PEER REVIEWED

Effect of live yeast (*Saccharomyces cerevisiae boulardii* CNCM I-1079) feed additive on health and growth parameters of high-risk heifers in a commercial feedlot

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Abstract

Saccharomyces cerevisiae boulardii CNCM I-1079 (live yeast; ProTernative®, Lallemand Animal Nutrition) was evaluated for effects on health and performance in high-risk feeder heifers. A total of 1,274 beef heifers (average body weight = 547 ± 28.7 lb; 248 ± 13.0 kg) were procured from auction markets in the southern United States. Heifers were randomly assigned to 1 of 2 treatments: 1) Control (CON; no yeast products) or 2) ProTernative® (PRO) fed at 1 gram/hd/day to provide 20 x 10^9 CFU/hd/day for the first 45 days-on-feed (8 pens/treatment). After 45 days-on-feed, PRO was removed from the diet and both the PRO and CON treatment groups were fed the same basal diets throughout the rest of finishing. Feeding PRO during the first 45 days decreased bovine respiratory disease first treatment 28.4% compared to CON (P=0.01), and improved average daily gain (P=0.05; +4.5%), feed:gain (P=0.02; -5.0%), cost of gain (P=0.04; -4.7%), percentage USDA quality grade Choice (P<0.01; +6.8%), and reduced A+ liver abscesses (P<0.01; -45.9%). Carcass weight and percentage USDA Choice carcasses decreased (P<0.01) concomitant with increased (P<0.01) percentage USDA Select carcasses as the number of times treated for bovine respiratory disease increased. Addition of PRO to the ration during the first 45 days improved health, performance, and carcass outcomes through closeout in high-risk feeder heifers.

Key words: bovine respiratory disease, BRD, feedlot, liver abscess, morbidity, preventative, yeast, ProTernative®

Résumé

L'effet de *Saccharomyces cerevisiae boulardii* CNCM I-1079 (levures vivantes) sur la santé et la performance a été évalué chez des génisses en engraissement à haut risque. Un total de 1274 génisses de boucherie (poids moyen = 547 ± 28.7 lb; 248 ± 13.0 kg) a été obtenu à partir d'encans dans le sud des États-Unis. Les génisses ont été allouées au hasard à l'un des deux traitements suivants : 1) témoin (sans levures), 2) le probiotique ProTernative à la dose de 1 gramme/tête/jour pour fournir 20 x 10^9 UFC/tête/jour durant les 45 premiers jours en engraissement (8 enclos par traitement). Après 45 jours, le probiotique a été retiré de l'alimentation et les génisses dans les deux groupes de traitement ont reçu la même alimentation de base pendant le reste de l'engraissement. La prévalence de premier traitement pour des maladies respiratoires bovines était 28.4% moins élevée dans le groupe recevant le probiotique pendant 45 jours que dans le groupe témoin (P=0.01). Le groupe avec probiotique avait aussi un gain moyen quotidien plus élevé (P=0.05; +4.5%), une meilleure conversion alimentaire (P=0.02; -5.0%), un moindre coût du gain (P=0.04; -4.7%), un pourcentage plus élevé de carcasses avec le grade *Choice* du *USDA* (P<0.01; +6.8%) et une plus faible prévalence d'abcès du foie du type 1A (P<0.01; -45.9%). Le poids de la carcasse et le pourcentage de carcasses avec le grade *Choice* du *USDA* diminuaient (P<0.01) alors que le pourcentage de carcasses avec le grade *Select* du *USDA* augmentait lorsque le nombre de traitements pour les maladies respiratoires bovines augmentait. L'ajout de ProTernative dans la ration durant les premiers 45 jours a amélioré la santé et la performance de même que le classement des carcasses à la finition chez les génisses en engraissement à haut risque.

Introduction

Yeast products have been reported to improve gastrointestinal function, which may improve health and performance outcomes in feedyard cattle.[23] Two types of yeast products commonly marketed to the cattle feeding industry include live (active) yeast and yeast cultures. *Saccharomyces cerevisiae boulardii* CNCM I-1079 is a live yeast which has been shown to survive the rumen environment.[11,13] Strain-specific identification of *Saccharomyces cerevisiae boulardii* has been identified as important, as beneficial outcomes are related to specific strains.[17,27]

Mice and swine models have shown *Saccharomyces cerevisiae boulardii* to reduce the ability for *Salmonella enterica* and *E. coli* to adhere to intestinal epithelium as well as prevent pathogens from translocating through the intestinal tract to the liver and mesenteric lymph nodes.[25,26] The prevention of translocation of pathogenic bacteria appears to be related to the prevention of breakdown of intestinal tight junctions.[12,28] Intestinal crypt depth was increased, whereas crypt width decreased in calves fed *Saccharomyces cerevisiae boulardii* compared to controls.[15] *Saccharomyces cerevisiae boulardii* also has been shown to produce a protease to inhibit toxin binding ability as well as making lipopolysaccharide nontoxic.[7-9]

Feeding *Saccharomyces cerevisiae boulardii* CNCM I-1079 to heifers has been shown to increase monocytes and decrease haptoglobin concentration, potentially reducing the catabolic effects associated with the acute phase protein response of animals to bovine respiratory disease (BRD).[22] Haptoglobin has been shown to increase after exposure to *Mannheimia hemolytica* challenge models.[6,34] Dairy calves fed milk replacer supplemented with *Saccharomyces cerevisiae boulardii* had improved innate immunity (oxidative burst and phagocytosis) compared to calves not fed supplements.[15]

Small pen studies have evaluated *Saccharomyces cerevisiae boulardii* CNCM I-1079's[a] effect on dry-matter intake and immune response,[22] but currently no large-pen studies in a commercial feedyard have been reported. The primary objective of the current study was to evaluate the effect of *Saccharomyces cerevisiae boulardii* CNCM I-1079 during the 45-day receiving period on health, growth performance, and carcass traits of cattle fed in a commercial feedlot environment. The secondary objective was to evaluate the impact of treatment for BRD on carcass outcomes. Our hypothesis was calves fed *Saccharomyces cerevisiae boulardii* CNCM I-1079 would have improved health and performance outcomes while in the feedlot.

Materials and Methods

The study was performed at Hy-Plains Feedyard, LLC located near Montezuma, Kansas. The study began September 27, 2018 and concluded June 7, 2019. All procedures were approved by the Veterinary Research and Consulting Services, LLC Institutional Animal Care and Use Committee (IACUC number 1002) prior to study initiation.

Study Heifers

A total of 1,274 crossbred beef heifers (body weight [BW] = 547 ± 28.7 lb; 248 ± 13.0 kg) were procured from auction markets in the southern United States in September and October 2018. Heifers were considered high-risk for developing BRD based upon origin, transportation distance (range 256 to 621 miles; 412 to 999 km), and shrink; all heifers were transported to the research site with unknown health, vaccination, or implant history. The heifers were unloaded and housed in pens by origin upon arrival to the feedlot and provided *ad libitum* access to grass hay and water.

Treatment Allocation

Just prior to processing, all heifers were evaluated by a veterinarian (MET) and severely morbid or injured heifers were identified based upon visual appraisal and excluded from the study. Heifers remained separated by origin and were randomized into treatments within blocks at the processing chute. Treatment sequence was determined by drawing treatment groups written on a piece of paper from a hat to determine treatment order for each block. The first treatment randomly selected was assigned to the first calf in the chute, and the second treatment was assigned to the second calf in the chute, and so on. Treatment order remained consistent for the entire block, and a new order was randomly chosen at the beginning of each block.

Heifers were randomly assigned to 1 of 2 dietary treatment groups: 1) Control (CON; no yeast products provided) or 2) ProTernative®[a] (PRO; *Saccharomyces cerevisiae boulardii* CNCM I-1079) fed at a targeted rate of 1 gram/hd/day to provide 20 x 10^9 CFU/heifer/day for the first 45 days-on-feed (DOF). PRO was administered in the diet by application through a micro-ingredient machine beginning the morning after enrollment. After 45 DOF, PRO was removed from the treatment ration, and for the balance of the trial both CON and PRO treatment groups were fed the same rations.

Arrival Processing

Heifers were allowed to rest a 12 to 36 hours prior to processing. All heifers were processed following the same protocol with the following products:

- Duplicate, serially numbered ear tags color-coded for each pen
- Tulathromycin[b] (1.1 mL/100 lb [45.4 kg] of BW) administered subcutaneously (SC)
- Modified-live virus vaccine[c] containing infectious bovine rhinotracheitis virus, bovine viral diarrhea virus (types 1 and 2), bovine respiratory syncytial virus, and parainfluenza 3 administered SC
- Recombinant *Mannheimia haemolytica* leukotoxoid vaccine[d] administered SC
- Moxidectin[e] (1.0 mL/110 lb [50 kg] of BW) administered SC
- Oxfendazole[f] (1.0 mL/110 lb [50 kg] of BW) administered orally
- Dinoprost trimethamine[g] (25 mg/heifer) administered intramuscularly
- Trenbolone acetate (140 mg)/estradiol (14 mg) growth promoting implant[h] (1 implant/heifer).

All products were administered in accordance with

Beef Quality Assurance guidelines. After processing, all heifers were weighed by pen in drafts on a livestock ground certified platform scale for starting pen weight.

Feed, Housing, and Water

Heifers were fed diets formulated to meet or exceed nutritional requirements for feedlot cattle (Table 1). Heifers were fed twice daily throughout the study using a slick bunk feeding program. Pens in the PRO group had ProTernative® added in the micro-machine for rations 1 and 2. Both pens within a block were transitioned to the next ration on the same day. Grass hay was supplemented to each pen for the first 7 DOF as well as during transition. Tylosin[i] was fed for reduction of liver abscesses, *Lactobacillus acidophilus and Lactobacillus buchneri*[j] for pathogen reduction and performance improvement, and monensin[k] was fed for improved feed efficiency. Melengestrol acetate[l] was included in the finish ration (0.4 mg/heifer/day). Ractopamine hydrochloride[m] (300 mg/heifer/day target) was included in the diet when the heifers were estimated to be 30 days from harvest, and each pen within a block was started on the same day. Tylosin[i] was removed from the ration when ractopamine hydrochloride was added to the diet.

The 2 pens within each block were housed in adjacent pens, and all pens were within the same feed alley of the feedlot. Water was provided *ad libitum* through an automatic float-activated system shared between pens. Common treatment groups were assigned to pens which shared waterers to eliminate the chance of the CON group receiving ProTernative® through the water. Approximately 80 heifers (range 69 to 84) were enrolled per pen with an average enrollment weight of 547.4 lb (248.3 kg: range 505.8 to 609.8 lb [229.4 to 276.6 kg]) across all blocks. Pen area per heifer averaged 239.0 ft^2 (22.2 m^2: range 225.9 to 275.0 ft^2 [21.0 to 25.5 m^2]) whereas average bunk space was 10.4 in (26.4 cm: range 9.9 to 12.0 in [25.1 to 30.5 cm]) per heifer. Pen metrics were similar (within 1 heifer) within each experimental block. One block had fewer head available to enroll, resulting in increased pen square footage and bunk space compared to other blocks.

BRD Case Definition and Treatment Regimen

A 7-day post-metaphylaxis interval was used following administration of tulathromycin during processing where cattle were not eligible for BRD treatment. Animal health was evaluated daily by pen riders. Pen riders were blinded to treatment group throughout the study, and the same pen rider evaluated all pens within a day.

Health abnormalities were identified in the home pen by pen riders and moved to the hospital for further evalu-

Table 1. Macro ingredient composition (dry-matter basis) and analyzed calculated nutrients for each of the rations fed throughout the study. ProTernative®* was fed for the first 45 days in the respective treatment group.

	Ration†					
Ingredient, %	**1**	**2**	**3**	**4‡**	**5**	**6§**
Steam flaked corn	23.48	44.33	74.52	72.65	73.37	71.60
Wet distillers grain	16.27	16.13	8.36	8.36	8.25	8.41
Ground alfalfa hay	44.95	24.00	3.47	4.44	4.18	7.29
Chopped corn stalks	5.31	4.05	5.86	6.83	6.52	4.90
Fat	0.00	1.50	2.84	2.78	2.78	2.78
Liquid finisher	6.30	5.65	4.95	4.94	4.90	5.02
Corn steep	3.69	4.34	0.00	0.00	0.00	0.00
Calculated nutrients						
Dry matter, %	64.50	63.89	71.06	71.16	71.19	71.21
Net energy maintenance, Mcal/lb	77.24	87.91	98.63	97.77	97.42	96.77
Net energy gain, Mcal/lb	49.07	60.00	69.36	68.56	68.26	67.65
Crude protein, %	19.10	17.51	13.32	13.31	13.36	13.35
Non-protein nitrogen, %	2.05	2.34	2.38	2.34	2.38	2.34
Crude fat, %	3.52	5.48	6.84	6.81	6.80	6.77
Crude fiber, %	19.22	12.54	6.27	6.75	6.81	7.04
Calcium, %	1.20	0.95	0.75	0.76	0.77	0.77
Phosphorus, %	0.39	0.40	0.36	0.36	0.36	0.35
Potassium, %	1.59	1.10	0.61	0.63	0.64	0.65
Magnesium, %	0.30	0.28	0.22	0.22	0.22	0.23
Sulfur, %	0.36	0.33	0.22	0.22	0.22	0.23

* Lallemand Animal Nutrition, Milwaukee, WI

† Formulated to provide 8 g/ton tylosin (90% DM basis), 26 g/ton monensin, 0.4 mg/heifer/day melengestrol acetate, and 50 mg/heifer/day *Lactobacillus acidophilus* and *Lactobacillus buchneri*

‡ Ration 4 was storm ration for ration 3

§ Ration 6 was storm ration for ration 5 ation. Feedlot protocol specified that cattle qualifying for BRD treatment have a rectal temperature ≥ 104.0°F (40°C), and display at least 1 of the following clinical signs: depression/lethargy, dyspnea, abnormal respiration, sunken eyes, dehydration, nasal discharge, ocular discharge, lowered head carriage, and/or depressed ruminal fossa. Rectal temperature was measured using a GLA digital thermometer.[n]

Heifers requiring first treatment for BRD were administered florfenicol[o] (18.1 mg/lb [40 mg/kg] of BW) with a 3-day post-treatment moratorium. Heifers that displayed clinical signs of BRD after the moratorium period were considered treatment failures and eligible for additional treatments. Heifers pulled for additional BRD treatment had to have a rectal temperature ≥ 104.0°F (40°C) or experience decreased body weight since previous treatment. Enrofloxacin[p] (4.5 mg/lb [10 mg/kg] of BW) and oxytetracycline[q] (9 mg/lb [19.8 mg/kg] of BW) were administered for second and third treatments for BRD, respectively; a 3-day post-treatment moratorium was observed following treatment with enrofloxacin. Treatment success was defined as heifers which did not require subsequent BRD treatment for the remainder of the feeding period and did not die due to BRD. Additional treatments for diseases not associated with BRD were managed according to standard operation procedures established with the consulting veterinarian.

All treated heifers were subjectively evaluated by feedlot personnel and returned to their home pen on day of treatment if deemed well enough to thrive. Hospital pens were available to house non-thriving heifers. Hospital pens were evaluated daily by feedlot personnel to monitor potential re-treatment eligibility and potential for heifers to return to their home pen. Feed consumed by heifers in the hospital pen was prorated to the appropriate home pen. Heifers (CON *n* = 6; PRO *n* = 0) not capable of reaching appropriate market weight in the same time frame as penmates due to illness (chronic respiratory disease, lameness, or failure to thrive due to undiagnosed condition) and were clear of pre-harvest withdrawals, were removed from the study and marketed via alternate channels. These animals were not included in growth performance analyses for deads-out evaluation. Health records for all treated heifers were maintained using the feedlot computer system.[r] Gross necropsy examination of heifers that died was performed by a veterinarian or trained feedlot personnel to determine most probable cause of death. No additional diagnostics were performed to differentiate cause of mortality.

Re-implant

A trenbolone acetate (200 mg)/estradiol (20 mg) growth promoting implant[s] was administered to all heifers at an average of 112 DOF (range 103 to 124 DOF). Both pens within a block were re-implanted on the same day. Prior to re-implant, heifers were weighed in drafts by pen for interim body weight on certified livestock ground platform scales. A topical pyrethroid[t] was administered for lice control at time of re-implant. No additional products were administered at time of re-implant.

Harvest, Carcass Outcomes, Liver and Lung Lesion Scoring

Heifers were harvested based on evaluation of feed intake and visual estimation of adequate finish for harvest based upon body weight and estimated percentage yield grade 4 or 5. Average DOF at time of harvest was 232 (range 217 to 243), and both pens within a block were harvested on the same day. Heifers were not fed the morning of shipment. All heifers were weighed in drafts on certified platform livestock scales by pen with a 4% shrink applied to final live weights, gain, and feed conversion calculations. Heifers were shipped to a commercial abattoir in Holcomb, Kansas from May 10, 2019 to June 7, 2019.

At the abattoir, trained personnel from West Texas A&M University–Beef Carcass Research Center cross-referenced individual animal identification tags with abattoir carcass identification. Quality grade and yield grade were provided on an individual animal basis based on the processors' visual camera grading system. Personnel from the Beef Carcass Research Center, blinded to treatment group, scored livers based on the Elanco Liver Scoring System.[u] Edible livers without any abnormalities were classified as normal. Livers with 1 or 2 small abscesses or inactive scars were classified as A-; livers with 1 to 2 large abscesses or multiple small abscesses were classified as A; and the A+ score was used to describe multiple large abscesses present. Ruptured abscesses and those with tissue adhesions were categorized as A+ liver scores. No samples were collected for culture or histopathology evaluation.

Lung lesions were scored as previously described.[5,24,33] Lungs were manually palpated and scored for lung consolidation: lungs with <5% consolidation were classified as normal; 5 to 15% consolidation; 15 to 50% consolidation; and >50% consolidation. The presence and severity of fibrin tissue was also assessed: no fibrin tissue present; minor amount of fibrin tissue; or extensive amount of fibrin tissue.

Economic Analysis

Cost-of-gain was calculated on a deads-in (the initial body weight and head days from mortalities and removals were included in the calculation) and deads-out (the initial body weight and head days from mortalities and removals were excluded from the calculation) basis. Cost-of-gain was determined by dividing total costs for the pen (feed costs, medicine costs, processing costs, and yardage) divided by the total pounds of weight gained during the feeding period. Commercial market prices of ProTernative® included by the sponsor were included in economic calculations ($0.09/heifer/day). Treatment costs were calculated by adding the costs for products used for treatment for each lot and dividing by the number of heifers shipped for harvest. All other feed and products used during the study were included in feedlot closeout expenses. Sale weight had a 4% shrink applied to all final weights, and head-days were used to determine performance outcomes.

Statistical Analysis

Data were evaluated using a commercial software program.[v] Pen served as the experimental unit for all outcomes comparing treatment groups. Continuous outcomes (body weight, average daily gain [ADG], feed to gain [F:G], dry-matter intake, cost of gain, treatment costs, carcass weight, and dressing percent) were evaluated on a pen mean basis as a randomized complete block design with linear mixed models. Binomial outcomes (BRD morbidity, BRD mortality, overall mortality, treatment success, BRD case fatality risk, removals, yield grade, quality grade, liver scores, and lung scores) were evaluated using generalized mixed models. All models included a fixed effect of treatment group and random effect of block. Health outcomes were evaluated at 45 DOF (day of removal of ProTernative® from ration in respective treatment group), re-implant, and closeout. Interim body weight and ADG performance outcomes were evaluated at time of re-implant. Performance calculations were evaluated on a deads-in and deads-out basis. Differences exhibiting a *P* value ≤ 0.05 were considered statistically significant. Descriptive cumulative BRD first treatment, overall mortality, and dry-matter intake were evaluated by treatment group and DOF.

Binary outcomes were created for quality grade, yield grade, liver scores, and lung scores. Individual animal carcass, liver, and lung score outcomes were also evaluated by the number of times treated for BRD at the feedlot (0, 1, 2, or 3 times) using generalized linear mixed models. Models included random effect for lot and block. Differences exhibiting a *P* value ≤ 0.05 were considered statistically significant. Pairwise comparisons between the number of times treated for BRD were performed when main effect was significant ($P \leq 0.05$).

Results

Enrollment information and health outcomes at 45 DOF (time when PRO was removed from rations) are shown in Table 2. The percentage of calves that required BRD first treatment was decreased in the PRO group compared to the CON group ($P=0.01$) at 45 DOF. No other health outcomes were different ($P \geq 0.21$) at 45 DOF between treatment groups.

Health outcomes were also summarized at time of re-implant (average 112 DOF; Table 3) and at harvest closeout (average 232 DOF; Table 4). The percentage of calves which required BRD first treatment continued to be fewer in the PRO group compared to CON at time of re-implant ($P=0.02$; 4.65 percentage point reduction) and harvest ($P=0.01$; -4.81%), suggesting the initial effects identified in the initial

Table 2. Model-adjusted least square means (± SEM) of enrollment weight and health outcomes during the first 45 days-on-feed when ProTernative® was removed from the rations in the ProTernative® treatment group in high-risk feedlot heifers.

Variable		Control			ProTernative®*		*P* value
No. calves (pens)		637 (8)			637 (8)		-
Enrollment weight, lb	548.8	±	10.48	545.9	±	10.48	0.52
BRD first treatment, %	15.41	±	1.82	10.76	±	1.48	0.01
BRD second treatment, %	6.53	±	1.16	5.16	±	1.01	0.29
BRD third treatment, %	3.43	±	0.76	2.81	±	0.68	0.52
BRD mortality, %	5.88	±	1.02	4.33	±	0.86	0.21
Overall mortality, %	6.12	±	0.95	4.71	±	0.84	0.27

* Lallemand Animal Nutrition, Milwaukee, WI

Table 3. Model-adjusted least square means (± SEM) health and performance outcomes at re-implant (average 112 days-on-feed) by treatment group in high-risk feedlot heifers. ProTernative® was fed for the first 45 days for the respective treatment group.

Variable		Control			ProTernative®*		*P* value
BRD first treatment, %	16.76	±	1.97	12.11	±	1.63	0.02
BRD second treatment, %	7.66	±	1.23	5.66	±	1.03	0.15
BRD third treatment, %	4.08	±	0.78	2.83	±	0.66	0.22
BRD mortality, %	7.38	±	1.04	5.65	±	0.91	0.21
Overall mortality, %	7.53	±	1.05	6.12	±	0.95	0.32
Interim body weight, lb	906.5	±	9.13	913.2	±	9.13	0.41
ADG, lb†	2.71	±	0.12	2.89	±	0.12	0.13
ADG, lb‡	3.15	±	0.10	3.28	±	0.10	0.03

* Lallemand Animal Nutrition, Milwaukee, WI

† Dead and removed heifers included in analysis

‡ Dead and removed heifers excluded in analysis

Table 4. Model-adjusted least square means (± SEM) of health outcomes at closeout (average 232 days-on-feed) by treatment group in high-risk feedlot heifers. ProTernative® was fed for the first 45 days for the respective treatment group.

Variable	Control			ProTernative®*			*P* value
BRD first treatment, %	16.92	±	1.98	12.11	±	1.63	0.01
Rectal temperature at BRD first treatment, °F	104.88	±	0.08	104.94	±	0.08	0.59
BRD second treatment, %	7.66	±	1.23	5.66	±	1.03	0.15
BRD third treatment, %	4.08	±	0.78	2.83	±	0.66	0.22
BRD first treatment success, %†	42.73	±	4.72	39.24	±	5.49	0.63
BRD second treatment success, %†	22.00	±	5.86	27.03	±	7.30	0.59
BRD third treatment success, %†	23.08	±	8.26	22.22	±	9.80	0.95
BRD case fatality risk, %	38.18	±	4.63	41.77	±	5.55	0.62
Overall mortality, %	8.94	±	1.13	7.06	±	1.01	0.22
BRD mortality, %	7.84	±	1.09	5.80	±	0.94	0.15
Digestive mortality, %	0.31	±	0.22	0.31	±	0.22	1.00
AIP mortality, %‡	0.47	±	0.27	0.16	±	0.16	0.34
Other mortality, %	0.31	±	0.22	0.78	±	0.35	0.42
BRD outs (deads + removals), %	7.97	±	1.12	5.80	±	0.96	0.12
Total outs (deads + removals), %	9.89	±	1.18	7.06	±	1.02	0.07

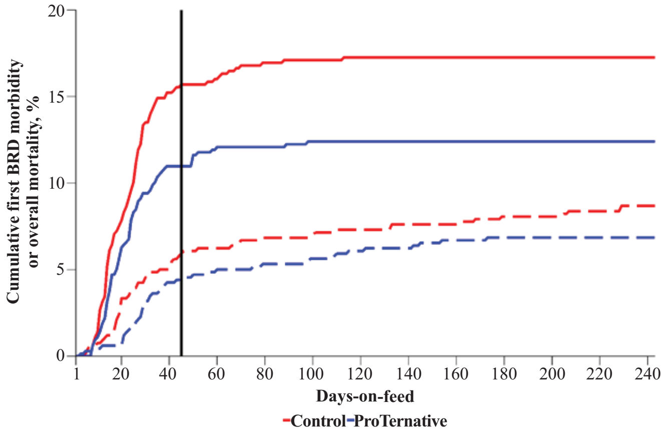
*Lallemand Animal Nutrition, Milwaukee, WI

† Treatment success defined as not requiring additional antibiotic treatment for BRD, cause of death was non-related to BRD, or removed due to BRD

‡ Acute interstitial pneumonia

45-day receiving period carried through to closeout harvest (Figure 1). At closeout, the number of calves which required BRD first treatment was fewer in 7 of the 8 blocks in the PRO groups compared to CON. Treatment success and case fatality were not different between treatment groups (*P*>0.59). There was a numerical reduction (12 heifers total) in overall mortality in the PRO treatment group compared to CON (*P*=0.22; Table 4). Total outs (deads and removals) tended to be less in the PRO treatment group (*P*=0.07) at closeout. Average daily gain (*P*=0.05; +4.5%), feed to gain (*P*=0.02; -5.0%), and cost-of-gain (*P*=0.04; -4.7%) were all improved in the PRO treatment group compared to CON when evaluated on a deads-in and deads-out basis (Table 5).

Figure 1. Cumulative bovine respiratory disease (BRD) first treatment (solid lines) and overall mortality (dashed lines) by days-on-feed and treatment group (Control-red line; ProTernative® [Lallemand Animal Nutrition]-blue line) in high-risk heifers. ProTernative was fed for the first 45 days-on-feed (vertical black line) for the ProTernative treatment group, and then the same basal diets were fed throughout the finishing period for both treatment groups.



Heifers in the PRO treatment group had an increased proportion of carcasses grading USDA Choice (*P*<0.01; +6.82 percentage points) and a decrease in A+ liver abscesses (*P*<0.01; absolute reduction 4.31 percentage points) compared to CON (Table 6). Liver and lung scores were not captured for 31 heifers from 2 different lots (23 from 1 lot and 8 from a different lot) because animal ID and abattoir carcass identification on the intestinal table could not be accurately matched. All of these were from the PRO treatment group. The denominator was changed to only the number of heifers for which data could be matched for these lots for analyses. The authors do not believe this impacted conclusions from the study because the missing data was due to loss of identity linkage.

Carcass, liver, and lung outcomes by number of times treated for BRD are shown in Table 7. Hot carcass weight, percentage of carcasses that graded USDA Choice, and percentage of carcasses that graded USDA Select were associated (*P*<0.01) with the number of times heifers were treated for BRD. Heifers treated 1, 2, or 3 times for BRD had hot carcass weights that were 5.5%, 9.7%, and 19.1%, respectively, lower than heifers not treated for BRD. Similarly, percentage of carcasses grading USDA Choice and better decreased from 84.1% for heifers not treated for BRD to 78.5%, 52.86%, and 18.40% for heifers treated 1, 2, or 3 times, respectively, for BRD; moreover, percentage of heifers with normal lungs at harvest decreased from 72.9% for heifers not treated for BRD to 39.6%, 10.3%, and 10.1% for heifers treated 1, 2, or 3 times, respectively, for BRD.

Table 5. Model-adjusted least square means (± SEM) of performance and economic outcomes at closeout (average 232 days-on-feed) by treatment group in high-risk feedlot heifers. ProTernative® was fed for the first 45 days for the respective treatment group.

Variable	Control			ProTernative®*			*P* value
Final body weight, lb[†]	1188.9	±	9.07	1192.8	±	9.07	0.46
ADG, lb[‡]	2.46	±	0.05	2.57	±	0.05	0.05
ADG, lb[§]	2.77	±	0.03	2.80	±	0.03	0.04
F:G*	7.35	±	0.14	6.98	±	0.14	0.02
F:G[†]	6.71	±	0.07	6.52	±	0.07	0.03
Average dry matter intake, lb	18.02	±	0.36	17.91	±	0.36	0.60
Cost-of-gain, $/100 lb*	104.31	±	2.10	99.39	±	2.10	0.04
Cost-of-gain, $/100 lb[†]	95.18	±	0.97	92.83	±	0.97	0.04
Treatment costs, $/heifer sold	6.27	±	0.84	4.24	±	0.84	0.10

* Lallemand Animal Nutrition, Milwaukee, WI

[†] Adjusted for 4% shrink

[‡] Dead and removed heifers included in analysis

[§] Dead and removed heifers excluded in analysis

Table 6. Model-adjusted least squares means (± SEM) of carcass outcomes, liver scores, and lung scores by treatment group in high-risk feedlot heifers. ProTernative® was fed for the first 45 days for the respective treatment group.

Variable	Control			ProTernative®*			*P* value
Hot carcass weight, lb	761.0	±	7.16	765.0	±	7.16	0.45
Dressing percent, %	64.00	±	0.23	64.14	±	0.23	0.61
Quality grade							
Prime, %	10.14	±	1.91	7.46	±	1.53	0.10
Choice, %	70.21	±	1.91	77.03	±	1.73	<0.01
Select, %	17.00	±	1.99	13.75	±	1.75	0.12
No roll/Other, %	0.87	±	0.60	0.41	±	0.31	0.17
Yield grade							
1, %	16.32	±	1.82	15.67	±	1.76	0.76
2, %	37.26	±	2.15	42.21	±	2.17	0.09
3, %	34.66	±	2.11	31.24	±	2.02	0.21
4, %	10.28	±	1.27	8.61	±	1.15	0.33
5, %	1.16	±	0.48	1.76	±	0.61	0.38
Liver abscesses							
Normal, %	80.48	±	4.17	82.16	±	3.92	0.47
A-, %	7.65	±	1.71	10.01	±	2.10	0.15
A, %	1.39	±	0.49	2.32	±	0.64	0.25
A+, %	9.38	±	2.61	5.07	±	1.58	<0.01
Total abscesses, %	19.52	±	4.17	17.84	±	3.92	0.47
Lung scores							
Normal, %	71.10	±	2.42	67.04	±	2.57	0.14
5-15, %	6.04	±	1.05	8.13	±	1.24	0.17
15-50, %	14.63	±	2.16	15.67	±	2.28	0.62
>50, %	7.58	±	1.33	8.42	±	1.44	0.60
Fibrin tissue presence							
None, %	64.40	±	4.16	62.46	±	4.26	0.50
Minor, %	19.79	±	3.43	21.13	±	3.60	0.58
Extensive, %	15.08	±	1.85	15.62	±	1.91	0.80
Lung condemned status							
Not condemned, %	68.33	±	4.21	71.85	±	4.21	0.20
Condemned, %[†]	31.67	±	4.21	28.15	±	3.98	0.20

* Lallemand Animal Nutrition, Milwaukee, WI

[†] Unfit for human consumption

Table 7. Model adjusted least square means (± SEM) carcass outcomes, liver scores, and lung scores by number of times treated for bovine respiratory disease in high-risk feedlot heifers.

	Number times treated for BRD						*P* value pairwise contrast					
Variable	**0**	**1**	**2**	**3**	**SEM***	***F*-test†**	**0 vs 1**	**0 vs 2**	**0 vs 3**	**1 vs 2**	**1 vs 3**	**2 vs 3**
Observations, *n*	1025	79	20	10	-	-	-	-	-	-	-	-
Hot carcass weight, lb	768.92	726.54	694.18	622.07	27.60	<0.01	<0.01	<0.01	<0.01	0.13	<0.01	0.03
Quality grade												
Prime, %	9.65	2.40	0.00	0.00	1.73	0.26	-	-	-	-	-	-
Choice, %	74.44	76.07	52.86	18.40	12.02	<0.01	0.75	0.04	<0.01	0.05	<0.01	0.08
Select, %	13.45	18.25	46.17	82.09	11.90	<0.01	0.24	<0.01	<0.01	0.01	<0.01	0.07
No roll/Other, %	0.58	1.23	0.00	0.00	1.16	0.82	-	-	-	-	-	-
Yield grade												
1, %	14.43	24.11	20.04	79.84	1.29	<0.01	0.02	0.49	<0.01	0.70	<0.01	<0.01
2, %	39.97	40.70	30.35	20.40	12.89	0.54	-	-	-	-	-	-
3, %	33.43	30.17	39.62	0.00	0.00	0.87	-	-	-	-	-	-
4, %	10.04	5.05	9.97	0.00	6.72	0.57	-	-	-	-	-	-
5, %	1.66	0.00	0.00	0.00	0.44	1.00	-	-	-	-	-	-
Liver abscesses												
Normal, %	82.41	73.38	82.56	72.00	15.21	0.24	-	-	-	-	-	-
A-, %	8.50	11.71	14.06	7.53	8.01	0.64	-	-	-	-	-	-
A, %	1.51	2.24	0.00	9.54	1.66	0.38	-	-	-	-	-	-
A+, %	6.69	10.37	4.05	9.47	9.43	0.56	-	-	-	-	-	-
Total abscesses, %	17.59	26.62	17.44	28.00	15.21	0.24	-	-	-	-	-	-
Lung scores												
Normal, %	72.91	39.63	10.28	10.10	9.61	<0.01	<0.01	<0.01	<0.01	0.02	0.10	0.99
5-15%, %	6.40	11.03	10.45	9.61	9.23	0.40	-	-	-	-	-	-
15-50%, %	13.01	26.96	72.47	48.21	16.26	<0.01	<0.01	<0.01	<0.01	<0.01	0.18	0.21
>50%, %	6.90	20.68	4.81	30.58	4.87	<0.01	<0.01	0.71	0.01	0.12	0.48	0.08
Fibrin tissue presence												
None, %	63.17	60.44	81.73	81.37	12.37	0.22	-	-	-	-	-	-
Minor, %	21.44	14.35	4.16	0.00	4.56	0.13	-	-	-	-	-	-
Extensive, %	14.64	24.46	14.53	20.02	12.78	0.14	-	-	-	-	-	-
Lung condemned status												
Not condemned, %	72.26	55.66	33.29	39.73	16.38	<0.01	<0.01	<0.01	0.04	0.08	0.36	0.73
Condemned, %‡	27.74	44.34	66.71	60.26	16.37	<0.01	<0.01	<0.01	0.04	0.08	0.36	0.73

* Largest standard error of the mean shown

† Overall *F*-test for treatment effect comparing number of times treated for BRD with outcome

‡ Unfit for human consumption

Discussion

Results of this study demonstrate improved health outcomes in high-risk heifers fed ProTernative® during the first 45 DOF. First treatment for BRD was decreased 28.4% through closeout in calves in the PRO group. The magnitude of reduction of BRD morbidity in small pen studies range from 17.7% to 42.6%, consistent with the current results.[23] Reduction of morbidity allows for more judicious use of antimicrobials in feedlots. To the authors' knowledge, this is the first study to evaluate feeding *Saccharomyces cerevisiae boulardii* CNCM I-1079 in a large pen commercial feedlot setting. The effect of *Saccharomyces cerevisiae boulardii* CNCM I-1079 on the gastrointestinal tract[15,25,26] and immune system[7-9,15,22] appears to be the reason for the improvement in health and performance outcomes identified in the current study.

Feed intake has been shown to increase in healthy steers supplemented with *Saccharomyces cerevisiae boulardii* CNCM I-1079 after administration of florfenicol.[23] In the current study, heifers were metaphylactically administered tulathromycin during arrival processing because tulathromycin is more effective in reducing morbidity and mortality compared to florfenicol.[1] Heifers were initially treated with florfenicol for BRD and returned to their home pen, and individual heifer intake patterns were not measured; however, there was no difference in feed intake on the pen level across treatment groups.

Other than metaphylaxis, there are few, large-scale published studies performed in commercial feedlots that reduced morbidity. Metaphylaxis research trials have consistently resulted in decreased morbidity and mortality.[1,40] Timing of vaccination or administration of immunostimulant research studies have resulted in decreased retreatment or mortality, respectively.[18,32] Additional studies are needed to determine methods to reduce morbidity to reduce antimicrobial use.

The increase in percentage of USDA Choice carcasses in the PRO treatment group was likely attributable due to decreased morbidity. Calves treated for BRD had a notable reduction in percentage of carcasses that graded USDA Choice.[36] Surprisingly, there was no difference in the lung lesion presence or severity between treatment groups. Identification of morbidity by pen riders has been shown to have poor sensitivity and specificity,[39] and the bovine lung has been shown to be a regenerative organ after challenge with *Mannheimia haemolytica*.[19] The poor diagnostic accuracy of identifying morbidity in feedlot cattle and the regenerative ability of the bovine lung make evaluation of lung lesion data difficult; however, the PRO group had decreased first BRD treatments, total outs (deads and removals), as well as improved performance indicators.

The reduction in severe liver abscesses was surprising, especially because PRO was only fed for the first 45 DOF and not throughout the entire feeding period. Liver abscessation has primarily been thought to occur secondarily to rumen acidosis allowing bacteria to access the portal vein.[29] *Fusobacterium necrophorum* is the primary etiologic agent of liver abscesses, and is ubiquitous in the rumen of cattle;[29] *Salmonella enterica* has been cultured from liver abscesses as well.[2] This organism is found throughout the gastrointestinal tract and feces of cattle.[10,14] We hypothesize that ProTernative® reduces the ability of gram negative bacteria to adhere to and translocate across the intestinal wall, thereby reducing severe liver abscesses. All heifers in the current study were fed tylosin from the beginning of the feeding period until approximately the last 30 days-on-feed, when a beta agonist was fed. Additional research is needed to evaluate effects of feeding PRO at varying time points and/or compared to tylosin to evaluate effectiveness in controlling liver abscesses. Tylosin has been shown to reduce liver abscesses,[40] and severe liver abscesses have resulted in decreased carcass weight and profitability.[4,29,31] Non-antimicrobial methods to control liver abscesses would appeal to feedlots and consumers alike; however, a 45.9% relative reduction (4.31% absolute reduction) in the prevalence of severe liver abscesses when feeding PRO warrants further evaluation.

Huebner et al evaluated feeding a *Saccharomyces cerevisiae* fermentation product in natural cattle consuming the finish ration, and identified no improvement in health, performance, or liver abscess prevalence.[21] That study evaluated a *Saccharomyces cerevisiae* fermentation product,[21] whereas the *Saccharomyces cerevisiae boulardii* CNCM I-1079 evaluated in the current study is a specific strain of a live yeast with activity in the lower gastrointestinal tract in ruminants.[13] Differences in the strain of *Saccharomyces cerevisiae* used, as well as how the product is produced, appear to have implications on clinical efficacy.

The reduction in carcass weight in relation to the number of times the heifers were treated for BRD was more severe than previously identified (Table 7).[16,20,30,36] The heifers in the current study were metaphylactically administered tulathromycin during arrival processing, whereas other studies differed in metaphylaxis status and sex. Surprisingly, there was no difference in the percentage of cattle that graded USDA Choice between heifers not treated for BRD and heifers treated 1 time for BRD; however, heifers treated 2 or 3 times had a significant reduction in the percentage grading USDA Choice and a corresponding increased percentage grading USDA Select. To the authors' knowledge, this is the first study to report liver abscess prevalence by number of times cattle were treated for BRD. Prevalence of lung scores by number of BRD treatments is consistent with the method of classification for scoring lung lesions.[5,24,33] In the current study, 27.09% of heifers never treated for BRD had some form of lung consolidation at the time of harvest, which was less than previously reported.[16,38] The high prevalence of lung lesions in heifers never treated for BRD agrees with previous reports, demonstrating the relatively poor diagnostic sensitivity of identifying morbid cattle.[36,37,39]

Limitations of the current study include the fact that the study population was high-risk heifers. Morbidity was relatively low in relation to the mortality outcomes; incidence of morbidity in this study was still greater than the industry average, and case fatality risk was within expectations.[35] All study heifers were administered tulathromycin during arrival processing to reduce morbidity, and the majority of morbidity occurred during the first 45 DOF. Probability of treatment failure has been reported to be greater in high-risk cattle pulled early in the feeding period.[3]

Conclusions

The addition of the live yeast to the ration during the first 45 DOF improved health and performance outcomes through closeout in high-risk heifers. Feeding PRO to high-risk heifers during the first 45 DOF decreased BRD first treatment 28.4% compared to CON, as well as improving ADG, F:G, and cost-of-gain. A higher percentage of heifers fed the live yeast graded USDA Choice, and A+ liver abscesses were reduced in the PRO group. Additional research is needed in a low-risk study population to determine potential value in different production systems.

Endnotes

[a] ProTernative®, Lallemand Animal Nutrition, Milwaukee, WI
[b] Draxxin®, Zoetis Animal Health, Parsippany, NJ
[c] Titanium® 5, Elanco Animal Health, Greenfield, IN
[d] Nuplura® PH, Elanco Animal Health, Greenfield, IN
[e] Cydectin®, Bayer Animal Health, Shawnee Mission, KS
[f] Synanthic®, Boehringer Ingelheim, Duluth, GA
[g] Lutalyse®, Zoetis Animal Health, Parsippany, NJ

[h] Revalor-H®, Merck Animal Health, Whitehouse Station, NJ
[i] Tylan™, Elanco Animal Health, Greenfield, IN
[j] Micro-Cell® FS Gold, Lallemand Animal Nutrition, Milwaukee, WI
[k] Rumensin®, Elanco Animal Health, Greenfield, IN
[l] MGA®, Zoetis Animal Health, Parsippany, NJ
[m] Optaflexx®, Elanco Animal Health, Greenfield, IN
[n] GLA M700 Thermometer, GLA, San Luis Obispo, CA
[o] Nuflor®, Merck Animal Health, Whitehouse Station, NJ
[p] Baytril® 100, Bayer Animal Health, Shawnee Mission, KS
[q] Biomycin® 200, Boehringer Ingelheim Vetmedica, Inc., Duluth, GA
[r] Animal Management System, Animal Health International, Greeley, CO
[s] Revalor-200®, Merck Animal Health, Whitehouse Station, NJ
[t] Exile® Pour-On, Aspen Veterinary Resources LTD, Greeley, CO
[u] Elanco Animal Health, Greenfield, IN
[v] RStudio Team 2016, Boston, MA

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