106 PROGESTATIONAL AGENTS, PROSTAGLANDINS AND PRETERM CERVICAL RIPENING: CRITICAL PATHWAYS FOR PRETERM PARTURITION

HUA XU[1], JUAN GONZALEZ[1], ELLA OFORI[1], BRIANNA LYTTLE[1], MICHAL ELOVITZ[1], [1]University of Pennsylvania, OBGYN; Maternal and Child Health Research Program, Philadelphia, Pennsylvania

OBJECTIVE: Progestational agents (PAs) have been demonstrated to decrease the rates of preterm birth (PTB) in high risk patients—most recently in patients with short cervices. The molecular mechanisms by which PAs prevent PTB—or more specifically cervical ripening are not understood. Prostaglandins (PGs) play a fundamental and complex role in parturition and cervical ripening. This study sought to determine if inflammation-induced PTB and/or PAs altered expression or regulation of mediators in the PG pathway in the cervix.

STUDY DESIGN: E15 CD-1 mice were randomized to 1) intrauterine infusion of saline 2) intrauterine infusion of LPS and 3) pretreatment with medroxyprogesterone acetate (MPA) (1mg/dam) 1 hour prior to intrauterine LPS. Cervices were harvested at 6 hrs for QPCR. In a separate set of experiments, E15 mice were randomized to MPA (1mg/dam) or vehicle and cervices were harvested at 24 hrs QPCR or for immunohistochemistry.

RESULTS: LPS and MPA significantly altered PG expression (TABLE). MPA alone induced the expression of Hpgd, EP2 and EP4 in the absence of inflammation. Hpgd protein expression was decreased by LPS and increased in cervical stroma by MPA.

Genes Involved in Prostaglandin Pathway

	LPS*	LPS+MPA*	MPA**
HPGD	-5.9	-2.2	2.3
COX-2	36.7	35.7	2.3
EP1	2.2	1.0	1.2
EP2	-2.0	1.3	3.7
EP4	-4.1	-1.8	1.8

*Fold change compared to control tissues at 6 hrs
**Fold change compared to vehicle treated at 24 hrs
Shaded cells were significant in pair-wise comparison with P<0.01

CONCLUSION: Intrauterine inflammation can effect PG metabolism in the cervix possibly leading to preterm cervical ripening. The ability of PAs to modulate this effect may be a critical mechanism by which PAs prevent PTB in women with short cervices. This study suggests that exogenous administration of PAs during pregnancy can forestall the natural process of cervical ripening through modulation of the PG pathway in the cervix.

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2008.09.133

107 NEURODEVELOPMENTAL OUTCOME AT 2 YEARS IN PRETERM TWINS TREATED BY AMNIOREDUCTION OR FETOSCOPIC LASER SURGERY FOR TWIN-TO-TWIN TRANSFUSION SYNDROME: COMPARISON WITH DICHORIONIC TWINS.

RICHARD LENCLEN[1], GIUSEPPINA CIARLO[1], ALAIN PAUPE[1], LAURENCE BUSSIERES[2], STEPHANIE STARACI[3], YVES VILLE[3], [1]Poissy/St Germain Hopsital, Department of neonatology, Poissy, France, [2]Unité de Recherche Clinique Paris-Ouest, Hopital Ambroise Paré, Boulogne, France, [3]Paris-Ouest University VSQ, Department of Gynecology and Obstetrics, Paris, France

OBJECTIVE: Long term neurodevelopmental outcome of premature infants from monochorionic pregnancies with twin-to-twin transfusion syndrome (TTTS) treated by amnioreduction (AR) or fetoscopic laser surgery (FLS) was compared with that of dichorionic pregnancies (DC).

STUDY DESIGN: TTTS cases treated and delivered at our center at 24-34 weeks′ of gestation between 2000-2005 were matched for gestational age at birth with dichorionic twins. At 2 years of corrected age, all 333 surviving children (AR=22, FLS=89; DC=222) were assessed with Ages and Stages Questionnaire (ASQ) and standardized physical and neurological examination. Neurodevelopmental impairment was defined by at least cerebral palsy, deafness or blindness.

RESULTS: 94% follow-up was obtained at a median of 24 months. Mean overall ASQ scores and risk of having 2 abnormal ASQ domains (34% v. 27%) were similar in FLS and DC infants. Normal development, minor and major neurological impairment were found in 77 (88.6%), 6 (6.8%) and 4 (4.6%) of the FLS children and this was not different from DC children. Multivariate logistic regression analysis showed that gestational age was the only significant factor associated with neurological impairment in infants born after FLS and in their DC controls. Mean ASQ scores were significantly lower (p=0.01) and risk of having 2 abnormal ASQ domains were higher (60% v. 27%, p=0.005) in AR compared with DC children. Normal development was found in 81% v.93.1% (p=0.07).

CONCLUSION: TTTS children treated in utero with serial amnioreduction have an increased risk of neurodevelopmental delay at 2 years of age. Neurodevelopmental outcome is similar in TTTS infants treated by FLS and in dichorionic controls.

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2008.09.134

108 ASSOCIATION OF VITAMIN D RECEPTOR (VDR) GENE POLYMORPHISMS WITH IDIOPATHIC PRETERM BIRTH (IPTB)

SORINA GRANOVSKY-GRISARU[1], ORLY ELSTEIN[2], ARON TEVET[3], GEONA ALTARESCU[4], MICHAEL S. SCHIMMEL[5], ARNON SAMUELOFF[6], DEBORAH ELSTEIN[7], [1]Shaare Zedek Medical Center, Hebrew University, Obstetrics, Jerusalem, Israel, [2]Shaare Zedek Medical Center, Gaucher Unit, Jerusalem, Jerusalem, Israel, [3]Shaare Zedek Medical Center, Jerusalem, Obstetrics and Gynecology, Jerusalem, Israel, [4]Shaare Zedek Medical Center, Genetics, Jerusalem, Israel, [5]Shaare Zedek Medical Center, Neonatology, Israel, [6]Shaare Zedek Medical Center, Hebrew University Jerusalem Israel, Obstetrics and Gynecology, Jerusalem, Israel, [7]Shaare Zedek Medical Center, Gaucher Clinic, Jerusalem, Israel

OBJECTIVE: Active form of vitamin D (1,25 (OH)(2)D(3) has been established to have potent antiproliferative, immunomodulatory and antimicrobial action, besides its well established effect on bone metabolism. Its receptor VDR is expressed in "non classic" tissues, among which the placenta-decidua. VDR- vitamin D complex regulates key genes associated with implantation. We hypothetized that VDR polymorphisms may be involved the placenta-decidua interface dysfunction intrinsic to IPTB. We aimeed to determine the relationship between IPTB and VDR polymorphisms.

STUDY DESIGN: Case control study (2007-2008). Paired maternal & neonatal blood samples from 21 mothers that had IPTB (24-35 weeks gestation): (excluded: multifetal pregnancy, fetal anomalies, prolonged PPROM, vaginal bleeding, chorioamnionitis, uterine malformations, cervical cerclages) compared to 98 cases of term uncomplicated births. PCR amplification with appropriate endonucleases to identify VDR polymorphisms: FokI, ApaI, TaqI, BsmI. Statistics: Descriptive, Fisher exact test. Software: PHASE 2.0 and SAS 9.2; to test additive effect of polymorphisms we used logistic regression.

RESULTS: Maternal age and ethnicity were comparable among the study groups. Parity and the number of live children were lower in the IPTB. All four VDR polymorphisms were in Hardy Weinberg equilibrium for the control group. The maternal **FokI VDR** polymorphism carrier frequency was significantly increased in the IPTB (p< 0.03) **5.5 OR** (95%CI: 1.14-9). The other genotypes showed non-significant variation between the study groups .The haplotype combinations analysis recapitulated a similar pattern. We found no significant difference for either genotype among the neonates.

CONCLUSION: We were able to identify **FokI VDR** as an inherited maternal risk trait for IPTB. This may provide an explanatory mechanism by which environmental/ dietary vitamin D can modulate the placenta- decidua relationship resulting in a tendency for IPTB. This selective population may benefit from vitamin D/VDR targeted therapeutic actions .

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2008.09.135

109 THE EFFECT OF EXPOSURE TO ANTENATAL CORTICOSTEROIDS ON THE RATE OF RESPIRATORY MORBIDITY AMONG LATE PRETERM INFANTS

KARIN FUCHS[1], KAREN SCOTT[1], PHYLLIS GYAMFI[2], CYNTHIA GYAMFI[1], [1]Columbia University, New York, New York, [2]ORC Macro, Applied Research Division, Atlanta, Georgia

OBJECTIVE: To evaluate whether exposure to antenatal corticosteroids affects the rate of respiratory morbidity among late preterm infants.

STUDY DESIGN: This was a retrospective cohort study of late preterm infants (defined as 34 0/7 and 36 6/7 weeks) delivered between January 2005 and December 2006. Records were reviewed to determine the gestational age at delivery, mode of delivery, plurality, gender, maternal diabetes, antenatal steroid exposure (ACS), and newborn respiratory outcome. Neonatal respiratory morbidity was defined as respiratory distress syndrome (RDS), transient tachypnea (TTN), or use of therapeutic CPAP or mechanical ventilation. Cases with major fetal malformations were excluded.

RESULTS: In a cohort of 722 infants, 136 (18.8%) had received a complete course of ACS prior to delivery (mean: 30.0 days; range: 1-82 days). Of neonates exposed to ACS prior to delivery, 36 (5%) had received ACS within 14 days of delivery. There was a higher frequency of respiratory morbidity among neonates exposed to ACS within 14 days of delivery (6/36; 16.7%) than among those never exposed (87/586; 14.8%). After controlling for other factors associated with respiratory morbidity, however, there was a trend towards decreased respiratory morbidity among neonates exposed to ACS within 14 days of delivery (OR 0.385; p 0.057). Only gestational age and mode of delivery were associated with a statistically significant impact on respiratory morbidity.

CONCLUSION: Although exposure to ACS within 14 days of delivery is associated with a trend toward decreased risk of respiratory morbidity, respiratory outcomes among late preterm infants appear to be influenced by gestational age at delivery and mode of delivery.

Influence of ACS exposure and obstetric factors on respiratory morbidity of late preterm infants:

	Adj OR	95% CI	p
ACS < 14 days	0.385	0.144, 1.030	0.057
GA	0.328	0.245, 0.440	<0.005
Cesarean delivery	1.817	1.066, 3.096	0.028
Male gender	1.383	1.066, 1.383	0.182
Maternal diabetes	0.922	0.443, 1.922	0.829
Twin	0.865	0.517, 1.450	0.583

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2008.09.136