

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

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## 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.

