Table of Contents

Research Week 2024

Effects of Diet Changes and Maternal Metformin Consumption during Pregnancy on both Maternal and Offspring Insulin Resistance

Anna Maior-Leichtfried, Hannah Blomenkamp, Tyler Dean, Melissa Kirigiti, Kristin Sauter, and Paul Kievit

Oregon National Primate Research Center

Keywords

Insulin resistance/sensitivity, glucose homeostasis, pregnancy, maternal diet, offspring development, metformin treatment, intravenous glucose tolerance tests, insulin enzyme-linked immunosorbent assays, rhesus macaques

Abstract

Background:

Pregnancy causes complex hormonal changes, leading to physiologic decreases of insulin sensitivity, onset of gestational diabetes (GDM), and worsening conditions associated with insulin resistance (IR). These factors, although not fully understood, are closely linked to the metabolic effects of elevated hormones during pregnancy. Studies suggest GDM can cause offspring to develop impaired glucose tolerance. Metformin reduces hepatic glucose production, increases hepatic insulin sensitivity, and combats GDM/IR conditions. It is unknown how metformin exposure during fetal development impacts glucose homeostasis in offspring.

Methods:

Female rhesus macaques were divided into four groups: CHOW/vehicle, CHOW/metformin, Western-style diet (WSD)/vehicle, and WSD/metformin. Baseline intravenous glucose tolerance tests (iv-GTTs) were performed prior to beginning treatments or breeding. Blood samples were taken prior to infusion and at several time-points post-infusion with dextrose. Dams started metformin treatment after confirming pregnancy at gestational age (G) 30 via ultrasound. Another iv-GTT was performed at G115. Infants were reared with mothers and underwent iv-GTTs at 6 months. Plasma insulin values were measured via insulin enzyme-linked immunosorbent assays to determine iv-GTT insulin levels.

Results:

Fasting glucose and GAUC showed no differences between groups at baseline. CHOW groups had decreased fasting glucose at G115 compared to baseline. WSD/metformin had increased glucose area under the curve (GAUC) at G115 compared to baseline. Comparing insulin area under the curve (IAUC) at baseline vs G115, there was a significant increase for CHOW/vehicle, CHOW/metformin, and WSD/metformin.

Conclusions:

We previously demonstrated that maternal WSD does not affect offspring iv-GTT GAUC or IAUC. This project supports this result despite maternal metformin treatment. Metformin did not alter gravid glucose homeostasis. WSD/metformin females had measurements that were significantly higher than other groups. At time of presentation, infant iv-GTT data will be analyzed and correlated to maternal conditions to assess how maternal glucose homeostasis affects offspring glucose homeostasis.