Hepatic and Placental Endocannabinoid System (ECS) in Maternal Obesity

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Introduction

Nonalcoholic fatty liver disease (NAFLD) has become the most prevalent form of liver pathology in the Western world and has been linked to obesity, insulin resistance, and type 2 diabetes with the incidence as high as 75-92% in the morbidly obese population. In general, pediatric population the prevalence of NAFLD has been reported to be in the 13-14% range. Fatty liver has already been documented in fetuses of obese women and in healthy pregnant women as early as the first trimester of pregnancy. Recent data showed a direct role of endocannabinoids (ECBs) in alcoholic and non-alcoholic (obesity-related) fatty liver diseases. In particular, the activation of endocannabinoid receptor 1 (CB1) has been associated with hepatic fat accumulation in the animals on the higher fat diet. However, the role of CB1 in maternal and fetal responses to the obesity (Figure 1) has not been yet elucidated. Our goal was to use the baboon model of maternal obesity to evaluate the expression of CB1 receptors in maternal and fetal livers and to compare the expression between the groups.

Objectives

The goal of this study was to evaluate the expression of the ECS receptor CB1 within the liver of maternal obese and non-obese baboons (Papio spp), as well as their fetuses, to determine whether or not maternal ECS expression can influence CB1 hepatic expression in offspring used as an indicator of the risk for developing NAFLD.

Methods

Archived liver and placental tissues from a previous study in which samples were collected from obese and non-obese baboons (Papio spp) (Farley et al., 2009), were evaluated using Reverse Transcription real-time quantitative PCR method (Q-RT-PCR) using the Light Cycler 96 from Roche. The T1R1/2 method was used to isolate RNA from tissue samples (Life Technologies, USA), and cDNA was synthesized according to the manufacturer’s instructions (Applied Biosystems/ Roche, USA). Q-RT-PCR was performed using Fast start Essential DNA Probe Master Mix (Roche, USA), and TaqMan Gene Expression Assay Probes (Life Technology USA). The TaqMan probes used were CB1 (Hs01308522_m1). A secondary analysis of the previously published data was also performed. IHC was done using the CB1 monoclonal primary antibody (ImmunoGenes, Budakeszi, Hungary), and the secondary antibody was included in the Vectastain ABC kit (Vector laboratories; Burlingame, CA); methodology for IHC was performed according to kit instructions. IHC slides were then scanned using the NanoZoomer-SV and quantification was done using Aperio software.

Results

This is the first report demonstrating the presence of ECS receptors in fetal and maternal hepatic tissues. Hepatic CB1 protein expression was decreased in pregnant obese mothers. Fetal CB1 mRNA expression correlated with fetal birthweight. A negative correlation is demonstrated between serum AEA and maternal liver weight, pointing out possible involvement of the ECS pathway in fetal growth and maternal metabolic adaptations to pregnancy. Changes in the ECBS might be the candidates for being markers of NAFLD in pregnancy.

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References
