Lipid and glucose metabolism gene expression in a NAFLD model of rat treated with a high fat diet and a low dose of streptozotocin

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Nonalcoholic fatty liver disease (NAFLD) is an increasingly common public health problem, characterized by the infiltration of triglycerides into hepatocytes, thereby inducing steatosis. Estimates of the NAFLD prevalence in the general population ranges from 5 to 20%, but in patients with diabetes mellitus this percentage rise up to 75%. (Chalasani et al., 2012). The aim of this study was to evaluate the lipid and glucose metabolism genes in a new non alcoholic fatty liver disease rat model induced with a high fat/cholesterol diet (HFD) and risen diabetic with a low dose of streptozotocin (STZ) (Srinivasan et al., 2005). Consequently, this rat model may better mimic NAFLD than HFD feeding alone. HFD/STZ rats developed hyperglycemia, hypertriglyceridemia, steatosis, oxidative stress and fibrosis. Treated rats, compared to control ones, showed a significant up regulation of marker genes of inflammation (TNFα, IL6), fibrosis (TGFβ) and oxidative stress at mitochondrial level (UCP2), but not CHOP, a marker of endoplasmatic reticulum stress. The HFD/STZ treatment caused an increased expression of genes involved in the lipogenic responses such as LXRα–dependent SREBP-1c and FAS, of CYP4A genes involved in the microsomal fatty acids (ω)-oxidation by PPARα activation, and in a strong induction of LXRα–regulated cytochrome CYP7A1, the key gene responsible of cholesterol biotransformation to bile acids. In the treated rats it was also observed a reduced expression of genes entailed in the cholesterol biosynthesis such as the SREBP-2–regulated HMG-CoA reductase, LDLr, and CPT-1, the entry door of fatty acids in the mitochondria for the β-oxidation. The HFD/STZ treated rats showed a significant up regulation of G6Pase gene, involved in gluconeogenesis and a significant decrease in the hepatic glycogen content indicating that, in the context of reduced glycogen stores and fatty acids β-oxidation, high glucose levels bring about *de novo* lipogenesis. Taken together with an our previous report (Vornoli et al., 2014), these results contribute to extend the characterization of the HFD/STZ rat new model, which better mimics the human NAFLD.

References

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