27 Single nucleotide polymorphisms in the oxytocin receptor and GRK6 are associated with oxytocin dosing requirements and labor outcomes

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OBJECTIVE: Oxytocin is a potent uterotonic agent widely used for induction and augmentation of labor. Oxytocin has a narrow therapeutic index and the optimal dosing for any individual woman varies widely. The objective of this study was to determine if genetic variation in the oxytocin receptor gene (OXTR) or in the gene coding GRK6, which regulates desensitization of the OXTR, could explain differences in oxytocin dosing and labor outcomes among women being induced near term.

STUDY DESIGN: Pregnant women with a singleton gestation residing in Durham County, NC were prospectively enrolled. DNA was available from 482 women undergoing induction of labor at 36 weeks or greater. 18 haplotype tagging (ht) single nucleotide polymorphisms (SNPs) in the OXTR and 7 htSNPs in GRK6 were genotyped using TaqMan assays. Linear regression was used to examine the relationship between maternal genotype and maximal oxytocin infusion rate, total oxytocin dose received, and duration of labor. Logistic regression was used to test for association of maternal genotype with mode of delivery. For each outcome, backward selection techniques were utilized to control for important confounding variables and additive genetic models were employed. Race/ethnicity was included in all models due to differences in allele frequencies across populations and Bonferroni correction for multiple testing was used.

RESULTS: Five SNPs in the OXTR were significantly associated with maximal oxytocin infusion rate and two SNPs in the OXTR were associated with total oxytocin dose received. One SNP in the OXTR and two SNPs in GRK6 were associated with duration of labor, one of which met the multiple testing threshold (p=0.0014, rs2731664 [GRK6], mean duration of labor 17.7 hours vs. 20.2 hours vs. 23.5 hours for AA, AC and CC genotypes, respectively). Three SNPs, two in the OXTR and one in GRK6, were significantly associated with mode of delivery. (Table)

CONCLUSION: Variation in genes coding the OXTR and GRK6 are associated with the amount of oxytocin required, as well as the duration of labor and risk for cesarean delivery among women undergoing induction of labor near term. Pharmacogenomic approaches may potentially be utilized to improve labor outcomes among women undergoing induction of labor.

28 First trimester alcohol exposure alters placental perfusion and fetal oxygen availability affecting fetal growth and development in a non-human primate model

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OBJECTIVE: Prenatal alcohol exposure leads to impaired fetal growth, brain development, and stillbirth. The placenta likely contributes to these adverse outcomes, but the mechanisms and specific vasoactive effects of alcohol linking placental perfusion and oxygenation to impaired fetal development are not known. Recently, we developed MRI techniques in non-human primate models to estimate placental oxygen reserve by measurements of T2*, and perfusion using dynamic contrast enhanced (DCE) MRI. Our objective was to evaluate the adverse effects of first trimester alcohol exposure on placental outcomes and to characterize fetal brain development in-vivo.

STUDY DESIGN: Timed-pregnant Rhesus macaques (n=12) were divided into 2 groups: control (CON, n=6) and ethanol exposed (EE, n=6). Animals were given either 1.5g/kg/day of ethanol (equivalent to 6 drinks/day) or an isocaloric control fluid from preconception until gestational day 60 (G60, term is G168). All underwent Doppler ultrasound (D-US) followed by MRI consisting of...