INTRODUCTION

- Fatty liver disease is the major cause of liver transplantation in 21st century.
- Maternal BMI: influences fetal liver and brain development and is the strongest predictor of fetal fat accumulation and offspring adiposity (PMID: 24740157).
- Maternal obesity (MO): links to autism spectrum disorders, non-alcoholic fatty liver diseases (NAPLD), diabetes and other life-threatening diseases.
- Endogenous cannabinoid (eCB) system (ECS): family of the biologically active lipids – derivatives of omega-3 fatty acids, which regulate vascular tone, metabolic rate, inflammatory and stress responses – all hallmarks of MO and play vital role in obesity, appetite regulation and lipogenesis (Fig. 1).

Information regarding eCBs physiology in obesity, associated with pregnancy, is sparse. The different patterns of maternal obesity: pre-pregnancy obesity vs. pregnancy-related weight gain, over-eating vs. high-fat vs. high-calorie diet make studies of mechanisms of developmental programming challenging. Animal models represent an opportunity to dissect specific mechanisms associated with dietary patterns and provide important data for development of interventional strategies in humans.

Fetal and maternal hepatic gene expression for CB1R, CB2R and FAAH did not differ between two groups. CB1R protein expression (full length receptor, ~ 55 kDa), was increased in HFD dams, carrying male fetuses by 40% and decreased in their fetuses by 75%. Full length hepatic CB1R was not detectable in the HFD female fetuses and their mothers (Fig. 2 and Fig. 3). Maternal hepatic CB2R and FAAH protein expressions did not differ between groups. Fetal hepatic expression of CB2R and FAAH were decreased in both – HFD male and female fetuses compared to CTR (Fig. 4 and Fig. 5).

OBJECTIVE

To describe the influence of a maternal high fat diet on the feto-maternal hepatic axis in baboon (Papio spp) model of obesity.

MATERIALS AND METHODS

Baboons (Papio spp) were fed a diet of 45% fat (HFD, n=11), while controls (CTR, n=9) ate 12% fat from at least 9 months prior to conception. Fetal and maternal sera samples were collected at term Cesarean Section. qRT-PCR, immunohistochemistry (IHC) and western blot analysis were performed to quantify expression of CB1 and CB2 receptors and the central enzyme regulating eCBs tone - Fatty Acid Amidohydrolase (FAAH) in maternal and fetal liver. Data were presented as mean ± SEM (Standard Error of Mean) and statistical analysis was performed using Mann-Whitney test.

RESULTS

- CB1R protein expression in the maternal and fetal livers of HFD (n=11) and CTR (n=10) animals. CB1R protein expression was increased in the maternal and fetal livers of HFD (n=11) and CTR (n=10) animals. A: Representative images of fetal livers from male fetuses in the CTR (n=3) and HFD (n=4) groups; B: Quantitative analyses. M to F: Maternal liver sections from male fetuses in the CTR (n=3) and HFD (n=4) groups; H: Quantitative analyses. M: Maternal liver sections of dams carrying male fetuses in the CTR (n=3) and HFD (n=4) groups. [Blue arrows: bile ducts, green arrow: arteries, orange: bile canaliculi, and yellow: portal vein].

Figure 2: CB1R protein expression in the maternal and fetal livers of HFD (n=11) and CTR (n=10) animals.

- CB2R protein expression in the maternal and fetal livers of HFD (n=11) and CTR (n=10) animals. CB2R protein expression was increased in the maternal and fetal livers of HFD (n=11) and CTR (n=10) animals. A: Representative images of fetal livers from male fetuses in the CTR (n=3) and HFD (n=4) groups; B: Quantitative analyses. M to P: Maternal liver sections from dams carrying male fetuses in the CTR (n=3) and HFD (n=4) groups. H: Quantitative analyses. M: Maternal liver sections of dams carrying male fetuses in the CTR (n=3) and HFD (n=4) groups. H: Quantitative analyses.

Figure 3: CB2R protein expression in the maternal and fetal livers of HFD (n=11) and CTR (n=10) animals.

DISCUSSION

To our knowledge this is the first report of decreased fetal systemic ECS concentration in response to a HFD. HFD stimulated maternal eCBs excess and was associated with hepatic and placent al eCB changes which suggest compensatory peripheral mechanisms to alleviate systemic eCB deficiency.

CONCLUSION

High fat diet consumption in pregnancy decreases the abundance of the main enzyme degrading endogenous cannabinoids and decreased ability of fetal liver to counteract changes, associated with hepatic fat deposition.

REFERENCES

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