The Effectiveness of Micotil for the Treatment of Bovine Respiratory Disease

John K. Merrill, *Ph.D.*
PROVEL
Division Eli Lilly Canada Inc.
Calgary, Alberta
Lealon V. Tonkinson, *Ph.D.*
Lilly Research Laboratories
Greenfield, Indiana

Introduction

Bovine respiratory disease (BRD), also called shipping fever, is a common occurrence in beef feedlots. It is especially common in lots receiving newly weaned calves. In Canada this occurs primarily in the fall of the year (September–December) when environmental stresses may be the largest and cattle movement and mixing is the most intense. Many of these animals pass through an auction market where the potential of mixing and exposure to disease organisms is great. Transportation for relatively long distances, mostly via truck, is usually necessary to get the animals from point of purchase to the feedlot. These stresses appear to interact with viruses and bacteria to cause the disease.

Morbidity and mortality related to BRD represents a significant cost to the beef industry. Estimates of 15–40% morbidity and 1–5% mortality are common.[1] Until effective methods or practices are developed to prevent BRD from occurring, treatment regimes that are more effective in reducing total cost of treatment as well as mortality, are desirable.

MICOTIL® (tilmicosin) is a new macrolide antibiotic developed by Lilly Research Laboratories, Indianapolis and Greenfield, Indiana. Micotil injection contains 300 mg tilmicosin per ml and is administered as a single subcutaneous injection. Tilmicosin has an in-vitro antibacterial spectrum that is predominantly gram-positive with activity against certain gram-negative micro-organisms and several mycoplasma species as well.[2] The antibacterial activity of tilmicosin led to its development for the treatment of BRD in cattle associated with *Pasteurella haemolytica* and *P. multocida*, and other sensitive organisms. Micotil was initially evaluated for the treatment of BRD in newly weaned, recently shipped feedlot beef calves in four Canadian and four U.S. studies. These were dose titration studies and will be reported elsewhere. A series of 11 product comparison studies were then conducted across Canada to compare the effect of a single injection of 10 mg tilmicosin/kg of body weight with other commonly used antimicrobial injection product treatment regimens (Table 1).

TABLE 1. Location, number of animals and year conducted for eleven canadian tilmicosin studies.

Trial Number	Location	Number of animals	Year
1	Alberta	60	1987
2	Ontario	60	1987
3	Alberta	317	1988
4	Ontario	36	1988
5	Ontario	31	1988
6	Ontario	118	1988
7	Ontario	120	1988
8	Alberta	329	1988
9	Saskatchewan	144	1988
10	Alberta	314	1988
11	Ontario	237	1988

Materials and Methods

Trials 1 and 2

Trials 1 and 2 compared tilmicosin at 10 mg/kg of body weight to long-acting oxytetracycline at 20 mg/kg of body weight for the treatment of naturally occurring bacterial pneumonia in feedlot cattle. A single injection of each drug was administered. Each experiment utilized 25 head per treatment with 10 animals per study kept as untreated controls. All calves had a temperature of at least 105°F and were diagnosed as having BRD at the time of treatment.

Trials 3–11

Trials 3–11 were conducted to compare the efficiency of tilmicosin to that of other drugs currently being used to treat BRD in Canada. Five trials compared tilmicosin to ceftiofur, two compared tilmicosin to trimethoprim/sulfa-

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doxine and two compared tilmicosin to oxytetracycline. These trials were all conducted under a similar protocol in that all calves pulled for treatment of BRD had a temperature of greater than or equal to 105°F. Tilmicosin was administered as a single injection at a dose of 10 mg/kg of body weight, ceftiofur at 0.5 mg/lb, trimethoprim/ sulfadoxine at 1.2 mg trimethoprim and 6 mg sulfadoxine per lb and oxytetracycline at 7 mg/lb in one study and 4 mg/lb in another. Ceftiofur and trimethoprim/ sulfadoxine were injected daily for either three or four days.

The number of animals per treatment varied from trial to trial and ranged from 14 to 167. Repull rates, treatment days and mortality rates were evaluated. No other treatments were allowed and strict treatment regimes were followed.

Results and Discussion

Table 2 shows the pooled results of trials 1 and 2. Both tilmicosin and oxytetracycline were effective in reducing body temperatures ($p<0.06$). Tilmicosin appeared to have a greater effect in reducing body temperature on day 1 than did oxytetracycline.

Twenty-eight day weight gain was not different between negative controls and tilmicosin but was less ($p<0.07$) for long-acting oxytetracycline. Mortality was 25%, 8% and 12% for negative control, tilmicosin and oxytetracycline treatment groups, respectively.

TABLE 2. Temperature reduction, weight gain and mortality of feedlot calves left untreated or treated with tilmicosin or long-acting oxytetracycline (Trials 1 and 2).

	Avg. temperature by treatment (°F + 100) Days post-treatment						
Treatment	0	1	4	10	Avg. 1-10	28 day weight gain(kg)	Died/ treated
Placebo	6.11	5.09	4.82	2.95	4.24[c]	43.64[ab]	5/20
Tilmicosin 10 mg/kg	6.22	3.14	3.58	3.20	3.24[d]	40.62[a]	4/50
LA oxytet 20 mg/kg	6.01	4.27	3.56	3.19	3.60[e]	32.52[b]	6/50

[a,b] Means in the same column without a common superscript differ ($p<0.07$). Contrasts comparing treatment groups to placebo are less powerful than the contrast comparing treatment groups, due to a smaller number of animals in the placebo group.

[c,d,e] Means in the same column without a common superscript differ ($p<0.06$).

Trials 3, 4, 5, 6 and 7 compared tilmicosin to ceftiofur for the treatment of BRD. A summary of the pooled results is shown in Table 3. First treatment success rate was 60.58% for tilmicosin and 55.16% for ceftiofur. Six animals in the tilmicosin treatment group became chronic while 14 became chronic in the ceftiofur group. Average treatment days were 1.39/animal for tilmicosin and 4.35/animal for ceftiofur. A total of four animals died from each treatment group. Two of the four in the tilmicosin treatment group were diagnosed as fibrinous pneumonia and three of the four in the ceftiofur group were diagnosed as fibrinous pneumonia. With the exception of trial 3, if animals were pulled again after being treated twice for BRD, they were removed from the trial and no further data was collected.

In trial 3 animals were treated for a third time, if necessary. In the tilmicosin group 16 out of 159 or 10.06% required a third injection while 34 out of 158 or 21.52% of the animals in the ceftiofur group required a third series of treatments ($p<0.01$). Four animals were pulled a fourth time and categorized as chronics with no further treatment in the tilmicosin group while there were nine from the ceftiofur group in this category.

TABLE 3. Summary of relapse and mortality data for trials 3, 4, 5, 6, and 7.

	Antibiotic treatment	
Item	Tilmicosin	Ceftiofur
# of cases	312	310
Treatment days, initial	312	930
# 1st repull	123	139
Treatment days, 1st repull	123	417
# of chronics	6	14
Total treatment days	435	1347
Average treatment days	1.39	4.35
Mortality (all cases)	4	4
Mortality (fibrinous pneumonia)	2	3

Trials 8 and 9 compared tilmicosin to trimethoprim/ sulfadoxine. A summary of the pooled results is shown in Table 4. First treatment success rate was 91.25% for tilmicosin and 78.54% for trimethoprim/sulfadoxine ($p<0.07$). One animal became chronic in the tilmicosin group while six animals became chronic in the trimethoprim/sulfadoxine group. Average treatment days (days in which an antibiotic injection was administered) were 1.10/animal for tilmicosin and 4.11/animal for trimethoprim/sulfadoxine. Three animals died in the tilmicosin group and four in the trimethoprim/sulfadoxine group.

None of the three mortalities in the tilmicosin group were diagnosed as fibrinous pneumonia while three of the four in the trimethoprim/sulfadoxine group were fibrinous pneumonia.

TABLE 4. Summary of relapse and mortality data for trials 8 and 9.

Item	Antibiotic treatment	
	Tilmicosin	Trimethoprim/ sulfadoxine
# of cases	240	233
Treatment days, initial	240	770
# 1st repull	21[a]	50[b]
Treatment days, 1st repull	2	40
# 2nd repull	2[c]	15[d]
Treatment days, 2nd repull	2	40
# of chronics	1	6
Total treatment days	263	957
Average treatment days	1.10	4.11
Mortality (all cases)	3	4
Mortality (fibrinous pneumonia)	0	2

[a,b] The number of 1st repulls were significantly less for tilmicosin treated group ($p<0.07$).
[c,d] The number of 2nd repulls were significantly less for tilmicosin treated group ($p<0.35$).

Tilmicosin was compared to oxytetracycline LP in trials 10 and 11. In trial 10 the oxytetracycline was injected intravenously for four days at 7 mg/lb of body weight and in trial 11 oxytetracycline was injected intramuscularly for three days at 4 mg/lb of body weight. The pooled results from these two studies are shown in Table 5. First treatment success rate was 80.37% for tilmicosin and 74.02% for oxytetracycline ($p<0.04$). Average treatment days per animal were 1.20 and 4.38, for tilmicosin and oxytetracycline treatment groups, respectively.

There was a significant difference in mortality due to fibrinous pneumonia between the tilmicosin and oxytetracycline. Two out of 270 cases (0.74%) in the tilmicosin group died while 17 out of 281 cases (6.05%) in the oxytetracycline group died ($p<0.11$). Tilmicosin was more effective than oxytetracycline for treatment of BRD in these feedlot calves.

TABLE 5. Summary of relapse and mortality data for trials 10 and 11.

Item	Antibiotic treatment	
	Tilmicosin	Oxytetracycline LP
# of cases	270	281
Treatment days, initial	270	987
# 1st repull	53[a]	73[b]
Treatment days, 1st repull	53	245
Total treatment days	323	1232
Average treatment day	1.20	4.38
Mortality (all cases)	7[c]	18[d]
Mortality (fibrinous pneumonia)	2[e]	17[f]

[a,b] Number was significantly less for tilmicosin group ($p<0.04$).
[c,d] Number was significantly less for tilmicosin group ($p<0.05$).
[e,f] Number was significantly less for tilmicosin group ($p<0.11$).

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