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A Comparison of Two *Mannheimia haemolytica* Vaccination Strategies in Freshly Weaned Southeastern Feedlot Heifers

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Abstract

A total of 1,017 southeastern crossbred heifer calves (average weight 572 lb; 260 kg) were utilized to determine the effect of administering Pyramid® 5 and Presponse® SQ (Fort Dodge Animal Health, Overland Park, KS) as two separate injections (SEP), or as a combination product (COMB) on health and performance in a commercial feedlot setting. There were no significant differences ($P > 0.05$) between the two vaccine treatments for morbidity, mortality, or realizers. The SEP group had significantly greater weight gain ($P=0.05$) and average daily gain ($P<0.01$) at reprocessing (day 119). These differences subsided by harvest. Hot carcass weights, estimated live-weights, and average daily gains at the end of the feeding period were similar between the vaccination groups ($P>0.05$).

Keywords: bovine, feedlot, BRD, *Mannheimia haemolytica* toxoid, MLV vaccine

Résumé

Un total de 1017 taures du sud-est et de race mélangée (poids moyen 572 lb; 260 kg) ont été utilisées afin de déterminer l'effet de l'administration de Pyramid® 5 et de Presponse® SQ (Fort Dodge Animal Health, Overland Park, KS) en deux injections séparées (SEP) ou en combinaison (COMB) sur la santé et la performance dans le contexte d'un parc d'engraissement commercial. Il n'y avait pas de différence significative (P>0.05) entre les deux groupes d'injection sur la morbidité, la mortalité et la performance des animaux. Le gain de poids (P=0.05) et le gain moyen quotidien (P<0.01) était plus élevé dans le groupe SEP au retraitement (jour 119). Ces différences s'amenuisaient à la récolte. Il n'y avait pas de différence entre les deux groupes en ce qui concerne le poids de la carcasse chaude, le poids vif estimé et le gain moyen quotidien à la fin de la période d'engraissement (P>0.05).

Introduction

Bovine respiratory disease (BRD) is the greatest contributor to morbidity and mortality of feedlot cattle in North America.[9] *Mannheimia haemolytica* serotype A1 has been identified as the most common pathogen involved in BRD during the receiving period,[2,5,6,8,15] with prevalence ranging from 65 to 75%.[5] Rarely does BRD stem from a single pathogen, but rather it has a multifactorial origin that relies on interaction between host susceptibility, pathogens, and the environment. A commensal organism of the nasopharynx and tonsillar crypts, *M. haemolytica* is an opportunist, gaining access to the lungs when host defenses are compromised by stress or infection with respiratory viruses or mycoplasma.[14] In several studies, aerosol exposure to bovine herpesvirus (BHV-1) facilitated lung infection by a usually non-infectious dose of *M. haemolytica*, thus demonstrating the immunosuppressive effect that other pathogens can impart.[15,18] Research efforts have identified a ruminant-specific leukotoxin produced by rapidly growing *M. haemolytica* organisms.[3,12,16] Leukotoxin is indirectly responsible for pneumonia and the subsequent tissue damage because it functionally impairs and lyses alveolar macrophages and neutrophils.[17] Dying neutrophils release proteolytic and other enzymes that contribute to lung lesions. The classic lung lesion associated with *M. haemolytica* infection is acute fibrinous pleuropneumonia.[2,5]

Production of antibodies to leukotoxin can prevent or reduce the occurrence of fibrinous pneumonia in experimentally challenged calves.[17] Various strategies have been employed to combat and mitigate BRD in stocker

and feedlot operations. A recent study in a commercial feedlot demonstrated a possible synergism when tilmicosin was used concurrently with *M. haemolytica* toxoid at arrival. As a result of the reduced morbidity and mortality, a $14.77 advantage was reported compared to using tilmicosin alone.[4]

Vaccination on arrival to prevent disease from both bacterial and viral BRD pathogens remains a commonly utilized practice in feedlots. One report, however, suggests a possible antagonistic interaction of modified-live virus (MLV) vaccine administered at the same time as *M. haemolytica* vaccine in stressed cattle.[7] Thus, scientists have questioned the practice of administering MLV vaccine and *M. haemolytica* toxoid on the same side of the neck, postulating interference with the immune response if both products drained to common lymph nodes. The purpose of this study was to compare the effect on animal health and performance of high-risk feedlot calves when *M. haemolytica* toxoid and MLV vaccine are administered as separate injections on opposite sides of the neck, or as a combination product given on one side of the neck. Outcomes of interest included morbidity, mortality, treatment cost, realizers, and average daily gain (ADG).

Materials and Methods

Cattle

A total of 1,017 English and Continental crossbred heifer calves were procured from auction-markets by an order-buyer in Montgomery, Alabama, and delivered to Ward Feed Yard in Larned, Kansas from May 24 to June 2, 2007. Cattle were then randomized to one of two vaccination treatments until each pen replicate was complete. As a result, calves were equally represented in both treatment groups and commingled within a pen. A total of 12 pen replicates were placed on trial, with an average of 85 calves per pen (range 72-93). Across all pens, average weight of the calves at processing was 572 lb (260 kg), and ranged from 414-742 lb (188-337 kg).

Processing

After arrival at the feedlot, cattle remained separated by truckload and were placed in receiving pens where hay and water were provided *ad libitum*. Calves were processed within 36 hours of arrival. Randomization of animals to a processing group was accomplished by sorting cattle within each truckload in a feedlot sorting alley, three at a time, into one of two treatments. Cattle were brought to the processing facility by replicate with their respective treatment group and temporarily staged in holding pens without feed or water. Treatment processing order alternated between each truckload of calves to neutralize any differences in shrink from standing prior to processing when initial weights were collected. An entire treatment group was processed prior to the start of the next group to ensure proper vaccines were administered. Initial processing included the following:

- Serially numbered lot ear tag
- Radio-frequency identification (RFID) tag
- Based upon randomization outcome:
    - Modified-live infectious bovine rhinotracheitis (IBR) virus, parainfluenza-3 (PI_3) virus, bovine viral diarrhea (BVD) virus (types 1 and 2), and bovine respiratory syncytial (BRS) virus combination vaccine + *Mannheimia haemolytica* toxoid[a] (2 mL) administered subcutaneously (SC) in right neck (COMB group)

    OR

    - Modified-live IBR virus, PI_3 virus, BVD virus (types 1 and 2), and BRS virus combination vaccine[b] (2 mL) administered SC in right neck and *Mannheimia haemolytica* toxoid[c] (2 mL) administered separately SC in left neck (SEP group)
- Tilmicosin[d] administered SC in the left neck at 4.54 mg/lb (10 mg/kg) of body weight
- Growth promoting implant[e]
- Doramectin[f] (6 mL) administered SC in the right neck
- Gender was assessed and all heifers were pregnancy checked

Four short-bred heifers (< 90 days of gestation) were confirmed and aborted at the time of processing; however, these were not included in the final headcount or study analysis. Cattle were individually weighed once at initial processing and again when they received their terminal implant,[g] ranging from 102 to 146 (average 119) days-on-feed (DOF). All calves were revaccinated with MLV IBR-BVD[h] vaccine when they were reimplanted.

Feed

Cattle were fed three times daily, and diet and bunk management were similar for all pens on trial. The ration consisted of steam-flaked corn, wet distillers grain, mixed silage, alfalfa hay, and liquid supplement. Monensin[i] and tylosin[j] were included in the diet for the entire feeding period.

Animal Health

Pen riders and treatment personnel were masked (blinded) to experimental treatment assignment. Cattle with signs of illness were removed from the home pen and evaluated by hospital personnel. A diagnosis of BRD was made when a calf demonstrated clinical signs of depression (e.g., unresponsive to activity in the pen, lowered head, drooped ears, inappetance), absence of signs ascribed to other body systems, and a rectal tem-

perature of 104°F (40°C) or higher. Treatment of cattle followed the standard protocol established at the feedlot. Cattle were allowed to recover in the hospital pens following treatment, and were then returned to their home pen. Health records for all treated cattle were maintained throughout the trial.[k] Cattle not expected to reach market weight at the same time as their pen mates due to illness (i.e., chronic respiratory disease, lameness, or failure to thrive due to an undiagnosed condition) were removed from the pen and marketed via alternate channels (culls or realizers). These animals were removed from the final growth performance analysis. All animals that died during the trial were necropsied by either a veterinarian or feedlot personnel. Digital images were recorded to aid in diagnostic description of gross lesions.

Marketing

The heifers were harvested when they were visually estimated to have adequate finish for market; DOF ranged from 181-224 (average 203). There were a total of seven slaughter dates, and all heifers from a pen (replicate) were harvested on the same day. All heifers were harvested at the Tyson plant in Emporia, Kansas. Kansas State University personnel collected individual identification and hot carcass weights (HCW) for final weight calculations. Live weight was estimated by dividing HCW by a standard dressing percentage of 63.5%.

Statistical Analyses

Individual animal was the experimental unit. Descriptive statistics including frequency counts and percentages were calculated to characterize the data and to check for any data entry errors prior to data analysis. Descriptive statistics including mean, median, standard deviation, and percentiles were also calculated for analyses based upon interval data. Evaluations of morbidity and mortality, including heifers that were removed from the feedlot and not marketed with their pen group (realizers), were conducted. Additionally, a subset of cattle in the study with respiratory diagnoses was analyzed. Chi-square statistics were used to evaluate the tabular data for significance. Cattle performance measures, including weight gain to reprocessing, treatment cost, and feedlot performance (weight gain, ADG, and HCW), were evaluated with an independent samples t-test. Statistical calculations were performed by using commercially available statistical software,[l] and a P-value of ≤ 0.05 was used to determine significance of results.

Results

No significant differences in morbidity between the two vaccine treatments were determined during the course of the trial (P=0.25). Morbidity rates were so nearly identical for the two experimental groups that the corresponding morbidity curves appear superimposed until approximately 28 DOF (Figure 1). The morbidity rate in the COMB group increased more rapidly than the SEP group during the second wave of BRD. The separation in curves was maintained throughout the remainder of the feeding period.

The death rate and realizer rate did not differ between groups (P>0.05; Table 1). The distribution within respiratory categories (i.e. fibrinous, chronic, and hematogenous pneumonia, data not shown) was not different for either mortality (P>0.05) or animals realized (P>0.05) between the two vaccine treatments.

Body weight and ADG were significantly higher in the SEP treatment group compared to the COMB group (P=0.05 and >0.01, respectively) at 119 DOF when calves were reimplanted. However, animal weight and ADG

Table 1. Morbidity, mortality, and realizer rates for each treatment group of high-risk heifer calves.

Item	SEP[a]	COMB[b]	P-value
No. animals[c]	511	506	
BRD morbidity, %[d]			
Total	44.42	48.02	0.25
First relapse	43.17	44.03	0.92
Second relapse	27.55	24.30	0.71
Treatment cost, $/hd[e]	20.86	20.85	0.99
Final disposition, %			
Normal harvest[f]	93.35	92.89	0.76
Realizer[g]	3.13	2.77	0.85
Mortality[h]	3.52	4.35	0.52

[a]SEP is Pyramid®5 and Presponse®SQ (Fort Dodge Animal Health, Overland Park, KS) administered as two separate injections.
[b]COMB is Pyramid®5 + Presponse®SQ (Fort Dodge Animal Health, Overland Park, KS) administered as a combination product.
[c]Calves were commingled among 12 study pens with an average of 85 head/pen.
[d]All calves received tilmicosin at initial processing. Total bovine respiratory disease (BRD) is the number of calves initially treated for BRD divided by the number of animals in the experimental group x 100. First relapse rate is the number of first relapses divided by the number of calves originally treated for BRD x 100. Second relapse rate is the number of second relapses divided by the number of first relapses x 100.
[e]Treatment cost includes costs associated with therapy plus $1.25 chute charge.
[f]Percentage of heifer calves harvested at study completion.
[g]Cattle that were culled because of respiratory disease or other conditions due to unsatisfactory response to treatment.
[h]Deaths due to all causes.

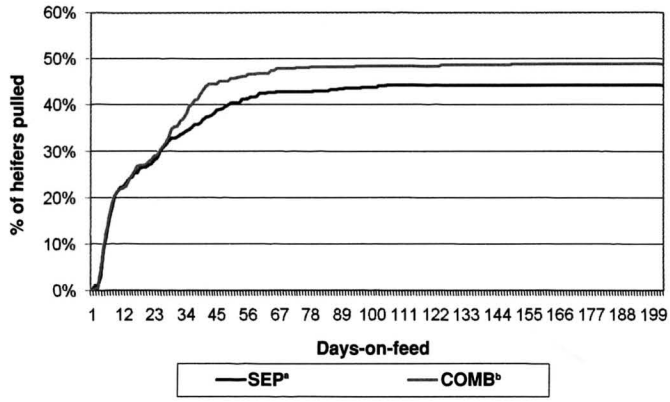

Figure 1. Cumulative morbidity (%) due to bovine respiratory disease (BRD) (first treatment only) in heifer calves comparing two *Mannheimia haemolytica* vaccination programs (P=0.25).
[a]SEP is Pyramid®5 and Presponse®SQ (Fort Dodge Animal Health, Overland Park, KS) administered as two separate injections.
[b]COMB is Pyramid®5 + Presponse®SQ (Fort Dodge Animal Health, Overland Park, KS) administered as a combination product.

were similar between the two experimental groups at time of harvest (P>0.05).

Discussion

Numerous studies have documented the benefits of vaccination with *M. haemolytica* toxoid at feedlot arrival, citing reduced risk of morbidity, relapse, and mortality.[1,8,10,11] Modern vaccines labeled for prevention of *M. haemolytica* infection are approximately 50-70% efficacious.[14] Optimal timing and frequency of administration remains debatable since varying results have been reported.[13] The potential negative interaction between MLV vaccine and *M. haemolytica* toxoid may explain some of the inconsistency seen between *M. haemolytica* vaccine trials.[7] However, the use of one dose of *M. haemolytica* at arrival in conjunction with a viral vaccine has generally been accepted as an industry standard. In the present study, there was no negative control (treatment without *M. haemolytica* toxoid); thus, these results are not comparable with other trials.

No significant differences in morbidity, mortality or realizers between treatments were detected (Table 1). For the purposes of this study, a chronic was defined as a calf that failed to respond to two treatments following metaphylactic treatment with tilmicosin. When animals realized exclusively for respiratory disease (chronics) were compared, no significant differences between vaccine treatments existed (P>0.05). Likewise, mortality due to type of respiratory disease (i.e., fibrinous pneumonia or chronic bronchopneumonia) did not differ between treatments (P>0.05).

Dry matter intake and feed conversion for calves within each treatment group could not be measured because of commingling. This information may have provided more insight into the differences in gain noted at reprocessing (Table 2). The second episode of morbidity that occurred at approximately 28 DOF likely resulted from stress associated with ration transition (Figure 1). Calves in each treatment group were commingled, resulting in identical feeding conditions; however, more calves required treatment for BRD in the COMB group than in the SEP group during the second outbreak that began at about 28 DOF (Figure 1). It is unknown why this divergence may have occurred. The increased incidence in respiratory disease may have temporarily impacted performance in the COMB group, but no differences were detected at closeout.

Table 2. Comparison of animal weight and average daily gain at various times during the course of the study.

Item	SEP[a]	COMB[b]	P-value
Animal weights, lb			
Initial processing (day 0)	569	574	0.18
Reprocessing (day 119)	940	928	0.05
Harvest (day 203)[c,d]	1139	1141	0.82
Hot carcass	724	725	0.82
Average daily gain, lb/day			
Reprocessing (day 0-119)	3.09	2.93	<0.01
Harvest (day 0-203)[c]	2.82	2.81	0.68

[a]SEP is Pyramid®5 and Presponse®SQ (Fort Dodge Animal Health, Overland Park, KS) administered as two separate injections.
[b]COMB is Pyramid®5 + Presponse®SQ (Fort Dodge Animal Health, Overland Park, KS) administered as a combination product.
[c]Calves were fed for an average of 203 days.
[d]Live-weight estimated by dividing hot carcass weight by a dressing percentage of 63.5%.

Conclusions

The primary objective of this trial was to determine if there was a negative impact on health or performance when *Mannheimia haemolytica* was administered on the same side of the neck and in combination with a MLV vaccine. Under the conditions of this study, no differences in animal health or performance at study completion were observed between the two treatment regimens. Since the study design did not incorporate a negative control (no treatment without a modified-live

IBR fraction), it is unknown whether interference and subsequent loss of efficacy of the *M. haemolytica* toxoid may have occurred. Previously published reports support the use of *M. haemolytica* toxoid to combat BRD in high-risk cattle at arrival. However, more research is needed to elucidate optimal timing of administration such that possible antigen interference is minimized and ultimate protection achieved.

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Endnotes

[a]Pyramid®5 + Presponse®SQ, Fort Dodge Animal Health, Overland Park, KS
[b]Pyramid®5, Fort Dodge Animal Health, Overland Park, KS
[c]Presponse®SQ, Fort Dodge Animal Health, Overland Park, KS
[d]Micotil®, Elanco Animal Health, Indianapolis, IN
[e]Synovex®C, Fort Dodge Animal Health, Overland Park, KS
[f]Dectomax®, Pfizer Animal Health, Exton, PA
[g]Synovex®Plus, Fort Dodge Animal Health, Overland Park, KS
[h]Pyramid®2 + Type II BVD, Fort Dodge Animal Health, Overland Park, KS
[i]Rumensin®, Elanco Animal Health, Indianapolis, IN
[j]Tylan®, Elanco Animal Health, Indianapolis, IN
[k]Turnkey, Amarillo, TX
[l]SPSS 15.0 Statistics; SPSS Inc., Chicago, IL

References

1. Bechtol DT, Ballinger RT, Sharp AJ: Field trial of a *Pasteurella haemolytica* toxoid administered at spring branding and in the feedlot. *Agri Pract* 12:6-14, 1991.
2. Booker CW, Abutarbush SM, Morley PS, Jim GK, Pittman TJ, Schunicht OC, Perrett T, Wildman BK, Fenton RK, Guichon PT, Janzen ED: Microbiological and histopathological findings in cases of fatal bovine respiratory disease of feedlot cattle in western Canada. *Can Vet J* 49:473-481, 2008.
3. Brown JF, Leite F, Czuprynski CJ: Binding of *Pasteurella haemolytica* leukotoxin to bovine leukocytes. *Infect Immun* 65:3719-3724, 1997.
4. Bryant TC, Nichols JR, Adams JR, Farmer TD, Miles DG: Effect of tilmicosin alone or in combination with *Mannheimia haemolytica* toxoid administered at initial feedlot processing on morbidity and mortality of high-risk calves. *Bov Pract* 42:50-54, 2008.
5. Confer AW, Clarke CR: Pasteurellosis in cattle, in Howard JL, Smith RA (eds): *Current Veterinary Therapy 4. Food Animal Practice.* Philadelphia, WB Saunders Co, 1999, pp 369-372.
6. Griffin D: Etiology, pathogenesis and clinical signs of bovine respiratory disease, in Smith RA (ed): *Bovine Respiratory Disease. Sourcebook for the Veterinary Professional.* Trenton, NJ, Veterinary Learning Systems Co., 1996, pp 6-11.
7. Harland RJ, Potter AA, van Drunen-Littel-Van den Hurk S, Van Donkersgoed J, Parker MD, Zamb TJ, Janzen ED: The effect of subunit or modified live bovine herpesvirus-1 vaccines on the efficacy of a recombinant *Pasteurella haemolytica* vaccine for the prevention of respiratory disease in feedlot calves. *Can Vet J* 33:734-741, 1992.
8. Ives S, Drouillard J, Anderson D, Stokka G, Kuhl G: Comparison of morbidity and performance among stressed feeder calves following vaccination with PYRAMID MLV 4 or PYRAMID 4 + PRESPONSE SQ. *Kansas State University, Cattlemen's Day, Report of Progress* 831:126-129, 1999.
9. Jensen R, Pierson RE, Braddy PM, Saari DA, Lauerman LH, England JJ, Keyvanfar H, Collier JR, Horton DP, McChesney AE, Benitez A, Christie RM: Shipping fever pneumonia in yearling feedlot cattle. *J Am Vet Med Assoc* 169:500-506, 1976.
10. Jim K, Guichon T, Shaw G: Protecting feedlot calves from pneumonic pasteurellosis. *Vet Med* 83:1084-1087, 1988.
11. MacGregor S, Smith D, Perino LJ, Hunsaker BD: An evaluation of the effectiveness of a commercial *Mannheimia (Pasteurella) haemolytica* vaccine in a commercial feedlot. *Bov Pract* 37:78-82, 2003.
12. Perino LJ: Immunology and prevention of bovine respiratory disease, in Smith RA (ed): *Bovine Respiratory Disease. Sourcebook for the Veterinary Professional.* Trenton, NJ, Veterinary Learning Systems Co., 1996, pp 18-29.
13. Perino LJ, Hunsaker BD: A review of bovine respiratory disease vaccine field efficacy. *Bov Pract* 31:59-66, 1997.
14. Rice JA, Carrasco-Medina L, Hodgins DC, Shewen PE: *Mannheimia haemolytica* and bovine respiratory disease. *Anim Health Res Rev* 8:17-28, 2007.
15. Roth JA: How cattle defend themselves against *P. haemolytica* pneumonia. *Vet Med* 83:1067-1072, 1988.
16. Samithamby J, Sreevatsan S, Maheswaran SK: Role of *Mannheimia haemolytica* leukotoxin in the pathogenesis of bovine pneumonic pasteurellosis. *Anim Health Res Rev* 3:69-82, 2002.
17. Shewen PE, Wilkie BN: Cytotoxin of *Pasteurella haemolytica* acting on bovine leukocytes. *Infect Immun* 35:91-94, 1982.
18. Yates WDG: A review of infectious bovine rhinotracheitis, shipping fever pneumonia and viral-bacterial synergism in respiratory disease of cattle. *Can J Comp Med* 46:225-263, 1982.