Administration of ceftiofur crystalline free acid (CCFA) to pony mares with placentitis

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Ascending bacterial equine placentitis initiates inflammation, uterine contractions and preterm delivery. Treatment protocols for placentitis have included antimicrobials, anti-inflammatory agents and progestins. In 2010, a long-acting preparation of ceftiofur crystalline free acid (CCFA) with broad-spectrum bactericidal activity was approved for use in horses. Our objectives were to determine the pharmacokinetics of CCFA in pregnant mares with placentitis, evaluate the disposition of CCFA in fetal fluids, fetal membranes, colostrum and serum from foals, and to obtain pilot data on the efficacy of CCFA for improving foal survival in mares with induced placentitis. We hypothesized that administration of CCFA to mares with placentitis would result in therapeutic concentrations of desfuroylceftiofur acetamide (DCA, the acetamide derivative of ceftiofur) in tissues and fluids of mares and foals. Twelve reproductively normal, pregnant pony mares were assigned to one of three groups: CEFT (n = 3; CCFA 6.6 mg/kg, IM, q96h; Excede® Pfizer Animal Health, Kalamazoo, MI); COMBO (n = 6; CCFA 6.6 mg/kg, IM, q96h; altrenogest, 0.088 mg/kg, PO, q24h; pentoxifylline 8.5 mg/kg, PO, q12h); UNTREAT (n = 3; infected, untreated controls). From March through May in 2010, each mare was inoculated intracervically with $10^7$ CFU $S. \text{zooepidemicus}$ on day 286 of gestation (range 280-294). Treatment began at the onset of clinical signs (ultrasonographic evidence of increased combined thickness of uterine and placental CTUP, placental separation, mammary gland development, or vulvar discharge).

Concentrations of DCA were measured in multiple tissue and fluid compartments from mares and foals. Serum DCA concentration versus time data was analyzed by noncompartmental pharmacokinetics. Significance was assigned for values $P < 0.05$. The serum half-life of DCA in pregnant mares with placentitis was $56.5 \pm 20.5$ h. Maximum and minimum serum concentrations of DCA at steady state in treated mares were $2.40 \pm 0.40 \mu g/mL$ and $1.06 \pm 0.29 \mu g/mL$, respectively, which is similar to that in non-pregnant horses. Concentration of DCA in colostrum was $1.51 \pm 0.60 \mu g/mL$. Concentrations of DCA in placental and fetal tissues (median = 0.03 µg/mL) were below the minimum inhibitory concentration of relevant pathogens (0.2 µg/mL); DCA was not detected in amniotic fluid or serum from live foals. Treatment did not improve foal survival (Group CEFT: 0/3; Group COMBO: 2/6; Group UNTREAT: 2/3). Bacteria were recovered from the uterus of most mares and fetal/neonatal blood samples regardless of treatment group. The survival data were complicated by the unexpected number of live foals from infected, untreated mares (attributed to technical failure when placing bacteria in the mare’s cervix). The results of this study do not support the use of CCFA at the recommended dose for the treatment of placentitis in mares.

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