36 A DOUBLE-BLINDED RANDOMIZED CONTROLLED TRIAL COMPARING NORMAL SALINE WITH AND WITHOUT DEXTROSE ON THE COURSE OF LABOR IN NULLIPARAS.

VINEET SHRIVASTAVA[1], THOMAS GARITE[1], SHERI JENKINS[2], LISA SAUL[1], PAMELA RUMNEY[1], CHRISTINE PRESLICKA[3], KENNETH CHAN[3], [1]University of California, Irvine, Orange, California, [2]University of Alabama at Birmingham, Birmingham, Alabama, [3]Long Beach Memorial Medical Center, Maternal-Fetal Medicine, Long Beach, California

OBJECTIVE: As previously seen in laboring nulliparae, increased maternal hydration has been demonstrated to shorten the frequency of prolonged labor. However, the effects of carbohydrate administration on labor duration have yet to be elucidated. The objective of this study is to compare intravenous normal saline with and without dextrose on the course of labor in nulliparae.

STUDY DESIGN: This was a double-blinded randomized controlled trial. Consenting term, nulliparae with singletons in active labor between 3-5 cm or with ruptured membranes were included. Subjects were randomized to normal saline (NS), NS with 5% dextrose (D5NS), or NS with 10% dextrose (D10NS) at 125 cc/hr. The primary outcome was total length of labor from onset of study fluid. Both maternal and neonatal outcomes were examined. A sample size of 95 patients in each group was needed for 80% power to detect shortening of total labor by 20% from 560 to 450 minutes.

RESULTS: Of 300 enrolled, 290 subjects met inclusion and exclusion criteria and completed study. There were no significant differences observed in the cesarean section rates between the groups ($p=0.21$). In vaginally delivered subjects, significant differences were noted in time to complete dilation [(NS) 461+402 min vs. (D5NS) 363+293 min. vs. (D10NS) 340+200 min. ($p=0.039$)], and total length of labor [(NS) 565+408 min. vs. (D5NS) 450+302 min. vs. (D10NS) 413+202 min. ($p=0.027$)]. No differences were noted in oxytocin use ($p=0.08$), epidural administration ($p=0.12$) or chorioamnionitis ($p=0.16$). There were no differences in neonatal jaundice ($p=0.12$), NICU admission ($p=0.16$) or neonatal hypoglycemia at one ($p=0.21$) or two hours following delivery ($p=0.38$).

CONCLUSION: This study presents the novel finding that administration of a dextrose solution to nulliparae in labor compared to normal saline resulted in shorter lengths of labor in subjects who deliver vaginally. This shortening of labor with the use of dextrose solutions was accomplished without any apparent adverse neonatal outcomes.

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.041

37 MATERNAL DIET INFLUENCES FETAL THYROID FUNCTION AND CHROMATIN REMODELING COMPLEXES IN A PRIMATE MODEL OF OBESITY

KJERSTI AAGAARD-TILLERY[1], SARAH WILLIAMS[2], HALEH SANGI-HAGHPEYKAR[1], MICHAEL VARNER[3], KEVIN GROVE[2], ROBERT H LANE[4], [1]Baylor College of Medicine, Houston, Texas, [2]Oregon National Primate Research Center, Beaverton, Oregon, [3]University of Utah, Obstetrics&Gynecology, Salt Lake City, Utah, [4]University of Utah, Pediatrics, Salt Lake City, Utah

OBJECTIVE: Hypothyroidism is associated with development of obesity and dysplidemia. Emerging evidence suggests that thyroid receptor associated proteins (TRAP) are key regulatory components of chromatin remodeling complexes. Our prior studies demonstrate that a high fat (HF) maternal diet induces fetal nonalcoholic steatohepatitis (NASH), while epigenetically altering chromatin structure of reprogrammed fetal genes. We hypothesized that a HF maternal diet influences the fetal thyroid and TRAP expression, thereby setting the stage for obesity via alterations in chromatin remodeling complexes.

STUDY DESIGN: Pregnant macaques were fed control (**n**12) or HF (**n**14) diet up to yr4, with a subset reverted to control diet in yr5 (**n**7). On e130 serum/tissue of delivered maternal-offspring pairs in successive gestations were obtained to assay thyroid hormones (TH: fT4,fT3,T3RU,TBG), lipids/FFA, cortisol, and leptin. Correlation of fetal TH to lipid levels was performed with Fishers **z** transformation in regression models stratified by maternal diet and controlling for maternal TH and leptin/bw ratio.

RESULTS: Consistent with marked disruption of fetal thyroxine regulation, maternal and fetal fT4 became inversely correlated with HF diet ($r+.43,-.57$ $p<.01$), and adjusted fetal fT4 was significantly less (1.97vs1.34, $p<.0001$). Moreover, while under control diet adjusted fetal TH to lipids trended in an inverse correlation ($r-.09, -.6$), HF diet reversed this correlation ($r+.01,+.57$) with a modest restoration following gestational diet reversal ($r-.02,+.4$). In Affymetrix (HG-U133 40K human genes) microarrays of fetal hepatic tissue, TRAP3 alone bore significant differential expression (>4.0-fold) among thyroid-related genes.

CONCLUSION: These data demonstrate that an obese in utero environment alters both fetal thyroid levels and correlative dyslipidemia in a reversible fashion, as well as hepatic TRAP3. We speculate this serves as a potential novel mechanistic link relating development of obesity with fetal hypothyroidism, NASH, chromatin remodeling complexes, and gene-specific regulation.

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.042

38 SIGNALING OF SOLUBLE FMS-LIKE TYROSINE KINASE-1 (SFLT-1) VIA THE GSK-3 PATHWAY IN CYTOTROPHOBLAST CELLS DEMONSTRATES A LINK BETWEEN PREECLAMPSIA AND HYPOXIA

ALICE ROBINSON[1], SUZY DAVIES[1], LAURA LAIDLER[1], SANG-JOON LEE[2], KIMBERLY LESLIE[1], [1]University of New Mexico, Dept. of Obstetrics and Gynecology, Albuquerque, New Mexico, [2]University of New Mexico, Dept. of Internal Medicine, CRTC, Albuquerque, New Mexico

OBJECTIVE: The quest to outline the pathogenesis of preeclampsia has yielded the discovery of several anti-angiogenic factors such as soluble Fms-like tyrosine kinase (sFlt-1). We and others have previously demonstrated that this endogenous inhibitor of vascular endothelial growth factor (VEGF) is significantly elevated in the sera of preeclamptic patients. We sought to map the downstream signaling pathways under the influence of sFlt-1 in cultured cytotrophoblast cells to further clarify the mechanisms underlying preeclampsia.

STUDY DESIGN: We cultured HTR-8/Svneo trophoblast cells in complete growth media until they reached 80% confluence, and then serum-starved them for 24 hours. The cells were then treated with recombinant VEGF165 which was premixed with excess heparin sulphate proteoglycans (HSPG), and either sFlt-1 or bevacizumab (Avastin, an exogenous anti-VEGF antibody inhibitor) for growth experiments, or sFlt-1 alone for the cell signaling experiments. Cells were harvested after 24 hours of treatment and counted using a Beckman Coulter counter. Protein lysates were prepared from cell suspensions, and analyzed utilizing the Kinetworks KPSS 1.3 screen to determine the phosphorylation targets.

RESULTS: Growth experiments revealed that, compared to bevacizumab, treatment with s-Flt1 at 10 ng/mL had the most suppressive effects on cultured HTR-8 cells ($p = 2.013E-12$), with cell count inhibition by as much as 20%. Phosphoproteomic mapping using the KPSS screen revealed that the central signaling effect of sFlt-1 treatment was a 40% inhibition of the phosphorylation of glycogen synthase kinase 3β (GSK-3β), which plays an important regulatory role in cell survival in hypoxic environments by inducing hypoxia-inducible factor-1α (HIF-1α).

CONCLUSION: Our results indicate that up-regulation of sFlt-1, as seen in preeclampsia, initiates a cascade that leads to defective angiogenesis and decreased cell survival. In addition, sFlt-1 signaling through GSK-3β is a mechanism that links preeclampsia to hypoxia.

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.043

39 TRANSGENERATIONAL EFFECT OF FETAL PROGRAMMING ON VASCULAR PHENOTYPE IN AN ENDOTHELIAL NITRIC OXIDE SYNTHASE (NOS3) KNOCKOUT MOUSE MODEL

LABIB M. GHULMIYYAH, ESTHER TAMAYO, MICHAEL MAKHLOUF, PHYLLIS GAMBLE, GARY D.V. HANKINS, GARLAND D. ANDERSON, GEORGE R. SAADE, MONICA LONGO, The University of Texas Medical Branch, Obstetrics and Gynecology, Galveston, Texas

OBJECTIVE: We have previously characterized a model of altered fetal programming of vascular function in first generation adult offspring using transgenic mice lacking a functional NOS3, a critical regulator of cardiovascular adaptation in pregnancy. Our purpose in this study was to determine the transgenerational effect of fetal vascular programming by examining the vascular phenotype of the second generation offspring.

STUDY DESIGN: Homozygous NOS3 knockout (C57BL/6J-Nos3tm1Unc, NOS3−/−KO) and wild type controls (NOS3+/+WT) were cross-bred to obtain heterozygous offspring (KOM) that developed in KO mothers lacking a functional NOS3 versus offsrping (KOP) born to wild-type control mothers. The first generation KOM and KOP female mice were then bred with WT males to obtain a second generation offsprng. The offspring were genotyped, and the second generation WT offspring (WT-F2) were used for in vivo blood pressure measurement by telemetry. A blood pressure (BP) catheter was inserted into the carotid artery and BP was monitored continuously for 8 days in the unrestrained and conscious 15 week old WT-F2. The mean arterial pressure (MAP), systolic (SBP), diastolic (DBP) and pulse pressure (PP) were obtained. Mean values of MAP, SBP, DBP and PP over an 8 day period were calculated, and Student t-test was used for statistical analysis (significance: $p<0.05$)

RESULTS: The WT-F2 mice born to KOM mice had a significantly higher SBP (153 ± 4.4 vs 120.2 ± 2.6 mmHg, $p=0.001$), MAP (110.5 ± 0.8 vs 107.2 ± 0.8 mmHg, $p=0.005$) and PP (59.4 ± 3.6 vs 21.6 ± 1.8 mmHg, $p=0.001$) compared to the WT-F2 mice born to KOP mice. A higher DBP was also noted in the WT-F2 mice from the KOM but the difference was not statistically significant.

CONCLUSION: Despite being wild type, offspring born to mothers who themselves developed in an adverse uterine environment have hypertension compared with the genomically-similar wild type offspring born to mothers who developed in a normal uterine environment. Our results show that fetal programming of adult vascular function can have transgenerational consequences.

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.044