Abstracts

PM.09 | THE EFFECT OF GLUCOCORTICIDS ON ANGIOGENESIS IN THE HUMAN PLACENTA

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Background Fetal growth restriction (FGR) is associated with glucocorticoid (GC) excess in human pregnancies and animal models. In mice and rats, GC treatment reduces placental angiogenesis and dysregulates the expression of angiogenic factors. It is not known whether GCs reduce angiogenesis in the human placenta.

Hypothesis Glucocorticoid excess in the human placenta inhibits angiogenesis by dysregulating angiogenic factors.

Methods Human umbilical vein endothelial cells (HUVECs) and human placental artery endothelial cells (HPAECs) were treated with hydrocortisone (HC), prednisolone (PRED) and dexamethasone (DEX) for 24–48 hours. Tube-like structure (TLS) formation on matrigel, cell migration, proliferation and apoptosis were assessed. Chorionic plate arteries (CPAs) from normal placentas (n = 10) were cultured for 48 hours with HC or DEX. mRNA expression of six angiogenic factors were quantified using real-time Q-PCR with normalisation to TBP.

Results In experiments in HPAECs (n = 40), tube formation (tr), cell migration (cm), proliferation (p) and apoptosis (a) were assessed. HC and DEX treatment reduced the expression of fibroblast growth factor-2 (FGF-2) (p < 0.001), matrix metalloproteinase-16 (p < 0.001), VEGF-A (p < 0.01), VEGF-C (p < 0.01), matrix metalloproteinase-1 (p < 0.05) and CCL-2 (p < 0.05) compared to vehicle control cells. GCs had no effect on cell proliferation, apoptosis or viability. HC and DEX treatment reduced the expression of fibroblast growth factor-2 (FGF-2) (p < 0.001), interleukin-8 (p < 0.001), VEGF-A (p < 0.01), VEGF-C (p < 0.01), matrix metalloproteinase-16 (p < 0.01), matrix metalloproteinase-1 (p < 0.05) and CCL-2 (p < 0.05).

Discussion GCs reduced tube formation and cell migration, key facets of angiogenesis, in HUVEC and HPAEC models. These findings indicate that GCs inhibit human placental angiogenesis, which could contribute to the pathogenesis of FGR. The downregulation of specific angiogenic factors by GCs identifies putative mechanistic pathways involved.

PM.10 | ARE LOW PAPP-A CONCENTRATIONS ASSOCIATED WITH PLACENTALLY-MEDIATED COMPLICATIONS IN WOMEN WITH ANTI-PHOSPHOLIPID SYNDROME (APS)?

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Women with antiphospholipid syndrome (APS) have pregnancies complicated by placenta-mediated events whereas women with antiphospholipid antibodies (aPL) have similar pregnancy outcomes to the normal population. Low PAPP-A concentrations are useful in predicting adverse pregnancy outcomes in the general population. We aimed to determine whether PAPP-A concentrations could identify women with APS at risk of adverse outcomes.

Methods This retrospective case control study included all women with singleton pregnancies (without fetal anomalies) with persistent aPL and PAPP-A concentrations between 2008 and 2012. The women were grouped as those fulfilling the classification criteria for APS and those who had persistent aPL without a history of thrombosis or adverse pregnancy outcomes. Data obtained included demographic details, medical comorbidities, aPL subtypes, nicotine use. Pregnancy outcomes included live birth, miscarriages > 10 weeks, pre-eclampsia, abortion, birthweight.

Results Sixty-one cases were identified. There were no significant differences in maternal baseline characteristics. Live birth rates were similar between both groups. There were significant differences (p < 0.05) between all placenta-mediated complications, birthweight and customised birthweight centiles. However, despite these complications, PAPP-A concentrations were similar. There was no trend towards adverse outcomes with lower PAPP-A concentrations.

Conclusion Despite the high rate of placenta-mediated complications in women with APS, a low PAPP-A was not useful in predicting these complications.

PM.11 | A LABEL-FREE SRM WORKFLOW IDENTIFIES A SUBSET OF PREGNANCY SPECIFIC GLYCOPROTEINS AS NOVEL PREDICTIVE MARKERS OF EARLY-ONSET PRE-ECLAMPSIA

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Objective The aim of this study was to identify and verify plasma protein markers which may add to predictive algorithms for pre-eclampsia (PE) in asymptomatic nulliparous women.

Methods We used a quantitative mass spectrometry (MS) approach to identify proteins with abundance changes in plasma (15 weeks) taken from women who subsequently develop PE recruited to the international SCOPE study. We developed a novel, targeted, label-free MS method, selective reaction monitoring (SRM) which enabled robust and reproducible verification of these proteins in a further 100 samples (16 early-onset PE, 42 late-onset PE, 42 controls).

Results We identified and quantified >500 plasma proteins, and prioritised a set of candidate predictive markers. The two most promising, Platelet Basic Protein (PBF/NAP-2) and Pregnancy-specific glycoprotein (PSG)-9 were selected for further verification. The SRM method was validated extensively using dilution experiments for PSG proteins and by comparison to a commercial ELISA for NAP-2. NAP-2 was only elevated in a subset of women with PE, however, peptides unique to PSG-9 and PSG-5 were consistently elevated in women with subsequent early onset PE (p < 0.01; AUCs 0.72–0.75). Other PSG peptides were not different between groups.

Conclusion This study has identified specific PSG proteins as being predictive of early-onset PE. Importantly, use of a highly specific MS method has enabled measurement of individual PSG family members which has not been possible using antibody-based techniques. Future work is needed to determine whether these proteins will improve current prediction algorithms for the identification of PE in low risk nulliparous women.