SAT-014

Background: Pregnant women with obesity are at increased risk for peripartum depression. Maternal obesity is also associated with reduced human placental lactogen (hPL) levels, and decreased hPL transcripts were reported in women with clinical depression. In addition, hPL production may be rescued in women with obesity that were subsequently diagnosed with gestational diabetes and treated with insulin (INS). **Objective:** Study the effect of INS treatment in pregnancy on the risk for postpartum psychological distress (PPD) in women with and without obesity. **Study Design:** Using data housed at the Manitoba Centre for Health Policy (2002–2017), cohorts of women (ages 15+) with a single live birth with and without obesity were developed using weight (≥85 and <65.6 kg, respectively) and an average (1.63 m) height. Pre-existing mood and anxiety disorders within 5 years preceding delivery as well as gestational hypertension were excluded. After randomly selecting 1 birth per mother, cohorts were stratified by INS treatment during the gestational period. The risk of PPD within 1 year of delivery was assessed by Poisson regression analysis. Models were adjusted for maternal age and area-level income at delivery. **Results:** The risk of PPD was 27% greater among women with obesity versus without (adjusted rate ratio (aRR)=1.27, 95% CI 1.16–1.4, p<0.0001). However, women with obesity treated with INS did *not* have a significantly different risk of PPD compared to women without obesity whether treated with INS (aRR=0.99, 95%CI 0.48–2.02, p=0.974) or not (aRR=1.16, 95%CI 0.86–1.56, p=0.328). This suggests that the risk of PPD among women with obesity may be reduced by INS treatment; however, our ability to detect a significant difference may be limited by small cohort numbers (46 women with obesity received INS in pregnancy) or confounders for receiving INS in pregnancy. Direct comparison of INS treatment within weight groups faced the same limitations but trended toward a reduction in women with obesity who received INS (aRR=0.91, 95%CI 0.68–1.22, p=0.531). The positive association between INS treatment in pregnancy and decreased risk of PPD in women with obesity was lost when pre-existing mood and anxiety disorder was not excluded. Inclusion of pre-existing diabetes in the adjusted models did not improve model fit or contribute significantly to the differences in PPD rates. **Conclusions:** Maternal obesity increases the risk for PPD but this risk may be reduced by gestational INS treatment in the absence of a pre-existing mood and anxiety disorders. This correlates with the decrease and increase in hPL levels reported previously with maternal obesity without and with INS treatment (for diabetes) in pregnancy, respectively. Thus, hPL levels may serve as a possible indicator of PPD risk and a potential target for gestational INS treatment.

Cardiovascular Endocrinology

PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE

Effect of the Combination of Conjugated Estrogens and Bazedoxifene on Muscle and Serum Lipidome in Obese Postmenopausal Women: A Placebo-Controlled Randomized Pilot Trial

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Background and Objectives: Menopause is characterized by estrogen deficiency and predisposes women to weight gain and metabolic disturbances including lipid abnormalities. Orally-administered estrogens increase high-density lipoprotein (HDL) and triglycerides (TG) cholesterol and decreases low-density lipoprotein (LDL) cholesterol levels. The increase in serum TGs is not well understood. The objective of this study was to assess the effect of CE/BZA on serum and skeletal muscle lipid species in obese postmenopausal women.

Methods: Randomized double-blind crossover pilot trial in 8 obese postmenopausal women (53± 3 years, BMI 35.7±3.2 kg/m^2) assigned to 8 weeks of CE/BZA or placebo with 8 weeks washout in between. At the end of each 8-week treatment period, intrahepatic and skeletal muscle lipids were measured by proton magnetic resonance spectroscopy (^{1}H-MRS) while serum and skeletal muscle lipidomics were assayed by ultrahigh performance liquid chromatography/mass spectrometry (UHPLC/MS).

Results: No treatment differences were observed in intrahepatic lipid, soleus intramyocellular lipid (IMCL) or extramyocellular lipid (EMCL) as well as tibialis anterior IMCL or EMCL.

The serum metabolome and lipidome comprised a total of 2002 biochemicals. Treatment with CE/BZA was associated with higher levels of diacylglycerols (DAGs) and triacylglycerols (TAGs) composed of long-chain saturated fatty acids (SFA, palmitic C16:0 and arachidic C20:0), monounsaturated FAs (MUFA, palmitoleic C16:1, oleic C18:1 and ecosenoic C20:1), and polyunsaturated FAs (PUFA, linoleic C18:2, arachidonic C20:4, eicosapentaenoic C20:5, and docosahexaenoic C22:6) compared to placebo (all p<0.05). Treatment with CE/BZA was also associated with lower levels of several acylcarnitine species, which are markers of FA oxidation, including long-chain SFA (C14, C16 and C18), MUFA (C18:1 and C24:1) and PUFA (C18:2, C20:2 and C20:4). In addition, treatment with CE/BZA was associated with higher levels of phosphatidylcholines (PCs), phosphatidylinositols (PIs), phosphatidylethanolamines (PEs), sphingomyelins (SMs), and ceramides (CER), as well as lower levels of lysophophatidylcholines (LPCs). There were no treatment differences in carnitine or ketones levels. The skeletal muscle analysis comprised a total of 652 biochemicals, but unlike in serum, no significant treatment differences were observed in the skeletal muscle lipidome.

Conclusions: Our lipidomic analysis supports a model in which CE/BZA (and likely all oral estrogens) increases hepatic de novo FA synthesis and esterification into TAGs for export into TAG-rich very low-density lipoproteins, as well as decreased FA oxidation, respectively. Although CE/BZA treatment inhibits FA oxidation, it is not associated with hepatic lipid accumulation as measured by MRS, or skeletal muscle lipid accumulation measured by MRS and lipidomics.