Gastroenterology addresses the question as to whether serum prohepcidin levels are associated with HCV infection activity as well as with the efficacy of PEG-interferon/ribavirin therapy. The studied group consisted of 53 chronic hepatitis C patients, who were followed during anti-HCV therapy with pegylated-IFN+ribavirin. Prohepcidin serum concentrations as well as other iron metabolism parameters were measured at many time-points, including baseline, 4th, 12th, 24th and 48th (genotype 1) week of antiviral therapy and 24th week after termination of the treatment (week 72).

The authors found comparable levels of serum prohepcidin in chronic hepatitis C and healthy individuals. Interestingly, baseline prohepcidin was significantly higher in HCV genotype 3a than in HCV-1. This new finding was explained by differences in iron metabolism in patients with genotype 3. Baseline serum prohepcidin in a study by Jaroszewicz et al showed a strong positive correlation with serum ferritin. Moreover, an association between baseline serum prohepcidin and ALT activity was

found. The new finding of the study was the association between serum prohepcidin and PEG-IFN/ribavirin efficacy in chronic hepatitis C. The authors demonstrated a statistically significant, gradual decrease of serum prohepcidin which occurred only during successful antiviral treatment in HCV-1 and 3a individuals. In contrast, in non-sustained viral responders the prohepcidin serum concentrations did not change significantly compared to baseline values.

Data obtained by the research group led by Professor R. Flisiak from the Department of Infectious Diseases and Hepatology of Medical University in Bialystok indicate that in situations of liver function impairment, the prohepcidin synthesis as well as activity or expression of converting enzymes might be altered and affect circulating prohepcidin concentrations. Their finding could also suggest HCV interference with hepcidin synthesis at the level of prohormone synthesis or maturation in the liver.

More information: Jaroszewicz J, Rogalska M, Flisiak I, Flisiak R. Successful antiviral therapy is associated with a decrease of serum prohepcidicin in chronic hepatitis C. World J Gastroenterol 2010; 16(14): 1747-1752. www.wjgnet.com/1007-9327/full/v16/i14/1747.htm

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