Tulathromycin metaphylaxis increases prevalence of multidrug resistant *Mannheimia haemolytica* while improving health in stocker calves

W. B. Crosby,1 DVM; B. B. Karisch,2 PhD; L. M. Hiott,3 MS; J. D. Loy,4 DVM, PhD; W. B. Epperson,1 DVM, DACVPM (Epidemiology); S. F. Capik,5 DVM, PhD; P. S. Morley,7 DVM, PhD, DACVIM-LA; A. R. Woolums,1 DVM, PhD, DACVIM-LA, DACVM

1Department of Pathobiology and Population Medicine, College of Veterinary Medicine, Mississippi State University, Mississippi State, MS, 39762
2Department of Animal and Dairy Sciences, College of Agriculture and Life Sciences, Mississippi State University, Mississippi State, MS, 39762
3Bacterial Epidemiology & Antimicrobial Resistance Research, U.S. National Poultry Research Center, USDA-ARS, Athens, GA, 30605
4Nebraska Veterinary Diagnostic Center, School of Veterinary Medicine and Biomedical Sciences, University of Nebraska, Lincoln, NE, 68583
5Texas A&M AgriLife Research, Texas A&M University System, Amarillo, TX, 79119
6Department of Veterinary Pathobiology, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, 77843

**Introduction**

Bovine respiratory disease (BRD) is commonly controlled by metaphylaxis, but increasing prevalence of antimicrobial resistant (AMR) *Mannheimia haemolytica* (MH) may decrease efficacy. The objective of this study was to determine the effect of macrolide metaphylaxis on 1) morbidity and mortality in stocker cattle over a 21-day period and 2) isolation rate and antimicrobial susceptibility of MH at arrival (d0) and d21.

**Materials and methods**

Commercial beef cross heifers (n = 335, 232 ± 17.8 kg) were purchased from regional auction markets for 4 trials from October 2019 to October 2021. Cattle were randomized to receive tulathromycin at 2.5 mg/kg subcutaneously (META, n = 168) or not (NO META, n = 167). Nasopharyngeal swabs were obtained on d0 and d21 for aerobic culture and susceptibility testing. Groups were separated with no contact; any calves requiring additional antimicrobial (AM) treatment were moved into separate pastures (META-TRT, NO META-TRT). Logistic regression models were constructed to evaluate effect of group (META, META-TRT, NO META, NO META-TRT), trial, and previous MH isolation with isolation of multi-drug resistant (MDR, MICs classified as not susceptible to AM in ≥ 3 classes) *M. haemolytica* on d21 as the outcome variable.

**Results**

Over all trials, total and BRD morbidity (animals given AM for BRD) was significantly lower in META (14.9%) animals than NO META (29.3%) ($\chi^2$, $P = 0.002$); however, difference in BRD morbidity was observed only in the spring and fall 2021 trials ($\chi^2$, $P = 0.002$ & $P = 0.037$, respectively). There was no difference in mortality, or d21 MH isolation risk between groups. Risk of isolation of MDR MH was significantly higher ($\chi^2$, $P = 0.0004$) at d21 (69/139) compared to d0 (17/72), and odds of recovery of MDR isolates at d21 was significantly higher from animals that received META (OR = 221.0, 95% CI = 12.602-3875.6; $P = 0.0002$) and META-TRT (OR = 25.35, 95% CI = 3.09-207.88; $P = 0.0026$) compared to NO META (Reference).

**Significance**

Tulathromycin metaphylaxis was associated with increased risk of MDR *M. haemolytica* isolation in high-risk heifers. Isolation of MH at d21 was not decreased in META cattle, possibly due to AMR. Metaphylaxis maintained efficacy in reducing morbidity, possibly through non-antimicrobial mechanisms; thus, future work investigating such mechanisms are warranted to develop approaches that decrease BRD without increasing AMR.