Evaluation of multiple ancillary therapies used in combination with an antimicrobial in newly received high-risk calves treated for bovine respiratory disease[1]

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ABSTRACT: Ancillary therapy (ANC) is commonly provided in conjunction with an antimicrobial when treating calves for suspected bovine respiratory disease (BRD) in an attempt to improve the response to a suspected BRD challenge. The first experiment evaluated the effects of 3 ANC in combination with an antimicrobial in high-risk calves treated for BRD during a 56-d receiving period. Newly received crossbred steers ($n = 516$; initial BW = 217 ± 20 kg) were monitored by trained personnel for clinical signs of BRD. Calves that met antimicrobial treatment criteria ($n = 320$) were then randomly assigned to experimental ANC treatment (80 steers/experimental ANC treatment): intravenous flunixin meglumine injection (NSAID), intranasal viral vaccination (VACC), intramuscular vitamin C injection (VITC), or no ANC (NOAC). Animal served as the experimental unit for all variables except DMI and G:F (pen served as the experimental unit for DMI and G:F). Within calves treated 3 times for BRD, those receiving NOAC had lower ($P < 0.01$) clinical severity scores (severity scores ranged from 0 to 4 on the basis of observed clinical signs and severity) and heavier ($P = 0.01$) BW than those receiving NSAID, VACC, or VITC at the time of third treatment. Between the second and third BRD treatments, calves receiving NOAC had decreased ($P < 0.01$) daily BW loss (−0.13 kg ADG) compared with those receiving NSAID, VACC, or VITC (−1.30, −1.90, and −1.41 kg ADG, respectively). There were no differences in rectal temperature, combined mortalities and removals, or overall performance among the experimental ANC treatments. Overall, morbidity and mortality attributed to BRD across treatments were 66.5% and 13.2%, respectively. After the receiving period, a subset of calves ($n = 126$) were allocated to finishing pens to evaluate the effects ANC administration on finishing performance, carcass characteristics, and lung scores at harvest. Ultrasound estimates, BW, and visual appraisal were used to target a common physiological end point for each pen of calves. There were no differences among the experimental ANC observed during the finishing period ($P \geq 0.11$). In summary, the use of NSAID, VACC, and VITC do not appear to positively impact clinical health and could potentially be detrimental to performance during the receiving period in high-risk calves receiving antimicrobial treatment for suspected BRD.

Key words: ancillary therapy, bovine respiratory disease, flunixin meglumine, high-risk calves, viral vaccine, vitamin C

INTRODUCTION

Bovine respiratory disease (**BRD**) is the most significant production problem for the feedlot industry, accounting for the majority of morbidity, mortality, and decreased production in feedlots with estimated annual economic losses in excess of $2 billion (Powell, 2013). The standard protocol when treating

for suspected BRD in feedlot cattle is to administer an injectable antimicrobial. However, it is also common for veterinarians to prescribe an additional treatment, or ancillary therapy (**ANC**), along with the antimicrobial. The goal of ANC is to improve the response to a BRD challenge in calves treated with antimicrobials, not to replace antimicrobial treatment. This can be accomplished by relieving the harmful effects of inflammation, blocking histamine activity, or boosting immune system function to aid in the defense against infectious pathogens (Apley, 1994).

In 1999, USDA's National Animal Health Monitoring System (**NAHMS**) surveyed feedlots in the top 12 cattle-feeding states and noted that only 12.8% of feedlots used a single antimicrobial for BRD treatment, whereas the use of multiple products in combination for the treatment of BRD was more common (NAHMS, 2001). Terrell et al. (2011) reported that 48% of veterinarians recommended some form of ANC for the treatment of BRD. Recently, NAHMS (2013) released an updated survey detailing additional ANC use in feedlots. The most common forms of ANC listed in the surveys included antihistamines, B vitamins, corticosteroids, direct-fed microbials, nonsteroidal anti-inflammatory drugs (**NSAID**), viral vaccines, and vitamin C (NAHMS, 2001; Terrell et al., 2011; NAHMS, 2013). Although these surveys provide evidence as to the scope of ANC use, there is limited published research on the efficacy of these ANC. Hence, the objective of this experiment was to evaluate the effects of 3 of the most common ANC used in combination with an antimicrobial on the performance, health, and immune response variables of newly received high-risk calves treated for clinical BRD.

MATERIALS AND METHODS

All procedures for the present experiment were approved by the Oklahoma State University Institutional Animal Care and Use Committee (Animal Care and Use Protocol AG-12–11).

Cattle Description and Initial Processing

Over the course of 1 wk, 516 crossbred steers and bulls (BW at arrival = 217 ± 20 kg) were purchased at livestock auctions throughout Oklahoma and transported (average distance = 135 km) to the Willard Sparks Beef Research Center at Oklahoma State University. Upon arrival at the feed yard, calves were individually weighed and visually inspected for noticeable deformities or abnormalities. Hide color, horn status, and sex were recorded, and a uniquely numbered ear tag was placed in the left ear of each

calf. Calves were then commingled into holding pens, given ad libitum access to prairie hay and water, and allowed to rest 24 to 48 h before initial processing.

Initial processing consisted of vaccination for infectious bovine rhinotracheitis (**IBR**) virus, bovine viral diarrhea virus (**BVDV**) types 1 and 2, parainfluenza 3 (**PI3**) virus, and bovine respiratory syncytial virus (**BRSV**; BRD Shield; Novartis, Greensboro, NC), vaccination for *Clostridium chauvoei*, *Clostridium septicum*, *Clostridium novyi*, *Clostridium sordellii,* and *Clostridium perfringens* types C and D (Caliber 7; Boehringer-Ingelheim, St. Joseph, MO), and treatment for the control of internal and external parasites (Ivomec Plus; Merial, Duluth, GA). Individual BW were obtained, and bulls (*n* = 355) were surgically castrated by incising the scrotum with a Newberry castrating knife followed by emasculation by a single individual. Any calves with horns (*n* = 57) had their horns tipped with a Keystone dehorner.

Receiving Phase Pen Management and Diet

After processing, groups of calves were gate cut and returned to receiving pens, where they received ad libitum access to a common receiving ration and water. Receiving pens were 12.2 × 30.5 m soil-surfaced open-air pens with a 12.2-m concrete bunk at the front of each pen. A 76-L concrete water tank (model J 360-F; Johnson Concrete, Hastings, NE) was shared between 2 pens and was cleaned 3 times/wk throughout the experiment. The common wet corn gluten feed–based receiving ration was formulated to meet or exceed NRC (2000) nutrient requirements (Table 1). The ration was fed to all cattle twice daily at 0700 and 1300 h in a 274-12B Roto-Mix Forage Express mixer wagon (Roto-Mix, Dodge City, KS) to the nearest 0.45 kg of that day's feed call. Feedings were equally split (50% of the day's feed call) between the 0700 and 1300 h feed deliveries. Long-stem prairie hay was fed at 0.454 kg/animal daily for the initial 5 d. Ration samples were collected once per week and dried in a forced-air oven for 48 h at 60°C to determine DM. Ration samples were composited gravimetrically and analyzed at a commercial laboratory (Servi-Tech Inc., Dodge City, KS) for nutrient composition (Table 1).

Assessment for Clinical Signs of BRD and Antimicrobial Administration

Calves remained in the receiving pens and were allocated to an experimental ANC only after they were identified as demonstrating subjective clinical signs of BRD, met treatment criteria, and were administered an antimicrobial. During the receiving period, calves

Table 1. Composition of the common receiving diet[1]

Item	Value
Ingredient, %	
Wet corn gluten feed[2]	48.8
Grain sorghum hay	30.0
Dry-rolled corn	15.0
Dry supplement B-273[3]	5.2
Nutrient composition[4]	
NE_m, Mcal/kg	1.69
NE_g, Mcal/kg	1.07
TDN, %	71.60
CP, %	17.40
Crude fat, %	1.90
NDF, %	39.90
ADF, %	21.40
Ca, %	0.68
P, %	0.67
Mg, %	0.36
K, %	1.15
S, %	0.27

[1]All values are presented on a DM basis.

[2]Sweet Bran (Cargill, Dalhart, TX).

[3]Dry supplement B-273 was formulated to contain (% DM basis) 38.46% ground corn, 30.36% limestone, 21.04% wheat midds, 6.92% urea, 1.03% magnesium oxide, 0.618% zinc sulfate, 0.38% salt, 0.119% copper sulfate, 0.116% manganese oxide, 0.05% selenium premix (contained 0.6% Se), 0.311% vitamin A (30,000 IU/g), 0.085% vitamin E (500 IU/g), 0.317% Rumensin 90 (Elanco Animal Health, Indianapolis, IN), and 0.195% Tylan 40 (Elanco Animal Health).

[4]Feed samples were analyzed for nutrient composition by an independent laboratory (Servi-Tech Laboratories, Dodge City, KS).

were visually monitored twice daily by trained evaluators throughout the experiment for clinical signs characteristic of BRD. The veterinarian that served as the primary evaluator was blinded to all experimental treatments until the conclusion of the experiment.

The evaluation employed criteria based on the DART system (Zoetis, Florham Park, NJ) with some modifications as described by Step et al. (2008). The subjective criteria used for pulling calves consisted of depression, abnormal appetite, and respiratory signs. Signs of depression included but were not limited to depressed attitude, lowered head, glazed or sunken eyes, slow or restricted movement, arched back, difficulty standing or walking, knuckling of joints or dragging toes when walking, and stumbling. Signs of abnormal appetite included an animal that was completely off feed, an animal eating less than expected or eating extremely slowly, a lack of gut fill or gaunt appearance, and obvious BW loss. Respiratory signs included labored breathing, extended head and neck (in an attempt to breathe), and audible noise when breathing. The evaluators assigned a calf a severity score from 0 to 4 on the basis of the clinical signs and the severity of those observed signs. A score of 0 was assigned for a calf that appeared clinically normal. A score of 1 was assigned for mild clinical signs, 2 for moderate clinical signs, 3 for severe clinical signs, and 4 for a moribund animal. For a calf to be assigned a score of 4, the calf had to be unable to rise, had to require assistance to rise, or had to have extreme difficulty standing, walking, or breathing. Calves with severity score of 4 required immediate attention.

The objective criteria used to determine if antimicrobial treatment was necessary was rectal temperature. All calves assigned a severity score of 1 to 4 were taken to the processing chute for rectal temperature measurement (GL M-500; GLA Agricultural Electronics, San Luis Obispo, CA), unless it was deemed necessary for a moribund calf (severity score = 4) to receive treatment in the home pen ($n = 5$). Any animal that was identified with a severity score of 1 or 2 and had a rectal temperature of 40°C or greater received an antimicrobial according to label instructions. If a calf was identified with a severity score of 1 or 2 and had a rectal temperature of less than 40°C, no antimicrobial treatment was administered, and the calf was returned to its receiving pen after evaluation. Any animal with severe clinical signs (severity score = 3 or 4) received an antimicrobial according to label instructions regardless of rectal temperature. In extreme cases the antimicrobial may have been administered in the home pen if the calf was deemed unable to make the trip to the processing facility.

Before antimicrobial administration, BW was obtained to calculate the appropriate dosage. Antimicrobial doses were calculated by rounding the calf's current BW up to the nearest 11.3 kg. All antimicrobials were administered subcutaneously per manufacturer's label directions following Beef Quality Assurance Guidelines (National Cattlemen's Beef Association, 2001). The first antimicrobial treatment was administered on the left side of the animal, and subsequent injections were given on alternating sides of the animal. The severity score, temperature, BW, and antimicrobial dosage administered (or no treatment administered) were recorded for every calf that was identified as exhibiting clinical signs of BRD. A maximum of 4 antimicrobial treatments were administered during the experiment.

The first time antimicrobial treatment criteria were met, gamithromycin 150 mg/mL (Zactran; Merial, Duluth, GA) was administered subcutaneously (**s.c.**) at the rate of 1 mL/24.9 kg of BW. A moratorium was observed after gamithromycin administration before a second antimicrobial treatment could be administered. This moratorium was 240 h for calves with a severity score of 1 or 2 and 96 h for calves with a severity score of 3 or 4 after the initial antimicrobial treatment. If antimicrobial treatment criteria were met a

second time, florfenicol 300 mg/mL (Nuflor; Intervet/ Schering-Plough, Desoto, KS) was administered s.c. at the rate of 1 mL/7.56 kg of BW. After florfenicol administration, a 96-h moratorium was observed before a third antimicrobial treatment could be administered regardless of severity score. If antimicrobial treatment criteria were met a third time, ceftiofur crystalline free acid 200 mg/mL (Excede; Pfizer, New York, NY) was administered s.c. at the base of the ear at the rate of 1 mL/30.2 kg of BW. After ceftiofur crystalline free acid administration, a 168-h moratorium was observed before a fourth antimicrobial treatment could be administered regardless of severity score. If antimicrobial treatment criteria were met a fourth time, a second dose of ceftiofur crystalline free acid was administered as previously described.

Allocation to Experimental ANC Treatments and ANC Administration

Once a calf was "pulled" for suspected BRD, met the treatment criteria described, and was administered an antimicrobial, it was then randomly assigned to 1 of 4 ANC treatments. Calves received their respective experimental ANC at the time of initial antimicrobial treatment and during all subsequent BRD treatments. The 4 ANC treatments consisted of an intravenous flunixin meglumine injection (NSAID), an intranasal viral vaccination (VACC), an intramuscular vitamin C injection (VITC), or no ANC (NOAC). The VITC experimental ANC treatment consisted of 10 mL per calf of Vita-Jec C (Aspen, Liberty, MO) containing 250 mg of sodium ascorbate per milliliter injected intramuscularly. The NSAID experimental ANC treatment consisted of 2 mL per 45.4 kg of BW of Suppressor (RXVeterinary, Westlake, TX) containing 50 mg of flunixin per milliliter injected intravenously. The VACC experimental ANC treatment consisted of 2 mL per calf of Inforce 3 (Zoetis, Florham Park, NJ) viral respiratory vaccine containing IBR-PI3-BRSV isolates administered intranasally. The NOAC experimental treatment consisted of no experimental ANC, and only an antimicrobial injection was administered at the time of BRD treatment.

After calves were administered their experimental ANC, they were allocated to a new home pen that previously had been randomly assigned to their respective ANC group. The calves remained in these pens for the duration of the experiment with the exception of mortalities and removals. These pens had the same dimensions and pen structure of the receiving pens previously described. A group of 4 pens (1 pen/ANC) remained open until 80 calves (20 steers/pen) were allocated to those pens. The average length of time required to fill a group of pens was 3 d, and half the pens on the experiment were filled in 2 d. The date when a group of pens were closed was determined to be d 0 for that group of 4 pens. A total of 4 pens per experimental ANC were used during the experiment, resulting in a total of 80 calves per experimental ANC group.

Removals, Postmortem Examinations, and Pathogens

Standards for defining chronically ill (CI) calves were instituted if it was determined by the trained evaluators that there was a potential animal welfare concern resulting from severe lameness or the inability to compete within the home pen. A calf could be removed from the experiment only once it was classified as CI. To be classified as CI, an animal must have previously been administered all 4 antimicrobial treatments according to protocol and at least 48 h must have passed after the last antimicrobial treatment was administered. The calf must have been enrolled in the experiment long enough to receive all 4 antimicrobial treatments and have experienced a net loss of BW during the experiment. In addition, the calf must have been assigned a severity score of 3 or 4 on the day it was removed from the home pen.

Gross postmortem examinations were performed on all mortalities by veterinarian-trained personnel to determine cause of death. All mortalities that occurred during the receiving period were attributed to BRD. Full postmortem necropsies were performed on 3 random mortalities by the Oklahoma Animal Disease Diagnostic Laboratory. Bacterial and viral pathogens identified in the necropsy reports included *Mannheimia haemolytica, Mycoplasma bovis, Pasteurella multocida,* bovine viral diarrhea virus, and bovine coronavirus.

Receiving Phase Data Collection, Calculations, and Statistical Analysis

A shrunk BW was obtained for all animals on arrival. Unshrunk BW were obtained at the time of initial BRD treatment and all subsequent BRD treatments. Interim BW were determined for all animals by weighing all pens and individual animals on d 28 and 56 after pens were closed. Body weights obtained at the time of BRD treatments and on d 28 and 56 are presented with a calculated 2% shrink. Individual BW and individual days on feed (DOF) were used to calculate individual ADG. Actual head days within a pen and total feed consumption were used to calculate DMI. Average DMI and ADG for the pen were used to calculate G:F.

Data were analyzed using the GLIMMIX procedure of SAS 9.4 (SAS Inst. Inc., Cary, NC) with ani-

mal serving as the experimental unit for all variables except DMI and G:F (pen served as the experimental unit for DMI and G:F). Means were separated using the PDIFF option. Pen replication, gender at the time of arrival (bull or steer), and horn status at the time of arrival (horned, polled, or scurred) were included in the model as random effects. Results were considered significantly different when $P \leq 0.05$. Tendencies are discussed when $0.05 < P \leq 0.10$. Data were analyzed with mortalities and removals included (deads in) and with mortalities and removals excluded (deads out). For the deads-out analysis, the feed consumptions for mortalities and off-trial calves were removed from the pen at a calculated maintenance intake level. The NRC (2000) equation $NE_m = 0.077$ Mcal/empty BW (**EBW**)$^{0.75}$ and ration NE_m concentration were used to calculate maintenance DMI.

Finishing Phase Cattle Management

After the receiving period, calves remained in their home pens and received ad libitum access to the common receiving ration (Table 1) and water for 2 to 3 additional weeks. After this additional period (average total DOF = 86), a subset of 126 calves were allocated to the finishing experiment. For the finishing experiment, all previous experimental ANC were maintained, but calves were also allocated by the number of antimicrobial treatments administered during the receiving period. This resulted in 6 pens or replications of each ANC treatment (2 pens of calves that received 1 antimicrobial treatment, 2 pens of calves that received 2 antimicrobial treatments, and 2 pens of calves that received 3 or 4 antimicrobial treatments).

Before allocation to finishing pens, all steers were administered 200 mg trenbolone acetate and 40 mg estradiol (Revalor XS; Merck Animal Health, Summit, NJ) in the caudal aspect of the right ear per manufacturer's directions. The goal was to harvest all calves at a common physiological end point regardless of DOF while still maintaining the integrity of the pen and shipping truck load lots. This was accomplished through the use of the ultrasound estimates, BW, and visual appraisal. Calves were harvested in 2 groups (DOF = 166 or 197). For the last 28 DOF, all steers were fed ractopamine hydrochloride (Optaflexx 45; Elanco Animal Health, Indianapolis, IN) at 300 mg·steer^{-1}·d^{-1}.

Finishing Phase Pen Management and Diet

Finishing pens were 4.57×15.24 m in area with a 4.57-m-long concrete bunk at the front of the pen. The pens contained a 4.57×4.42 m concrete pad, with the remainder of the pen being soil surfaced. The pens

Table 2. Composition of the common finishing diet[1]

Item	Value
Ingredient, %	
Dry-rolled corn	48.14
Wet corn gluten feed[2]	15.00
Dried distillers grains plus solubles	15.00
Prairie hay	9.00
Liquid supplement[3]	6.54
Dry supplement B-273[4]	3.12
Dry supplement B-283[5]	3.20
Nutrient composition[6]	
NE_m, Mcal/kg	2.23
NE_g, Mcal/kg	1.54
TDN, %	89.55
CP, %	18.85
Crude fat, %	5.00
NDF, %	22.35
ADF, %	10.40
Ca, %	0.96
P, %	0.52
Mg, %	0.28
K, %	1.03
S, %	0.31

[1]All values are presented on a DM basis.

[2]Sweet Bran (Cargill, Dalhart, TX).

[3]Synergy 19-14 (Westway Feed Products, New Orleans, LA).

[4]Dry supplement B-273 was formulated to contain (% DM basis) 38.46% ground corn, 30.36% limestone, 21.04% wheat midds, 6.92% urea, 1.03% magnesium oxide, 0.618% zinc sulfate, 0.38% salt, 0.119% copper sulfate, 0.116% manganese oxide, 0.05% selenium premix (contained 0.6% Se), 0.311% vitamin A (30,000 IU/g), 0.085% vitamin E (500 IU/g), 0.317% Rumensin 90 (Elanco Animal Health, Indianapolis, IN), and 0.195% Tylan 40 (Elanco Animal Health).

[5]Dry supplement B-283 was formulated to contain (% DM basis) 40.47% limestone, 36.26% ground corn, 19.73% wheat midds, 2.47% salt, 0.312% zinc sulfate, 0.071% copper sulfate, 0.064% manganese oxide, 0.029% selenium premix (contained 0.6% Se), 0.202% vitamin A (30,000 IU/g), 0.056% vitamin E (500 IU/g), 0.207% Rumensin 90 (Elanco Animal Health, Indianapolis, IN), and 0.127% Tylan 40 (Elanco Animal Health).

[6]Feed samples were analyzed for nutrient composition by an independent laboratory (Servi-Tech Laboratories, Dodge City, KS).

were under partial cover, with the bunk and pad being covered by an overhang. A 76-L concrete water tank (model J 360-F; Johnson Concrete, Hastings, NE) was shared between 2 pens and was cleaned 3 times/wk throughout the experiment.

The common finishing ration was formulated to meet or exceed NRC (2000) nutrient requirements (Table 2). Adaptation to the finishing diet was accomplished using a 2-ration blend method where each day the percentage of finishing diet delivered was increased by approximately 4.6% DM, and the percentage of receiving diet (Table 1) delivered was decreased by approximately 4.6% DM until only the finishing diet was being fed. Following adaptation, the finishing ration was fed to all cattle twice daily at 0700 and 1300 h in a 274-12B Roto-Mix Forage Express mixer wagon (Ro-

to-Mix) to the nearest 0.45 kg of that day's feed call. Ration samples were collected once a week and were dried in a forced-air oven for 48 h at 60°C to determine DM. Ration samples were composited gravimetrically and analyzed at a commercial laboratory (Servi-Tech Inc.) for nutrient composition (Table 2).

Finishing Phase Data Collection, Calculations, and Statistical Analysis

Unshrunk BW were obtained at the time of allocation to finishing pens and at approximately 45-d intervals thereafter. All BW were shrunk a calculated 4%. Ultrasound estimates were taken at 91 and 138 DOF. Carcass data along with lung consolidation and lung adhesion scores were obtained at the harvest facility by trained personnel from West Texas A&M University. Lung consolidation scores ranged from 0 to 3, with 0 being a clinically normal, healthy appearing lung with less than 5% consolidation of lung tissue; 1 being approximately 5% consolidation of lung tissue or mycoplasma-like lesion; 2 being greater than 5% but less than 50% consolidation of lung tissue, missing lung, or mycoplasma-like lesion; and 3 being greater than 50% consolidation of lung tissue, missing lung, or mycoplasma-like lesion. Lung adhesion scores ranged from 0 to 2, with 0 being a clinically normal, healthy-looking lung; 1 being a lung with minor threadlike fibrous adhesion; and 2 being a lung with extensive fibrous adhesion. Data were analyzed using the GLIMMIX procedure of SAS 9.4 (SAS Inst. Inc.) with animal serving as the experimental unit for all variables except DMI and G:F (pen served as the experimental unit for DMI and G:F). Means were separated using the PDIFF option. Initially, data were analyzed for an interaction between experimental ANC and the number of antimicrobials administered. Because of the lack of significant interactions, data were subsequently analyzed on the basis of only ANC. Results were considered significantly different when $P \leq 0.05$. Tendencies are discussed when $0.05 < P \leq 0.10$. Data were analyzed with mortalities (4, with 3 digestive and 1 BRD) included in the analysis (deads in). One NOAC calf, 1 VACC calf, and 2 VITC calves died during the finishing phase of the experiment. Because calves were harvested at varying DOF, harvest group was included in the model as a random effect for the analysis of marbling number and the percentage of USDA Prime and Choice carcasses.

RESULTS

Receiving Phase Calf Performance within BRD Treatment Intervals

Calf performance within BRD treatment intervals is presented in Table 3. The BW of calves at the time of the initial BRD treatment was not different between the 4 experimental ANC ($P = 0.78$). There was also no difference ($P = 0.82$) in the BW of calves among ANC groups at the time of second antimicrobial administration for BRD. Between the first and second BRD treatments, calves on all experimental ANC treatments lost an average of 0.66 kg/d, but there was no difference among ANC ($P = 0.63$).

By the time calves received a third antimicrobial treatment for BRD, those calves receiving NOAC had significantly heavier BW compared with the other 3 ANC groups ($P = 0.01$). This was a result of the calves receiving NOAC losing only 0.13 kg/d between the second and third BRD treatments, whereas the calves receiving NSAID, VACC, and VITC lost an average of 1.54 kg during the same interval. The ADG of the NOAC calves was significantly greater than the ADG for the other 3 ANC groups during this time period ($P < 0.01$). There were no differences ($P = 0.60$) in BW among ANC by the time a fourth antimicrobial was administered. In addition, ADG between the third and fourth BRD antimicrobial treatments and the overall ADG between the first and fourth BRD antimicrobial treatments were not different between ANC groups ($P = 0.99$ and $P = 0.94$, respectively).

Retreatment Percentages and BRD Retreatment Intervals

The data for BRD retreatment percentages and the length of time between BRD treatments are also presented in Table 3. Calves that received NOAC required a fourth antimicrobial treatment for BRD less frequently than calves receiving VITC and tended to require a second antimicrobial treatment for BRD less frequently than calves receiving VACC ($P = 0.05$). Calves that received NSAID tended to require a fourth antimicrobial treatment for BRD less often than calves receiving VITC ($P = 0.05$). However, when comparing individual ANC means, there was no difference between calves receiving NOAC or NSAID, and NSAID was also not different from VACC ($P \geq 0.63$). There were no differences ($P \geq 0.26$) between ANC for any other BRD retreatment percentages. There were no differences ($P \geq 0.30$) between ANC for the length of time until the first, second, or fourth BRD antimicrobial treatments. However, it should be noted that calves receiving NOAC received their third BRD treatments at significantly greater days after arrival ($P < 0.001$).

Table 3. Effects of ancillary therapies used in combination with an antimicrobial on performance, retreatment percentages, and retreatment intervals

Variable	Experimental ancillary treatment[1]				Pooled SEM	Overall P-value[2]
	NOAC	NSAID	VACC	VITC		
Treatment BW,[3] kg						
First treatment	215	214	212	213	3.32	0.78
Second treatment	214	209	212	212	6.97	0.82
Third treatment	211[a]	192[b]	192[b]	192[b]	5.63	0.01
Fourth treatment	193	181	190	194	12.1	0.60
Average daily gain,[4] kg						
First to second	−0.54	−0.48	−0.61	−1.01	0.40	0.63
Second to third	−0.13[a]	−1.30[b]	−1.90[b]	−1.41[b]	0.42	<0.01
Third to fourth	−0.31	−0.28	−0.48	−0.45	0.72	0.99
First to fourth	−0.89	−0.97	−1.16	−1.01	0.34	0.94
Retreatments,[5] %						
Second treatment	48.8	51.3	37.5	43.8	11.4	0.26
Third treatment	55.1	42.7	50.4	44.7	13.5	0.67
Fourth treatment	29.7[a,x]	35.7[a,y]	59.2[y,z]	67.2[b,z]	12.1	0.05
Third treatment, % of first	30.0	25.0	21.3	22.5	9.63	0.54
Fourth treatment, % of first	8.75	8.75	12.5	15.0	5.48	0.50
Time to treatment,[6] d						
First treatment	7.53	7.28	7.30	7.27	1.36	0.82
Second treatment	19.4	16.7	18.0	16.9	3.34	0.31
Third treatment	26.4[a]	18.2[b]	18.3[b]	17.9[b]	2.22	<0.001
Fourth treatment	31.0	26.7	24.7	25.8	2.66	0.30

[a,b]Within a row means with different superscripts differ ($P \leq 0.05$).

[x–z]Within a row means with different superscripts tend to differ ($P \leq 0.10$).

[1]Experimental ancillary therapy treatments administered at each antimicrobial treatment for bovine respiratory disease: NOAC = antimicrobial only, no ancillary therapy; NSAID = intravenous flunixin meglumine injection; VACC = revaccination with an intranasal viral vaccine; VITC = intramuscular vitamin C injection.

[2]P-values are included for the overall F test.

[3]Treatment BW was the BW in kilograms with a calculated 2% shrink at the time of bovine respiratory disease (BRD) treatment.

[4]Treatment ADG was calculated from the shrunk (2%) BW in kilograms and individual days on feed between the BRD treatments.

[5]Retreatment percentages were calculated by taking the number of calves treated for BRD divided by the number of calves treated for BRD the previous time in the case of second treatment, third treatment, and fourth treatment or by taking the number of calves treated for BRD divided by the number of calves treated for BRD initially in the case of third treatment percentage of first and fourth treatment percentage of first.

[6]Average length of time in days from arrival until the BRD treatment.

Subjective Clinical Severity Scores and Rectal Temperatures

The data for subjective clinical severity scores and rectal temperatures at the time of BRD treatment are reported in Table 4. There was a tendency ($P = 0.06$) for calves receiving VACC to have lower clinical severity scores than calves receiving NOAC, NSAID, or VITC at the time of initial BRD treatment. At the time of the second BRD treatment, calves receiving NOAC had lower ($P < 0.01$) clinical severity scores than calves

Table 4. Effects of ancillary therapies used in combination with an antimicrobial on clinical severity scores, rectal temperatures, and mortalities and removals

Variable	Experimental ancillary treatment[1]				Pooled SEM	Overall P-value[2]
	NOAC	NSAID	VACC	VITC		
Severity score[3]						
First treatment	1.14[a,x]	1.13[a,x]	1.04[b,y]	1.18[a]	0.06	0.06
Second treatment	2.37[a]	2.83[c]	2.53[ab]	2.69[b,c]	0.27	<0.01
Third treatment	2.50[a]	2.84[b]	2.98[b]	3.11[b]	0.23	<0.01
Fourth treatment	2.84	3.05	2.99	2.83	0.30	0.72
Rectal temperature,[4] °C						
First treatment	40.7	40.7	40.8	40.8	0.08	0.27
Second treatment	40.3	40.3	40.5	40.3	0.19	0.87
Third treatment	39.6	39.4	39.4	39.4	0.33	0.86
Fourth treatment	39.5	39.4	39.0	39.1	0.31	0.55
Off trial, %						
Mortality	17.5	22.5	20.0	23.8	8.97	0.74
Removals[5]	6.17[a]	0.00[b]	3.65[a,b]	1.16[b]	1.92	0.08
Combined off trial[6]	23.8	22.5	23.8	25.0	9.85	0.98

[a–c]Within a row means with different superscripts differ ($P \leq 0.05$).

[x,y]Within a row means with different superscripts tend to differ ($P \leq 0.10$).

[1]Experimental ancillary therapy treatments administered at each antimicrobial treatment for bovine respiratory disease: NOAC = antimicrobial only, no ancillary therapy; NSAID = intravenous flunixin meglumine injection; VACC = revaccination with an intranasal viral vaccine; VITC = intramuscular vitamin C injection.

[2]P-values are included for the overall F test.

[3]Subjective clinical severity score (1 = mild clinical signs, 2 = moderate clinical signs, 3 = severe clinical signs, and 4 = extreme clinical signs or a moribund animal) assigned by trained personnel. For a calf to be assigned a clinical severity score of 4, the calf had to be unable to rise or had to have extreme difficulty standing, walking, or breathing.

[4]Rectal temperature at the time of bovine respiratory disease (BRD) treatment.

[5]Percentage of calves removed from the experiment because of lameness or the inability to compete in the home pen (includes surviving chronic BRD cases).

[6]Combined percentage of mortalities and removals for the experiment.

receiving NSAID or VITC, whereas the severity scores of calves receiving VACC were lower ($P < 0.01$) than the clinical severity scores of calves receiving NSAID but not different ($P \geq 0.30$) from those for NOAC or VITC. At the time of the third BRD treatment, calves receiving NOAC had lower ($P < 0.01$) clinical severity scores than calves receiving any of the 3 other ANC. Upon receiving a fourth antimicrobial treatment, there was again no difference among any of the ANC groups ($P = 0.72$). There were no differences ($P \geq 0.27$) in rectal temperatures among any of the ANC at any BRD treatment event throughout the experiment.

Removals and Mortality Attributed to BRD

Data concerning mortality attributed to BRD and removal of calves from the experiment are reported in Table 4. There were no differences ($P = 0.74$) in the mortality percentages among the ANC groups, whereas the calves receiving NOAC did exhibit numerically decreased mortality compared with the other ANC groups. There was a tendency ($P = 0.08$) for calves receiving NOAC to be removed from the experiment more frequently than calves receiving NSAID or VITC. The numerical decrease in mortality and tendency for increased removal for calves receiving NOAC resulted in no difference ($P = 0.98$) in the combined percentage of calves that were not able to complete the experiment due to BRD-related mortality or removal from the home pen as a result of severe lameness or the inability to compete.

Receiving Phase Performance with Mortalities and Removals Included

The performance data including mortalities and removals (deads-in data) are included in Table 5. No differences ($P \geq 0.23$) existed between any of the individual ANC for any of the performance or efficiency data when evaluated on a deads-in basis.

Receiving Phase Performance with Mortalities and Removals Excluded

The performance data with mortalities and removals excluded (deads-out data) are given in Table 6. Although calves receiving NOAC had numerically heavier BW on d 28 and 56, there were no differences ($P \geq 0.15$) between any of the individual ANC for any of the performance or efficiency data when evaluated on a deads-out basis.

Finishing Performance, Efficiency, Lung Scores, and Carcass Characteristics

Body weight at the time of arrival (BW before the initiation of the receiving experiment) was not different for the subpopulation of calves used for the finishing experiment ($P = 0.48$). No ANC differences were observed in the overall model for any of the variables analyzed in the finishing experiment ($P \geq 0.11$; Table 7). There were also no differences observed in ultrasound measurements, lung scores, or carcass characteristics among any of the ANC ($P \geq 0.26$; Table 8).

Table 5. Effects of ancillary therapies used in combination with an antimicrobial on receiving performance with mortalities and removals included

Variable	Experimental ancillary treatment[1]				Pooled SEM	Overall P-value[2]
	NOAC	NSAID	VACC	VITC		
BW,[3] kg						
First treatment	215	214	212	213	3.32	0.78
d 28	251	244	245	244	4.12	0.45
d 56	290	281	282	280	5.21	0.28
ADG,[4] kg						
First treatment to d 28	1.19	1.02	1.16	1.03	0.11	0.47
d 29 to d 56	1.30	1.25	1.32	1.24	0.12	0.64
First treatment to d 56	1.29	1.16	1.23	1.18	0.07	0.36
DMI,[5] kg						
First treatment to d 28	5.04	4.57	4.80	4.82	0.54	0.40
d 29 to d 56	7.95	7.29	7.58	7.48	0.24	0.23
First treatment to d 56	6.34	5.77	6.04	6.05	0.41	0.32
G:F[6]						
First treatment to d 28	0.238	0.232	0.246	0.219	0.02	0.72
d 29 to d 56	0.157	0.165	0.167	0.164	0.01	0.75
First treatment to d 56	0.200	0.205	0.202	0.196	0.01	0.93

[1]Experimental ancillary therapy treatments administered at each antimicrobial treatment for bovine respiratory disease: NOAC = antimicrobial only, no ancillary therapy; NSAID = intravenous flunixin meglumine injection; VACC = revaccination with an intranasal viral vaccine; VITC = intramuscular vitamin C injection.

[2]P-values are included for the overall F test.

[3]Treatment BW was the BW in kg with a calculated 2% shrink.

[4]Treatment ADG was calculated from the shrunk (2%) BW in kg and days on feed between the time periods.

[5]Treatment DMI was calculated by taking DMI in kg for a pen for the period shown divided by the actual number of head days within each pen including mortalities and removals (deads in).

[6]Treatment G:F was calculated by taking the pen ADG in kg divided by the pen average DMI in kg for the time periods.

DISCUSSION

The goal of ANC administration is to focus on the overall health of the calf or improving the calf's clinical signs rather than treating the invading pathogens responsible for the illness, as would be the case with antimicrobials. The use of vaccines as an ANC would be 1 of the few exceptions, in that they may boost the immune system by providing a pathogen-specific antibody response. The improvement in the calf's response resulting from ANC administration can be theoretically accomplished through a variety of mechanisms, and these mechanisms can subsequently be divided into 3 broad classes. The 3 classes of ANC can potentially impact overall calf health or the calf's clinical signs by relieving the harmful effects of inflammation, decreasing histamine activ-

Table 6. Effects of ancillary therapies used in combination with an antimicrobial on receiving performance with mortalities and removals excluded

Variable	NOAC	NSAID	VACC	VITC	Pooled SEM	Overall P-value[2]
BW,[3] kg						
First treatment	216	214	212	213	2.81	0.58
d 28	253	246	245	246	3.67	0.23
d 56	290	281	282	280	5.21	0.28
ADG,[4] kg						
First treatment to d 28	1.30	1.11	1.17	1.14	0.08	0.36
d 29 to d 56	1.30	1.25	1.32	1.24	0.12	0.64
First treatment to d 56	1.29	1.16	1.23	1.18	0.07	0.36
DMI,[5] kg						
First treatment to d 28	5.43	4.76	5.04	5.14	0.46	0.19
d 29 to d 56	8.05	7.37	7.58	7.66	0.22	0.21
First treatment to d 56	6.70	6.03	6.28	6.37	0.31	0.15
G:F[6]						
First treatment to d 28	0.238	0.245	0.233	0.220	0.02	0.81
d 29 to d 56	0.155	0.164	0.167	0.160	0.01	0.69
First treatment to d 56	0.189	0.194	0.193	0.185	0.01	0.87

[1]Experimental ancillary therapy treatments administered at each antimicrobial treatment for bovine respiratory disease: NOAC = antimicrobial only, no ancillary therapy; NSAID = intravenous flunixin meglumine injection; VACC = revaccination with an intranasal viral vaccine; VITC = intramuscular vitamin C injection.

[2]P-values are included for the overall F test.

[3]Treatment BW was the BW in kg with a calculated 2% shrink.

[4]Treatment ADG was calculated from the shrunk (2%) BW in kg and days on feed between the time periods.

[5]Treatment DMI was calculated by taking DMI in kg for a pen for the period shown divided by the actual number of head days within each pen excluding mortalities and removals (deads out). Mortalities and removals were backed out of the pen at a calculated maintenance DMI (NEm = 0.077 Mcal/empty BW$^{0.75}$).

[6]Treatment G:F was calculated by taking the pen ADG in kg divided by the pen average DMI in kg for the time periods.

Table 7. Effects of ancillary therapies used in combination with an antimicrobial on subsequent finishing performance and efficiency of crossbred steers

Variable	NOAC	NSAID	VACC	VITC	Pooled SEM	Overall P-value[2]
Days on feed,[3] d	181	182	190	182	2.98	0.11
BW,[4] kg						
Initial	294	289	287	297	5.98	0.60
d 45	375	368	365	374	6.80	0.62
d 91	441	432	429	432	7.61	0.66
d 138	503	498	495	500	8.65	0.92
Final	562	561	565	565	9.12	0.98
ADG,[5] kg						
Initial to d 45	1.81	1.75	1.74	1.72	0.06	0.70
d 46 to d 91	1.43	1.41	1.40	1.26	0.07	0.24
d 92 to d 138	1.33	1.40	1.40	1.44	0.08	0.43
d 139 to final	1.44	1.52	1.39	1.55	0.08	0.44
Initial to final	1.49	1.50	1.47	1.48	0.05	0.98
DMI,[6] kg						
Initial to d 45	8.57	8.65	8.73	8.58	0.23	0.96
d 46 to d 91	9.71	9.75	10.1	10.1	0.33	0.73
d 92 to d 138	10.1	9.78	10.2	10.5	0.31	0.48
d 139 to final	10.2	9.87	9.91	10.4	0.30	0.60
Initial to final	9.63	9.49	9.74	9.82	0.23	0.76
G:F[7]						
Initial to d 45	0.212	0.203	0.198	0.197	0.01	0.26
d 46 to d 91	0.149	0.145	0.139	0.130	0.01	0.31
d 92 to d 138	0.132	0.145	0.140	0.144	0.01	0.49
d 139 to final	0.140	0.155	0.140	0.151	0.01	0.54
Initial to final	0.155	0.159	0.151	0.154	<0.01	0.61

[1]Experimental ancillary therapy treatments administered at each antimicrobial treatment for bovine respiratory disease: NOAC = antimicrobial only, no ancillary therapy; NSAID = intravenous flunixin meglumine injection; VACC = revaccination with an intranasal viral vaccine; VITC = intramuscular vitamin C injection.

[2]P-values are included for the overall F test.

[3]Average of days on feed for all pens within an experimental treatment.

[4]Treatment BW was the BW in kilograms with a calculated 4% shrink.

[5]Treatment ADG was calculated from the shrunk (4%) BW in kilograms and days on feed between the time periods.

[6]Treatment DMI was calculated by taking DMI in kilograms for a pen for the period shown divided by the actual number of head days within each pen.

[7]Treatment G:F was calculated by taking the pen ADG in kilograms divided by the pen average DMI in kilograms for the time periods.

ity, or improving immune system function to aid in the defense against BRD pathogens (Apley, 1994).

The objective of this experiment was to evaluate the effects of 3 of the most commonly used ANC that also had significantly different intended effects and modes of action in combination with an antimicrobial within a common population of newly received, high-risk calves that were treated for BRD. It has been established that there is widespread use of ANC within the feedlot industry through surveys conducted by NAHMS (2001, 2013) and Terrell et al. (2011). However, there is limited published controlled research concerning the effectiveness of the various forms of ANC, and there is no published research, to our

Table 8. Effects of ancillary therapies used in combination with an antimicrobial on ultrasound estimates, lung scores, and carcass characteristics of crossbred steers

Variable	Experimental ancillary treatment[1]				Pooled SEM	Overall P-value[2]
	NOAC	NSAID	VACC	VITC		
Ultrasound estimates[3]						
d 91 REA, cm[2]	80.5	79.4	77.0	80.6	1.80	0.44
d 91 12th-rib fat, cm	0.81	0.77	0.81	0.77	0.04	0.73
d 91 IMF	4.21	4.17	4.47	4.31	0.16	0.53
d 138 REA, cm[2]	87.7	87.6	83.5	87.2	1.77	0.26
d 138 12th-rib fat, cm	0.92	0.91	0.93	0.90	0.05	0.98
d 138 IMF	4.45	4.20	4.49	4.33	0.17	0.55
Lung scores[4]						
Consolidation[5]	0.60	1.03	0.92	0.79	0.20	0.33
Adhesion[6]	0.80	0.70	1.00	0.86	0.16	0.58
HCW, kg	363	360	364	363	6.69	0.97
Dressing percentage	64.5	64.2	64.5	64.3	0.53	0.97
REA, cm[2]	92.4	90.9	91.0	91.6	2.04	0.94
12th-rib fat, cm	1.33	1.26	1.42	1.32	0.09	0.67
KPH fat, %	2.00	2.00	2.06	2.11	0.07	0.58
Marbling score[7]	407	415	436	440	20.6	0.29
Prime and choice,[8] %	43.0	56.3	61.8	53.6	12.6	0.51
Yield grade	2.67	2.63	2.84	2.72	0.17	0.81
Liver score[9]	0.54	0.36	0.35	0.29	0.25	0.87

[1]Experimental ancillary therapy treatments administered at each antimicrobial treatment for bovine respiratory disease: NOAC = antimicrobial only, no ancillary therapy; NSAID = intravenous flunixin meglumine injection; VACC = revaccination with an intranasal viral vaccine; VITC = intramuscular vitamin C injection.

[2]P-values are included for the overall F test.

[3]Ultrasound estimates of rib eye area (REA), 12th-rib fat thickness, and intramuscular fat (IMF) were taken on d 91 and 138 by Chad Gordon of Ultrasound Technologies, Fletcher, OK.

[4]Lung scores were obtained by trained personnel from West Texas A&M University.

[5]Lung consolidation: 0 = clinically normal, healthy lung with <5% consolidation of lung tissue; 1 = ±5% consolidation of lung tissue or mycoplasma-like lesion; 2 = >5% but <50% consolidation of lung tissue, missing lung, or mycoplasma-like lesion; 3 = >50% consolidation of lung tissue, missing lung, or mycoplasma-like lesion.

[6]Lung adhesion: 0 = clinically normal, healthy lung; 1 = minor thread-like fibrous adhesion; 2 = extensive fibrous adhesion.

[7]Marbling scores: 400 = Small[00], 500 = Modest[00].

[8]Pecentage of calves with prime or choice carcasses within each pen.

[9]Liver Score: 0 = no abscesses, 1 = A−, 2 = A, 3 = A+, 4 = telangiectasis, 5 = distoma (fluke damage), and 6 = fecal contamination.

knowledge, comparing multiple commonly administered ANC within a single experiment or across similar groups of calves. According to the most recent survey detailing ANC use conducted by NAHMS (2013),

the 3 ANC used in this experiment were the 3 most frequent forms of ANC given on a percentage of cattle treated basis in commercial feedlots.

In addition to comparing multiple ANC within a single experiment across a similar group of calves, the present experiment aimed to observe the effects of ANC in a group of newly received, high-risk exposed calves originating from multiple livestock auctions. If only a small incidence of BRD were to occur within an experiment, any observed responses to the ANC could be viewed as less valid. The calves in this experiment experienced a significant natural immune challenge resulting in a first-treatment morbidity of 66.5% and mortality attributed to BRD of 13.2% when considering the initial population of 516 animals. The final goal of the experiment was to make sure that calves were experiencing a natural BRD challenge before receiving an ANC. In the present experiment, only calves that met the case definition for antimicrobial treatment were enrolled in the experiment to ensure that the effects observed were evaluated only in morbid calves.

The observed responses to the 3 ANC used in this experiment were largely negligible with the only positive response to ANC administration being a decrease in the removal of calves receiving NSAID and VITC. This difference in removals is likely explained by the numerical increase in mortality observed with ANC administration in this experiment. In addition, there were numerical differences in time from arrival to mortality and from the first BRD treatment to mortality among experimental treatments. Of calves that suffered BRD-attributed mortality, the calves receiving NOAC lived numerically longer from the time of arrival (average DOF = 26) and lived at least 4 d longer after receiving their initial BRD treatment (average 23 d after initial antimicrobial treatment) than any of the calves receiving ANC.

For many of the variables measured, calves receiving NOAC demonstrated statistically or numerically positive responses in relation to the other ANC. Regardless of one's opinion of ANC use, the improvements observed in cattle receiving NOAC were somewhat surprising. Some of these advantages for NOAC are of clinical importance, whereas others may serve to simply advocate that there is little justification for ANC use in high-risk calves suffering from an extreme natural immune challenge.

Calves receiving NOAC had heavier BW at the time of third BRD treatment and improved ADG between the second and third BRD treatments compared with the use of ANC. These differences must be critically evaluated since calves receiving NOAC received their third BRD treatment approximately a week after calves receiving NSAID, VACC, or VITC received their third BRD treatment. As a result, it would be expected

that the calves receiving NOAC would weigh more at this time. However, the fact that calves receiving the 3 ANC lost an additional 1.41 kg of BW compared with the NOAC calves during this BRD treatment interval should not be disregarded. In addition, the subjective clinical scores at the time of the second and third BRD treatments were significantly lower for calves receiving NOAC compared with other ANC. Although this is a subjective measurement, it suggests that calves receiving NOAC exhibited less visible depression and had improved appetites and respiratory signs at this time compared with calves receiving the other ANC.

Although calves receiving NOAC exhibited numerically improved performance over certain intervals, no statistical differences existed for any of the performance variables measured during the receiving period on a deads-in or deads-out basis. The expectation would be that any performance differences observed in the 56-d receiving period would likely decrease because of compensatory gain responses by the time calves were fed for an additional 166 or 197 d. It would also be expected that any ANC treatment administered within 30 d of arrival would not significantly impact finishing performance or carcass characteristics. This was the case, and at the end of the finishing period, no ANC differences were observed for any of variables analyzed.

It is difficult to compare the results of this experiment to others published in the literature. When reviewing the published research concerning the use of these 3 specific ANC in calves treated for BRD, it becomes obvious that this area of research is deficient and has produced very inconsistent results to date. Much of the research that exists consists of the evaluation of a single ANC. These studies may or may not include a negative control, and they are often conducted on a small number of animals and are not well replicated. The use of NSAID as an ANC for BRD has been researched to a greater extent than the use of any of the other ANC, and NSAID seems to provide the most consistent response of all the ANC that have been examined. There are a couple recent reviews conducted by Apley (2010) and Francoz et al. (2012) concerning the use of ANC that bear mentioning. These ANC reviews are primarily reviews of anti-inflammatory drugs, and more specifically NSAID, because of the lack of published controlled field experiments for other ANC.

When reviewing the published research concerning the use of these 3 specific ANC in calves treated for BRD, very few controlled well-replicated studies are found except in the case of NSAID. A recent review of the research concerning ANC conducted by Apley (2010) chose to focus on the published data concerning the use of anti-inflammatory drugs as an ANC for BRD. In this review, multiple studies that demonstrated some beneficial effect of NSAID as an ANC are cited, with the most typical response observed being a decrease in rectal temperature in calves treated with an NSAID. Apley (2010) determined that other clinical responses to NSAID as an ANC in the research were inconsistent.

Francoz et al. (2012) also conducted a comprehensive review of the literature concerning ANC use. For an experiment to be included in the review, the authors determined that the experiment must have involved the antimicrobial treatment of naturally occurring BRD and must have included experimental ANC treatments with and without at least 1 ANC. As a result of these criteria, experimental models, BRD prevention studies, studies evaluating an ANC without a control group, or studies including different antimicrobials within the treatment groups were not included. When studies not meeting these stipulations were removed from consideration, only 15 articles met the criteria. Of those 15 experiments, 14 dealt with anti-inflammatory drugs (12 NSAID experiments, 1 steroidal anti-inflammatory drug experiment, and 1 experiment containing both a steroidal anti-inflammatory drug and NSAID), and 1 dealt with immune modulators (Francoz et al., 2012). Upon reviewing the data related to the use of NSAID as an ANC to BRD, Francoz et al. (2012) concluded that NSAID caused a more rapid decrease in rectal temperature of calves but did not in any way benefit clinical signs, mortality, or calf performance. The authors did mention that published data were lacking and too inconsistent to conclusively determine the effects on calf performance or mortality when NSAID were used as an ANC for BRD. Francoz et al. (2012) also suggested that NSAID have the potential to decrease lung lesions at slaughter but noted that lung consolidation was only evaluated in 2 of the studies. On the basis of the results of this review, it could be argued that the decrease in rectal temperature and the potential decrease in lung lesions at slaughter resulting from NSAID administration may be important from an animal welfare perspective. However, it would be extremely difficult to justify the economics of NSAID use based on inconsistent improvements in clinical signs and the lack of performance benefits seen in calves receiving an NSAID as ANC for BRD (Francoz et al., 2012).

The observation of a decrease in rectal temperature without an associated improvement in clinical outcomes, mortality, or performance would be supported by research conducted evaluating an NSAID and an antimicrobial combination. In a clinical efficacy experiment, florfenicol, florenicol and flunixin meglumine, and saline were alternatively administered to 486 calves treated for suspected BRD at 4 research sites (Food and Drug Administration [**FDA**], 2009). Calves

receiving the florenicol and flunixin meglumine combination product as treatment for BRD had a greater mean decrease in rectal temperature 6 h after administration compared with calves receiving florenicol alone as treatment for BRD. However, the researchers also concluded that the combination of florenicol and flunixin meglumine was not different from florenicol alone when calves were evaluated for BRD treatment successes at the end of an 11-d period (FDA, 2009).

In both the FDA (2009) clinical efficacy experiment and the reviews conducted by Apley (2010) and Francoz et al. (2012), the most consistent response observed when an NSAID is used as an ANC for BRD calves is a more rapid decrease in rectal temperature after NSAID administration. However this response is often short-lived, and typically, there is no difference in rectal temperature when measured at the end of an extended evaluation period. The observation of a rapid decrease in rectal temperature shortly after NSAID administration with no difference in rectal temperature among treatments at the end of the evaluation period was likely a function of the pharmacokinetics of flunixin meglumine. When flunixin meglumine is administered according to label dose rates to healthy cattle, total body clearance has been reported to range from 90 to 151 mL·kg^{-1}·h^{-1}, and the terminal half-life has been shown to vary from 3.14 to 8.12 h (Anderson et al., 1990; Odensvik, 1995).

In the current experiment, the administration of NSAID as an ANC did not decrease the rectal temperature of calves at subsequent BRD treatments. Granted, rectal temperature was measured only in calves that met treatment criteria at the time of BRD treatment. It is quite possible that calves receiving NSAID could have demonstrated decreased rectal temperatures if rectal temperature was obtained a few hours after NSAID administration. This experiment attempted to mimic commercial production settings as much as possible, and pulling multiple calves up at short intervals to obtain hourly rectal temperatures was not a priority of the current experiment. That is not to say that changes in rectal temperature were unimportant in the current experiment, but rather, the concern was with prolonged or sustained changes in rectal temperature over the course of time. It should also be noted, however, that the interval between BRD treatments was relatively short for many calves, and this was especially the case with the first and second BRD treatments. As such, if calves receiving NSAID demonstrated any prolonged improvement in rectal temperatures it could have been detected, and that was not the case. It has also been suggested in the research that NSAID have the potential to decrease lung lesions at harvest in treated calves. Our data did not support these findings. In the present experiment, the administration of NSAID as an ANC did not decrease lung consolidation or adhesion at harvest. Calves receiving NSAID actually had numerically increased lung consolidation compared with calves receiving NOAC. Conversely, calves receiving NSAID had a slight numerical decrease in lung adhesion scores when compared with calves receiving NOAC.

In regard to the use of other ANC, reviewers have not observed reasons to justify their use. In the review conducted by Apley (2010), the author concluded that no data published at the current time supported the use of vaccines, vitamin C, or other ANC for BRD. Similarly, Francoz et al. (2012) concluded that there were no published data that currently supported the use of vaccines, vitamin C, or other ANC for BRD. This lack of support was primarily a result of Francoz et al. (2012) being able to evaluate only 1 additional ANC experiment outside of the anti-inflammatory drug experiments included in the review.

When reviewing the existing research, no experiment utilizing VACC as an ANC for BRD was found. This is extremely surprising given that NAHMS (2013) reported that a respiratory vaccine was used as a component of the initial BRD treatment program in 39.3% of feedlots and that 48.5% of cattle received a respiratory vaccine as part of initial BRD treatment. It is well established that the vaccination of healthy calves for respiratory pathogens is important for preventing BRD and maintaining optimal calf health. However, there is little justification for the vaccination of high-risk calves at arrival to the feedlot even though it is a widespread and accepted management practice (Edwards, 2010; Taylor et al., 2010). Some epidemiologic studies have suggested that vaccinating calves on arrival to the feedlot for respiratory viruses actually leads to increased BRD incidence (Taylor et al., 2010). The data are somewhat confounded as preconditioned low-risk calves would be less likely to be vaccinated on arrival. As a result, the increased BRD incidence observed in calves vaccinated on arrival to the feedlot is not necessarily a causal response. In addition, most published vaccine research has focused on comparing different multivalent vaccines, and the majority of vaccine studies do not include a nonvaccinated negative control. As a result, it is extremely difficult to determine if vaccination of high-risk calves at or shortly after arrival aids in the prevention of BRD or if it actually may be detrimental. Because no published research was found evaluating the use of VACC as an ANC for BRD, comparisons to the data in the present experiment are not possible. It is interesting to note that although not significant, calves that died after receiving VACC in the current experiment did so numerically sooner than any other ANC treatment. This observation was true

regardless of whether the interval was measured from the time of arrival to the feedlot or from the time of the first BRD treatment. This response ultimately resulted in the VACC group receiving the fewest total antimicrobial treatments (137 doses) for BRD. However, this was only 8 to 13 total antimicrobial treatments less than the other 3 ANC groups.

When reviewing individual research trials concerning ANC use for calves with BRD, a few experiments utilizing VITC as an ANC for BRD were identified. In an experiment conducted by Cusack et al. (2005), the authors examined the effects of injectable vitamin C given at the time of BRD treatment on subsequent cattle health. At the time of BRD antimicrobial treatment, 176 cattle were alternately administered injectable vitamin C (5 g/animal) or not injected. Fewer of the cattle injected with vitamin C at the time of BRD treatment died later in the experiment compared with those cattle that were not injected (11% vs. 23%, respectively; Cusack et al., 2005). The results led the authors to conclude that mortality rate in cattle with BRD may be decreased by administering injectable vitamin C at the time of antimicrobial administration. Urban-Chmiel et al. (2011) evaluated the effects of vitamin E and vitamin C on the development of inflammation processes and selected defense mechanisms against MH-induced infections. Calves were assigned to 3 treatments and received subcutaneous injections of vitamin E (750 IU), vitamin C (2.5 g per head), or no vitamin injection. Calves receiving either of the vitamin injections demonstrated a difference in the sensitivity of leukocytes to the cytotoxic effect of LKT when compared with the control group (Urban-Chmiel et al., 2011). There were no differences observed in the percentage of cells sensitive to LKT between the calves receiving vitamin E and those receiving vitamin C. The authors concluded that both vitamin E and vitamin C exerted a protective effect on leukocytes aiding in the defense against MH virulence factors when administered by injection. Urban-Chmiel et al. (2011) also suggested that these vitamins can be used to support the treatment of BRD in cattle following transport.

In the current experiment, VITC had no major effects on morbidity or mortality. In fact calves administered VITC had numerically higher mortality and combined mortality and removals when compared to NOAC calves. Although leukocyte sensitivity was not measured in the current experiment as in Urban-Chmiel et al. (2011), there was no evidence from the current experiment to support the use of VITC as an ANC for BRD as those authors suggested. Calves that died after receiving VITC in the current experiment did so at the same time interval as calves receiving NSAID but numerically sooner than calves receiving

NOAC. This result was true regardless of whether the interval was measured from the time of arrival to the feedlot or from the time of the first BRD treatment.

Conclusions

There is widespread use of ANC for BRD in commercial feedlots as evidenced by multiple published surveys. The goal of ANC therapy is to improve the response to a BRD challenge in calves treated with antimicrobials, and there is potential justification for ANC use based on the modes of actions of various ANC. However, published research has yet to suggest that ANC other than NSAID are effective in commercial settings in response to a natural BRD challenge. Although NSAID have demonstrated the ability to decrease rectal temperatures in treated calves, the response is usually short-lived and not evident at the end of the evaluation period. It has also been suggested that NSAID may decrease lung consolidation at harvest, but this has been demonstrated in only a few experiments. For all of the variables measured in the current experiment, observed responses to the 3 ANC were negligible during both the receiving and finishing periods. The lack of observed positive responses in calves given the 3 ANC used in this experiment compared with calves receiving NOAC leads us to conclude that the use of NSAID, VACC, and VITC as an ANC for BRD does not appear to be warranted. In addition, this experiment suggests that ANC use could potentially have negative effects on calf performance during the receiving period if administered to calves experiencing a severe natural immune challenge.

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