Prophylactic Administration of Hyperimmune Serum when Processing Feedlot Cattle

R. L. Morter, *D.V.M., Ph.D.*
H. A. Amstutz, *D.V.M.*
A. J. Roussel, *D.V.M., M.S.*
Department of Large Animal Clinic
School of Veterinary Medicine
Purdue University
West Lafayette, Indiana 47907

Calves after leaving the farms of origin east of the Mississippi River spend an average of 4.5 days in market channels and transit before arriving at the feedlot with much of the time spent in markets or assembly points. During the marketing process, groups of calves are assembled by sex, weight, breed, frame size and muscling to enhance their market value. Further, most of the producers have small cow herds and frequently market small lots of uneven calves. Grading and sorting of the calves to assemble lots of uniform calves that are attractive to buyers and feeders is a major function of the marketing system. The net result is a load of calves that originated from a number of farms, were co-mingled, passed through several markets and assembly points over a period of days, before being loaded for final transit to the feedlot.

During the movement through market channels, the calves are exposed to viral and bacterial respiratory pathogens, may be on a limited plain of nutrition, and have access to water in a variety of devices with which they are not familiar. Upon arrival at the feedlot, though not showing overt signs of bovine respiratory disease (BRD), many are prodromal. Processing calves at the time of arrival at the feedlot, a widely accepted practice includes vaccination, but the immune response does not occur quickly enough to protect those calves already incubating one or more of the respiratory pathogens. The widespread incidence of *Pasteurella hemolytica* strains that are resistant to antimicrobials approved for use in feedlot cattle further compounds the problems of the lot management in attempting to minimize the losses from BRD in cattle from these sources.[1]

It was stated at the North American Symposium on Bovine Respiratory Disease that the industry needed to be able to provide calves with instant immunity upon their arrival at the markets.[2] Genetically engineered bovine interferons may provide instant immunity, but are as yet in developmental stages. Passive immunity offered another alternative to provide fast immunity. This study was undertaken to evaluate the efficacy of a commercially available hyperimmune serum (HS) of bovine origin administered to calves at the time of arrival at the feedlot in reducing the incidence and severity of respiratory disease as well as the effect it might have on the immunoresponse to vaccines.

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Materials and Methods

Two hundred head of large framed, well muscled, mixed breed steer calves were procured by a Kentucky order buyer in October, 1983. The calves were assigned to one of two barns and one of six pens within each barn by a computer generated random number assignment; sixteen calves allotted to each pen. Eight calves were excluded from the study due to weight extremes, clinical signs of disease, or erratic behaviour. Two pens in each barn were randomly assigned to one of three treatment groups: a) untreated controls (UTC), b) 5 ml of HS (5-HS) per 100 pounds of body weight, and c) 10 ml HS per 100 pounds of body weight (10-HS).

Processing of calves on arrival included weighing individually, identifying by ear tag, degrubbing and delousing, deworming, intramuscular (IM) administration of 2.5 million units of vitamin A, vaccinating with an IM multivalent modified live virus product for protection against infectious bovine rhinotracheitis (IBR), a bovine virus diarrhea (BVD) and parainfluenza 3 (PI:3), a 7-way clostridial bacterin-toxoid, and a *Haemophilus somnus bacterin*®. Immediately following processing, the calves were sorted by barn and pen assignment. The HS was administered subcutaneously to the assigned calves.

The receiving ration was good quality first cutting mixed orchard grass-alfalfa hay free choice, plus one pound of natural protein supplement and one pound of rolled corn per head per day. Automatic waterers served two adjoining pens. The amount of supplement was increased to 1.5 pounds on day 7, to 2.0 on day 11 and continued on that level. The corn was increased to 1.5 pounds on day 11, to 2.0 pounds on day 14, the level for the rest of the trial. Corn silage was included on day 14 and increased incrementally

until all hay was withdrawn by day 18. The ration for the remainder of the 42 day observation period was corn silage to appetite with 2.0 pounds of supplement and 2.0 pounds of corn fed as a complete mixed ration. The feed was weighed for each pen daily and periodic weigh-back of feed left in the bunks subtracted to determine consumption by pen.

All calves were observed daily for the first 28 days by the principal investigators and by technical staff for the remainder of the trial. Any with clinical signs of disease were cut from their group for further examination. A diagnosis was established for each sick calf. The severity of the signs of BRD was graded and recorded on treatment sheets previously described.[3] The judgment of the investigators of the clinical condition of the calf, not just a temperature of 104 F or greater, determined initiation of antimicrobial treatment. The primary antibiotic was oxytetracycline administered IM at a dose 5 mg/lb once a day. Improvement of clinical condition and a marked drop in rectal temperature after 24 hours indicated a response to treatment, and calves were continued on oxytetracycline until the temperature was at least below 104 F for 2 consecutive days. Calves that did not have a marked improvement in clinical signs of respiratory disease and drop in temperature after 1 day of treatment were classified as non-responsive to oxytetracycline. The secondary antibiotic was chloramphenicol administered IM at 8 mg/lb. Other intracurrent disease, e.g. coccidiosis or foot rot, was treated with accepted regimens of therapy.

Specimens were taken for the isolation and identification of pasteurella by thrusting a sterile swab deep into the nares, taking care to avoid contact with the external nares. Thirty-six of the first calves diagnosed as having clinical BRD and prior to having received any antibiotics at the feedlot were sampled. Antibiograms were determined for the pasteurella strains isolated by the disc diffusion technique for susceptibility testing.[4] All calves were bled at the initiation of the trial and again on day 42 to provide sera for establishing the initial and final titers for IBR, BVD, PI:3, and *Haemophilus somnus*.

The variables analyzed to determine efficacy of the treatment were: a) average daily gain (ADG), b) feed per pound of gain (FPG), c) number of steers treated for BRD, d) day of trial on which a steer was first treated, e) number of days of treatment for BRD of individual steers, f) seroconversions, and g) effects of barn or pen. Computer analysis of the data utilized the Statistical Package for Social Sciences and Biological Medical Data Processing.

Results

Feedlot Performance: The overall average weight on arrival was 494 pounds with a variation of 12± between the average weight of steers by pen. The ADG for 42 days by treatment group was: UTC 2.1 pounds with a range of 1.83 to 2.28 between pens, 5-HS 2.25 pounds with a range of 2.12 to 2.49 and 10-HS 2.2 pounds with a range of 2.10 to 2.31. The 5-HS treatment steers gained 6.6% and the 10-HS steers 6.5% more than the UTC. The UTC consumed an average of 5.7 FPG, range between pens 5.2 to 6.5; 5-HS 5.5, range 5.0 to 6.0 and 10-HS 5.5, range 5.3 to 5.7, which varied within treatments but was not significantly different between treatments.

Clinical BRD: Eighteen steers in each HS treatment group developed clinical BRD and 19 in the UTC group. None died. Eighteen steers responded to oxytetracycline therapy; 4 UTC treated an average of 3.3 times, 9 on the 5-HS, with 3.1 treatments and 5 on the 10-HS with 3.4 treatments. The average number of treatments for steers that did not respond to oxytetracycline and were treated with chloramphenicol was 4.9 for UTC, 4.7 for 5-HS and 4.4 for the 10-HS group. Subsequently, retreatment of 2 of the UTC group, 3 of the 5-HS and 1 of 10-HS was required. The average time to onset of BRD was not significantly different between treatment groups.

Bacteriology: A total of 18 strains of pasteurella were isolated, predominantly *Pasteurella hemolytica*. The sensitivity of the strains to various antibiotics varied greatly from 100% sensitive to gentamycin, 89% to chloramphenicol, 44% to neomycin, 27.5% to ampicillin, 22% to tetracyclines, 22% to penicillin and 5.5% to lincomycin. (Table 1)

TABLE 1. Antibiotic Sensitivity of Eighteen Isolates of Pasteurella Hemolytica.

Antibiotic	Number of Isolates		
	Resistant		Sensitive
	Total	Intermediate	
Streptomycin (10 mcg)	13*	3	2
Chloramphenicol (30 mcg)	2	0	16
Lincomycin (2 mcg)	17	0	1
Tetracycline (30 mcg)	13	1	4
Neomycin (30 mcg)	2	8	8
Ampicillin (10 mcg)	13	0	5
Gentamycin (30 mcg)	0	0	18
Penicillin (10 units)	13	1	4

* Thirteen isolates totally resistant to Streptomycin, Tetracyclines, Ampicillin, Lincomycin and Penicillin.

Serology: Only 4 steers had IBR titers of 2 or greater on the initial serology; 2 a titer of 4, 1 of 8 and 1 of 16. One hundred twenty eight steers were seronegative to BVD and 64 positive. The initial BVD titers ranged from 2 to 4096 with a geometric mean titer (GMT) of 4.6. The PI:3 titers ranged from 4 to >512 with 66 seronegative steers. The reactivity to *H. somnus* ranged from 24 titers of 32, 96 of 64 and 36 of 256

to 1024 with an initial GMT of 91 and all steers seropositive. Forty one percent (26/64) of the UTC steers failed to seroconvert to IBR, 40% of the 5-HS and 52% of the 10-HS. All of the 124 steers seronegative to BVD on arrival seroconverted. Seven titers to BVD dropped 2 or more dilutions, e.g. 4096 to 1024; 2 of the UTC, 3 of 5-HS and 2 of 10-HS. The final *H. somnus* GMT were UTC-215, 5HS-239, and 10HS-223. The GMT to *H. somnus* of the revaccinated steers was 239 compared to 208 for the singly vaccinated. (Table 2)

TABLE 2. Serologic Response of Steers Treated With Bovine Hyperimmune Serum At Time of Vaccination.

	Titers**							
Dose of*	IBR		BVD		PI:3		H. somnus	
Serum	I***	F***	I	F	I	F	I	F
0	1.0	2.6	4.3	187	8.0	95	79	215
5	107	2.5	4.6	181	3.5	78	91	239
10	1.0	2.0	4.8	169	5.9	101	97	223

* Dose as ml per 100 pounds of body weight
** Geometric Mean Titers
*** I=initial sera and F=final sera taken on post-vaccination day 42

Discussion

This study, during the fall of 1983, while policy on the extra-label use of drugs in food animals was being developed, was undertaken before the restrictions on the use of chloramphenicol had been issued. The experimental design evaluated passively administered antibodies for control of BRD in cattle following arrival at the feedlot. Highly resistant *P. hemolytica* had been isolated from cattle from the same source in previous trials.[1] Passive immunity appeared to provide an alternative to extra-label use of drugs for the treatment of BRD in cattle with indigenous pasteurella resistant to antibodies approved for use in feedlot cattle. The HS is labeled for use in young calves at a dose of 15 ml per 50 pounds, i.e. 30 ml per 100 pounds. The 2 much smaller doses of HS, 5 ml and 10 ml per 100 pounds of body weight were arbitrarily selected to keep both the cost and ease of administration within practical limits. A larger dose would have been unduly expensive with little probability of being cost-effective and would have been time-consuming to administer. The quality of the commercial hyperimmune serum relative to pathogens known to be involved in BRD was not considered.

The experimental design, 4 replicates of 16 steers for each treatment, with an overall 28% incidence of BRD, provided a sound basis for statistical analysis of the data. The hyperimmune serum treatment did not affect the incidence of BRD with 18 of 64 affected in each of 2 treatment groups and 19 in the other. It had also been postulated that the passive immunity would reduce the severity of BRD as measured by response to treatment. The response to treatment, the number of days a steer had to be treated, was not significantly different between experimental groups ($P<0.10$). Further, it was thought that the passive immunity could delay the onset of BRD by aiding the host defense mechanisms in suppressing the buildup of the pathogens in an individual steer or within an experimental group. As measured by the number of days from processing to the occurence of clinical BRD, the average number of days to the onset of clinical BRD was not significantly different ($P<0.10$). Thus, the incidence, severity, or time of onset of BRD were not significantly affected by the passively administered antibodies.

Improved performance is an important indicator of the cost effectiveness of an experimental regimen. The overall ADG of 2.18 on the low energy ration was very good, though biased by initial shrink weights on arrival and final weights on filled cattle. The shrink from pay weight to weight on arrival was 4.8%. Based on the initial pay weight, the ADG was 1.62. The 6.6% and 6.5% increase in ADG in the 5-HS and 10-HS groups respectively as compared to the UTC suggested a positive effect of the treatments; however, the increase in ADG was not significantly different ($P<0.75$) nor was 0.2 of a pound difference in FPG significant.

These steers were considered typical of feeder calves originating in the southeastern states, except for the time in transit. The order buyer purchased them at three different auction markets, and in 2 cases, the cattle arrived within 12 hours after the sale. Various means of identification, e.g. numbered or a variety of insecticide ear tags or notched ears, indicated multiple farms of origin. No history of vaccination or previous disease was available. The IBR virus is reported to be ubiquitous and considered widespread in cattle in the United States.[4] Finding only 4 of 192 steers serologically positive to IBR on arrival did not substantiate this, at least in cattle from this source. Eighty of the 192 steers were still seronegative 42 days after vaccination with the MLV-IBR virus. The optimum time to determine seroconversion following vaccination is 14 to 28 days and by 42 days the low level postvaccination SN titers may well have declined. Further, IBR serologic results are difficult to interpret as titers and may have little correlation with protection immunity. Protective immunity can only be truly determined by challenge with virulent virus. The initial titers of >2 excluded low levels of persistent colostral antibodies as a cause of the failure to seroconvert. The HS was not a factor as the seroconversion rates were not significantly different between the UTC and those that received the HS. The vaccine was properly handled, being reconstituted as used, not unduly exposed to sunlight or extreme temperatures, and administered with new disposable syringe and needles. It is obvious that field strain virulent IBR virus did not circulate in this group of steers or higher postinfection SN titers would have been found. The data do not indicate that the MLV IBR vaccine was not efficacious.

All of the steers were seropositive to BVD at the end of the trial with a final GMT of 181, compared to an initial GMT

of 4.6. The drop in titer of two dilutions or more in seven steers indicated either recent infection or vaccination prior to the initial sampling. If due to infection, those steers could have been actively shedding field strain BVD virus during the trial, which could have contributed to the 100% seroconversion. More likely, the vaccine contributed to the seroconversions as clinical BVD was not diagnosed. The HS did not influence the response as there was no significant difference in GMT between the three treatment groups.

At the end of the trial, all steers were seropositive to PI:3. The final GMT of 91 was significantly greater ($P>0.05$) than the initial GMT of 5.4 for PI:3. It is difficult to rationalize the significantly lower PI:3 titer of the 5-HS group ($P>0.01$). As with IBR, it was surprising to find that 66 of the steers were seronegative on arrival. It is frequently difficult to find PI:3 seronegative animals at the farm or ranch of origin before the exposure to the virus in market channels.

Titers to *H. somnus* may be interpreted: 256 and above as active infection, 128 heavy exposure or recent vaccination, 64 moderate exposure or vaccination and 32 as susceptible. Thus, 36 of the steers with titers of 256 to 1024 were in the category of active infection. Recent active infection was further substantiated by the drop in titer of 11 of these steers. Eight of the steers classified as susceptible based on initial titers of 32 had final titers of 256 or greater, a further indication of active *H. somnus* infection in the cattle. The initial GMT was 91 compared to the final GMT of 223, a significant increase ($P>0.05$). Revaccination 21 days after arrival of the cattle in one barn did not significantly affect the final GMT by barn, 239 as compared to 208, The apparent active infection in both barns could have negated the anticipated serologic response to revaccination.

The reasons for the failure to demonstrate efficacy of hyperimmune bovine serum administered when processing cattle into the feedlot were not determined. The doses administered were selected arbitrarily for practical reasons, not on the basis of quality of the serum. The amount of antibodies specific for given bovine respiratory pathogens might have been inadequate in the arbitrary doses, 1/3 and 1/6 of the label recommendations. The unexpectedly high rate of calves seronegative to IBR and PI:3 indicates that the steers had little previous experience with these common pathogens of BRD and represented an unusually susceptible population. Thus, a higher level of passive immunity would have been required than necessary if some actively acquired immunity had been present. Administration of the recommended label dose of 30 ml per 100 pounds might have achieved protective passive immunity but could not be a cost effective practice.

The indications of recent or active BVD and *H. somnus* infections among some of the steers may have resulted in a level of exposure that overwhelmed the passive immunity. The feedlot industry is still faced with the problem of preventing or treating BRD in calves of Southeastern origin whose indigenous pasteurella are very resistant to antibiotics approved for use in feedlot cattle. Current restrictions on antibiotics known to be effective compounds the problem. The stated need for a product that would provide fast immunity at the point that calves enter market channels still exists. Hyperimmune serum of greater potency, genetically engineered bovine interferons or monoclonal antibodies may provide the desired instant immunity providing protection until active immunity following vaccination can provide ongoing protection.

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