The effect of oral iron supplements on serum hepcidin, insulin and glucose metabolism in pregnancy

Project 555

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Background

Type 2 diabetes mellitus (T2DM) is characterized by insulin resistance, usually secondary to adiposity and physical inactivity. Several observational studies have linked disturbances in glucose metabolism, including increased risk of T2DM, with greater iron stores. A common disorder during pregnancy is gestational diabetes mellitus (GDM), defined as hyperglycemia with blood glucose values above normal but below those diagnostics of DM, occurring during pregnancy. Iron deficiency is common among pregnant women, and iron deficiency anemia is associated with a greater risk of neonatal morbidity such as preterm birth as well as with a variety of negative effects on different aspects of child development. WHO recommends routine iron supplementation during pregnancy. Whether iron supplementation during pregnancy to prevent or treat iron deficiency increases the risk of GDM is uncertain; data from existing clinical trials are equivocal.

The overarching objective of this study was to assess whether oral iron supplementation acutely increases plasma hepcidin and affects glucose metabolism by decreasing insulin sensitivity during the second trimester of pregnancy.

Materials and methods

The study was conducted between September 2019 - today. Pregnant women were enrolled in week of pregnancy 24 – 28. Participants in the *high iron group* received 200 mg oral iron on study days 3-6. Participants in the *low iron group* received a multivitamin supplement containing 15 mg iron on days 0-14. On days 0 and 7 (after the iron intervention) we performed an oral glucose tolerance test (OGTT). On day 14 we collected a final blood sample.

Preliminary results

Data from seventeen women (*high iron group:* n=14*; low iron group:* n=3) were included into this report. At baseline, mean (SD) gestational age was 25 (1) weeks, mean (SD) pre-pregnancy BMI was 21.4 (2.7) kg/m^2, mean (SD) age was 34 (5) y, mean (SD) hemoglobin was 11.6 (1.1) g/dl and median (IQR) serum ferritin was 11.5 (7.4-14.8) µg/L. Linear mixed model analysis showed a significant effect of the high-dose iron intake on serum hepcidin ($p=0.011$) (Table 2). Serum hepcidin was increased at 24h after the high-dose iron intake on day 7 compared to day 0 ($p<0.05$) and day 14 ($p<0.05$) (Figure 1). There was no effect of the supplement intake on hemoglobin and iron and inflammatory status parameters. There was no effect of the supplement intake on fasting glucose and fasting insulin.

The blood glucose increase during the OGTT was significantly higher on study day 7 (after the iron intake) compared to day 0 in the high iron group ($p = 0.022$) (Figure 1). There was no difference in blood glucose increase during the OGTTs done on days 0 and 7 in the low iron group ($p = 0.214$).

Preliminary conclusion

In conclusion, the data collected so far show that high oral iron doses administered in the second trimester of pregnancy acutely increase serum hepcidin at 24 hours and affect glucose metabolism by increasing delta glucose concentration after performing an OGTT. Furthermore, there is a trend showing greater fasting insulin and delta insulin after OGTT at 24h after high iron supplementation compared to baseline. However, these findings are only preliminary and the further analyses including the complete dataset of the control group are needed.