Effect of Levamisole on Respiratory Disease in Feedlot Cattle

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Successful vaccination enhances the host's resistance to a specific disease agent. Vaccination could be considered a means of regulating acquired immunity. The objective of a vaccination program is to provide protection against challenge by exposure to the virulent agent. The postvaccinal response may not be adequate to provide such protection. The response to vaccination, particularly with bacterins and toxoids, has been enhanced by the incorporation of immunoadjuvants with the antigen. Better adjuvants than the commonly used aluminum hydroxide gel, e.g., preparations of mycobacterium cells, produce an undesirable granulomatous reaction and sensitize the animal to tuberculin which has eliminated their use in veterinary practice. A number of immunostimulatory chemical agents have been identified. These agents are not specific relative to the response to a given antigen, but may be highly specific relative to the immune system. Some affect only the humoral component and others the cellular. Immunoregulation is not a new concept as cortisones and antihistamines have long been used to depress the immune response. The concept that the immune respone can be enhanced by chemical agents is an intriguing one.

Levamisole not only has anthelmintic activity, but is known to potentiate the immune response in combination with antigenic stimulation. Levamisole has little effect on the normal immune response or on the humoral response. It is effective in restoring cellular immunity to normal levels in the compromised animal. A common therapeutic dose of levamisole for immunopotentiation is 2.5 mg/kg, less than half the anthelmintic dose for cattle. Further, it is commonly repeated for 3 days with a second 3 day course a week later.[1]

It has been suggested that the deworming dose of levamisole administered at the time of processing cattle into the feedlot could be immunostimulatory and result in a reduced incidence of respiratory disease.[1-4] This controlled field trial was undertaken to evaluate the effect of a single dose of 6.0 mg/kg of levamisole administered at the time of processing on the incidence and severity of bovine respiratory disease (BRD) in feedlot cattle.

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Material and Methods

Three hundred and eighteen crossbred steers were purchased by an order buyer in Kentucky. The movement of cattle in sales channels was not known, nor was any history of prior treatment or preconditioning available. All cattle were processed on arrival, weighed individually, ear-tagged, implanted with Ralgro, injected IM with 2.5 million IU units of vitamin A, vaccinated intranasally with infectious bovine rhinotracheitis and parainfluenza 3 modified live viruses and subcutaneously with a heptavalent clostridial bacterin-toxoid. The steers were not deloused or degrubbed.

Twelve steers were excluded from the study due to clinical signs of disease or weights at the extremes for the group as a whole. The random number program assigned 17 steers to each of 18 pens and 9 pens to each of 2 treatment groups. The assignment to treatment groups was not known to the investigators to preclude biasing subsequent observations. One treatment group received 6.0 mg/kg of levamisole subcutaneously at the time of processing and the other group served as untreated controls.

The receiving ration was coarsely chopped good quality alfalfa-orchard grass hay ad lib plus 0.5 lbs rolled corn per head for the first 3 days. On day 4, 0.5 lb of a 32% natural protein supplement was added, and the corn increased to 1.0 lb; on day 9 the supplement increased to 1.0 lb and the corn to 2.0 lbs, on day 16, corn silage was introduced and over a 3 day period substituted for all of the hay to bring the ration to corn silage ad lib plus 2.0 lbs of supplement and 2.0 lbs of corn. During the remainder of the trial, the supplement was held constant and the corn increased and corn silage decreased incrementally to bring the cattle on to full feed.

All steers were observed daily and any animal with clinical signs of BRD examined individually. The Food and Drug Administration, Bureau of Veterinary Medicine requires that cattle on a drug trial must have a rectal temperature of 104° F. or greater to be diagnosed as having BRD, regardless of other clinical signs. Thus, a rectal temperature of 104° F. or greater was the primary criteria

for a diagnosis of BRD. A subjective rating system to evaluate the severity of other clinical signs of BRD used a scale of 0 to 3, with 3 being the most severe for depression, weakness, dehydration, nasal discharge, respiratory rate and auscultatory sounds. Recumbency, encrusted muzzle, oral breathing and cough were recorded as plus or minus. *(Figure 1).* Steers undergoing treatment for BRD remained in their assigned pens.

Figure 1
HEALTH RECORD

Pen Number 25 Veterinarian Amstutz/Morter
Cattle/Pen 17

Date	Calf No.	Recumbent	Depression	Weakness	Dehydration	Nasal Discharge	Encrusted Muzzle	Oral Breathing	Cough	Temperature	Respiratory Rate	Auscultation	Diagnosis	Treatment
10/14	221	–	1	1	1	1	–	–	+	7^2	1	1	shipping fever	23 ml Oxytet & 18 ml Tylan
10/15		–	1	1	1	2	+	+	+	5^0	1	1		23 ml Oxytet & 18 ml Tylan
10/16		–	3	2	2	2	+ + +	–	–	4^7	2	1		23 ml Oxytet & 18 ml Tylan
10/17		–	1	1	1	2	–	–	–	3^6	2	1		23 ml Oxytet & 18 ml Tylan
10/18	DT	–	1	0	1	2	+	–	–	2^1	1	–		23 ml Oxytet & 18 ml Tylan

Form courtesy of American Cyanamid Company, Princeton, N.J. 05840

The primary treatment for BRD was 11 mg/kg oxytetracycline and 17.5 mg/kg of tylosin administered at different sites. Response to treatment was evaluated on a reduction in rectal temperature and severity of clinical signs. Treatment was terminated with the rectal temperature less than 104° F. for 2 consecutive days. Steers that had not responded after 2 days of treatment with the primary antibiotic were treated with 24% w/v sulfonamide preparation (8% each of sulfamethazine, sulfathiazole and sulfapyridine) with an initial dose of 41 ml/100 lbs and maintained with 28 ml/100 lbs daily. Steers that did not respond to the sulfonamide therapy were subsequently treated intramuscularly with 36,000 IU/kg of procaine penicillin G.

Data collected included the ratings of the severity of BRD in individual animals, the number treated, the number of treatments per animal, response to the antimicrobials, deaths, average daily gain (ADG) and feed per pound of gain (FPG). No fecal examinations for parasite ova were conducted. The steers were weighed individually on day 42 and the trial terminated.

Results

The overall incidence of BRD was 21%, 65 of 306 steers. The number treated for BRD was almost identical for the treatment groups: 33 in the levamisole-treated group (LTG) and 32 in the untreated controls (UTC). The average rectal temperature of steers with BRD were almost identical for the 2 groups at the time of the first treatment—LTG 105.35° F. and UTC 105.3° F. The values assigned to other signs of BRD were low in both groups, most values being slightly more than 1 out of a possible maximum of 3 for severe signs *(Table 1).* Those signs that were recorded as either being present or not are given as the percent of the group with a given sign. The only notable difference is in coughing, 60% of the LTG and 30% of the UTC.

TABLE 1

ASSIGNED VALUES FOR SIGNS OF RESPIRATORY DISEASE

	Average Values*							Percent With Signs**		
Treatment	Depression	Weakness	Dehydrated	Nasal Discharge	Respiratory Rate	Auscultation	Temperature	Encrusted Muzzle	Cough	Oral Breathing
Levamisole 6.0 mg/kg	1.4	1.2	1.0	1.25	1.1	1.1	105.35	8	60	3
Controls	1.2	0.87	0.87	1.1	1.4	1.2	105.3	10	30	3

* Values assigned from 0 with no signs to 3 for severe signs

** The signs recorded as present or not

TABLE 2

DECREASE IN RECTAL TEMPERATURE OF STEERS
24 HOURS AFTER FIRST TREATMENT
FOR RESPIRATORY DISEASE

Treatment	Responders*	Non-Responders**
Levamisole 6.0 mg/kg	2.55***	0.65
Controls	2.44	0.48

* Responding - therapy completed with primary antibiotics

** Non-Responding - shifted to secondary drug to obtain response

*** Degrees F.

The 2 groups responded to treatment with the primary drugs at similar rates; 51.5% for LTG and 56.3% for UTC with the average number of days on treatment 3.6 and 3.3 respectively. The response to the secondary and tertiary drugs was not satisfactory in either group with many days of additional treatment required. The rectal temperatures of the steers that responded to the primary antibiotics had dropped remarkably 24 hours after the initial treatment, 2.55° F. for LTG and 2.44° F. for the UTC. The 24 hour decrease recorded for those that did not respond subsequently was 0.65° F. and 0.48° F. *(Table 2).*

Eleven of the LTG steers died, 10 due to pneumonia and one with a perforated abomasal ulcer and liver abscesses. Seven deaths occurred in the UTC group, 1 dying of peracute pneumonia did not receive any treatment.

The average weight of the steers in both groups at the time of processing was 479 pounds. The average weight of the steers at the end of the trial was LTG 562 pounds and UTC 559 pounds. The ADG for the 2 groups was 1.96 and 1.83 respectively. The FPG for the LTG steers was 5.46 and for the UTC 5.66.

Discussion

Identifying animals early in the course of BRD and timely initiation of treatment increases the probability of a good response. The well-established criteria of a rectal temperature of 104° F. or greater may not be a valid criteria for selecting animals for treatment. The Bureau of Veterinary Medicine has adopted this standard in an attempt to preclude biasing results of drug trials by treating animals that are not clinically ill. It does not follow that 104° F. should be a standard for the diagnosis of BRD in the feedlot. Early in the disease, the temperature may be only slightly elevated. The clinical signs are often discrete, not the classic textbook signs of markedly depressed, ears lowered, oral breathing, gaunt, encrusted muzzle and paroxysmal coughing. The criteria for examining individual animals were some loss of herding instinct, a serous nasal discharge that was cleansed from the muzzle with the tongue, rapid but shallow respirations, some loss of coordination of the rear legs, soft coughing often only associated with forced activity, and some degree of deviation from normal behaviour patterns. The required 104° F. temperature caused treatment of some animals to be deferred for 24 hours, permitting the pneumonic process to progress unchallenged by treatment.

The response to treatment with the combination of oxytetracycline and tylosin was unsatisfactory, but typical of the response obtained when the infecting pastuerella are highly resistant to the drugs. Poor response to treatment also resulted from continuing the primary drugs for the second day in spite of the lack of response. This practice of giving the antibiotic time to work became established when the levels of resistant bacteria were not as great. The almost 2.0° F difference in the drop in temperature after 24 hours in the animals that were responding to the treatment as compared to those that were not should have been an early indication to adjust the therapeutic regimen. The response to treatment with the sulfonamides and penicillin was also unsatisfactory, partly due to advanced state of the pneumonia. Further, the pasteurella isolated were also resistant to the sulfonamides. Sensitivity to penicillin was not determined, but our past experiences suggest that resistance was a problem. The deaths due to pneumonia were not significantly different between the 2 groups.

The only significant difference between the LTG and UTC steers was in the ADG (P 0.05). The lower FPG for the LTG steers was not significant. This increased efficiency of the LTG might be attributed to the effects of deworming. However, this is only speculative as pre- and post-treatment fecal examinations for parasite ova were not done. It would be equally speculative to attribute the benefit to some other activity of the levamisole in view of the fact that none of the other parameters were affected. In this trial, treatment with the anthelmintic dose of levamisole at the time of processing cattle into the feedlot did not affect the incidence or severity of BRD.

References

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