Mycoplasma bovis and *Mannheimia haemolytica* dynamics during acute bovine respiratory disease in feedlot cattle

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Introduction

Mycoplasma bovis is a bacterium member of the family Mycoplasmataceae, characterized by a small genome, lack of cell wall, and high nutritional requirements for in vitro growth (Li et al., 2011; Parker et al., 2018; Dudek et al., 2020). Traditionally, *M. bovis* has been linked to chronic BRD cases and treatment failures (Booker et al., 2008; Hermeyer et al., 2012; Gershwin et al., 2015; Becker et al., 2020). Several virulence factors have been implicated in *M. bovis* ability to persist in the lungs of cattle with BRD, such as variable surface proteins (Vsp), adhesins, nucleases, H2O2 production and biofilm formation (Burki et al., 2015; Perez-Casal, 2020). Due to the difficulties of growing *M. bovis* in the lab, the inherent culture bias (Prakash et al., 2021) could have shaped our current knowledge of *M. bovis* in BRD.

Recent evidence has emerged linking *M. bovis* presence in the upper respiratory tract with acute BRD status (Timsit et al., 2018; Centeno-Martinez et al., 2022). However, the association between *M. bovis* and other BRD agents, especially *Mannheimia haemolytica*, over time remains unknown during the first month on the feedlot. A more comprehensive understanding of the dependencies among BRD pathogens over time will help develop new non-antibiotic control strategies and subsequently reduce the burden of BRD on beef cattle production. Therefore, this study aimed to evaluate the association of *M. bovis* and *M. haemolytica* during acute BRD in feedlot cattle.

Materials and methods

Nasal swabs from an experiment evaluating the effect of anti-BRSV vaccination on BRD in feedlot cattle were used for the molecular detection of BRSV, *Histophilus somni, M. haemolytica, Pasteurella multocida*, and *M. bovis* via multiplex qPCR assays using TaqMan chemistry. Inverse probability weighted (IPW) logistic regression models were built, in which *M. haemolytica* prevalence on day 28 post arrival was regressed on *M. bovis* presence on arrival, 7 days and 14 days post arrival. An IPW Cox proportional hazards model to infer the association between time-to-first BRD antibiotic treatment and *M. bovis* presence on arrival, 7 days and 14 days post arrival, was also created.

Results

The presence of *M. bovis* in nasal swabs on day 7 post arrival was significantly associated with an increase in the prevalence of *M. haemolytica* on day 28 post arrival (prevalence difference: 0.28; 95% CI: 0.18, 0.38; *P* value < 0.001). Significant time-varying coefficients for M. bovis presence were detected in all evaluated time points in the IPW Cox model (*P* value < 0.001). The shortest median time-to-first BRD antibiotic treatment was 29 days in cattle *M. bovis*-positive on day 0, 7 and 14 post-arrival, and in those positive on day 0 and 14 post-arrival.

Significance

Our findings suggest that *M. bovis* may be influencing the respiratory environment during the acute phase of BRD, increasing the abundance and prevalence of *M. haemolytica*. Therefore, the relevance and dynamics of *M. bovis* in BRD should be revisited.