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Hypoglycaemia increases during pregnancy after gastric bypass: the Bariatric surgery And consequences for Mother and Baby In pregnancy (BAMBI) study

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Background and aims: Roux-en-Y Gastric bypass surgery (RYGB) is complicated by subsequent alterations in glucose profiles partly due to an enforced incretin response. The increased insulin resistance during pregnancy poses an additional challenge to glucose metabolism in women treated by RYGB. However, the magnitude and impact of this has only been sparsely investigated. The aims of the BAMBI study were to investigate the interstitial glucose (IG) profiles during the course of pregnancy and the incidence of hypoglycemic events in pregnant women previously treated by RYGB compared to matched controls.
Materials and methods: In the prospective BAMBI study, 23 pregnant women with RYGB and 23 BMI- and parity-matched pregnant controls were studied with continuous glucose monitoring (CGM) in the 1st, 2nd, and 3rd trimester as well as 4-6 weeks postpartum. Time in range (TIR) was defined as time with IG of 3.5-7.8 mmol/l. The primary outcomes were time below range (TBR) (%), and the incidence of hypoglycemic events (< 3.0 and 3.5 mmol/l) quantified by CGM.
Results: Pregnancies occurred 30 (IQR: 15.4-98.1) months following RYGB with a reduction of BMI from 45.2 kg/m^2 (IQR: 42.0-54.3) pre-surgery to 31.5 kg/m^2 (IQR: 26.5-39.1) pre-pregnancy. TIR was significantly lower throughout pregnancy and postpartum for the RYGB group compared to controls (87.3-89.5% vs. 93.7-96.1%, p<0.01). TBR increased from the 1st trimester (1.0%, SD 1.5) to the 2nd (2.1%, SD 3.2) and 3rd trimester (2.0%, SD 2.7) and returned to a reduced TBR postpartum (0.6%, SD 0.7). Similarly, the median weekly number of hypoglycemic events increased during pregnancy for the RYGB group with 0, 0.8, 0.4 and 0 weekly events < 3.0 mmol/l, and 1.6, 2.4, 2.9 and 1.1 weekly events < 3.5 mmol/l in the 1st, 2nd, and 3rd trimester and postpartum, respectively. The median weekly number of hypoglycemic events for the controls was 0 for both the 3.0 and 3.5 cut-off.
Conclusion: The results of the BAMBI study show that women treated by RYGB pre-pregnancy spend more time in TBR and are more exposed to hypoglycemia than matched controls. Further research is warranted investigating if the increased risk of fetal growth restriction among pregnant women treated with gastric bypass is associated with exposure to hypoglycemia during pregnancy.
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Body composition and effect of insulin treatment during pregnancy in *Socs2*$^{-/-}$ mice with gestational diabetes and macrosomia

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Background and aims: The Suppressor of Cytokine Signaling 2 (SOCS2) protein modulates cytokine response, growth, inflammatory processes, and cytokine-mediated metabolism of lipids and carbohydrates. Thus, its ablation in mice (Socs2$^{-/-}$) generates gigantism and insulin-resistance as well as gestational diabetes (GDM) and macrosomia with high mortality rates (>88%). Our aim is to evaluate the body composition variations in pregnant Socs2$^{-/-}$ as a potential early diagnostic tool for macrosomia. Additionally, we assess the potential use of insulin to prevent foetal macrosomia.
Materials and methods: Body Weight (BW) and composition (lean, fat and fluid) were evaluated in 7 Socs2$^{-/-}$ and 4 C57BI/6J pregnant females (age: 196.3±28 days,) using an NMR-TD spectrometer (Minispec+ LF90II). Basal glucose was measured at days 7 and 14 of pregnancy (first and second gestational thirds) using a glucometer (Glucomen Areo Menarini). Besides, Socs2$^{-/-}$ mothers and offspring were retrospectively analyzed and compared for the presence of macrosomia, based on whether the mother was insulin-treated (0.5U/kg, Glargine) or not during pregnancy (3 females with 22 neonates *vs* 21 females with 137 neonates, respectively). Macrosomia in this strain was previously defined as >1.43 g birth weight. Mann-Whitneys's U, Student's test and Chi^2 test were used for comparisons.
Results: Basal blood glucose did not differ between groups for the whole evaluation (Socs2$^{-/-}$: 151±2.19 mg/dL; control: 144±13.63 mg/dL) (p=0.46). BW of Socs2$^{-/-}$ tended to be greater at day 7 compared to controls (29.5±2.2 *vs* 25.7±2.1g, respectively; p=0.063) and was significantly higher at day 14 of pregnancy (36±3.2 *vs* 28.2±2.3g, respectively; p=0.006). Fat percentage was higher in controls (7d: 26.2±3.1%; 14d: 21.3±2.8%) than in Socs2$^{-/-}$ (7d: 10.6±2.1%; 14d: 11±2.9%) (p=0.016; p=0.012). Fluid content was reduced in Socs2$^{-/-}$ compared to controls at 7d (6.06±1.16 *vs* 9.3±0.7%, p=0.016), but not at 14d (10.3±1.0 *vs* 11.7 ±1.5%; p=0.16). Finally, differences were no significantly (p>0.05) in lean percentage on days 7 and 14 between control (7d: 79.9±2.9%; 14d: 80.5±3.0%) and Socs2$^{-/-}$ (7d: 63.3±16.3%; 14d: 71.9±6.9%). Neonates from untreated mothers were heavier than offspring of mice receiving insulin (1.5±0.2g vs 0.8±0.4g, respectively; p<0.001) and the prevalence of macrosomia was higher, too (65.9 ±24.01% vs 20 ±34.6%, respectively; p=0.007).
Conclusion: Although it is necessary to extend the analysis of body composition to more animals and later pregnancy periods to assesses if these variables indeed predict macrosomia, actual results show weight, fat and fluid as parameters with potential noninvasive pre-diagnostic interest for macrosomia. Insulinization of pregnant *Socs2*$^{-/-}$ resulted in almost 50% decreased occurrence of macrosomia, reinforcing a novel *in vivo* model for GDM. New specific insulin evaluations will be conducted to define its potential to ameliorate the severity of macrosomia. Further studies should be performed to fully elucidate the potential role of SOCS2 in the development of GDM.
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Insulin sensitivity, growth differentiation factor-15 and fetuin-B during pregnancy after assisted reproductive therapy in the STORK cohort

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Background and aims: Assisted reproductive therapy (ART) may increase the risk of gestational diabetes (GDM) and glucose intolerance after pregnancy. We have previously shown reduced insulin sensitivity (IS) in pregnant women after ART. To gain more insight in this