Evaluation of response to vaccination on the feedlot performance of weaned calves

J.J. Gaspers[1], K.C. Swanson[1], F.E. Doscher[1], M. Rodenhuis[1] and G.L. Stokka[1]

The objective of this study was to evaluate the response of a vaccination protocol for bovine respiratory disease complex on feedlot performance in newly weaned backgrounding steers. The results indicate that vaccination protocols for bovine respiratory disease complex did not affect feedlot performance negatively in newly weaned backgrounding cattle.

Summary

Bovine respiratory disease complex (BRD) is one of the most costly diseases for beef production in the U.S. To help combat this costly inefficiency, cattle producers have implemented vaccination protocols for their beef herds. To investigate the effects of vaccination on feedlot performance, newly weaned calves (n = 76) were adapted to the Insentec roughage feeders at NDSU's Beef Cattle Research Center. Treatment one was a sterile saline negative control, treatment two was Bovishield Gold with One Shot, treatment three was Inforce 3 and Bovishield BVD with One Shot, and treatment four was Bovishield Gold with One Shot and Inforce 3. The Bovishield Gold with One Shot and Bovishield BVD with One Shot were injected subcutaneously in the neck. Inforce 3 was administered via the intranasal route. Calves were vaccinated on day 0 of the trial, and weights and blood samples were collected on days 0, 1, 3, 6 and 28 of the trial. Haptoglobin, an indicator for an inflammatory immune response, as well as antibody titers for bovine respiratory syncytial virus (BRSV) and infectious bovine rhinotracheitis (IBR), were collected to determine if vaccination immunity took place. All vaccines initiated an inflammatory response ($P < 0.001$). Treatments two and four induced an increase in plasma antibodies by day 28. Feeding intake and behavior were unaffected by the use of vaccines. The average daily gain (ADG) tended to be higher in treatment two ($P = 0.06$). All other feedlot performance variables were not different among treatment groups.

Introduction

In livestock, the major causes of death preceding slaughter are due to infectious diseases (Babiuk, 2002). Bovine respiratory disease complex (BRD) persists as the single most costly disease syndrome associated with the commercial beef production in the U.S., accounting for losses in 2010 of 1,055,000 animals valued at $643 million (NASS, 2011). Increased morbidity and mortality and decreased weight gains, feed utilization and carcass quality account for the economic losses associated with BRD (Edwards, 2010).

BRD originally was termed "shipping fever" because signs often occur shortly after arrival at the feedlot. The morbidity risk of BRD cases in feedlot cattle occur in the first 45 days after arrival at the feedlot, and the highest risk for cattle occurs in weeks one to three; thereafter, morbidity declines (Buhman et al., 2000)

Vaccination for viruses and bacteria associated with BRD is widespread (Taylor et al., 2010). The viral component of BRD consists of bovine herpesvirus type 1, also known as infectious bovine rhinotracheitis (IBR), bovine viral diarrhea (BVD), parainfluenza virus type 3 (PI-3) and bovine respiratory syncytial virus (BRSV). The bacterial component of BRD consists of *Mannheimia haemolyticam, Pasteurella multocida* and *Histophilus somni.*

Killed and modified live vaccines (MLV) are available in different combinations of viral pathogens. The appropriate use of these vaccines can reduce the risk of BRD (Urban-Chmiel and Grooms, 2012). The immune responses, which include antigen-specific antibodies, have been shown to confirm vaccine-induced protection against numerous diseases (Casadevall, 2004).

To elicit a vaccine response, the vaccine must provide enough signals from the antigen, or with an adjuvant, to trigger the inflammatory reaction that is mediated by cells of the innate immune system (Hoebe et al., 2004). Injection of a vaccine antigen initiates an acute phase inflammation response, which develops within minutes (Tizard, 2013). Upon injection of an antigen, sentinel cells synthesize and secrete a mixture of molecules that triggers inflammation and initiates the first steps of the adaptive immune

[1]Department of Animal Sciences, NDSU

system (Tizard, 2013). Exposing an animal to an antigen can affect their performance in the feedlot negatively (Stokka et al., 1994).

The protein Haptoglobin (hp) is one of a number of acute phase proteins synthesized and secreted during the initial inflammatory response. Hp concentrations in healthy cattle often are undetected, but during the inflammatory reaction to a vaccine, they can increase 50 to 100 times (Conner et al., 1988). Hp concentrations will increase with bacterial and viral infections (Idoate et al., 2015).

Hp can be used as a tool to measure respiratory disease in feedlot conditions (Idoate et al., 2015). The objective of this study was to evaluate the response of a vaccination protocol for bovine respiratory disease complex on feedlot performance in newly weaned backgrounding steers.

Experimental Procedures

Animal care and use was approved by the Institutional Animal Care and Use Committee at North Dakota State University, Fargo. This study utilized 76 weaned Angus, Shorthorn and Simmental steers born at North Dakota State University beef barns in the winter of 2014 (Jan. 1, 2014, to March 31, 2014). At birth, calves were vaccinated with Inforce 3 (Zoetis; 100 Campus Drive, Florham Park, N.J. 07932), administered via the intranasal route, and Ultrabac C & D (Zoetis; 100 Campus Drive, Florham Park, N.J. 07932), administered via the subcutaneous route.

On April 2, 2014, calves were vaccinated with Bovishield Gold 5 and Ultrabac 7 subcutaneously and received Dectomax pour-on. On Sept. 3, 2014, calves received Bovishield Gold VL5 and One Shot Ultra 7 subcutaneously and received Dectomax pour-on. Calves were weaned for 30 days and then shipped to the NDSU's Beef Cattle Research Complex. Upon arrival on Oct. 21, 2014, calves (n = 76, body weight [BW] = 741 ± 69.7 pounds) were trained for 21 days to the Insentec Roughage Feeders (Insentec; Insentec B. V. Repelweg 10, 8316 PV Marknesse, The Netherlands).

Insentec Roughage Feeders measure feed intake and time of each visit, dry-matter intake (DMI), time spent at the feeder measured in minutes and number of visits; the number of meals can be calculated. Body weight was determined on days minus 21, 0, 1, 3, 6, 28 and 29, and average daily gain (ADG), feed conversion ratio (FCR) and gain-to-feed (G:F) were calculated. Time spent at the feeder, number of visits and meals were calculated on a 24-hour cycle. A meal is defined as a distinct, separate eating period and visit not separated by intervals longer than seven minutes.

On day 0, calves were blocked by weight, randomly assigned and administered one of four possible treatment groups. Treatment one was a 2-milliliter (mL) sterile saline negative control subcutaneously injected in the neck, treatment two was Bovishield Gold with One Shot (Zoetis; 100 Campus Drive, Florham Park, N.J. 07932), treatment three was Inforce 3 and Bovishield BVD with One Shot, and treatment four was Bovishield Gold with One Shot and Inforce 3. The Bovishield Gold with One Shot and Bovishield BVD with One Shot were injected subcutaneously in the neck. Treatments two, three and four were administered as a 2-mL dose subcutaneously on the left side of the neck. Inforce 3 was a 2-mL dose administered in one nostril via the intranasal route.

Blood samples were collected via jugular venipuncture into heparinized tubes in the morning on days 0, 1, 3, 6 and 28. Samples were placed on ice and centrifuged for 20 minutes at 1,380 x g to separate plasma, which then was pipetted into cryo-vials and frozen until later analysis. Plasma samples from days 0, 1, 3, 6 and 28 were sent to the University of Guelph Animal Health lab for hp concentrations analysis. Plasma samples from days 0, 3, 6 and 28 were sent to the Oklahoma State University diagnostic lab for BRSV and IBR antibody titers.

All data were analyzed using the mixed procedure of SAS. Variables analyzed were average dry-matter intake, average time at bunk, average visits per day, average meals per day, average two-day start weight, average two-day end weight, three-day weight change, six-day weight change, gain-to-feed ratio, time per visit, time per meal, feed intake per visit, feed intake per meal, feed intake per minute, gain, average daily gain, hp, BRSV antibody titers and IBR antibody titers. Antibody titers were converted using the natural log to normalize data. Significance was determined when $P \leq 0.05$.

Results and Discussion

The inflammatory response upon injection was observed for all injections with the exception of sterile saline ($P < 0.001$; Figure 1). Plasma hp concentrations increased beginning 24 hours post injection ($P < 0.001$) and peak response occurred 72 hours post injection ($P < 0.001$). By day 6, hp concentrations declined and returned to concentrations observed at 0 hour. This reaction across time is consistent with the innate immune response observed during exposure to an antigen. At day 6, the inflammatory response of the innate immune system returned to homeostatic levels observed on day 0.

However, day 6 showed the start of antibody production of the adaptive immune system. Treatment two, Bovishield Gold with One Shot, and treatment four, Bovishield

Gold with One Shot and Inforce 3, had significantly higher plasma antibody levels for BRSV and IBR, compared with treatment one, sterile saline, and treatment three, Bovishield Gold BVD with One Shot and Inforce 3 ($P < 0.001$; Figures 2 and 3). Although treatment three, Bovishield BVD with One Shot and Inforce 3, did initiate an inflammatory response ($P < 0.001$; Figure 1), it did not show an increase in IBR and BRSV antibody titer levels by day 28.

Treatments two and four had Bovishield Gold, which contains modified live IBR, PI3, BRSV, and BVD type 1 and 2 viral antigens, whereas treatment three, Bovishield BVD, only contains modified live BVD type 1 and 2 viral antigens, with the IBR, PI3 and BRSV antigens administered via the intranasal route as Inforce 3. Treatments two, three and four contain One shot, a *Mannheimia haemolytica* toxoid that includes an adjuvant. Adjuvants are added to vaccines to stimulate the immune response and enhance antibody production.

The lack of an antibody response to treatment three is likely due to the route of administration of these specific antigens: IBR, PI3 and BRSV. Because this entire group of calves previously received three doses of vaccine containing the IBR, PI3 and BRSV antigens, we assume that the defense mechanisms present at the natural route of infection, the nasal passages, were able to resist these live vaccine viral particles administered via the intranasal route. Treatment two and four received the same antigens but via the subcutaneous route of administration, thus bypassing the natural route of infection and the natural defense mechanisms that exist in the previously immunized animals.

During an immune response to a pathogen, upregulated signal

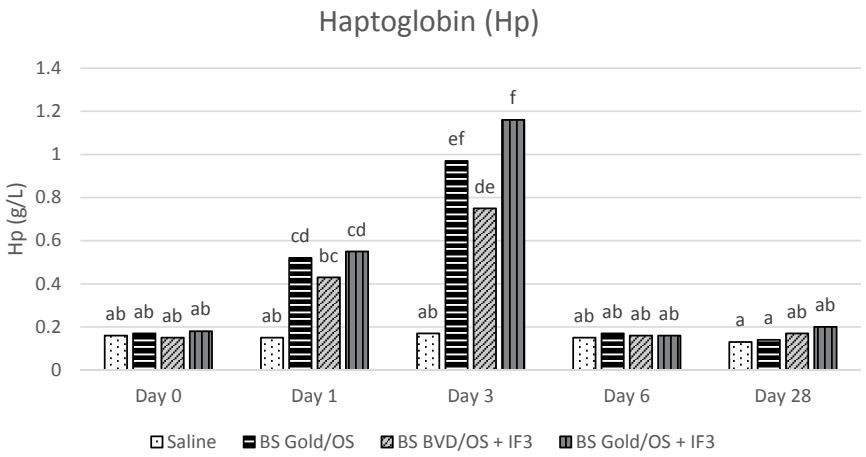

Figure 1. Haptoglobin levels (g/L) by vaccination treatment across time.
Treatment and time bars with differing letters differ by $P < 0.05$.

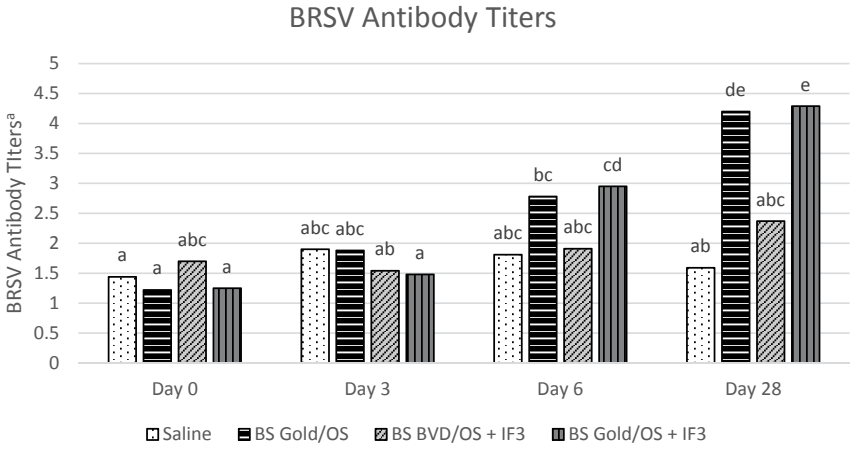

Figure 2. BSVR antibody titers by vaccination treatment across time.
[a]SN titer values were normalized using the Natural Log.
Treatment and time bars with differing letters differ by $P < 0.05$.

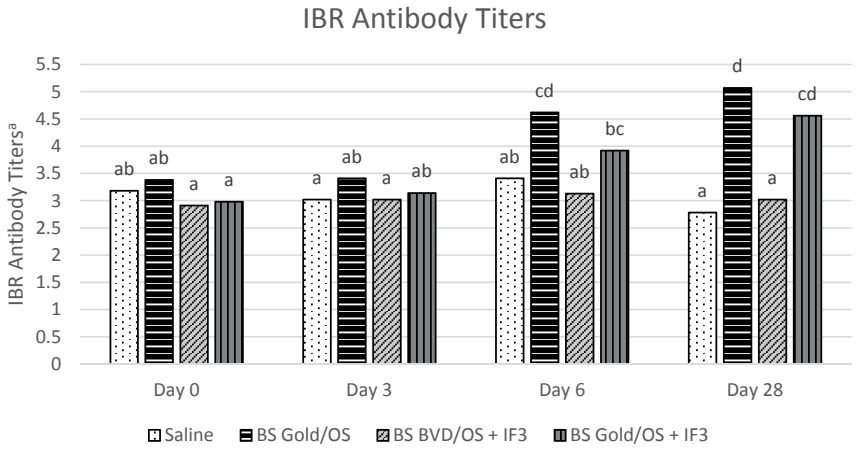

Figure 3. IBR antibody titers by vaccination treatment across time.
[a]SN titer values were normalized using the Natural Log.
Treatment and time bars with differing letters differ by $P < 0.05$.

molecules can have adverse effects on temperature regulation, appetite, energy metabolism and endocrine functions (Klasing, 1988). This could be induced by vaccines with enough antigenic load or adjuvant to elicit a significant immune response. However, in this study, feeding behavior and growth performance were not affected negatively by the injection of a modified live vaccine and adjuvant (See tables 1 and 2). On the contrary, treatment two tended to have an increased average daily gain, compared with the other three treatment groups ($P = 0.06$).

This group did receive a subcutaneous shot of Bovishield Gold; however, it did not receive Inforce 3. This group had the second largest hp and BRSV response at 3 and 28 days, respectively, as well as having the largest IBR response at 28 days. At low doses, signals used to upregulate hp also can increase feed intake and growth (Klasing, 1988). This could be the reason for the tendency for an increase in average daily gain observed in treatment two.

The calves used in this study were exposed to vaccine antigens three times prior the study. They were from the same herd, and were allowed to acclimate to their new environment for 21 days before the start of this study. Results on high-stress animals that are weaned, vaccinated and comingled with calves from different herds may be different. Further research is needed to evaluate unvaccinated, immune-naïve calves that are weaned and brought together in a backgrounding feedlot environment.

Table 1. Influence of vaccination on feeding behavior in backgrounding steers.

	Treatment					
Item	1	2	3	4	SEM[a]	*P*-value
DMI	19.5	20.2	19.9	19.4	0.39	0.41
Eating events, no./d						
Visits	42.6	42.2	41.5	36	2.97	0.36
Meals/d	12.0	12.1	11.8	11.2	0.42	0.43
Eating time, min.						
Per visit	4.54	4.51	4.70	5.31	0.37	0.39
Per meal	14.8	14.9	15.3	16.4	0.83	0.49
Per day	172	175	176	178	5.06	0.85
Feed DMI, lb.						
Per visit	0.52	0.52	0.52	0.57	0.04	0.70
Per meal	1.66	1.71	1.72	1.79	0.08	0.70
Per min	0.12	0.12	0.11	0.11	0.004	0.44

[a]Standard Error of the mean (n = 19).

Table 2. Influence of vaccination on growth performance in backgrounding steers.

	Treatment					
Item	1	2	3	4	SEM[a]	*P*-value
Initial BW, lb.	795	782	785	782	11.9	0.85
Final BW, lb.	847	850	843	839	13.0	0.95
Gain, lb.	52.2	67.8	58.1	57.5	4.28	0.06
Weight change						
3 day	6.07	7.98	9.49	9.25	3.96	0.92
6 day	5.64	13.1	10.1	10.3	3.60	0.50
ADG[b]	1.86	2.42	2.08	2.05	0.15	0.06
G:F	0.10	0.12	0.10	0.10	0.01	0.11

[a]Standard error of the mean (n = 19).

[b]Calculated by dividing the total gain calculated from the average initial and final weights by 28 days.

Acknowledgments

The authors thank Zoetis for the financial support of this project and the staff of the NDSU Beef Cattle Research Complex for assistance with sampling, animal husbandry and handling.

Literature Cited

Babiuk, L.A. 2002. Vaccinations: a management tool in veterinary medicine. Vet. J. 64:188-201.

Buhman, M.J., L.J. Perino, M.L. Galyean, T.E. Wittum, T.H. Montgomery and R.S. Swingle. 2000. Association between changes in eating and drinking behaviors and respiratory tract disease in newly arrived calves at a feedlot. Am. J. Vet. Res. 61:1163-1168.

Casadevall, A., 2004. The methodology for determining the efficacy of antibody-mediated immunity. J. Immunol. Methods. 291:1-10.

Conner, J.G., P.D. Eckersal, A. Wiseman, T.C. Aitchison and T.A. Douglas. 1988. Bovine acute phase response following turpentine injection. Res. Vet. Sci. 44:82-88.

Edwards, T.A. 2010. Control methods for bovine respiratory disease for feedlot

cattle. Vet. Clin. N. Am-Food An. 26(2)-273-284.
Hoebe, K., E. Janssen and B. Beutler. 2004. The interface between innate and adaptive immunity. Nat. Immunol. 5:971-974.
Idoate, I., B. Vander Ley, L. Schultz and M. Heller. 2015. Acute phase proteins in naturally occurring respiratory disease of feedlot cattle. Vet. Immun. Immunopath. 163:221-226.
Klasing, K.C. 1988. Nutritional aspects of leukocytic cytokines. J. Nutr. 118:1436-1446.
NASS. 2011. Cattle and calf death losses. http://usda.mannlib.cornell.edu/usda/current/CattDeath/CattDeath-05-12-2011.pdf (accessed June 10, 2015)
Stokka, G.L., A.J. Edwards, M.F. Spire, R.T. Brandt Jr. and J.E. Smith. 1994. Inflammatory response to clostridial vaccines in feedlot cattle. J. Am. Vet. Med. Assoc. 204:415-419.
Taylor, J.D., R.W. Fulton, T.W. Lehenbauer, D.L. Step and A.W. Confer. 2010. The epidemiology of bovine respiratory disease: what is the evidence for preventive measures? Can. Vet. J. 51(2):1351-1359.
Tizard, I.R., 2013. Innate immunity: The proinflammatory and antimicrobial mediators. In: I.R. Tizard, editor, Veterinary immunology an introduction 9th ed. W. B. Saunders, Philadelphia, Pa. p. 21-29.
Urban-Chmiel, R., and D.L. Grooms. 2012. Prevention and control of bovine respiratory disease. J. Livestock Sci. 3:27-36.