CARDIOVASCULAR DETERIORATION IN FETAL GROWTH RESTRICTION (FGR)

PROGRESSES IN THREE CHARACTERISTIC PATTERNS

OBJECTIVE: To identify the temporal sequence of arterial and venous Doppler abnormalities from the onset of placental insufficiency until delivery in FGR.

STUDY DESIGN: Singleton FGR (abdominal circumference <5th %ile) were studied prospectively, with umbilical artery (UA), middle cerebral artery (MCA), ductus venous (DV) and umbilical vein (UV) Doppler. Time intervals between progressive Doppler abnormalities and the sequence of Doppler changes defined characteristic patterns.

RESULTS: 688 longitudinal exams were performed in 104 fetuses identifying 3 patterns of progression. 1) Mild placental dysfunction (n=34): abnormality was confined to the UA/MCA. UA normal until 32 weeks (w, median) but never escalated >3 SD. Progression took 33 days requiring delivery at 35 w. 2) Progressive placental dysfunction (n=49): In 9 day intervals, normal UA Doppler (29 w) increased >3 SD, followed by onset of abnormal MCA, UA diastolic flow absent/reversed, abnormal venous Doppler requiring delivery by 33 w. III. Severe early placental dysfunction (n=21). UA Doppler markedly elevated by 27 w with rapid progression (7 day interval) to abnormal venous Doppler with delivery at 30 w. Gestational age at onset, time to delivery and progression intervals were significantly different between patterns (p<0.05 for all).

CONCLUSION: Cardiovascular manifestations in fetal growth restriction progress in three characteristic patterns that differ significantly in their gestational age at onset, speed of progression and degree of cardiovascular compromise. Recognition of these characteristics is critical for planning fetal surveillance in FGR.

0002-9378/$- see front matter
doi:10.1016/j.ajog.2007.10.542

PAPP-A AS A PREDICTOR FOR PREGNANCY OUTCOME IN EARLY-ONSET FETAL GROWTH RESTRICTION

Nathan Fox1, Stephen T. Chase1, Weill Cornell Medical College, Obstetrics and Gynecology, New York, New York

OBJECTIVE: Fetal growth restriction is associated with poor neonatal outcomes. Early-onset growth restriction may represent very early placental dysfunction. Low first-trimester levels of PAPP-A have been associated with subsequent fetal growth restriction. Our hypothesis is that low PAPP-A can be used to identify those fetuses with early-onset growth restriction at risk for poor perinatal outcome.

STUDY DESIGN: We analyzed outcomes for pregnancies in our unit with evidence of growth restriction in the second trimester who also had 1st trimester serum PAPP-A measured for aneuploidy risk assessment. We excluded multiple pregnancies and pregnancies with aneuploidy, major anomalies, fetal infection, or second trimester PPROM.

RESULTS: 199 pregnancies with early onset growth restriction and 1st trimester serum PAPP-A measurements were identified. PAPP-A below the 5th percentile was associated with an increased rate of third trimester SGA (<10th percentile; 50% vs. 11% p=0.011), IUFD (10% vs. 0%, p=0.03), preterm birth (33% vs. 8%, p=0.04), NICU admission (33% vs. 8%, p=0.04), IUFD or neonatal death (20% vs. 0%, p=0.002), smaller median birth weight (2795g vs. 3085g, p=0.03), and earlier median gestational age at delivery (38 1/7 vs. 39 6/7, p=0.004). PAPP-A percentile was positively correlated with birthweight (Pearson correlation .22, p=0.002) and gestational age at delivery (Pearson correlation .20, p=0.006).

CONCLUSION: PAPP-A is a useful marker for neonatal outcome in patients diagnosed with early-onset fetal growth restriction.

0002-9378/$- see front matter
doi:10.1016/j.ajog.2007.10.543

ACUTE ALCOHOL EXPOSURE INDUCES SIGNIFICANT APOPTOSIS IN THE MID-GESTATION EMBRYONIC LUNG

XIANGYU WANG1, PRASRA GOMUTPUTRA2, DEBRA WOLGEMUTH3, LAXMI BAVK1.

OBJECTIVE: Maternal alcohol abuse during pregnancy produces an array of birth defects comprising fetal alcohol syndrome with craniofacial and neural defects. A hallmark of fetal alcohol syndrome, intrauterine growth restriction, is associated with elevated apoptosis of placental cytrophoblasts. Acute exposure to ethanol of selected cells in day 7, 8, and 9 mouse embryos (late first trimester and early second trimester of gestation) can initiate apoptosis leading to altered differentiation within 12 hrs. Lung development depends greatly upon the balance between cell proliferation and apoptosis. In the present study, we therefore tested the hypothesis that acute exposure to alcohol during mid-gestation can also induce apoptosis and affect differentiation and subsequent function of developing organs and tissues, specifically the lung.

STUDY DESIGN: Pregnant C57BL/6j mice at day 13.5 of gestation were injected intra-peritoneally with 2 doses of 25% ethanol (3.75g/kg ), 4 hours apart (Alcohol-exposed: AE) or with Ringer’s solution (Controls: C). Six AE and five C fetuses were retrieved 16 hours later and the lungs were fixed and processed for morphological evaluation and for TUNEL assay. Three areas were selected randomly from each sample and the total number of cells and apoptotic-positive cells were counted in the bronchial epithelium and in the mesenchyme and analyzed for statistical significance.

RESULTS: In embryonic day 13.5 lung tissue exposed to alcohol, there were 8% apoptotic cells in the mesenchyme and 17% in the epithelium, while there were < 2% in the control tissues. (P < 0.0001; P < 0.05, respectively).

CONCLUSION:

1. Acute alcohol exposure at mid-gestation induced significant apoptosis in the embryonic lung, which is consistent with our previous studies showing delayed lung development in AE mice.

2. Additionally, this finding concurs with epidemiologic studies showing a higher risk of fetal lung malformations in intrauterine alcohol exposure

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.544