

Abstracts

THE DETECTION OF PLACENTAL DRUG TRANSFER IN EQUINE ALLANTOIC FLUID

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Placentitis is the most prevalent cause of equine abortion, and remains a large source of economic loss to the breeding industry. Current treatment modalities have been inconsistent in preventing infection-associated premature labor. The primary objective of this study was to determine the ability of selected drugs to pass through the blood–placental barrier in normal mares and mares with experimentally induced placentitis. We hypothesized that placentitis would not alter the pharmacokinetic profiles or the free concentrations of selected therapeutic agents in allantoic fluid. Ten late-gestational mares (276–300 d of gestation) were used for this study. Placentitis was induced in five mares using an intracervical inoculation of *Streptococcus equi* subspecies *zooepidemicus* (10^7 CFU) prior to sample collection. Five mares served as uninfected controls. Allantoic fluid drug concentrations were determined for all mares by *in vivo* microdialysis. Prior to drug treatments, a microdialysis probe was implanted in the allantoic cavity using transabdominal ultrasound guidance. Trimethoprim–sulfamethoxazole (TMP–SMZ, 30 mg/kg, q 12 h, PO) and pentoxifylline (PTX, 8.5 mg/kg, q 12 h, PO) were administered until abortion or parturition for a maximum period of 2 wk. Microdialysate samples were collected continuously for a period of 36 h in conscious, free-standing mares. Drug concentrations were analyzed by reverse-phase high performance liquid chromatography with ultraviolet spectroscopy. Peak drug concentrations, time-to-peak intervals, and total drug concentrations (reported as area-under-the-curve) were recorded as means $\pm$ standard error. Control versus infected groups were statistically compared using a non-parametric Wilcoxon Rank-Sum Test ($p < 0.05$). Mean TMP and SMZ levels were compared to the minimum inhibitory concentration (MIC) reported for *in vitro* control of *S. equi zooepidemicus*. Mean PTX levels were compared to concentrations reported to inhibit

inflammatory responses in vitro. All drugs exhibited placental transfer and were detectable by microdialysis sampling. No significant differences were detected between control and infected mares with regard to peak levels of TMP, SMZ, or PTX in allantoic fluid. Maximal drug concentrations in control versus infected mares were $0.5 \pm 0.1 \mu\text{g/ml}$ versus $0.6 \pm 0.2 \mu\text{g/ml}$ (TMP; $p = 0.89$), $7.8 \pm 1.1 \mu\text{g/ml}$ versus $7.0 \pm 0.7 \mu\text{g/ml}$ (SMZ; $p = 0.67$), and $1.3 \pm 0.2 \mu\text{g/ml}$ versus $1.2 \pm 0.4 \mu\text{g/ml}$ (PTX; $p = 0.89$). Based upon reported MIC values against *S. equi zooepidemicus*, the levels of TMP and SMZ in allantoic fluid should be sufficient to elicit an antibiotic effect for up to 4 h following each treatment in control and infected mares. However, it is unclear whether allantoic levels of PTX are sufficient to elicit any therapeutic action in vivo. The passage of the selected drugs through the blood–placental barrier was unchanged in mares with experimentally induced placentitis, and there were non-linear relationships between drug levels in plasma and allantoic fluid.

Keywords: Placentitis; Microdialysis; Trimethoprim; Sulfamethoxazole; Pentoxifylline