Effect of topical treatment of claw horn lesions with tetracycline-derivatives on plasma and milk concentrations

J. Coetzee, BVSc, Cert CHP, PhD, DACVCP 1; K. Kleinhenz, DVM, MS 1; B. Pingsterhaus, BS 1; J. Schleining, DVM, MS, DACVS 1; P. Wulf, PhD 1; J. Shearer, DVM, MS, DACAW 1;

1Veterinary Diagnostic and Production Animal Medicine, Iowa State University, Ames, Iowa

Introduction:

Claw horn lesions frequently result in lameness, and these types of lesions are associated with environment and animal husbandry practices rather than infectious pathogens. The paucity of scientific literaturerepertiing to intervention strategies for these lesions promote therapeutictrimming techniques with or without the application of a hoof block to the contralateralclaw and producer-dependent use of systemic antibiotics and analgesics. In a recent survey of hoof trimmers andveterinarians, 53% of trimmers and 59% of veterinarians reported using topicalapplication of medications to solar lesion, with extra-label use oftetracycline-derivatives being the most frequently reported topicalmedication. In the advent of modernanalytical technology, more sensitive assays are available to detectpharmaceuticals present in consumable animal products. These assays offer amore sensitive evaluation of residues involving the topical application oftetracycline-derivatives, which warrants concerns over the potential forviolative residues. Given these lesions resultin exposure of raw corium and granulation tissue, the potential of topicalmedications entering the systemic blood circulation in treated animals ispossible, and yet, no research has assessed if extra-label use oftetracycline-derivatives results in violative drug residues in plasma and milk. Our hypothesis is extra-label use oftetracycline-derivatives results in drug residues in both plasma and milk;however, the concentrations would not surpass the Food and Drug Administration’sreprinted acceptable level, 300 ppb.

Materials and Methods:

Eight Holsteins and 3 Jerseys diagnosed with either a sole ulcer or a white line lesion at hooftrimming events were topically treated with either oxytetracycline HCl (7animals) or tetracycline (4 animals). Digitalimages were taken of each lesion. The 7animals treated with topical oxytetracycline HCl received 7.3 grams of activeingredient. Prior to treatment, milk andplasma samples were collected. Following treatment, plasma was collected once a day for 3 days, and milk was collectedat each milking (3 times per day) for 3 days. The 4 animals topically treated with tetracycline had milk and plasmasamples collected prior to treatment. Following treatment, milk and plasma samples were collected twice a dayfor 3 days. Plasma and milk samples weredrozen after collection and submitted to Iowa State’s Pharmacology AnalyticalSupport Team
(PhAST) laboratory where drug concentrations were quantified using liquid chromatography-mass spectrometry. To calculate lesion surface area, the digital images were evaluated using free software, ImageJ, available through U. S. National Institute of Health. Statistical analysis was performed using JMP (JMP 10.00, SAS Institute, Cary, NC).

**Results:**

The Cmax for tetracycline in plasma (mean ± SEM, 4.78 ± 2.82 ng/ml; 95% confidence interval [CI], -4.40 to 13.95 ng/ml) was recorded at the time the medicated bandage was applied, and the Cmax for tetracycline in milk (mean ± SEM, 20.64 ± 14.51 ng/ml; 95% CI, -12.17 to 53.46 ng/ml) was recorded at the 3rd milking (milking 2x/day). The Cmax for oxytetracycline in plasma (mean ± SEM, 2.15 ± 1.20 ng/ml; 95% CI, -0.52 to 4.81 ng/ml) was recorded at 48 hours post topical application, and the Cmax for oxytetracycline in milk (mean ± SEM, 20.81 ± 19.90 ng/ml; 95% CI, -27.88 to 69.51 ng/ml) was recorded at the 7th milking (milking 3x/day). Greater log-transformed surface area measurements of lesions tended to be positively associated with higher log-transformed drug concentrations in both plasma (R²=0.51; P=0.03) and milk (R²=0.44; P=0.03).

**Significance:**

Results suggested cows with larger claw lesions exposed to tetracycline derivatives tend to absorb more drug into systemic circulation. Tetracycline concentrations are inclined to peak faster in both plasma and milk when compared to oxytetracycline HCl. It was noted that the time zero concentration for the 3 of the 4 tetracycline plasma samples contained a trace of drug, and due to the levels being so low, we hypothesize this is contamination from the trimmer’s hands at the time of plasma collection. Plasma drug levels were lower than milk concentrations likely because the sampling schedule was designed to capture drug depletion in milk as opposed to the systemic circulation. Milk concentrations therefore represented the cumulative secretion of drug in the milk between milkings. Although it is shown that tetracycline-derived residues do enter systemic circulation and ultimately milk following topical application of medicated hoof wraps, the level of drug reported is unlikely to result in residue violations if administered to individual cows.