HIGH FAT DIET INDUCES NONALCOHOLIC FATTY LIVER DISEASE AND IMPAIRS LIVER MITOCHONDRIAL METABOLISM IN ADULT MICE

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INTRODUCTION: Insulin resistance is the main consequence of obesity, which favors the development of nonalcoholic fatty liver disease (NFD). High Fat Diet rich in saturated fats is very important for the development of obesity and NFD. The nutritional and hormonal signals answer to regulate mitochondrial oxidation of fatty acids and carbohydrates stock or fuel in the form of triglycerides in the hepatocytes.

OBJECTIVE: The aim of this study was to investigate the liver mitochondrial metabolism of obese adult mice fed with High Fat Diet (rich in saturated fat).

MATERIALS AND METHODS: 21 days old male mice were divided in two groups: fed with control diet (CD) or High Fat Diet (HFD), for 112 days. At 133 days of life the animals were sacrificed for evaluation of biometric parameters, fasting glucose, fasting insulin, acylated ghrelin, triglycerides, hepatic glycogen, liver histology, liver mitochondrial function and proteins involved in the signaling cascade of ghrelin and insulin by Western Blotting (GHSR 1a, IRβ, PI3K, pAKT/AKT, CPT1, UCP2, GLUT2, GLUT4, PPARγ, and α-tubulin).

DISCUSSION AND RESULTS: Animals subjected to HFD showed increased body weight (p<0.0001), visceral fat (p<0.0001), liver weight (p<0.0001), hepatic glycogen (p<0.01), glycemia (p<0.0133), insulinaemia (p<0.001), triglyceridemia (p<0.01) compared to CD group. The liver of HFD group presented damaged parenchymal cells with accumulation of lipid droplets and alterations in protein content compared to CD: reduced level of GHSR1a (p<0.0282) and pAKT/AKT ratio (p<0.0053), increased content of PI3K (p<0.0149), IRβ (p<0.0539), CPT1 (p<0.0417), PPARγ (p<0.023) and decreased content of GLUT4 (p<0.012), UCP2 (p<0.0196). Through High resolution respirometry we observed a reduction in carbohydrate oxidation (p<0.0481) and increased fatty acid oxidation (p<0.0008) in the liver of HFD group.

CONCLUSIONS: The group subjected HFD presented hyperphagia, obesity, with increase in biometric parameters such as body mass, Lee index, epididymal and retroperitoneal fat, liver mass, changes in insulin and ghrelin signaling pathways, non-alcoholic fat liver disease, and decreased content of GHSR-1a receptor and the acylated ghrelin levels; decreased oxidation of carbohydrates and increase in fatty acid oxidation.

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KEY WORDS: Western diet, Ghrelin, Non-alcoholic fat liver disease.