MATERNAL OBESITY DURING GESTATION AND LACTATION PROGRAM OFFSPRING TO A DELETERIOUS RESPONSE TO A HIGH-FAT DIET EXPOSURE IN ADULT MICE

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Introduction and Objectives: Many studies have shown that nutritional status in intrauterine and early post-natal life plays a critical role in susceptibility to various diseases, including non-alcoholic fatty liver disease (NAFLD), a disease considered to be the hepatic manifestation of metabolic syndrome. Maternal overnutrition during gestation and lactation leads offspring to weight gain and impaired glucose metabolism, however the effect of re-exposure to a HFD in adult life on hepatic lipid metabolism need to be clarified. Thus, we aimed to investigate whether maternal obesity leads to a more harmful response in lipid metabolism after a HFD exposure in adult offspring.

Material and Methods: Control or obese female Swiss mice were mated with control male. At birth, litters were normalized to 8 pups to dam. At d18, pups were weaned and fed a control diet until d42. Part of the offspring from control and obese dams (CC and HH) were re-exposed to a HFD (CC-HF and HH-HF) until adult life (d82). We evaluated some parameters prior to HFD exposure and, at d82, we analysed body weight and adiposity, caloric intake, serum parameters, hepatic lipid content, gene expression (qRT-PCR) of Cpt1a, Acadvl, Agpat, Gpam, miR-122 and miR-370 and immunoblot to analyze proteins in liver fragments.

Results and Conclusion: At d42, offspring of obese dams (HH) presented higher body weight and adiposity, elevated serum TAG, glucose and insulin. At d82, HFD exposure in HH-HF resulted in higher weight gain, caloric intake, CHOL and TAG levels, fasting glucose and hepatic lipid content, increased Agpat and Gpam and decreased Cpt1a hepatic expression, compared to CC-HF. In conclusion, maternal overnutrition during critical periods of development programs offspring to an impaired lipid metabolism and to a harmful response to a HFD exposure in adult life, and this could be an important factor in the NAFLD pathogenesis.

Acknowledgements: The study was supported by grant #2011/22156-7 and #2013/07607-8, São Paulo Research Foundation (FAPESP). The contributing authors report no conflict of interest.

Key Words: maternal obesity, fatty liver, high-fat diet reexposure