PEER REVIEWED

Effect of an Immunostimulant Administered at or Near Weaning on Weight Gain and Health of Beef Calves

B. R. Hoar, *DVM, PhD, DACVPM*[1]; **D. M. Myers,** *BS*[2]
[1] *Department of Medicine and Epidemiology, School of Veterinary Medicine, University of California, Davis, CA 95616*
[2] *Sierra Foothill Research and Extension Center, University of California, Agriculture and Natural Resources, Browns Valley, CA 95918*

Abstract

Weaning is generally regarded as a very stressful event in the life of calves, and is often associated with an increase in morbidity and reduced weight gain. Various management strategies are employed in an effort to reduce the impact of weaning on calf health and productivity. This study examined the effects of a nonspecific immune stimulant, mycobacterial cell wall (MCW), administered at or near weaning on the subsequent morbidity and growth of beef calves. Heifer calves (n = 137) were administered either MCW or saline two weeks prior to weaning, while steer calves (n = 60) were administered either MCW or saline on the day of weaning. Calves were monitored for 120 days. There were no observed differences between treatment groups in either weight gain or number of disease events. Under the conditions of this trial, administration of MCW at or near weaning did not have a significant effect on calf health or weight gain.

Keywords: bovine, beef calves, weaning, immunostimulant, immunity

Résumé

Le sevrage est généralement considéré comme une période très stressante dans la vie des veaux et s'associe souvent à une hausse de la morbidité et à une réduction du gain de poids. Plusieurs stratégies de régie sont employées dans le but de réduire l'impact du sevrage sur la santé des veaux et la productivité. Cette étude se penchait sur les effets d'une stimulation immunitaire non spécifique, soit l'extrait de paroi cellulaire mycobactérienne (MCM), administrée dans la période entourant le sevrage sur la morbidité et la croissance subséquente de veaux de boucherie. Les veaux femelles (n = 137) ont reçu une administration de MCM ou de saline deux semaines avant le sevrage alors que les veaux mâles (n = 60) ont reçu les mêmes deux traitements au moment du sevrage. Les veaux ont été surveillés pendant 120 jours. Il n'y avait pas de différence entre les deux traitements tant au niveau du gain de poids que du nombre d'événements de maladie. Dans les conditions de cet essai, l'administration de MCM dans la période entourant le sevrage n'a pas eu d'effet significatif sur la santé des veaux ou le gain de poids.

Introduction

Keeping calves healthy at or near weaning can be challenging. The abrupt separation of the dam from the calf has been shown to be stressful to the calf, as measured by changes in behavior,[9] acute-phase protein response[3] and neutrophil:lymphocyte (N:L) ratio.[5,8] Stress has been associated with attenuation of immune function and increased disease susceptibility. The first three to four weeks after weaning is typically regarded as a period when calves are most susceptible to poor performance, disease and death.[10]

Some management tools available to minimize the impact of weaning and subsequent risk of disease include fence-line weaning,[9] two-step weaning,[7] and feeding or injection of prophylactic doses of antibiotic.[11] With increasing concern over risk of antibiotic resistance in animals and people, veterinarians and cattle producers should look for means other than antibiotics for prevention of infectious diseases. Stimulation of the calf's immune system is an obvious alternative that can be used to one's advantage. This can be achieved by various specific and nonspecific means. Specific immunostimulation through vaccination provides stimulation of the immune system to produce antibodies against specific antigens such as infectious bovine rhinotracheitis (IBR), parainfluenza-3 virus (PI3), bovine respiratory syncytial virus (BRSV) and bovine viral diarrhea virus (BVDV). Nonspecific immunostimulation arises from the sum of immune responses, not necessarily including specific antibody formation.[4] Mycobacterium cell wall (MCW)

fractions have been shown to be nonspecific immune stimulants that activate cell-mediated immune responses.[1] Immunoboost®[a] is a MCW fraction product licensed by the US Department of Agriculture to reduce death loss and clinical signs associated with *Escherichia coli* (K99) in calves.

While no data on use of this product are present in peer-reviewed publications, the company that produces Immunoboost® has made results of some in-house trials available. In newborn calves, treatment resulted in significantly greater numbers of MHC Class II CD-4 T-lymphocytes when compared to controls. In an *E. coli* (K99) challenge study, 90% of treated calves survived, compared to 42% survival in the controls. Over a 75-day feeding period, day-old calves treated with MCW had 15% greater average daily gain compared to control calves. In a trial using 500-600 lb (227-273 kg) calves over a 38-day feeding period, those treated with MCW gained 0.25 lb (0.11 kg)/day more than untreated controls. Morbidity was reduced by 62% and treatment cost by 54% in animals receiving a 3-mL subcutaneous dose of MCW in a study using 250 lb (114 kg) Holstein calves arriving at a feedlot (http://immunoboost.info).

The primary objectives of this study were to determine whether a single administration of a MCW immunostimulant can reduce the incidence of morbidity and increase average daily gain of recently weaned beef calves. A secondary objective was to assess effects of a single dose of MCW on white blood cell parameters when given on the day of weaning.

Materials and Methods

The study was performed on a cow-calf ranch in the Sierra Nevada foothill range of northern California, consisting of approximately 350 adult cows and their calves. In accordance with ranch protocol, all calves were vaccinated with a 4-way modified-live virus vaccine containing IBR, PI3, BRSV and BVDV at approximately three months of age, and again two weeks prior to weaning at approximately seven months of age. Calves were vaccinated against clostridial diseases at three months of age and on the day of weaning. A pour-on endectocide was also applied the day of weaning.

Using a random numbers table, 137 heifer calves were randomly assigned to receive either 3-mL of MCW subcutaneously or 3-mL of saline subcutaneously administered at the same time as the 4-way viral vaccine, 14 days prior to separation from their dams. This resulted in 72 heifers being allocated to the MCW group and 65 to the control group. Calves were weighed at this time, at weaning, and approximately every month for four months. During the trial period, animals were monitored and treated for any clinical disease event that occurred. Treatments and responses were recorded by ranch personnel, who were masked (blinded) to the membership of the treatment groups. Heifer calves were pastured on native rangelands throughout the trial.

Similarly, a random numbers table was used to allocate 60 steer calves to receive either 3-mL MCW subcutaneously or 3-mL of saline subcutaneously. This resulted in 31 calves being allocated to the MCW group and 29 to the control group. Unlike the heifers, this was administered on the day the steers were weaned. Animal weight and clinical disease events were monitored as for the heifer calves. Steer calves were pastured on native range for 60 days, then transferred to a commercial feedlot for the final 60 days of the trial.

Blood samples were drawn from a randomly selected subset of 21 steer calves (10 treated with MCW and 11 controls) at the time of weaning and treatment (0 hours), at 24 hours and at 48 hours post-treatment. Samples were submitted for complete blood counts.

Data were entered into and analyzed using a commercially available software program (SPSS, version 14, Chicago, IL). Initial weight, final weight and average daily gain were compared with two-sided t-tests. Differences in proportion of animals requiring treatment was assessed using either a chi-square test of homogeneity or a Fishers exact test, as appropriate. Time to first treatment was analyzed using a Kaplan-Meier survival analysis. For changes in white cell parameters, a generalized linear model was used, with treatment group as the between-subjects factor, and white cell parameter count as the within-subjects factor.

Results

Treatment with MCW did not have statistically significant ($P<0.05$) effects on weight gain in either steers or heifers (Table 1). Over the 120 days of the trial, heifer calves combined gained an average of 0.82 lb (0.37 kg)/day, while steer calves combined gained an average of 2.25 lb (1.02 kg)/day.

No differences between groups were observed in the proportion of calves that required treatment for any illness (Table 2). Fifteen of 94 (16%) control animals required at least one treatment, while 21 of 103 (20%) treatment animals required at least one treatment. All but one of the treatments was for suspected infectious bovine keratoconjunctivitis (IBK); the other treatment was for a subcutaneous abscess. There was no difference between groups in time to first treatment using Kaplan-Meier survival analysis (Figure 1).

Average daily gain for calves treated for IBK was significantly less than for those not treated. For heifers, untreated animals gained 0.88 lb (0.40 kg)/day during the trial, while treated animals gained 0.61 lb (0.28 kg)/day (P-value = 0.02). This resulted in a difference of 40.6 lb (18.5 kg)/heifer during the 120 days of the trial.

Table 1. Effect of a single dose of mycobacterial cell wall immunostimulant (MCW) on calf weight and average daily gain over a 120-day trial. MCW treatment was administered to 72 heifers and 31 steers, while 65 heifers and 29 steers were included in the control groups.

		MCW treatment*	Control*	*P*-value
Initial weight (lb)	Heifers	537.8 (55.4)	526.4 (59.6)	0.25
	Steers	569.0 (69.9)	567 (69.6)	0.90
Final weight (lb)	Heifers	641.9 (64.0)	647.4 (82.7)	0.66
	Steers	854.5 (69.5)	846.4 (73.8)	0.66
Average daily gain (lb/day)	Heifers	0.77 (0.51)	0.87 (0.62)	0.27
	Steers	2.28 (0.27)	2.20 (0.36)	0.35

*Mean (SD)

Table 2. Effect of a single dose of mycobacterial cell wall immunostimulant (MCW) on calf morbidity over a 120-day trial.

		Number of treatments for disease				
		0	1	2 or more	Total	*P*-value
Heifers	MCW	53	14	5	72	0.79
	Control	51	10	4	65	
Steers	MCW	29	2	0	31	0.59
	Control	28	1	0	29	

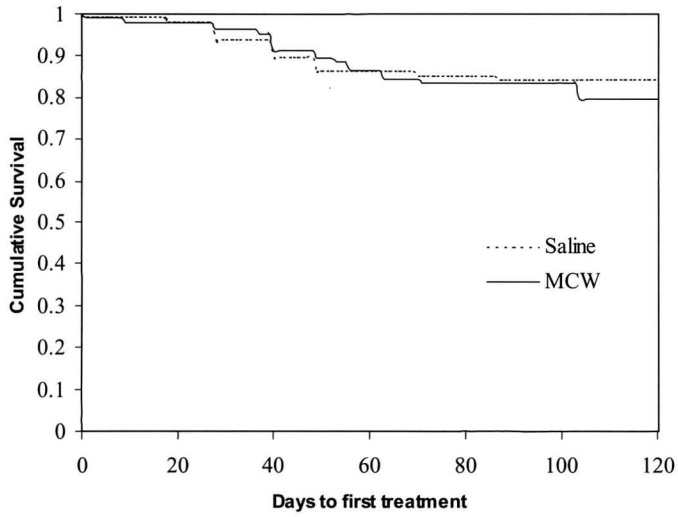

Figure 1. Comparison of a single dose of mycobacterial cell wall immunostimulant (MCW) to saline on the number of days to first treatment for disease.

For steers, the differences were not statistically significant, although there was a tendency for untreated animals to gain more weight than treated animals (2.25 lb [1.02 kg]/day compared to 2.10 lb [0.95 kg]/day, *P*-value = 0.45).

The effect of weaning, vaccination and simultaneous administration of MCW on white cell parameters is shown in Table 3. There were no differences between treatment groups in any of the parameters examined. Total white blood cell count, neutrophil count and neutrophil:lymphocyte ratio were significantly increased at 24 hours for both the MCW treated and control calves ($P<0.001$), and returned to baseline levels at 48 hours. Lymphocyte counts were not significantly different at any time period.

Discussion

We did not find significant differences in weight gain or morbidity rates between animals treated with MCW and those not treated. The rate of gain of calves throughout the study was minimal due to marginal late-season nutritional value of the native pasture that the cattle grazed, and better nutrition may have resulted in greater differences between the groups. Because IBK was the only disease that occurred in the calves, it is possible that disease exposure was not sufficient for a beneficial response to treatment with MCW to be detected. Calves were housed on pasture, were not transported and did not commingle with other cattle immediately after weaning; all factors believed to lower exposure to infectious pathogens. A trial involving calves weaned directly into

Table 3. Effect of weaning and simultaneous administration of mycobacterial cell wall immunostimulant (MCW) on white blood cell parameters in 21 steer calves.

		Treatment group		
Variable	Time (hrs)	MCW treatment (n = 10)	Control (n = 11)	*P*-value
White blood cells, 10^9/L	0	12.8 (1.9)[a]*	11.5 (2.8)[a]	0.24
	24	20.2 (4.1)[b]	20.1 (3.0)[b]	0.96
	48	14.0 (1.6)[a]	12.8 (2.6)[a]	0.26
Neutrophils, 10^9/L	0	2.5 (0.7)[a]	2.0 (0.7)[a]	0.12
	24	11.0 (3.8)[b]	11.2 (1.7)[b]	0.88
	48	3.6 (1.0)[a]	3.2 (1.0)[a]	0.37
Lymphocytes, 10^9/L	0	9.3 (1.4)	8.5 (2.4)	0.37
	24	7.9 (1.3)	7.6 (2.0)	0.72
	48	8.8 (1.3)	8.2 (1.6)	0.37
Neutrophil:lymphocyte ratio	0	0.27 (0.07)[a]	0.26 (0.14)[a]	0.83
	24	1.45 (0.56)[b]	1.57 (0.49)[b]	0.59
	48	0.42 (0.16)[a]	0.39 (0.09)[a]	0.64

*Mean (SD)

[a,b] Values within columns having different superscripts are significantly different (*P*-value ≤ 0.001).

a feedlot where nutrition is optimal and disease exposure is greater may prove more interesting.

The sample size of this study may also have limited the ability to detect a significant treatment effect. Based on the observed mean and standard deviation of the MCW treatment group, our sample would have declared a difference in average daily gain of 0.2 lb (0.09 kg)/day to be significantly different at the standard 5% level of significance.

The effect of IBK on weight gain was significant. Heifers treated one or more times for disease had significantly lower average daily gain than those not treated, and gained 40.6 lb (18.5 kg) less than unaffected herd mates over the course of the trial. Similar findings have been reported in a number of previous studies.[6,12,14,15]

The stress effect of weaning on leukocyte parameters is consistent with that shown previously. Our finding that the N:L ratio was elevated at 24 hours after weaning is consistent with an earlier study by Hickey and co-workers.[8] In contrast, Church and Hudson reported an elevation in the N:L ratio for up to 14 days after dam removal in wapiti (*Cervus elaphus*) calves.[5] In a study designed to simulate acute stress, administration of dexamethasone resulted in neutrophilia and marked lymphopenia that led to a dramatic increase in the neutrophil:lymphocyte ratio.[2] While the calves in our study were simultaneously vaccinated with a multivalent clostridial vaccine at weaning, we believe changes observed were most likely due to the stress of weaning, since it has been shown that vaccination with either a 2-way or 7-way clostridial vaccine has no significant effect on WBC, neutrophil or lymphocyte counts.[13]

Conclusions

With low disease exposure and marginal nutrition as observed in this trial, use of MCW fraction at or near weaning had no effect on weight gain, morbidity, or white blood cell parameters in beef heifer calves. While we observed no effect on these parameters in beef steer calves, the sample size limited our ability to draw definitive conclusions. IBK had a significant effect on weight gain, regardless of treatment group. White blood cell count, neutrophil count and N:L ratio were dramatically affected by weaning.

Acknowledgement

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Endnote

[a] Immunoboost®, Bioniche Animal Health USA, Inc., Athens, GA

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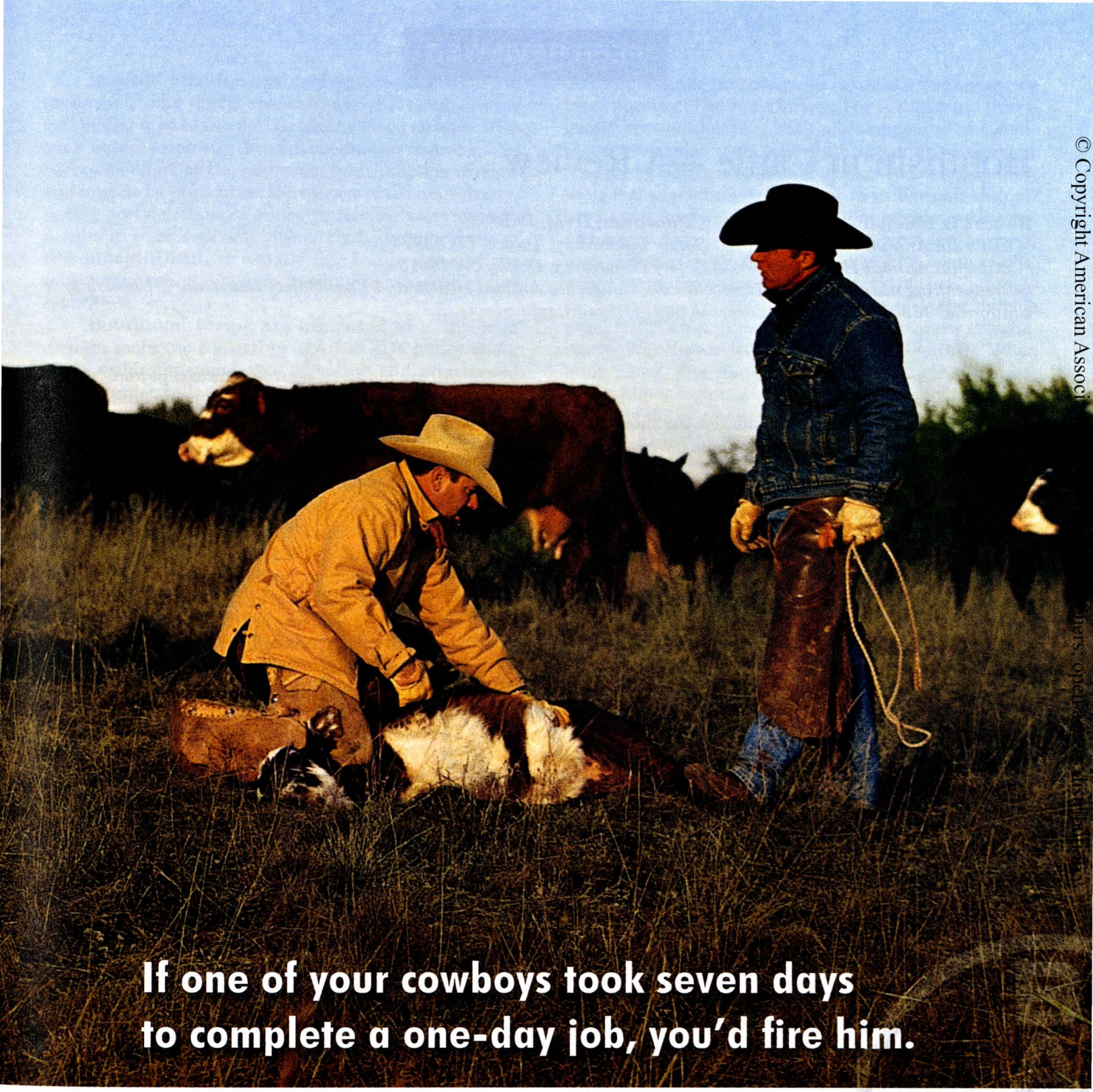

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