

Poster Presentations

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Betamethasone: a novel therapeutic intervention for preeclampsia

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The early pathogenesis of preeclampsia (PE) involves a systemic inflammatory immune response. Recent data demonstrate that increased circulating arginine vasopressin (AVP) in humans is predictive of PE and that infusion of AVP in mouse dams phenocopies the pregnancy-specific cardiovascular and immune alterations observed in human PE. Specifically, AVP suppresses anti-inflammatory cytokines and cells. Betamethasone (BMTZ), commonly given to women at risk for preterm birth, is both an AVP and immune response modulator. We hypothesize that early treatment with BMTZ will prevent the development of AVP-induced PE.

C57BL/6J dams were infused with AVP (24 ng/hour) or saline throughout gestation via osmotic minipump. AVP dams received a single subcutaneous injection of BMTZ (100ug) early post-placentation (gestational day (GD) 7). Blood pressure was measured throughout pregnancy. Total protein was measured on 24 hour urine collected on GD 17. Maternal and fetal tissues were collected on GD 18. Cytokine concentrations were determined via commercially available ELISAs and normalized to total protein.

BMTZ reversed the hypertension (ANOVA n=11, p=0.007) and proteinuria (ANOVA n=11, p=0.025) induced by

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AVP. BMTZ reversed the AVP-induced decreases in the maternal and fetal anti-inflammatory responses. In maternal kidney, both anti-inflammatory IL-4 (AVP: 0.034, n=10 vs BTMZ: 0.092, n=5 ug/g, p<0.05) and TGFb (AVP: 4.3, n=10 vs BTMZ: 9.2, n=5 ug/g, p<0.05) were increased in BMTZ-treated dams. Decreases in fetal kidney IL-4 (AVP: 0.013, n=5 vs BTMZ: 0.043, n=5 ug/g, p<0.05), IL-10 (AVP: 1.2, n=5 vs BTMZ: 2.1, n=5 ug/g, p=0.05), and TGFb (AVP: 1.8, n=5 vs BMTZ: 2.9, n=5 ug/g, p<0.05) were reversed with BMTZ treatment. Lastly, placental concentrations of IL-4 (AVP: 0.002, n=5 vs BTMZ: 0.005, n=5 ug/g, p<0.05) and TGFb (AVP: 0.090, n=5 vs BTMZ: 1.4, n=5 ug/g, p<0.05) were also improved following BMTZ in AVP-infused dams.

Supportive of our hypothesis, early BMTZ treatment prevented hypertension and reduced proteinuria in AVP-infused dams. BMTZ also reversed AVP-induced inhibition of anti-inflammatory responses, creating a more tolerogenic milieu. These data support the concept for the potential use of BMTZ in early gestation as a novel preventative agent for PE.

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