

Time-dependent changes in lipid metabolism and intrahepatocellular lipid content after high-fat feeding of rats

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Введение

Global epidemics of type 2 diabetes mellitus (T2DM) and obesity have spread extensively during the past two decades. Most obese individuals exhibit increased circulating levels of free fatty acids (FFAs) in plasma, the source of which are diet, adipose tissue lipolysis and hepatic de novo lipogenesis. The elevated levels of FFAs reaching liver override its oxidation capacity and, through esterification process, excessive energy is stored as triacylglycerols (TAG) and diacylglycerols (DAG) fractions. It is hypothesized that fatty acid composition of lipid fractions is more important rather than lipid species itself and it may explain, why particular obese patients do not develop insulin resistance and NAFLD.

Цель исследования

The main goal of the study was to evaluate the relationship between time-dependent changes caused by high-fat diet and fatty acid composition of selected lipid fractions as well as the lipogenesis and oxidation pathway in hepatocytes. Such study is essential in order to clarify changes in liver metabolic routes during overnutrition, thus it may contribute to finding new potential biomarkers associated with metabolic disorders.

Материалы и методы

The study was conducted on male Wistar rats, which were exposed to high-fat feeding for five weeks. The liver samples were collected from sacrificed animals after every week of experiment. Total expression of selected enzymes from de novo lipogenesis (fatty acid synthase-FAS), desaturation (stearoyl-CoA desaturase-SCD) and elongation (Elovl-6, Elovl-3) pathway was determined in liver homogenates using the Western Blot (WB) method. The contents of TAG, DAG and FFA accumulated in the liver, together with a detailed analysis of their fatty acid composition, were assessed by GLC.

Результаты

In our studies we demonstrated time-dependent changes in lipids content and composition, what may affect development of numerous metabolic disorders. It is possible that such a quick occurrence of lipids accumulation in the liver is the first protective mechanism of the whole body against lipotoxicity. FFA, DAG and TAG content increased during 5 weeks of high fat feeding, but only TAG elevation was linear. Considering the changes in protein expression, our research indicated a decreased expression of FAS after 5 weeks, which is widely involved in the synthesis of unsaturated fatty acids. In contrast, expression of SCD, enzyme responsible for desaturation of fatty acids, was higher at the end of our study. Furthermore, our research demonstrated increased expression of both Elovl-3 and Elovl-6, a long chain fatty acid elongases that contribute to formation of fatty acids with longer chains. de novo fatty acids synthesis. Our study revealed that after 5 weeks of high-fat feeding, the greatest fatty acid component of FFA fraction is the 18:0 and 22:0 fatty acid, in TAG fraction-16:0, 18:0, 20:0 and 22:0. Moreover, in DAG fraction high-fat diet resulted in excessive accumulation of mainly long chain fatty acids, namely 20:0, 22:0 and 24:0.

Выводы

The high-fat diet leads to significant changes in lipid metabolism and fatty acid composition of the above mentioned lipid fractions in liver. Our results showed that changes in DAGs fatty acid composition may be the most dangerous because of the possible inflammation development.