Endocrinol Diabetes Nutr. 2021;68(Espec Cong 1):121

Endocrinología, Diabetes y Nutrición

P-069 - EXACERBATED HEPATIC STEATOSIS AND STEATOHEPATITIS IN DIABESIC MICE FED A HIGH-FAT DIET

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Resumen

Introduction and objectives: Type 2 diabetes mellitus (DM2) is a risk factor of non-alcoholic fatty liver disease (NAFLD) and might eventually progress to advanced stages of hepatic damage. Excessive hepatic fat accumulation denotes a typical feature of diabetic patients and plays an important pathogenic role. Actually, now evident is that NAFLD, may have deleterious impact for diabetic individuals increasing the risk to develop cardiovascular complications. Thus, we aimed at analyzing whether the high-fat diet impaired the hepatic phenotype of diabetic mice.

Material and methods: Both groups of diabesic (db/db) and non-obese, db/+ mice (on a C57BKS genetic background) were fed with a high-fat (HFD) diet for 2 months. Gross parameters, plasma and hepatic biochemistry, and hepatic histology were assessed at the end of the study.

Results: Obesity and excess adiposity was exacerbated in db/db mice with a hypercaloric, HFD diet. In addition to the concomitant increase in body weight (1.6-fold, p 0.05) mainly due to enlarged adiposity (4.3-fold, p 0.05), the HFD-fed db/db mice presented an enhanced dyslipidemia, as shown by a marked increase in plasma levels of triglycerides (2.3-fold, p 0.05) and free-fatty acids (1.7-fold, p 0.05) as compared to non-obesemice. Importantly, this unhealthy metabolic phenotype was accompanied by an exacerbated ectopic accumulation of lipids in the liver and myocardium, as well as impaired insulin signaling, as revealed by increased plasma concentrations of glucose (3.4-fold, p 0.05) and insulin (2.5-fold, p 0.05), and concomitant elevations in HOMA-IR (3.6-fold, p 0.05) and Adipo-IR (2.8-fold, p 0.05) indices, common surrogates of global and adipose-specific insulin resistance. Furthermore, the histological analysis of the liver also revealed signs of steatohepatitis.

Conclusions: Caloric overfeeding in diabesic mice further aggravated insulin signaling, dyslipidemia, and worsened hepatic accumulation of lipids and steatohepatitis.