

Antimicrobial susceptibility in *Mannheimia haemolytica* isolated from high-risk stocker cattle after metaphylaxis and treatment

A. Woolums,¹ DVM, PhD, DACVIM, DACVM; B. Karisch,² PhD; D. R. Smith,¹ DVM, PHD, DACVPM (Epi); J. Blanton,² PhD; F. Austin,¹ DVM, PhD; J. Frye,³ PhD; L. Hiott,³ MS; M. McClelland,⁴ PhD

¹Department of Pathobiology and Population Medicine, Mississippi State University, Mississippi State, MS 39759

²Department of Animal and Dairy Science, Mississippi State University, Mississippi State, MS 39759

³US National Poultry Research Laboratory, USDA ARS, Athens, GA 30605

⁴Department of Microbiology and Molecular Genetics, University of California, Irvine, CA 92697

Introduction

Metaphylaxis (mass antimicrobial treatment) is commonly administered to high-risk cattle to limit bovine respiratory disease (BRD). While metaphylaxis decreases BRD morbidity and mortality, some cattle still require subsequent BRD treatments. Moreover, widespread application of antimicrobial drugs with extended duration of therapeutic concentrations in lung could increase antimicrobial resistance (AMR) in bacteria that cause BRD. Reports indicate increasing prevalence of AMR in *Mannheimia haemolytica*, the leading bacterial contributor to BRD in feedlot and stocker cattle. The role that metaphylaxis has contributed to the recognized increase in AMR prevalence in *M. haemolytica* has not been well described. The impact of AMR on health outcomes in cattle managed to treat and control BRD is also not clear. The objective of this research was to describe the prevalence of AMR *M. haemolytica* in auction market-derived stocker cattle that received a long acting macrolide for metaphylaxis, followed by treatment as necessary for BRD with other antimicrobials, over the first 21 days after receiving

Materials and Methods

Fifty auction market-derived bulls and steers weighing 330 to 471 lb (150 to 214 kg) received tildipirosin metaphylaxis on d. 0. A modified live 5-way viral BRD vaccine and a clostridium bacterin-toxoid was administered to all cattle on d. 0; cattle were not treated with an anthelmintic. Cattle were evaluated daily for signs of BRD and were eligible for treatment with different AM beginning on study d. 3, and a 2-day post treatment interval was observed after treatment with each antimicrobial. The antimicrobial administered for first BRD treatment was florfenicol, the second was ceftio-

fur, and the third was enrofloxacin. Nasopharyngeal swabs were collected from all cattle for aerobic bacterial culture before metaphylaxis and on d. 7, 14, and 21. Antimicrobial susceptibility was determined by disc diffusion and broth microdilution. Isolates were classified as multi drug resistant (MDR) if they were resistant to at least one antimicrobial in each of at least 3 classes. Pulse field gel electrophoresis (PFGE) was used to assess genetic relatedness of isolates, and a diverse subset of 36 isolates was subjected to whole genome sequencing (WGS).

Results

Forty-eight percent of the cattle required one BRD treatment, 22% required two treatments, and 8% required three treatments. One steer died and lesions of severe BRD were found on necropsy. The prevalence of *M. haemolytica* shedding was 10% on day 0; the prevalence of MDR Mh shedding was 6% on day 0 and increased to a high of 88% on day 14. All *M. haemolytica* isolates were resistant to at least one antimicrobial, and by day 7 all *M. haemolytica* shed by cattle were MDR. Multiple PFGE types were identified, indicating that the MDR isolates were not all from a single clone. Whole genome sequencing identified multiple recognized AMR genes.

Significance

Multi drug resistant *M. haemolytica* shedding can be highly prevalent following treatment of high risk cattle with antimicrobials for metaphylaxis and BRD therapy. Further research in larger groups is warranted to confirm the impact of MDR respiratory bacteria on health outcomes in stocker cattle, and to determine management practices that minimize the impact of AMR in cattle managed to treat and control BRD.