Endometrial tissue concentrations of ceftiofur following intrauterine infusion in mares
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Evidence based guidelines on appropriate dosing intervals for intrauterine ceftiofur treatment of bacterial endometritis are lacking. The aim of this study was to determine endometrial concentrations of ceftiofur for 48 h following intrauterine infusion in a healthy uterus. It was hypothesized that endometrial tissue concentrations of desfuroylceftiofur-acetamide (DCA; active metabolite of ceftiofur) would remain above the MIC90 for *Streptococcus equi zooepidemicus* (*S. zooepidemicus*) and *Escherichia coli* (*E. coli*) for greater than 24 h.

Six clinically healthy, non-pregnant mares, of various breeds (age 5-21 years; weight 525-578 kg) were included in the study. Samples were taken during estrus for uterine biopsy, culture, and cytology. Only mares that were free from uterine pathology were included in the study (Kenney-Doig biopsy score of I or IIA, negative uterine cultures and less than 3 polymorphonuclear neutrophils per high power field on cytology). Endometrial biopsy samples were taken immediately prior to the intrauterine infusion of 1g ceftiofur (diluted in sterile saline to a total volume of 60 ml). Further endometrial biopsy samples were taken at 4, 8, 12, 24, 36 and 48 h after ceftiofur infusion. Tissue samples were stored at -20°C until analysis. Desfuroylceftiofur-acetamide levels in endometrial tissue were measured using liquid chromatography-mass spectrometry at each time point. Data were analyzed with a Wilcoxon signed-rank test.

At all time points, endometrial tissue concentrations of DAC were well above the MIC90 for *S. zooepidemicus* (0.25 mcg/ml) and *E. coli* (0.5 mcg/ml). At 24 h DCA concentrations were different from the MIC90 for *S. zooepidemicus* and *E. coli*, (*P* =0.031, *N*=6, range 8-660 mcg/ml). At 48 h after infusion DCA endometrial tissue concentrations were still elevated above the MIC90 for *S. zooepidemicus* and *E. coli*, however one mare was removed from the study at 24 h (*P* =0.065, *N*=5, range 3-114 mcg/ml).

The results of this study support the clinical use of once daily intrauterine infusions of ceftiofur. They also suggest that less frequent dosing may be appropriate as all mares tested at 48 h had levels above therapeutic concentrations. Further studies are required to determine the effects of inflammation on tissue concentrations of DCA and if endometrial tissue levels of DCA remain above therapeutic concentrations for greater than 48 h and therefore if even less frequent dosing intervals can be justified.

**Keywords:** Bacterial endometritis, ceftiofur, Endometrial biopsy

**Reference**