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Systemic and local immune responses of weaned beef calves vaccinated post-transportation and at the time of a mild respiratory tract infection

Victor S. Cortese, DVM, PhD, DABVP[1]; **Amelia R. Woolums**, DVM, MVSc, PhD[2]; **Brandi B. Karisch**, MS, PhD[3]; **Thomas H. Short**, PhD[4]; **Merrilee Thoresen**, MS, PhD[2]; **Peres Badial**, DVM, MS, PhD[2]
[1] Zoetis, Inc., 8601 Glenfield Way, Louisville, KY 40241
[2] Department of Pathobiology and Population Medicine, Mississippi State University, Mississippi State, MS 39762
[3] Department of Animal and Dairy Sciences, Mississippi State University, Mississippi State, MS 39762
[4] Zoetis, Inc., Parsippany, NJ 07054
Corresponding author: Dr. Victor Cortese; victor.cortese@zoetis.com

Abstract

To examine the effects of transport stress and concurrent respiratory infection on bovine vaccine responses, 75 previously weaned beef calves were randomly assigned to 1 of 3 treatments (n=25/group). Group 1 calves were not transported, but were vaccinated (NTV). Both Groups 2 (vaccinated TV) and 3 (not vaccinated TUV) were transported for 12 h. Twelve h after transport, calves in NTV and TV groups were vaccinated intranasally with modified-live bovine respiratory syncytial virus (BRSV), bovine herpesvirus −1 (BHV-1), and parainfluenza virus type 3 (PI3V), and subcutaneously with modified-live bovine viral diarrhea virus (BVDV) types 1 and 2 vaccine with *Mannheimia hemolytica* (Mh) leukotoxoid vaccine. Nasal secretions and serum were collected pre- and post-vaccination for measurement of nasal interferon alpha, beta, and gamma, IgA to BHV-1 and BRSV, and serum neutralizing (SN) titers to BHV-1, BRSV, and BVDV types 1 and 2.

At vaccination some calves had nasal discharge and fever. Pre-vaccination nasal swabs, tested for respiratory viruses, were negative. During the 21-d study, 6 calves developed BRD and eventually recovered. BHV-1 and BVDV 1 and 2 SN titers were significantly higher in vaccinated than nonvaccinated calves on d 14 and 21. BVDV2 titers were significantly higher in TV than NTV. Vaccination stimulated systemic, but not mucosal, antibody responses. Cattle can mount a humoral response to vaccination in spite of transport and mild respiratory disease.

Key words: bovine, mucosal immunity, vaccination, stress, shipping

Résumé

Afin d'examiner l'effet du stress relié au transport et de l'infection respiratoire concomitante sur la réponse à la vaccination chez les bovins, 75 veaux de boucherie sevrés au préalable ont été alloués au hasard dans trois traitements (n=25/groupe). Dans le groupe 1, les veaux n'étaient pas transportés mais vaccinés (NTV) alors que dans le groupe 2 (TV vacciné) et dans le groupe 3 (TUV non-vacciné) les veaux étaient transportés pendant 12 heures. Douze heures après la fin du transport, les veaux NTV et TV ont reçu par voie intranasale un vaccin à virus vivants modifiés contenant le virus respiratoire syncytial bovin (VRSB), l'herpèsvirus bovin de type 1 (HVB-1) et le virus parainfluenza de type 3 (VPI-3) en combinaison avec le virus de la diarrhée virale bovine de type 1 et de type 2 (VDVB-1, 2) et une leukotoxine de *Mannheimia hemolytica* (Mh). Les sécrétions nasales et le sérum ont été recueillis avant et après la vaccination afin de mesurer les interférons nasaux de type alpha, bêta et gamma, la production d'IgA contre le HVB-1 et le VRSB, et les titres d'anticorps neutralisants contre le HVB-1, le VRSB et le VDVB-1 et 2.

À la vaccination, quelques bovins avaient des écoulements nasaux et de la fièvre. Les écouvillons nasaux testés pour les virus respiratoires étaient négatifs avant la vaccination. Durant les 21 jours de l'étude, six bovins ont développé le syndrome respiratoire bovin et aucun n'est mort. Les titres d'anticorps neutralisants contre le VHB-1 et le VDVB-1 et 2 étaient significativement plus élevées chez les veaux vaccinés que chez les veaux non-vaccinés aux jours 14 et 21. Les titres contre le VDVB-2 étaient plus élevés dans le groupe TV que dans le groupe NTV. La vaccination a stimulé la production d'anticorps au niveau systémique mais pas au niveau des muqueuses. Les bovins peuvent produire une réponse humorale à la vaccination en dépit du transport et d'affection respiratoire bénigne.

Introduction

Bovine respiratory disease remains the costliest disease of feedlot cattle.[13] A review of systemic vaccination studies in arrival cattle showed that vaccination had little

impact on BRD outcomes.[15,23] However, many beef calves are still vaccinated within 24 to 48 h of arrival at stocker, backgrounder, or feedlot facilities. These protocols often include a systemic modified-live pentavalent viral vaccine, *Mannheimia hemolytica* bacterin or toxoid, and a multivalent clostridial vaccine. Some evidence suggests that this practice is not beneficial[15,21,23], and may even have harmful effects in some cases.[1,9] The variable impact of parenteral vaccinations in newly arrived cattle has led to studies incorporating not only systemic, but also locally administered vaccines.[7,22]

Some studies evaluating humoral immune responses in high-risk cattle vaccinated at arrival found diminished antibody responses in those cattle, as compared to cattle receiving delayed vaccination,[18] but not in another study.[16] Rogers et al reported on-arrival vaccination with a parenterally administered modified-live viral (MLV) vaccine was associated with an increased rate of second treatment for BRD in high-risk heifers although there was no difference in morbidity.[19] No differences in BRD morbidity was seen when viral vaccine was administered on arrival or delayed by 28 days in another large high-risk heifer study.[10] A small trial evaluating on-arrival vaccination with MLV 5-way vaccine and a multivalent clostridial vaccine found increased rates of morbidity and mortality in high-risk bulls and steers vaccinated at arrival, compared to cattle not vaccinated until 56 d later.[9] In contrast, Cortese et al[3] compared the response of dairy cows to intranasal (IN) vaccination 3 weeks before calving to vaccinating the day of calving, and found higher nasal IgA titers in cows vaccinated on the day of calving. These studies indicate that stressful events can sometimes have a negative effect on the response to systemic vaccinations. Additionally, stress-induced immunosuppression may not negatively impact the mucosal immune system to the same degree as systemic immunity.[3]

Overall, the reported response of cattle to vaccination at the time of a stressful event varies considerably. This is likely related to variables affecting response, including age and immune status of cattle, nature of stressors encountered by the cattle, and type of vaccine. Ongoing research indicates the ability of dendritic cells to stimulate homing of immune responses that can primarily stay within the mucosal immune systems.[5,13] This further evidence of the division of systemic and mucosal immune systems may contribute to disparate responses to mucosal vs parenteral vaccination at the time of stress. Thus, much is still unclear regarding the effects of various stressors on vaccine responses in cattle.

Transportation is commonly superimposed on other stressors in many cattle vaccination studies. The relative effect of transportation, without other stressors commonly imposed on high-risk calves, has not been well characterized. The objective of this study was to evaluate the effect of transportation 12 h before vaccination on local and systemic immune responses to combined IN and subcutaneous (SC) vaccination with virus vaccines. Since cattle in the study had been weaned for a month and not commingled, the study design was intended to evaluate the sole effect of transportation on vaccine response. However, a natural outbreak of undifferentiated respiratory disease began at the onset of the study, which allowed assessment of both mucosal and systemic immune responses in vaccinated calves experiencing mild disease, with or without transport.

Materials and Methods

All procedures in this study were approved by the Institutional Animal Care and Use Committee at Mississippi State University (IACUC # 17-227).

Animals

The study was conducted at the Leveck Animal Research Center, and utilized calves from the resident herd. Calves were weaned approximately 30 days prior to the initiation of the study and were managed as a single group until assignment to their respective study groups. Calves ranged from 196 to 203 d of age, and were either Angus, Hereford, or Angus x Hereford cross. Forty-one heifers and 34 steers were enrolled in the study.

Calves from a single herd were enrolled to decrease potential exposure to BRD pathogens often observed when commingling calves from multiple sources. On study d -2, baseline samples were obtained (sera and nasal secretions), calves were blocked by age and sex, and randomly assigned to 3 treatments with 25 calves/group: not transported, vaccinated (NTV); transported, vaccinated (TV); and transported, not vaccinated (TUV). The NTV group was maintained at the research facility while the TV and TUV groups were transported as described below. After d 1 processing, cattle were housed by treatment in grass traps with free-choice access to a commercially available self-limited feed.[a] Cattle were provided medicated free- choice mineral formulated to provide 54 to 198 mg/hd/d of monensin.[b]

Transportation

On d 0, cattle in TV and TUV groups were loaded onto a single truck with each group equally distributed on the top and lower decks, then transported on county roads and state highways for 6 h. After initial transport, cattle were unloaded into separate small pastures at a different location with access to water and hay, and no contact with any other cattle during the rest period. After 3 h rest, calves were reloaded, transported for another 3 h, and then returned to their original pastures. The total transit time, with the rest stop, was 12 h.

Vaccination

Approximately 1 month before the study began, all calves were vaccinated SC with a MLV containing BVDV types 1 and 2, BHV-1, BRSV, and PI3V[c], *Clostridium chauvoei-septicum-novyi-sordellii-haemolyticum-perfringens* Types C and D bacterin-toxoid,[d] and *Campylobacter fetus ss venerealis-Leptospira pomona-hardjo-grippotyphosa-canicola-ictero-*

haemorrhagiae bacterin.[e] Each calf was uniquely identified with a numbered ear tag prior to weaning.

On d 1, calves in NTV and TV groups were vaccinated by the IN route with a modified-live bovine respiratory syncytial virus (BRSV), modified-live temperature-sensitive bovine herpesvirus 1 (BHV-1), and temperature-sensitive parainfluenza virus type 3 (PI3V) vaccine.[f] A modified-live bovine viral diarrhea virus (BVDV) types 1 and 2 vaccine in combination with a *Mannheimia haemolytica* (Mh) inactivated leukotoxoid vaccine[g] was administered SC as well. All vaccines were administered according to label instructions. Rectal temperatures were taken from NTV and TV calves before vaccination to determine whether transported calves were febrile. Calves in the 3 treatment groups were housed in separate pens to eliminate potential shedding of virus from vaccinated calves to unvaccinated calves.

Sample collection

Beginning on study d -2 and continuing through the 21 d study period (d 2, 4, 7, 10, 14, and 21), nasal secretion samples were collected for analysis of alpha, beta, and gamma interferon, as well as BRSV and BHV-1 IgA. Nasal secretions were collected by placing a soft sponge[h] into the nostril for 3 min. A loop of yarn was sewn through the sponge to facilitate removal. For nasal secretion retrieval, the sponges were placed into the barrel of a 30 mL syringe and pressed with the plunger so that secretions were expressed into a 12 x 75 mm polypropylene tube. No calves had clinical signs of disease on d -2. Serum samples were collected to measure BVDV types 1 and 2, BRSV, and BHV-1 serum neutralization (SN) titers via jugular venipuncture on d -2, 7, 14, and 21, and frozen for later analysis. Sera were sent as a complete set by overnight transport after the end of the study for SN antibody assays. On all sampling days, TUV calves were sampled first, and the working facility was cleaned and disinfected after all calves were sampled to prevent contact of TUV calves with vaccine virus on the chute or other structures on subsequent sampling days. Calves were weighed on each sampling/processing day using commercial livestock scales.[i]

In order to determine whether transport led to increased body temperature, rectal temperatures of calves in NTV and TV were measured on d 1 at the time they were vaccinated. Nasal swabs from 12 calves in TV were collected prior to vaccination using 6-inch (15.2 cm) polyester swabs and placed into Dulbecco's modified Eagle's medium + 10% horse serum and stored at -112°F (-80°C) until they were shipped for viral testing after the completion of the study. Nasal swabs were analyzed by real-time PCR for BRSV, BHV-1, BVDV1, and bovine coronavirus at the Veterinary Diagnostic Center, University of Nebraska-Lincoln, Lincoln, NE.

Measurement of respiratory mucosal IgA and interferon and SN titers

After collection each day, nasal secretions were diluted 1:2 with an equal volume of 0.5% Pluronic® F127 detergent[j] in PBS, mixed to disperse the gel portions of the sample, and stored at -112°F (-80°C) until assay following study completion. The concentration of IgA against BHV-1 and BRSV in nasal secretions was measured as previously described using a 2-fold dilution series starting at 1:100.[3] Titers were reported as the inverse of the last dilution yielding greater than or equal to twice the mean optical density of the negative control.

Bovine interferon (IFN)-gamma, IFN-alpha, and IFN-beta were measured by ELISA using commercially available antibodies and standards.[k] For each assay, the plates were coated with 100 µL of the respective polyclonal capture antibody (0.4 µg/mL for IFN-alpha [PB0474B-100] and 0.6 µg/mL for IFN-beta [PB0444B-100] and IFN-gamma [PB0156B-100]) diluted in Dulbecco's Phosphate-Buffered Saline (DPBS). Plates were covered with a plate sealer, incubated overnight at 39°F (4°C), and washed 3 times with 300 µL of the washing buffer solution (0.05 % Tween-20 diluted in DPBS). Plates were then blocked with 300 µL of the blocking buffer solution (4% BSA, 0.05% Tween-20 diluted in DPBS) for 2 h and washed as before. A 2-fold standard curve from 5,000–78 pg/mL was plated in duplicate. Nasal secretions previously diluted 1:2 with 0.5 % Pluronic® F127 detergent[l] in PBS were plated in duplicate. Following incubation of the samples and standards for 1 h at room temperature, plates were washed 4 times, incubated for 1 h at room temperature with 100 µL of the respective polyclonal detection antibody (0.5 µg/mL for IFN-alpha [PBB0483B-050], IFN-beta [PBB0450B-050], and IFN-gamma [PBB0267B-050]) diluted in blocking buffer, and washed again 4 times. Plates were incubated for 30 min at room temperature with 100 µL of horseradish peroxidase-conjugated streptavidin (0.3 µg/mL for IFN-alpha and 0.6 µg/mL for IFN-beta and IFN-gamma) diluted in blocking buffer and washed as before. Reactions were developed in the dark over 30 min at room temperature using 100 µL of TMB substrate and stopped with 100 µL of the stop solution (0.5 M of H_2SO_4). Absorbance was measured using an Epoch™ microplate spectrophotometer[m] at 450 nm. BHV-1, BRSV, BVDV types 1 and 2 SN titers were determined by the Athens Veterinary Diagnostic Laboratory, University of Georgia, Athens, GA.

Statistical Analysis

Antibody titer results (IgG and IgA) were analyzed both as actual titers and log 2 transformed titers. The log 2 transformed titers are reported here. All response variables were analyzed using a linear mixed model[n] with calf as the experimental unit. A repeated measures model was used with experimental treatment group, day, and their interaction included as fixed effects. Concentrations of antibodies and interferons were analyzed both as observed and log 2 transformed. The d -2 level was used to determine IFN-alpha, IFN-beta, and IFN-gamma baseline values. The model for antibody and interferon analysis also included the fixed effects of

experimental treatment group, day of sampling for antibody titer assay, and interaction of treatment and day of sampling. Calf was included in the model as a random effect. Statistical significance was set at p-value ≤ 0.05.

Results

Animals

Average daily gain of calves in the NTV and TV groups from d -2 to 1 did not differ (P>0.68). Average daily gain through d 21 for calves in the NTV, TV, and TUV groups was 2.70 ± 0.39, 3.18 ± 0.38, and 2.96 ± 0.40 lb/d (1.22 ±0.18, 1.44 ± 0.17, and 1.34 ± 0.18 kg), respectively. There were no significant differences in weight gain between the groups at any time point during the study (Figure 1).

At the time of vaccination of calves in the NTV and TV groups (12 h after transport), rectal temperatures were measured to determine whether TV calves were febrile. Although the ambient temperature at the time of processing was mild (68°F; 20°C), 11 calves in the non-transported (NTV) group had a rectal temperature ≥104°F (40°C); 1 also had a mucoid nasal discharge flecked with purulent material. Five calves in TV were also febrile. No cattle showed signs of disease before transport, and the rectal temperature was not taken in TUV calves since they were not scheduled to be sampled or vaccinated on d 1. Five more calves developed mucoid nasal discharge, and 6 calves began coughing during the study. It was determined that the fever was most likely due to a naturally occurring respiratory disease outbreak. Nasal swabs were not collected from NTV calves because they were vaccinated just prior to the decision to collect samples for diagnostics. Nasal swabs were collected from 12 TV calves before vaccination. The PCR testing of nasal swabs collected on d 1 were negative for BVDV, BRSV, PI3, BHV-1, and bovine coronavirus. Nasal swabs were negative for *Mycoplasma bovis*, *Mannheimia haemolytica,* and *Histophilus somni*, but positive for *Pasteurella multocida* at cycle times of 27-36.

Nine calves had clinical signs of BRD between study d 2 and 19; 6 calves (2 NTV, 3 TV, and 1 TUV) met farm criteria for antibiotic treatment (≥104°F [40°C]; rectal temperature combined with clinical signs such as elevated respiratory rate, shallow cough, depression). The 6 calves were treated with ceftiofur crystalline free acid,[o] and all recovered. One calf in the TUV group died of an intestinal intussusception, and 3 calves were treated for lameness, as determined by the attending veterinarian.

Serum neutralizing antibody titers

Serum neutralizing antibody titers to BHV-1, BRSV, BVDV1, and BVDV2 did not increase significantly between day – 2 and day 21 in TUV calves (Figures 2 through 5). There was a significant overall effect of treatment on BHV-1 SN titers occurring between d -2 and day 21 in both TV and NTV groups (P<0.0005). Vaccinates had significantly higher BHV-1 titers after vaccination than TUV; however, the increase in BRSV titers in vaccinates was not significantly higher than in TUV calves. Transported vaccinates had numerically higher BRSV antibody titers starting at d 7 after vaccination compared to NTV calves (Figure 3; P≥0.10). The majority of calves in all experimental groups had higher type 1 than type 2 BVD SN titers when first tested; however, vaccinated calves had greater BVDV 1 and BVDV 2 titer increases than calves in the TUV group (P<0.02). There were no significant differences

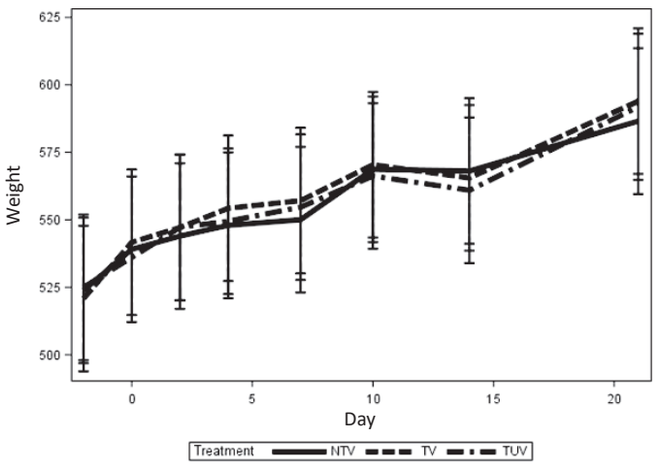

Figure 1. LS means body weights (lb) by study day (error bars represent 95% CI).
NTV=non-transported, vaccinated, TV=transported, vaccinated; TUV=transported, unvaccinated

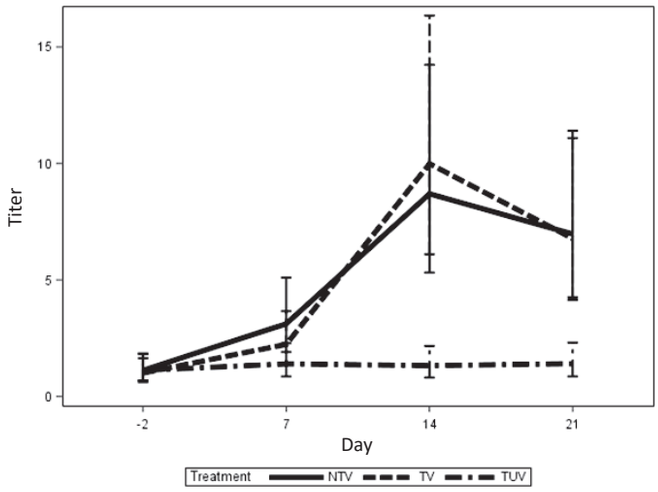

Figure 2. Back transformed LSmean serum neutralizing antibody titers to BHV-1 in weaned beef calves subjected to transportation or not and/or vaccination, by day.
NTV=not transported, vaccinated; TV=transported, vaccinated; TUV=transported, unvaccinated. Overall treatment effect p-value, P = 0.0005; treatment*time interaction p-value, P < 0.0001 Differences at 1) day -2, NS; 2) day 7, NTV & TUV P = 0.0241; 3) day 14, NTV & TUV P < 0.0001, TV & TUV, P <0.0001; 4) day 21, NTV & TUV P < 0.0001, TV & TUV P < 0.0001

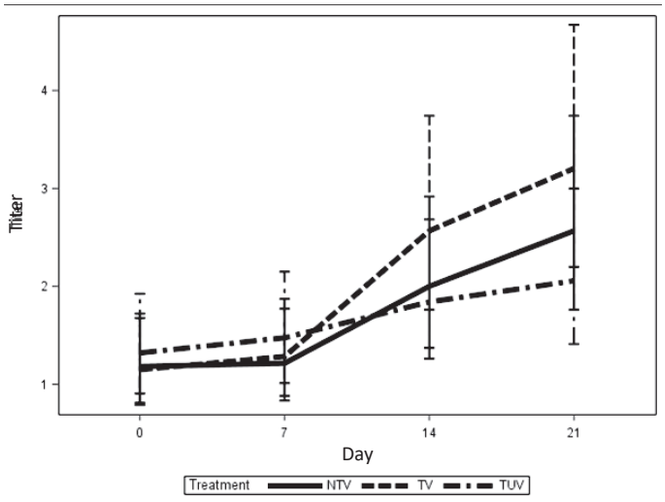

Figure 3. Back transformed LSmean serum neutralizing titers to BRSV in weaned beef calves subjected to transportation or not and/or vaccination, by day.
Error bars represent upper and lower 95% confidence intervals. NTV=not transported, vaccinated; TV=transported, vaccinated; TUV=transported, unvaccinated. Overall treatment effect p-value, *P* = 0.7722; treatment*day interaction p-value, *P* < 0.3553.

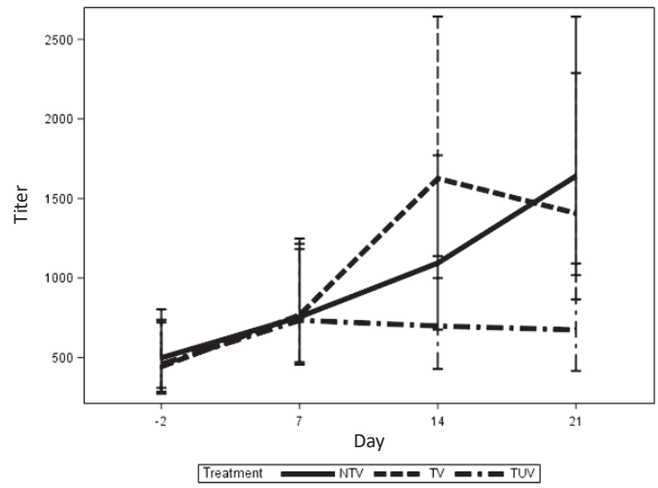

Figure 4. Back transformed LSmean serum neutralizing antibody titers to BVDV-1 in weaned beef calves subjected to transportation or not and/or vaccination, by day.
Error bars represent upper and lower 95% confidence intervals. NTV=not transported, vaccinated; TV=transported, vaccinated; TUV=transported, unvaccinated. Overall treatment effect p-value, P = 0.3074; treatment*day interaction p-value, P = 0.011. Differences at 1) day - 2, NS; 2) day 7, NS; 3) day 14, TV & TUV P = 0.0166; 4) day 21, NTV & TUV P = 0.0104, TV & TUV P = 0.0353

(*P*>0.30) in BVDV 1 and BVDV 2 antibody titers between TV and NTV groups (Figures 4-5).

Nasal IgA and interferon

No differences in the IgA titers for BHV-1 or BRSV were seen between calves in the TV and NTV vaccinated groups (*P*>0.28). While TUV calves did have significantly higher BHV-1 IgA titers (*P*<.02) than the NTV calves, it was not different from the TV calves (Figure 6). For BRSV IgA, there were no differences (*P*>0.35) between groups (Figure 7).

There were no significant differences in alpha, beta, or gamma interferon levels between treatments (Table 1, *P*>0.77, *P*>0.64, *P*>0.08 respectively). While not significant, TUV had increased interferon (alpha, beta, and gamma) levels over baseline. Similarly, interferon gamma levels were increased over baseline in NTV calves, while interferon gamma levels in TV remained relatively low (*P*>0.10; Table 1).

Discussion

The interaction of stress and respiratory pathogens with the bovine immune system has been reported to increase BRD morbidity and mortality over the past several years in spite of newer antibiotics and vaccines.[8,12,20,26,27] Transportation has been identified as a major stressor[2,4,6] impacting immune responses in cattle.[17,21,24,25,28] Chen et al[1] noted that transportation has been a common model of inducing and studying stress in cattle, but added that multiple stressors might be necessary to induce disease consistently. In the current study, a second stress was added with the addi-

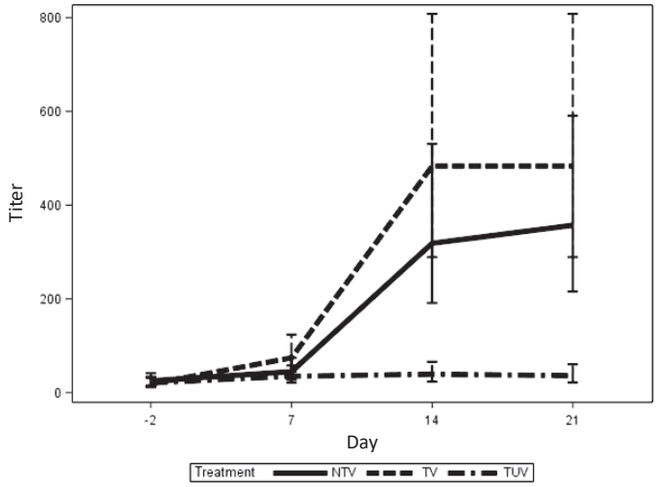

Figure 5. Back transformed LSmean serum neutralizing titers to BVDV-2 in weaned beef calves subjected to transportation or not and/or vaccination, by day.
Error bars represent upper and lower 95% confidence intervals. NTV=not transported, vaccinated; TV=transported, vaccinated; TUV=transported, unvaccinated. Overall treatment effect p-value, P < 0.0001; treatment*day interaction p-value, P < 0.0001. Differences at 1) day - 2, NS; 2) day 7, TV & TUV P = 0.0402; 3) day 14, NTV & TUV P < 0.0001, TV & TUV P<.0001; 4) day 21, NTV & TUV P < 0.0001, TV & TUV P < 0.0001

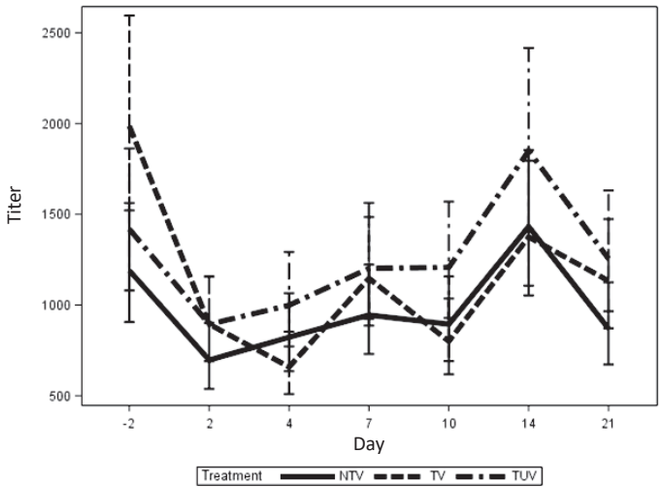

Figure 6. Back transformed LSmean nasal IgA titers to BHV-1 in weaned beef calves subjected to transportation or not and/or vaccination, by day.

Error bars represent upper and lower 95% confidence intervals. NTV=not transported, vaccinated; TV=transported, vaccinated; TUV=transported, unvaccinated. Overall treatment effect p-value, P=.0835, treatment by day interaction P=.0556 and difference between NTV and TUV P=.0264.

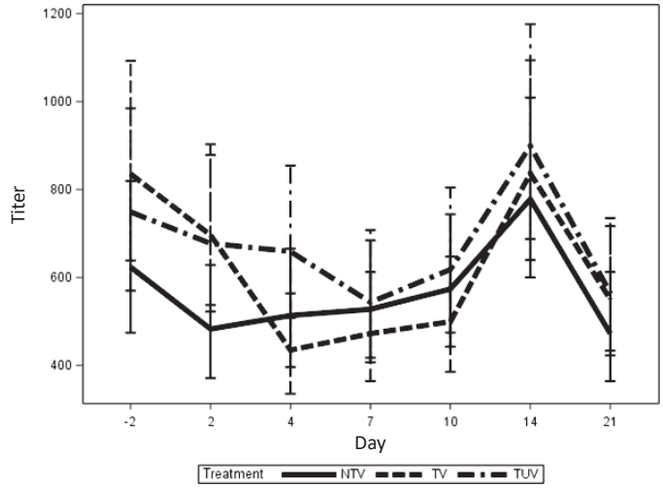

Figure 7. Back transformed LSmean nasal IgA titers to BRSV in weaned beef calves subjected to transportation or not and/or vaccination, by day.

Error bars represent upper and lower 95% confidence intervals. NTV=not transported, vaccinated; TV=transported, vaccinated; TUV=transported, unvaccinated

tional unloading and reloading of cattle. A measurement of the level of stress (i.e. corticosteroid levels) induced in this model would have provided additional information as to the severity of stress the model induced. The delay between transportation and weighing could have given transported

Table 1. IFN alpha, beta, and gamma LSMean concentrations in nasal secretions of weaned calves by day.*†

Item							
Study day	**-2**	**2**	**4**	**7**	**10**	**14**	**21**
				IFN alpha (pg/mL)			
NTV	36.4	14.1	26.3	22.7	29.5	26.0	11.1
TV	54.3	14.0	15.4	22.7	42.2	42.8	8.9
TUV	47.0	18.7	45.1	42.7	26.4	75.8	41.1
				IFN beta (pg/mL)			
NTV	0.0	17.6	55.9	49.8	101.5	97.6	14.0
TV	61.7	83.7	0.0	97.0	164.8	83.7	29.1
TUV	82.1	71.1	138.3	67.6	140.63	311.1	70.1
				IFN gamma (pg/mL)			
NTV	1.7	33.6	10.5	26.1	23.3	55.1	34.0
TV	0.0	0.5	3.9	0.0	7.0	0.0	12.0
TUV	2.8	42.5	4.3	27.4	21.8	43.7	63.1

* NTV=not transported, vaccinated; TV=transported, vaccinated; TUV=transported, vaccinated

† Treatment x day interactions for all 3 interferons: $P > 0.10$

calves time to compensate for any trucking weight loss that may have occurred. Similarities in weight gain between the 3 groups differs from other studies in which administration of MLV vaccines at arrival cattle decreased average daily gain for varying amounts of time.[17,18] This may have been due to inclusion of the intranasal vaccine rather than solely using vaccines administered systemically or that multiple sampling impacted growth similarly in all 3 groups.

Although cattle appeared healthy on study d -2, the elevated rectal temperature (≥104°F; 40°C) found in several NTV and TV calves on study d 1 (before vaccination) suggested a naturally-induced inflammatory process was occurring. Because *P. multocida* is a commensal of the upper respiratory tract, it is not clear whether the PCR results indicate that *P. multocida* was causing the inflammatory response associated with the elevated rectal temperatures. It is possible that an unidentified virus, such as bovine rhinitis virus, bovine rhinovirus, adenovirus, or influenza D virus was circulating among the calves at the time the study began.

The low initial mean SN titers for BHV-1 and BRSV was surprising considering that calves were vaccinated with a MLV 1 month prior to the start of the study. The BVDV titers and antibody levels to BHV-1 and BRSV on d -2 in some individual calves suggest that vaccine had been administered properly. Whether there was a decay of antibody levels post-vaccination or there was a poor vaccination response due to maternal interference or other factors cannot be determined by this study. The slight increase in BRSV SN titers in the TUV cattle from d -2 to d 14 suggests that naturally occurring BRSV infection may have occurred in the cattle. However, lack of BRSV virus identified by RT-PCR of nasal swabs collected from 12 febrile TV calves makes this uncertain. It is possible that

BRSV SN titers increased because of bystander activation of immune cells due to infection by another agent.[11]

All serologic titers following vaccination on d 1 can be considered an anamnestic response induced by vaccination at the beginning of this study. This vaccine served as the booster dose for vaccine administered a month prior to the study. The similar BVDV SN antibody response in the 2 vaccinated groups is consistent with results seen when vaccine was administered on arrival or delayed.[16] However, the numerically higher levels seen in the TV group should be further investigated.

In spite of the low serum antibody levels at the first sampling, all 3 treatment groups initially had high IgA BHV-1 and BRSV antibodies levels. This may be an indication that the respiratory immune system was already being stimulated at that time by the naturally occurring outbreak of respiratory disease, even though the animals had not shown signs of respiratory disease prior to study d 1.[11]

The lack of differences in nasal interferons between study groups may have been caused by the superimposed naturally occurring respiratory disease outbreak at the time cattle were sampled. Thus, the presence of a naturally occurring respiratory infection of uncertain etiology likely influenced the nasal IgA and alpha, beta, and gamma interferon responses in the calves, interfering with our ability to measure specific effects of vaccination and/or stress on the local immune system.

In this study, calves stressed by transportation mounted a systemic immune response as evidenced by seroconversion, similar to previous work in dairy cows.[3] That research showed that cows mounted significant mucosal IgA responses when vaccinated on the day of parturition. Though less dramatic than responses measured in post-partum dairy cows, transport-stressed calves (TV) in the current study had a similar humoral immune response to intranasal vaccination with BHV-1 as calves not transported before vaccination (NTV). The difference in relative degree of response over baseline in these 2 studies may be due to immaturity of the immune system in the current study calves and/or the hormonal changes in dairy cows resulted in immune shifting to a strong mucosal response. These results indicate that transported calves can have similar immune responses to intranasal BHV-1 vaccination and parenteral BVDV2 vaccination when compared to calves not stressed by transportation before vaccination.

Conclusions

The goal of this study was to define immune responses in cattle administered local (mucosal) and systemic vaccine after transport, without other stressors. While the natural respiratory disease outbreak was unexpected, it provided the opportunity to evaluate the immune responses of cattle in a practical, relevant situation. Although vaccination of cattle experiencing acute respiratory infection after transport is not ideal, in certain situations it may be necessary. The current study indicates that cattle exposed to certain stressors may still respond to a vaccination program that includes an intranasal virus vaccine. Results of this study should not be extrapolated to vaccination programs in different risk categories of cattle. Differences in serum and nasal responses further demonstrate the division between the local and systemic immune systems. Results of this study improves the understanding of the interactions between local and systemic immune responses in cattle, and supports continued advancement of effective vaccine strategies.

Endnotes

[a] Cattle Limiter 1, Purina Animal Nutrition, Nashville, TN
[b] CS Balancer R1200 Medicated, Purina Animal Nutrition, LLC, Shoreville, MN
[c] Pyramid® 5, Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO
[d] Ultrabac® 8, Zoetis Inc., Parsippany, NJ
[e] TriVib 5L®, Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO
[f] Inforce™ 3, Zoetis Inc., Parsippany, NJ
[g] One Shot® BVD, Zoetis Inc., Parsippany, NJ
[h] Identi-Plug® Plastic Foam Plugs, Jaece Industries Inc., North Tonawanda, NY
[i] Tru-test™ Scales, Datamars Livestock™, Lamone, Switzerland
[j] MilliporeSigma, Burlington, MA
[k] Bio-Rad Antibodies, Hercules, CA
[l] Kingfisher Biotech Inc., Saint Paul, MN
[m] Biotek®, Winooski, VT
[n] SAS Institute Inc., Cary, NC
[o] Excede®, Zoetis Inc., Parsippany, NJ

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