Matthias A. Brunert
Dr. med. dent.

Impact of Hepatitis C virus on key fat metabolizing enzymes in human end stage liver cirrhosis

Promotionsfach: Chirurgie
Doktorvater: Prof. Dr. med. Peter Schemmer

A growing body of evidence suggests a direct impact of Hepatitis C virus (HCV) on hepatic fat accumulation. The purpose of this study was to determine the activity of key fat metabolizing enzymes in the presence of HCV. To investigate this as a potential mechanism present within HCV infected human livers, human liver tissue was obtained during liver transplantation from explanted livers due to HCV-associated cirrhosis. Samples from ethanol-induced liver cirrhosis served as internal control. RNA was isolated from human liver tissue, followed by reverse transcription. Quantitative real-time PCR was performed to identify gene expression.

All investigated key fat metabolizing enzymes, [liver fatty acid binding protein (LFABP), very long chain acyl-CoA synthetase 2 (VLACS2), very long chain acyl-CoA synthetase 3 (VLACS3), medium chain acyl-CoA dehydrogenase (MCAD) and acyl-CoA oxidase (AOX)] are significantly down regulated in HCV-induced liver cirrhosis compared to their respective control (healthy liver).

In addition VLACS2, VLACS3 and AOX are significantly down regulated in HCV-induced liver cirrhosis compared to ethanol induced liver cirrhosis (internal control). MCAD and LFABP show a down regulation tendency, but no significant difference between HCV-induced liver cirrhosis and EtOH-induced liver cirrhosis.

However, no significant differences in gene expression of fat metabolizing enzymes was observed between normal human liver tissue and EtOH-induced cirrhotic liver tissue, (except for MCAD, which was significantly downregulated in EtOH-induced liver cirrhosis).

The significant down regulation of VLACS2, VLACS3, AOX and the down regulation tendency of LFABP, can therefore be attributed to the direct impact of HCV.

In summary, the presence of HCV in humans with end stage liver cirrhosis results in an impaired hepatic lipid metabolism. This study presents a potential mechanism that explains the increase in hepatic lipid accumulation after HCV infection. Modulation of this pathway might prove to be useful in a clinical setting of Hepatitis C infection with amelioration of the onset and severity of HCV-associated hepatosteatosis, a pathology that likely contributes to increased development of hepatic fibrosis and cirrhosis.