PEER REVIEWED

Effects of Intranasal Versus Intramuscular Modified Live Vaccines and Vaccine Timing on Health and Performance by Newly Received Beef Cattle

G. C. Duff, *PhD,* **K. J. Malcolm-Callis,** *PhD,* **D. A. Walker,** *MS,* **M. W. Wiseman,** *BS*
Clayton Livestock Research Center
New Mexico State University
Clayton, NM 88415
M. L. Galyean, *PhD*
Department of Animal Science and Food Technology
Texas Tech Universtiy
Lubbock, TX 79409-2141
L. J. Perino, *DVM, PhD*
Division of Agriculture
West Texas A&M University
Canyon, TX 79016

Abstract

Two studies were conducted to evaluate the effects of viral vaccines and vaccination programs on health and performance of newly received beef cattle. In Exp. 1, two loads (120 steer and bull calves and 108 heifer calves for Load 1 and 2, respectively) were used to evaluate the effects of an intranasal vs an intramuscular IBR-PI_3 vaccine on performance and health of newly received beef cattle. Treatments were: 1) no vaccine (Control); 2) an intranasal modified-live IBR-PI_3 vaccine (IN); and 3) an intramuscular modified-live IBR-PI_3 vaccine (IM). No treatment x load interactions were observed for performance data. For the 28-d receiving period, cattle given IN IBR-PI_3 vaccine had greater daily gain ($P < .05$) than cattle given IM IBR-PI_3 vaccine. No differences ($P > .10$) were noted for daily dry matter (DM) intake, however, the feed:gain ratio was increased ($P < .05$) for the IM group as compared to the IN group. No differences ($P > .10$) were noted among treatments in the percentage of cattle treated for BRD. In Exp. 2, 102 steer and bull calves were used to evaluate vaccine timing on health and performance of newly received calves. Treatments included: 1) no vaccine (Control); 2) no vaccine at processing, with an IM multiple antigen (IBR-PI_3-BVD-BRSV) viral vaccine given on d 7; 3) intranasal IBR-PI_3 administered at processing with IM IBR-PI_3-BVD-BRSV vaccine given on d 7; and 4) IM IBR-PI_3-BVD-BRSV vaccine administered both at processing and on d 7. No differences were noted for daily gain or daily DM intake during the 28-d receiving period. Feed:gain was improved ($P < .10$) for vaccinated calves as compared to controls. Results suggest that an intranasal IBR-PI_3 vaccine might have beneficial effects on gain and feed efficiency compared with an intramuscular IBR-PI_3 vaccine. There was no advantage or disadvantage to delaying vaccination with viral vaccines until 7 d after arrival. In terms of overall 28-d gains and morbidity, vaccines did not enhance gains or effect morbidity, compared to negative controls. However, statistical power to detect differences was marginal in both experiments.

Introduction

Infectious bovine rhinotracheitis and parainfluenza$_3$ (IBR-PI_3) pathogens are associated with the bovine respiratory disease (BRD) complex. Feedlots typically vaccinate against IBR-PI_3 as part of routine processing. These vaccines can be administered by either intranasal (IN) or intramuscular (IM) routes, but data are limited concerning the effects of route of administration on performance. It might be advantageous to delay vaccination with IBR-PI_3-BVD-BRSV vaccine

until animals have an opportunity to recover from stresses associated with shipping. In addition, because of the potential stress of multiple injections given to the animals at arrival, administration of an IN IBR-PI_3 vaccine might prove beneficial. Two experiments were conducted at the Clayton Livestock Research Center to evaluate the effects of IBR-PI_3 vaccines and IBR-PI_3-BVD-BRSV vaccination on health and performance of newly received beef cattle.

Materials and Methods

Experiment 1. Two loads of cattle were used in the experiment. Load 1 consisted of 120 steer and bull calves. Cattle were purchased from an order buyer in Meridian, MS. Average time in transit was 17.5 h with an average shrink of 6.1% from a pay weight of 366 lb (166 kg). There were 82 (68.33%) bulls and 37 animals (31.83%) that required horn tipping. Processing occurred immediately after arrival and included weighing each calf individually, individual identification, branding, castration of bulls, horn tipping as necessary, injection with vitamin A/D_3[a], treatment for internal (oxfendazole[b]) and external parasites (fenthion[c]), vaccination with a multivalent clostridial bacterin-toxoid[d] and sorting into treatment pens. In addition, cattle received one of three treatments: 1) no IBR-PI_3 vaccine (Control); 2) an IN modified-live virus (MLV) IBR-PI_3 vaccine[d]; or 3) an IM MLV IBR-PI_3 vaccine[e]. The IN vaccine was administered using 2 mL syringes to give 1 mL per nostril. The IM vaccine was administered as a 2 mL injection in the neck. Treatments were assigned randomly to individual animals based on processing order using a predetermined random number table. Pens were randomly assigned to treatments using a random number table (four pens per treatment with 10 calves per pen). Although not blocked by sex (steer versus bull) and horns, the number of bulls (29, 27, and 26 bulls for

Table 1. Ingredient composition of 70% concentrate diets fed to steers and heifers receiving modified live vaccines

Ingredient/Item	Experiment 1 Load 1	Experiment 1 Load 2	Experiment 2
Sorghum sudangrass hay	10.30	30.72	10.00
Alfalfa hay	19.48	-	19.37
Whole corn	10.12	9.91	10.12
Steam-flaked corn	46.01	46.05	45.95
Soybean meal	3.51	3.26	3.95
Molasses	4.89	4.73	5.12
Fat (yellow grease)	2.06	1.91	1.90
Limestone	0.75	0.71	0.74
Dicalcium phosphate	0.50	0.48	0.49
Salt	0.35	0.33	0.30
Urea	0.50	0.48	0.83
Ammonium sulfate	0.50	0.48	0.24
Premix[a]	1.03	0.94	0.99
Chemical composition			
Dry matter	85.6	83.8	84.5
Ash	8.1	7.9	8.2
Crude protein	14.7	12.0	14.4
Acid detergent fiber	12.3	20.5	13.6

[a]Premix contained (DM basis): wheat midds (83.11%), vitamin A - 30,000 IU/g (0.66%), vitamin E - 500 IU/g (1.98%), Rumensin-80 (1.125%), Tylan-40 (1.125%), and trace mineral package (12%). Trace mineral package contained (DM basis): calcium iodate (0.269%), cobalt carbonate (0.362%), copper sulfate (3.268%), ferrous sulfate (19.445%), magnesium oxide (29.762%), manganous oxide (6.944%), zinc sulfate (28.169%), wheat midds (7.831%), and mineral oil (3.95%).

[a]AgriLabs, St Joseph, MO.
[b]Synanthic, Ft. Dodge Animal Health, Overland Park, KS.
[c]Tiguvon, Bayer Corp., Shawnee Mission, KS.
[d]Ultrabac7 or TSV-2, SmithKline Beecham, West Chester, PA.
[e]IBR-PI_3, Sanofi, Overland Park, KS.

control, IN, and IM, respectively) and animals requiring horn tipping (12, 13, and 12 for control, IN, and IM, respectively) were similar across treatments. After processing, steers were placed in their respective pens, offered sorghum-sudangrass hay (first week only) and a 70% concentrate diet (Table 1) in quantities sufficient for *ad libitum* consumption throughout the 28-d receiving period. Cattle were monitored daily for signs of BRD, including nasal and (or) ocular discharge, labored breathing, lethargy, and (or) depressed appetite. Cattle displaying signs were removed from their pens, taken to a processing facility, and their rectal temperature was measured. Cattle with a rectal temperature greater than 103°F (39.4°C) were treated with tilmicosin phosphate[f] at 4.55 mg/lb (10 mg/kg) of body weight (1.5 mL/100 lb) and long-acting oxytetracycline[g] at 9 mg/lb (19.8 mg/kg) of body weight (4.5 mL/100 lb).* After treatment, cattle were returned to their assigned feedlot pens. All cattle were weighed on d 28, at which time feed bunks were swept, and any feed remaining was weighed and sampled for DM determination. Bunk samples were obtained at weekly intervals during the study and dried at 212°F (100°C) for approximately 22 h to determine DM matter content. Dietary ingredient samples were obtained every 2 weeks for DM determination.

For Load 2, 108 heifer calves averaging 423 lb (192 kg) were purchased from an order buyer in Southwestern Arkansas. Cattle from this order buyer are typically purchased from auction barns in Southwestern Arkansas and Eastern Texas with an assembly time of 4 days. The transit time was 13.75 h. Except for using a different brand clostridial bacterin-toxoid,[h] heifers were processed similarly to steers in Load 1. The number of heifers that required horn tipping was not recorded. Rectal temperatures were recorded at processing, and any heifer with a temperature greater than 103.5°F (39.7°C) was treated with tilmicosin phosphate at 4.55 mg/lb (10 mg/kg) of body weight (1.5 mL/100 lb) and 10 mL of penicillin.* Thirty-one heifers required treatment at processing with 10, 13, and 8 heifers in the control, IN, and IM groups, respectively. Heifers treated at processing were represented in all pens. Experimental treatments were assigned randomly to individual heifers using a random number table (4 pens per treatment and 9 heifers per pen) and were identical to Load 1. All other procedures were similar to Load 1.

Performance data were analyzed using General Linear Models (GLM) procedures of SAS.[8] Pen was the experimental unit. For daily gain, the model included effects for IBR-PI_3 treatment, block (load), treatment x block, and pen within treatment x block. Orthogonal contrasts were used to evaluate treatment responses. Contrasts were: 1) control vs vaccines and 2) IN vs IM. Feed intake data and calculated feed:gain ratio were analyzed with a model that included treatment, block, and treatment x block. Percentage of morbid calves were calculated for each pen and analyzed using GLM procedures of SAS.[8] Statistical power was evaluated by calculating the detectable differences in outcomes using published formulas[4] for growth and morbidity data. Calculations were carried out with alpha = 0.05 and beta = 0.20.

Experiment 2. One hundred-two beef steer and bull calves weighing 455 lb (207 kg) were purchased from the same order buyer as for Load 2 of Exp. 1. The transit time was 12 h. Processing procedures were similar to Exp. 1. Using a random number table, individual cattle were randomly allotted to one of three treatments: 1) no vaccine (**Control**); 2) no vaccine at processing, with IM MLV IBR-PI_3-BVD-BRSV[g] vaccine administered on d 7 (**CON/IM**); 3) an IN MLV IBR-PI_3[d] vaccine administered at processing, with IM MLV IBR-PI_3-BVD-BRSV[g] vaccine given on d 7 (**IN/IM**); and 4) IM MLV IBR-PI_3-BVD-BRSV[g] vaccine given at processing and on d 7 (**IM/IM**). After processing, calves were placed in their respective treatment pens (4 pens per treatment with 8 to 9 calves per pen). Calves were observed daily for sickness, and animals with a rectal temperature greater than 103.5°F (39.7°C) were treated with 1.0 mg ceftiofur equivalents/lb (2.2 mg/kg) of ceftiofur hydrochloride[i] (2 mL/100 lb of BW) at 48-h intervals, plus 10 mL of penicillin.* Animals not responding to the initial treatment were given tilmicosin phosphate[f] at 4.55 mg/lb (10 mg/kg) of body weight (1.5 mL/100 lb of BW). Animals were returned to their respective pens after medical treatments. The feeding regimen was the same as for Exp. 1, with animals receiving a 70% concentrate diet (Table 1), with *ad libitum* access to hay during the first week only. All other procedures were similar to Exp. 1.

Performance data were analyzed using GLM procedures of SAS.[8] Pen was the experimental unit. For daily gain, the model included effects for vaccine treatment and pen within treatment. Orthogonal contrasts were used to evaluate treatment responses. Contrasts were: 1) Control vs vaccines, 2) CON/IM vs the average of IN/IM and IM/IM, and 3) IN/IM vs IM/IM. Feed intake data and calculated feed:gain ratio were analyzed with a model that included treatment. Percent-

[f]Micotil, Elanco Animal Health, Indianapolis, IN.
[g]Liquamycin LA-200 or Bovishield-4, Pfizer Animal Health, Exton, PA.
[h]7-way, Aspen, Kansas City, MO.
[i]Excenel, Pharmacia & Upjohn, Kalamazoo, MI.
*Some doses and uses described constitute extralabel treatment and were done under veterinary supervision.

Table 2. Effects of infectious bovine rhinotracheitis-parainfluenza$_3$ (IBR-PI$_3$) vaccines on performance and health of newly received beef cattle in Exp. 1.*

Item	Treatment[1]			SE[2]	Contrast[3]
	Control	IN	IM		
No. of pens	8	8	8		
Initial body weight, lb	382.8	383.1	388.2	3.87	-
Day-28 body weight, lb	444.4	449.6	444.3	6.00	-
Average daily gain, lb					
Days 0 to 28	2.20	2.37	2.00	0.12	2 (.05)
Daily DM intake, lb					
Days 0 to 28	10.27	10.37	9.80	0.26	NS
Feed:gain					
Days 0 to 28	4.80	4.60	5.11	0.17	2 (.05)
Morbidity, %	40.8	38.2	41.8	4.85	NS

*No treatment x load interactions were detected (P > .10); therefore, data were analyzed across loads.
[1]Control - no IBR-PI$_3$ vaccine at processing; IN - intranasal administration of IBR-PI$_3$ at processing; IM - intramuscular IBR-PI$_3$ vaccine at processing.
[2]Pooled standard error of treatment means, n = eight pens per treatment.
[3]Contrasts evaluated were: 1) control vs vaccines and 2) intranasal vs intramuscular. Observed significance (in parentheses). NS = not significant (P > .10).

Table 3. Effects of timing of modified-live vaccine administration on performance and health of newly received beef cattle, Exp. 2.

Item	Treatment[1]				SE[2]	Contrast[3]
	Control	Con/IM	IN/IM	IM/IM		
No. of Pens	3	3	3	3		
Initial body weight, lb	451.2	460.2	454.4	454.8	8.3	-
Day-28 body weight, lb	511.5	527.6	529.4	528.7	12.8	NS
Average daily gain, lb						
Days 0 to 28	2.16	2.41	2.68	2.64	0.25	NS
Daily DM intake, lb						
Days 0 to 28	10.77	11.13	11.66	10.88	0.71	NS
Feed:gain						
Days 0 to 28	5.23	4.63	4.38	4.15	0.39	1(.10)
Morbidity, %	56.0	60.2	51.4	61.1	9.62	NS

[1]Control - no vaccine; Con/IM – no vaccine at processing with IM vaccine on d 7; IN/IM - IN vaccine at processing with IM vaccine on d 7; and IM/IM - IM vaccine at processing and on d 7.
[2]Pooled standard error of treatment means, n = three pens per treatment.
[3]Contrasts evaluated were: 1) Control vs vaccines, 2) Con/IM vs the average of IN/IM and IM/IM, and 3) IN/IM vs IM/IM. Observed significance (in parentheses). NS = not significant (P > .10).

age of calves treated for each pen were analyzed using GLM procedures of SAS.[8] Statistical power was evaluated by calculating the detectable differences in outcomes using published formulas[3] for growth and morbidity data. Calculations were carried out with alpha = 0.05 and beta = 0.20.

Results

Exp. 1. Performance data are presented in Table 2. No treatment x load interactions were observed for performance data. For the 28-d receiving period, cattle given IBR-PI_3 vaccine by the IN route had greater daily gain ($P < .05$) than cattle given an IM injection of IBR-PI_3 vaccine. Twenty-eight day ADG of vaccinates did not differ from controls ($P > .10$). No differences ($P > .10$) were noted for daily DM intake, however, the feed:gain ratio was increased ($P < .05$) for the IM group compared to the IN group. No differences ($P > .10$) were noted among treatments for the percentage of cattle treated for BRD. Statistical power was adequate to detect a change of approximately 21 percentage points from the baseline morbidity rate of 40%.

Exp. 2. No differences were noted among treatments for initial or final body weight of steers given different vaccination programs (Table 3). Likewise, no differences were noted for daily gain or daily DM intake for the overall 28-d receiving period. Feed:gain was improved ($P < .10$) for vaccinated calves vs controls. No morbidity differences ($P > .10$) were noted among treatments (Table 3). Statistical power was adequate to detect a change of approximately 46 percentage points from the baseline morbidity rate of 57%.

Discussion

Results from Exp. 1 suggest there might be an advantage in performance when using an IN IBR-PI_3 vaccine at processing as compared to an IM vaccine. Responses to IN IBR-PI_3 vaccine could be related to the rapid onset of protection with this product. An IN temperature-sensitive IBR vaccine has provided protection within 24 h after vaccination, thereby providing protection almost immediately.[5] However, an IM IBR vaccine has provided protection within 48 h against a simulated natural exposure to virulent IBR virus.[9] Another possible reason for the increased performance for IN vs IM in Exp. 1 might be related to reaction to the vaccine. Anecdotal information suggests that some IM vaccines may cause an elevated body temperature, or "sweating". Data in these two experiments do not support or refute these anecdotes. Body temperature was not measured in the present experiment. Calves initially given IN vaccine and then given an IM booster vaccination on d 7 of the receiving period showed no advantage in performance over those receiving an IM injection of vaccine followed by an IM booster vaccination on d 7 (Exp. 2).

No differences in morbidity were noted between the IN and IM IBR-PI_3 vaccinated groups in Exp. 1. Statistical power to detect differences was marginal. Early research[1] noted that an IN IBR vaccine did not protect cattle against the respiratory form of IBR, however, subsequent research suggested that IBR-PI_3 vaccination of calves decreased repiratory disease in a bull test station in Canada.[2] A recent review[7] of field trials using various respiratory vaccines reported mixed performance benefits. Likewise, IBR, IBR-PI_3, or IBR-PI_3-Pasteurella haemolytica vaccination within two weeks of arrival increased mortality.[6]

Anecdotal observations suggest that there might be an advantage to delaying vaccination programs until the animals have time to recover from the stressors of shipping. In contrast to such observations, data from Exp. 2 suggest that such a management program makes little difference on growth performance or morbidity. As in Exp. 1, statistical power to detect differences was marginal. Martin et al.[6] reported that vaccination for respiratory disease within 2 weeks of arrival increased death losses and health costs. Delaying vaccination for respiratory disease (including IBR, IBR-PI_3 [IN and IM], and IBR-PI_3-PAST) in cattle fed corn-silage-based diets decreased the negative effects of vaccination; however, no decrease was observed when dry hay-based diets were fed.[6] The disease dynamics in small pens likely differs from that in large pens. Likewise, the calves in this study were only observed for 28-d. Longer term studies under commercial feeding conditions may further define differences in processing and vaccination strategies.

Conclusions

These data marginally support the need for vaccination with infectious-bovine rhinotracheitis vaccines to improve performance by newly received cattle. There might be an advantage to an intranasal vaccine at processing as compared to an intramuscular vaccine when the animals are not revaccinated. Delaying vaccination did not seem to be a beneficial management program.

Acknowledgments

This research was supported by funds from the New Mexico Agric. Exp. Sta., Las Cruces 88003. We thank Elanco Animal Health, Ft. Dodge Animal Health, Pharmacia & Upjohn, and Roche Animal Health for product support.

References

1. Curtis RA, Angulo A: A field trial to evaluate an intranasal infectious bovine rhinotracheitis vaccine. Can Vet J 15:327-330, 1974.
2. Durham PJK, Hassard LE, Donkersgoed JV: Serological studies of infectious bovine rhinotracheitis, parainfluenza 3, bovine viral di-

arrhea, and bovine respiratory syncytial viruses in calves following entry to a bull test station. Can Vet J 32:427-429, 1991.
3. Kastenbaum MA, Hoel DG, Bowman KO: Sample size requirement: one-way analysis of variance. Biometrika 57:421-430, 1970.
4. Kastenbaum MA, Hoel DG, Bowman KO: Sample size requirement: randomized block designs. Biometrika 57:573-577, 1970.
5. Kucera CJ, Beckenhauer WH: Time required to stimulate protection with intranasal administration of a temperature-sensitive, infectious bovine rhinotracheitis virus vaccine. Vet Med Small Anim Clin 73:83-87, 1978.
6. Martin SW, Meek AH, Davis DG, Johnson JA, Curtis RA: Factors associated with mortality and treatment costs in feedlot calves: The Bruce County Beef Project, years 1978, 1979, 1980. Can J Comp Med 46:341-349, 1982.
7. Perino LJ, Hunsaker BD: A review of bovine respiratory disease vaccine field efficacy. Bov Practitioner 31(1):59-66, 1997.
8. SAS. SAS/STAT® Guide for Personal Computers, ed 6th, SAS Inst. Inc., Cary, NC, 1987.
9. Sutton ML: Rapid onset of immunity in cattle after intramuscular injection of a modified-live-virus. Vet Med Small Anim Clin 75:1447-1456, 1980.

Penicillin Residues in Milk Following Subconjunctival Injection of Procaine Penicillin G*

K Liljebjelke, LD Warnick, and **MF Witt**
Department of Population Medicine and Diagnostic Sciences, Cornell University, Ithaca, New York 14853

Introduction

Subconjunctival injection of procaine penicillin G is used to treat infectious bovine keratoconjunctivitis. The purpose of this project was to find out how long pencillin can be detected in milk after a single 1 ml bulbar subconjunctival injection of procaine penicillin G.

Materials and Methods

Forty-six healthy, lactating Holstein cows were randomly assigned to receive either the penicillin injection or no treatment. A few drops of proparacaine were administered topically before injecting penicillin. Cow weights ranged from 1177 to 1716 lb (535 - 780 kg) (median = 1342 lb (610 kg) resulting in a penicillin dose of about 385 to 560 units per kg body weight. Milk samples were collected before treatment and at each of the next 4 milkings (4 hr, 16 hr, 28 hr, 40 hr) after treatment. Some cows were also sampled at 10 hr and 22 hr post-treatment to determine the number of positive tests midway between milkings.

Results

No milk samples from untreated cows were positive for B-lactam antibiotic residues using the SNAP® test (IDEXX Laboratories Inc., Westbrook, Maine 04092). The earliest positive tests for treated cows occurred at 4 hours and the latest at 22 hours after treatment. The percentages positive among treated cows were 0, 9, 92, 52, 33, 0, and 0% for pretreatment, 4, 10, 16, 22, 28, and 40 hours after treatment, respectively. These results suggest that a 36 hour milk withholding period should be adequate following this therapy. However, we did not evaluate the potential effect of clinical pinkeye infections on the duration of milk penicillin residues.

*This article was originally published in the 1999 *Proceedings* of the American Association of Bovine Practitioners (p. 259). An error was made during editing of the original version. The editor regrets this error.