Abstract

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Alteration of transport proteins expression during obstructive cholestasis in rats I

Diploma thesis

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Background:

The purpose of the diploma thesis was the confirmation of liver cholestatic damage induced by bile duct obstruction lastnig for 28 days by biochemical analysis and analysis of mRNA and protein expression of liver uptake transporters in rats (Ntcp, Oatp1a1, Oatp1a4, Oatp1b2, Oat2).

Methods:

Wistar rats (n = 6, in each group; 280 – 320g) were dividend in two groups: control group of sham-operated animals (Sham) and group with bile duct obstruction lastnig for 28 days (BDO). Biochemical analysis of serum was performed by Cobas Integra ® 800. Changes of mRNA and protein expression of transport proteins were evaluated by qRT-PCR and Western blot.

Results:

In BDO group, level of bile acids increased to 454%, level of total bilirubin to 4111% and level of conjugated bilirubin to 7313% as compared to control group. In comparison to control group, activity of ALP was elevated to 238%, activity of GMT to 2826%, activity of ALT to 1200% and activity of AST to 1378%. As compared to Sham group BDO group showed decreased mRNA levels of Ntcp to 51% and of Oatp1a4 to 38%. No signifiant changes were found in Oatp1a1, Oatp1b2 and Oat2 mRNA levels. Protein levels decreased for Oatp1a1 to 25%, for Oatp1a4 to 31% and for Ntcp to 79%. No changes in Oatp1b2 and Oat2 protein expresion were observed.

Conclusion:

The results of biochemical analysis confirmed liver damage caused by obstructive cholestasis. The results of mRNA and protein analysis showed reduced expression of basolateral uptake transporters during biliary cirhosis in an effort to prevent accumulation of potentionaly toxic compounds such as bile acids or bilirubin in the liver.