Experimentally induced placentitis in late gestation mares with *Streptococcus equi* zooepidemicus: therapeutic prevention of preterm birth

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Placental infection due to opportunistic pathogens (i.e., *Streptococcus equi* subspecies *zooepidemicus* (*S. equi*)) is the single most common cause of abortion, stillbirth and premature delivery in horses. Recent evidence suggests that placentitis increases proinflammatory cytokine expression leading to premature delivery. The objective of this study was to evaluate the efficacy of using antibiotics alone or in combination with immunomodulators to prevent preterm birth and increase foal viability in mares experimentally infected to induce ascending placentitis.

Twenty three pregnant (299.4 ± 1.7 d; light breed) mares were assigned to one of four treatments. Seventeen were infected (298 ± 1.6 d) by intra-cervical inoculation with *Streptococcus equi* zooepidemicus (∼2\times10^6 CFU) and assigned to receive trimethoprim sulfamethoxazole (TMS; 30 mg/kg, q 12 h, PO, n = 6) alone; or with either dexamethasone (D) given over 6 d with decreasing doses every two d (TMS+D; 40, 35, 25 mg, respectively, q 24 h, IV, n = 6) or acetylsalicylic acid (TMS+A; 50 mg/kg, q 12 h, PO for 6 d, n = 5). Six mares served as uninfected controls (CN). Blood samples were collected pre- and post-infection at 12, 24, 48, 72 h and 3x/week thereafter until delivery for progesterone (P4) analysis. Fetal and placental well-being was evaluated daily by ultrasonography. Treatment commenced upon signs of vaginal discharge and/or placental changes. Blood was collected from foals at 0 and 24 h post-partum for CBC, IgG and P4. Inoculation induced vaginal discharge within 48 h and increased (P<0.05) combined thickness of uterus and placenta in all mares (0.83 ± 0.03 to 1.5 ± 0.1 cm). Mean serum P4 was not affected by inoculation or drug treatment, but P4 concentrations in foals of infected dams ranged from 4.6 to 24.5 and 0.9 to 15.3 ng/mL, and from 1.8 to 9.9 and 0.5 to 1.8 ng/mL in foals of control dams at 0 and 24 h, respectively. Mean gestational age at term was less (307.6 ± 3.7 d; P < 0.05) in TMS+D mares than in the other groups (CN, 338 ± 5.0; TMS, 318.8 ± 5.0; TMS+A, 322.6 ± 6.6 d). Birth weights were lower in TMS+D foals (36. 8 ± 1.7 kg; P <0.05) compared to foals of mares in the other treatment groups (CN, 45.5 ± 4.0; TMS, 44.6 ± 2.9; TMS+A, 45.2 ± 3.0 kg), but birth weight-placental weight ratio was higher (P <0.05) in all infected mares compared to controls. Placental pathology confirmed necrosuppurative placentitis in all inoculated mares. Mares delivered six viable foals in the CN group, four in each of the infected groups, two aborted in the TMS group, one live (euthanized at 24 h) and one aborted in the TMS+D group and one aborted in the TMS+A group. In these studies, four of the six (67%) mares treated with antibiotics alone had successful pregnancy outcomes compared with 8 of 11 (73%) mares treated with the drug combination, suggesting that aggressive therapy with antibiotics can substantially improve pregnancy outcome.
Acknowledgement
Funded by MSU-SRI #341080

Keywords: Mare, placentitis, antibiotics, immunomodulators