

Pharmacokinetics of two dry-cow intramammary antimicrobials in dairy goats

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Introduction

There are currently no intramammary antimicrobials approved for use goats in the United States. However, mastitis – both clinical and subclinical – is a major challenge for dairy goat producers. Determining plasma pharmacokinetic parameters of various intramammary antimicrobials in goats can assist in treatment recommendations and meat and milk withhold recommendations.

Materials and methods

This study included 24 healthy lactating does, of which 12 were treated with 300 mg of cephapirin benzathine (ToMORROW[®], Boehringer Ingelheim Vetmedica, Duluth, GA) per half (600 mg per goat) and 12 others with 500 mg cloxacillin benzathine (Orbenin[™] DC, Merck & Co., Rahway, NJ) per half (1,000 mg per goat) via intramammary infusion. Plasma samples were collected before treatment and at 1, 3, 6, 12, 24, 36, 48, 73, 96, 120, 144 and 168 hours post-treatment. Samples were analyzed by liquid chromatography with tandem mass spectroscopy (LC-MS-MS). Pharmacokinetic parameters were determined using noncompartmental methods with commercial software (MonolixSuite, Lixoft, Antony, France) and reported as geometric means except time-associated parameters (T_{max} , $T_{1/2}$, λ_z , and MRT), which are reported at harmonic means.

Results

The C_{max} for cloxacillin was 0.077 $\mu\text{g/mL}$ and occurred at an average T_{max} of 24 hours. The $AUC_{0 \rightarrow \infty}$ was 8.22 $\text{h} \times \mu\text{g/mL}$ (CV 21.09). MRT_{last} was 65.72 hours (CV 39.68) and $MRT_{0 \rightarrow \infty}$ was 139.02 hours (CV 39.68) while $T_{1/2}$ was 93.83 hours (CV 46.96). CEPH was detected in all does through 48 hours post-treatment and then dropped below the LOQ for all but one by 60 hours post-treatment. A single doe had a C_{max} of 0.007 $\mu\text{g/mL}$ which was 1/7 the mean with residues persisting to 144 hours post-treatment. The C_{max} for cephapirin was 0.069 $\mu\text{g/mL}$ (CV 64.73) which occurred at an average T_{max} of 7.75 hours (CV 41.95). The $AUC_{0 \rightarrow \infty}$ was 1.02 $\text{h} \times \mu\text{g/mL}$ (50.26). MRT_{last} was 14.34 hours (CV 27.04) $MRT_{0 \rightarrow \infty}$ was 18.87 hours (CV 77.4) while $T_{1/2}$ was 10.16 hours (CV 88.3).

Significance

This study described the plasma pharmacokinetic parameters of intramammary dry-cow products in dairy goats. It was noted that cloxacillin had a substantially longer $T_{1/2}$ and AUC as compared with cephapirin, likely due to differences in solubility. The results of this study can be used to plan tissue and milk residue depletion studies more accurately.

