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MEETING ABSTRACTS

EFFECTS OF CARVEDILOL ON BILE ACID HOMEOSTASIS IN MICE WITH NON-ALCOHOL STEATOHEPATITIS

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Bile acids (BAs) play a significant regulatory role in the pathophysiology of non-alcoholic steatohepatitis (NASH). The present study evaluates the modulation of BAs homeostasis by carvedilol, a nonselective blocker beta adrenoreceptor that is routinely used to treat cardiovascular complications accompanying NASH. NASH was induced in mice by a continuous 24-week high-fat diet (HFD) with glucose/fructose in drinking water. At week 21, individual groups of animals received carvedilol (10 mg/kg/day, p.o.) for three weeks. Biochemical and histological analysis has shown the effectiveness of a high-fat diet in inducing NASH. The spectrum of bile acid was analyzed in bile, stool, and plasma by the LC-MS method and the molecular determination of BAs-related enzymes and transporters. Carvedilol significantly increased plasma concentrations of BAs in healthy mice via downregulation of Ntcp and Bsep transporters. Carvedilol did not significantly affect net BAs plasma concentrations or BAs biliary and fecal excretions in animals with developed NASH. However, it shifted spectra of BAs toward more hydrophilic and less toxic αMCA and HCA. Carvedilol also significantly reduced liver fibrosis in NASH mice and *in vitro* suppressed profibrogenic response in human hepatic stellate cells. Our results suggest the hepatoprotective effect of carvedilol in NASH and support using this agent as a part of cardiovascular regimens in patients with metabolic syndrome and a high risk of NASH development.

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