

Modest increase in hepatic lipid content in early postnatal female offspring of non-obese mice with gestational diabetes mellitus

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Background

Clinical studies indicate that gestational diabetes mellitus (GDM) increases the risk for mother and child to develop non-alcoholic fatty liver disease (NAFLD) in later life. In order to define preventive or curative therapies, we need to better understand the course and mechanisms underlying NAFLD development in GDM mothers and offspring.

Objectives

In this preclinical study we therefore quantified hepatic lipid content in non-obese GDM mouse dams and their offspring.

Study design

Female mice challenged with a high fat diet (HF) and low-dose streptozotocin (STZ, 60 mg/kg) injections were mated to induce GDM. Livers from GDM dams were collected at gestational day 17.5 (GD17.5) or at the end of lactation, postnatal day 15 (PN15). We additionally collected livers from male and female offspring at PN15. Separate control groups to establish the independent effects of HF and STZ on maternal and offspring lipid contents were included.

Results

Total hepatic lipid content were comparable between GDM and controls at GD17.5. At PN15, hepatic triglyceride (TG) contents were higher in GDM dams compared to controls (TG 108 vs 76 nmol/mg, $p < 0.05$). TG and cholesteryl-ester (CE) contents were higher in female offspring from GDM dams at PN15 as compared to non-GDM offspring (TG 15 vs 8 nmol/mg, $p = 0.058$; CE 5.2 vs 1.3 nmol/mg, $p < 0.001$), while no changes were observed in male offspring. Increased hepatic lipid content in PN15 female GDM offspring was paralleled by higher TG/phospholipid ratios, suggestive of increased lipid droplet size.

Conclusion

Non-obese GDM does not affect maternal liver lipid content during gestation, while hepatic TG content is elevated at the end of lactation. Hepatic TG and CE levels are modestly increased in female GDM offspring by the end of lactation. Follow up research will establish whether these early changes may predispose towards NALFD development in later life, and potentially provide insight into the underlying mechanisms.