Systematic review and meta-analysis comparing arrival versus delayed vaccination of high-risk beef cattle with 5-way modified-live viral vaccines against BHV-1, BRSV, PI3, and BVD types 1 and 2

E.R. Snyder, DVM, MFAM; **B.C. Credille**, DVM, PhD, DACVIM; **R.D. Berghaus**, DVM, MS, PhD, DAVCPM;
B.D. Heins, DVM, MFAM
Food Animal Health and Management, Department of Population Health, University of Georgia, Athens, GA, 30602

Introduction

Bovine respiratory disease (BRD) is the leading cause of morbidity and mortality in North American beef cattle, and thus a major economic and welfare concern of individuals involved in the beef cattle industry. The most common viruses implicated in BRD are Bovine Herpesvirus 1 (BHV-1), Bovine Respiratory Syncytial Virus (BRSV), Parainfluenza 3 (PI3), and Bovine Viral Diarrhea Viruses types 1 and 2 (BVD 1 and 2), and it is common practice to administer vaccines against these viruses to cattle entering feedlots and stocker operations at arrival. However, there have long been concerns that cattle may not mount an optimal immune response when vaccinated at this time. A number of studies have been conducted to evaluate the effects of vaccination timing on morbidity and mortality, but often include other interventions that might confound interpretation of the results. This can make an objective evaluation of the effects of only vaccination timing difficult. It is therefore our goal to provide a systematic review of these studies, and extract relevant data to perform a meta-analysis of vaccine timing on BRD morbidity, retreatment rate, and mortality.

Materials and Methods

A literature search of PubMed, CAB, and Bovine Practitioner was performed with the following inclusion/exclusion criteria to find studies comparing the efficacy of arrival vaccination to delayed vaccination of high-risk beef cattle with a MLV pentavalent vaccine against viral BRDC pathogens. The vaccines needed to be labeled for the prevention of or the aid in prevention of disease caused by BHV-1, PI3, BRSV, and BVD types 1 and 2. Time points for interventions needed to include vaccination at arrival, or at a time point greater than 7 days following arrival. Studies needed to be conducted on high-risk beef cattle, and report clinically relevant outcomes; that is, morbidity, mortality, and retreatments, either as total case numbers or percentage of a population, and disease had to be naturally occurring. Means of diagnosis of respiratory disease had to be clearly described, and had to have a case definition that included clinical signs of BRD. After identification of all suitable studies, a MantelHaenszel risk ratio was calculated using a random effects model, along with a 95% CI and presented in a Forest plot, for BRD morbidity, retreatment risk, and mortality. The Cochran Q statistic was also calculated. A $P \geq 0.10$ for this statistic, and an $I2 > 50\%$ were used to indicate potential heterogeneity of the studies. A confidence interval that crosses 1 was considered indicative of no significant difference between the compared variables.

Results

A total of eight studies were identified that met all search and inclusion/exclusion criteria. In regards to morbidity, when all studies are evaluated, the overall risk ratio is 0.99 (95% CI 0.93, 1.06), indicating that there is no difference in regards to morbidity between vaccination at either time point. The overall risk ratio for retreatment risk is 1.01 (95% CI 0.91-1.13), indicating that retreatment risk is not impacted by vaccine timing. Regarding mortality risk, there does appear to be a trend toward delayed vaccination being advantageous; the risk ratio is 0.78. However, the 95% CI still crosses 1 (0.57, 1.10), again indicating no difference in mortality risk between calves vaccinated at arrival or delayed.

Significance

Based on the data from the studies analyzed, it would appear that there is not an advantage or disadvantage in terms of morbidity, retreatment rate, or mortality in delaying vaccination. In light of the results of this meta-analysis, and especially when we consider the very high morbidity rates observed in many of these studies, it may be that vaccination of high-risk beef cattle in the feedlot or stocker setting is equally ineffective regardless of when timing. More research is needed in larger groups of cattle with fewer confounding variables to evaluate the timing of vaccination as a factor in the control of bovine respiratory disease.