

Evaluation of Responses to Vaccination of Angus Cattle for Four Viruses that Contribute to Bovine Respiratory Disease Complex

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Summary and Implications

Initial antibody titers are maternally-derived from colostrum, then decay with age. Change in antibody titer levels were compared between four viruses contributing to the Bovine Respiratory Disease Complex (BRDC), and evaluation of response to vaccination indicated that antibody production will not occur when high levels of maternal antibodies are present. The maternal antibodies were found to decay with calf age for each of the four viruses, which allowed for the estimation of a maximum circulating titer level under which a positive antibody response to vaccination could occur. Phenotypic correlations were calculated between the antibody titers for the four viruses across multiple time points. Results indicate a difference in the response to vaccination between the four virus antigens.

Introduction

BRDC is an economically important disease causing concern for the US cattle industry. More than \$800 million dollars are lost a year due to incidences of this disease complex, yet despite this an effective treatment has not been sufficiently developed. Frequently occurring during transport to feedlots due to close exposure to other individuals, BRDC quickly circulates through herds and can lead to reduced growth, increased medical costs, and mortality in animals. Current preventative measures recommend vaccination of individuals three weeks prior to transportation, although improper administration or timing of the vaccination remains the primary cause of ineffective treatment. Identification of genomic regions controlling response to vaccination would allow for selection on more responsive individuals, resulting in herds with improved welfare and less morbidity. Circulating antibody levels were evaluated at several times for four viruses in Angus calves to characterize antibody titer trends. The viruses were Bovine Viral Diarrhea Virus 1 and 2 (BVDV-1, BVDV-2),

Bovine Respiratory Syncytial Virus (BRSV), and Bovine Herpes Virus 1 (BHV-1). This work was done to explore the relation between calf age, time of weaning, and time of vaccination, to determine potential mechanisms controlling response to vaccination.

Materials and Methods

The vaccine Bovi-Shield GOLD 5 was administered to some 1,600 – 2,300 animals, which had antibody titer levels measured at four different time points, at three week intervals: Pre-vaccination (-3 weeks), Initial vaccination (0 weeks), Booster vaccination (3 weeks), Booster Response (6 weeks). Blood samples collected at these time points were analyzed for circulating antibody titer levels for each of the four viruses and converted to a base 2 log scale, with two to five replicates per sample. Maternal antibody decay was calculated for BVDV-1 and BVDV-2 by determining decay between -3 and 0 week time points. Initial response was calculated as the titer increase between 0 and 3 weeks; booster response was calculated as the titer increase between 3 and 6 weeks; overall response was calculated as the titer increase between 0 and 6 weeks.

Models for vaccine response included class effects of Year-Season, Sex (bull, steer, cow), Initial Treatment Time (3 weeks prior, or at weaning), Pink Eye Score (infected or not), and Dam Age (2-14 years). Covariates of titer level, titer level squared, calf age within year-season, and average daily gain were fitted. Dam was fit as a random effect. Effect of weaning time on response to vaccination was characterized in terms of Least Square Means. Phenotypic correlations were calculated between responses to the four viruses in terms of initial response, booster response, overall response, and final antibody titer level to characterize the similarity in response to vaccination (Table 1).

Results and Discussions

Initial antibody titer concentration by calf age showed that maternally-derived antibodies from colostrum for BVDV-1 and BVDV-2 were circulating at higher initial levels than antibodies for BRSV or BHV-1. Antibodies for all four viruses showed a decline in circulating levels as calf age increased (figure 1), with BRSV declining the least. Visualization of overall response by initial circulating concentration indicates the maximum circulating antibody levels that can still result in an antibody response to vaccination within the animal (figure 2). This explains why responses to BVDV-1 and BVDV-2 antigens did not occur until animals were vaccinated at the booster time point (figure 3), as older animals had lower circulating antibody

levels than younger animals and most animals at weaning were around 130 days of age. As such, these animals had circulating antibody levels above the concentration required to achieve a response to the antigen.

Treatment time (3 weeks prior or at weaning) showed a difference between BVDV-1/BVDV-2 and BRSV/BHV-1. Weaning at initial vaccination resulted in a greater overall response for BVDV-1 and BVDV-2 while weaning at booster vaccination resulted in a greater overall response for BRSV and BHV-1 (figure 4). These differences in overall response levels by weaning time point indicate a potential causal reason why vaccination has not been as successful at reducing incidence of BRDC as hoped. The variety of viruses which can contribute to BRDC must be taken into account in the design of the vaccine, and results point towards variation in optimal times for vaccination. Further work to identify genomic regions controlling response to vaccination will provide additional insight into potential regions of selection for improved animal health.

Acknowledgement

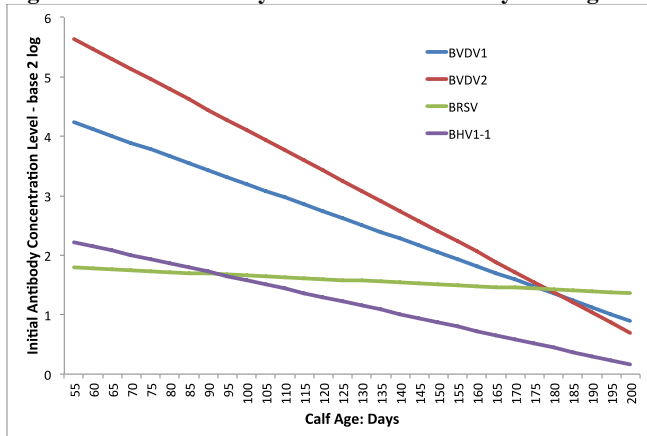
We would like to acknowledge the NIFA Award No-2013-67015-21344 for funding this project.

Table 1: Phenotypic Correlation of Overall Response¹

Overall Response	BHV-1	BRSV	BVDV-1	BVDV-2
BHV-1	1	0.32	0.37	0.18
BRSV		1	0.08	0.03
BVDV-1			1	0.67
BVDV-2				1

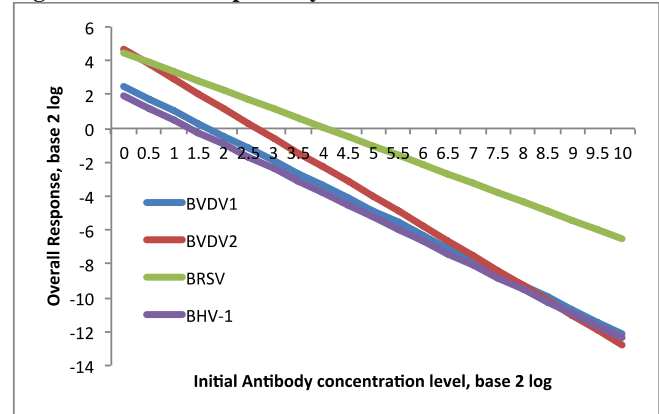
¹Initial Response, Booster Response, and Final level not shown

Figure 1: Initial Antibody Titer Concentration by Calf Age



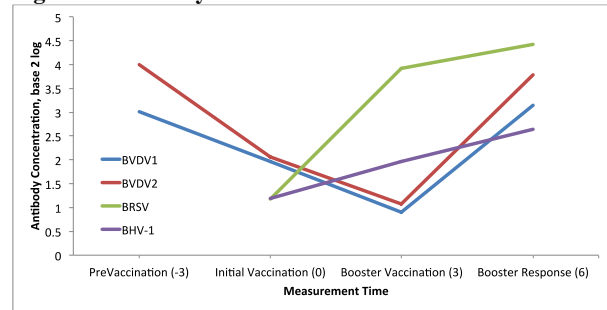
Average trend lines of initial antibody titer by age between the four viruses.

Figure 2: Overall Response by Initial Concentration



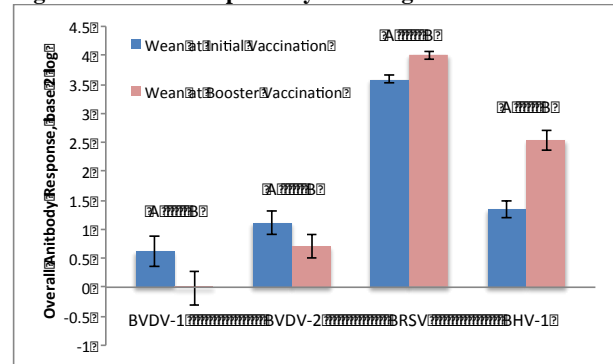
Average trend lines of overall response against initial titer between the four viruses.

Figure 3: Antibody Concentration Level Over Time



Antibody titer level change by virus across the four measurement time points. No pre-vaccination data for BRSV or BHV-1.

Figure 4: Overall response by Weaning Time Point



Least squares means estimates of overall response on time of weaning. Different letters within a virus represent significantly different responses (P<0.05).