

HYPERCHOLESTEROLEMIA LEADS TO METABOLIC AND PATHOLOGICAL ALTERATIONS IN THE LIVER WITHOUT AFFECTING THE PANCREAS

Tamás Baranyai^{*1,2}, Krisztina Kupai^{*1}, László Tiszlavicz⁴, Hedvig Fébel⁵, Gergő Szűcs¹, Zoltán V. Varga^{1,6}, Péter Ferdinandy^{3,6}, Csaba Csonka^{1,3}, László Czakó², Tamás Csont^{1,3}

*authors contributed equally

¹Cardiovascular Research Group, Department of Biochemistry, University of Szeged, Szeged, Hungary;

²1st Department of Internal Medicine, University of Szeged; Szeged, Hungary;

³Pharmahungary™ Group, Szeged, Hungary;

⁴Department of Pathology, University of Szeged, Szeged, Hungary;

⁵Research Institute of Animal Breeding and Nutrition, Herceghalom, Hungary

⁶Department of Pharmacology and Pharmacotherapy, Semmelweis University, Budapest, Hungary

Running title:

Word count:

Address for correspondence:

Csont Tamás

Cardiovascular Research Group,

Department of Biochemistry, University of Szeged

Dóm tér 9, Szeged, H-6720, Hungary

Tel: +36 62 545096, fax: +36 62 545097

E-mail: csont.tamas@med.u-szeged.hu

<http://www.cardiovasc.com>

HYPERCHOLESTEROLEMIA LEADS TO METABOLIC AND PATHOLOGICAL ALTERATIONS IN THE LIVER WITHOUT AFFECTING THE PANCREAS

Tamás Baranyai, Krisztina Kupai, László Tiszlavicz, Hedvig Fébel, Gergő Szűcs, Zoltán V. Varga, Péter Ferdinandy, Csaba Csonka, László Czakó, Tamás Csont

Abstract

Combined hyperlipidemia (hypercholesterolemia and hypertriglyceridemia) is established as a contributing factor to the structural alterations in pancreas and liver related to lipid accumulation. In addition, isolated hypercholesterolemia was shown to affect histology and lipid profile of the liver, however, its effects on the pancreas are not known. Therefore, our aim was to investigate whether isolated hypercholesterolemia leads to alterations in both pancreatic and hepatic histology and lipid profile in rats.

Isolated hypercholesterolemia was induced by feeding male Wistar rats with 2% cholesterol + 0.25% cholate supplemented diet for 12 weeks characterized by elevated serum cholesterol level and unchanged triglyceride level at the end of the diet. Histological evaluation demonstrated increased lipid accumulation in the liver, and accordingly, biochemical analysis confirmed elevation of tissue cholesterol and triglyceride contents in the liver tissue due to isolated hypercholesterolemia. However, in the same experimental setup the pancreas was not affected at week 12 in terms of histology and tissue lipid content. Isolated hypercholesterolemia caused a significantly increased fatty acid level in the liver and serum, which was associated with a marked alteration of fatty acid profile as assessed by GC/MS analysis.

In conclusion, isolated hypercholesterolemia leads to histological and metabolic alterations in the liver, however, under the same conditions the pancreas is not affected. Alterations in fatty acid composition may contribute to the morphological changes in the liver in isolated hypercholesterolemia.

Keywords: experimental hypercholesterolemia, liver, pancreas, tissue cholesterol, tissue triglyceride, fatty acid profile, rat