A Comparison of Tilmicosin and Ceftiofur for the Treatment of Bovine Respiratory Disease

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Introduction

Bovine respiratory disease (BRD), or "Shipping Fever", continues to be the most costly disease of stocker and feeder cattle. Recent weaning, movement through auction markets, commingling and shipment are significant stressors. Recently received, stressed calves are particularly vulnerable to infection with respiratory viruses and bacteria, especially *Pasteurella hemolytica.* Morbidity rates in stocker calves of southeastern origin often exceed 50%, and mortality rates are commonly 2-4%. The objective of this study was to compare efficacy of tilmicosin and ceftiofur, the two drugs most recently approved by the FDA for treatment of BRD.

Methods

Two hundred and thirteen calves were purchased from auction markets in Georgia (Trial 1) or Kentucky (Trial 2) and shipped to the Pawhuska Oklahoma Research Station backgrounding feedlot. Upon arrival, calves were weighed individually, eartagged with individually numbered tags, and randomly allotted to 10 pens for a nutrition study. Calves had free choice access to water and long stem grass hay. The following morning, all calves were processed as follows:

- vaccinated with IBR/PI_3[a], MLV, IM
- vaccinated with 7-way clostridial bacterin[b] subcutaneously
- dewormed with injectable ivermectin[c]

Georgia calves were adapted to a 72% concentrate ration which was limit fed to produce gains of 2.0 lbs per day (Trial 1). The Kentucky calves (Trial 2) were fed two pounds per head daily of a 40% natural protein pellet and offered prairie hay free choice. Any calves showing respiratory signs upon arrival were treated and were not included in the comparative respiratory treatment study.

Beginning on day 1, calves showing visual signs of BRD and also having a rectal temperature of 104°F or higher were treated with tilmicosin[d] or ceftiofur[e]. Alternate cattle received each treatment. Tilmicosin was administered as a single subcutaneous injection at 1.5 ml per hundredweight (10 mg/kg). Ceftiofur was administered IM once daily for three days at 1 ml per hundredweight (1.1 mg/kg). All calves were assigned a severity of illness score by the blinded investigator immediately before initial treatment. On day four following initial treatment, the rectal temperature was taken and the severity of illness was scored. Tilmicosin treated calves were then classified as responders (not requiring further treatment) or retreats, calves which required treatment with a different drug beyond the initial three days. Cattle initially treated with tilmicosin and classified as a retreat were treated with spectinomycin[f] and did not receive a second injection of tilmicosin. Cattle initially treated with ceftiofur and not satisfactorily recovered on day four, received ceftiofur treatments on days four and five or were treated with spectinomycin on day four if their condition had worsened by day four. Because the label for ceftiofur suggests treatment on days four and five for calves improving but not fully recovered, calves receiving ceftiofur on days four and five were not classified as retreats. Calves that died during the study were necropsied at the Oklahoma Animal Disease Diagnostic Laboratory. At the end of 28 days, bulls were castrated, horns were tipped, cattle were individually weighed, branded, implanted, re-vaccinated with IBR/

PI_3 and moved to pasture.

All data were analyzed using the general linear model of SAS with the main effects of drug and a combined effect of nutritional treatment and origin. F tests were used to identify significant effects of drug treatments. The data were analyzed by separate origin and with origins combined in order to demonstrate marked differences in response to therapy between origins.

Results and Discussion

Trial 1

Heifers included in trial 1 originated from Georgia. These heifers were high quality, fresh auction origin calves. Thirty-six of these heifers experienced BRD and were treated with either tilmicosin or ceftiofur. Response to treatment is shown in Table 1. The response rate following treatment with either drug was excellent, with an 88.9% response rate for tilmicosin and an 83.3% response rate in calves treated with ceftiofur. Retreat rates were 11.9 and 16.7% for tilmicosin and ceftiofur, respectively. There were no repulls and no death loss during the 28 day receiving period. Calves treated with tilmicosin had significantly improved severity of illness scores ($p<.01$) and lower rectal temperatures ($p<.01$) on day four than calves treated with ceftiofur.

Table 1. Effect of tilmicosin or ceftiofur on treatment response (Trial 1)[a].

	Tilmicosin	Ceftiofur	Probability (p<)
Number	18	18	
Response (%)	88.9	83.3	
Retreat (%)[b]	11.1	16.7	
Repulls (%)[c]	0	0	
Mortality (%)	0	0	
Severity score[d]			
Day 1	2.3	2.5	
Day 4	1.1	1.7	.01
Temperature			
Day 1, °F	104.8	104.9	
Day 4, °F	102.5	103.5	.01

[a]Data expressed as least squares means.
[b]A retreat was defined as a calf that required a second treatment regimen without a break in treatment days.
[c]A repull was defined as a calf that had a break in treatment days between initial and subsequent treatments.
[d]1=normal; 2=slightly ill; 3=moderately ill; 4=severely ill; 5=downer, dead.

Trial 2

Steers and bulls included in trial 2 originated from Kentucky and were considered lower quality and much more stale than the Georgia heifers. The purchase price for the steers and bulls was $34 per hundredweight less than the heifers. As shown in Table 2, the response rate for calves treated with either drug was markedly lower than the response rate of calves in trial 1. Calves treated with tilmicosin had a 65.9% response to first therapy while those treated with ceftiofur had a 43.9% response rate ($p<.02$). Retreats were high. The retreat rate for calves receiving tilmicosin was 29.5% as compared to 53.7% for calves treated with ceftiofur ($p<.02$). The repull rate was 6.8 and 14.6% for tilmicosin and ceftiofur treated calves, respectively.

Table 2. Effect of tilmicosin or ceftiofur on treatment response (Trial 2)[a].

	Tilmicosin	Ceftiofur	Probability (p<)
Number	44	41	
Response (%)	65.9	43.9	.02
Retreat (%)[b]	29.5	53.7	.02
Repulls (%)[c]	6.8	14.6	
Mortality (%)	2.3	14.6	.03
Severity score[d]			
Day 1	3.0	2.9	
Day 4	2.0	2.3	.01
Temperature			
Day 1, °F	105.4	105.7	
Day 4, °F	103.6	104.2	.05

[a]Data expressed as least squares means.
[b]A retreat was defined as a calf that required a second treatment regimen without a break in treatment days.
[c]A repull was defined as a calf that had a break in treatment days between initial and subsequent treatments.
[d]1=normal; 2=slightly ill; 3=moderately ill; 4=severely ill; 5=downer, dead.

On day 4, calves treated with tilmicosin had lower, or more favorable, severity of illness scores. The mean severity of illness score of 2.0 for tilmicosin treated calves was significantly ($p<.01$) lower than the mean score of 2.3 for ceftiofur treated calves. In addition, mean rectal temperatures were lower ($p<.05$) on day 4 in calves treated with tilmicosin.

One calf treated with tilmicosin died while six calves treated with ceftiofur died. This resulted in case fatality rates of 2.3 and 14.6%, respectively ($p<.03$). The one mortality in the tilmicosin group occurred on day 2 following initial treatment and was diagnosed by the diagnostic laboratory as having fibrinous pneumonia and infectious bovine rhinotracheitis (IBR). Ceftiofur treated calves which died were diagnosed as either fibrinous or chronic pneumonia and died between days 2 and 27 after initial treatment.

Combined Trials

After pooling the results obtained in trials one and two (Table 3), calves treated with tilmicosin had a statistically more favorable ($p<.03$) response rate than ceftiofur treated calves, 72.6 vs 55.9%, respectively. The

retreat rate for calves treated with tilmicosin was lower (24.1% vs 42.4%). These differences were statistically significant (p<.02). Repull rates did not differ, however, the case fatality rate of 1.6% in tilmicosin treated calves were markedly lower (p<.05) than the 10.2% case fatality rate experienced by the ceftiofur treated calves.

Table 3. Effect of tilmicosin or ceftiofur on treatment response (Trial 1 and 2 combined)[a].

	Tilmicosin	Ceftiofur	Probability (p<)
Number	62	59	
Response (%)	72.6	55.9	.03
Retreat (%)[b]	24.1	42.4	.02
Repulls (%)[c]	4.8	10.2	
Mortality (%)	1.6	10.2	.05
Severity score[d]			
Day 1	2.8	2.8	
Day 4	1.7	2.2	.01
Temperature			
Day 1, °F	105.2	105.4	
Day 4, °F	103.3	104.0	.01
Treatment days[e]	1.8	5.5	.01
Weight[e]			
Day 1	506	508	
Day 4	521	509	

[a]Data expressed as least squares means.
[b]A retreat was defined as a calf that required a second treatment regimen without a break in treatment days.
[c]A repull was defined as a calf that had a break in treatment days between initial and subsequent treatments.
[d]1=normal; 2=slightly ill; 3=moderately ill; 4=severely ill; 5=downer, dead.
[e]Because tilmicosin was a single injection treatment and ceftiofur was administered a minimum of 3 days, a statistical bias exists. Calculation of treatment days was based upon the number of times the calf was injected with an antimicrobial.

Severity of illness scores on day 4 were lower for tilmicosin treated calves (p<.01). A lower severity of illness score suggests that calves treated with tilmicosin "looked better" to the blinded investigator on day 4, which would strongly influence the retreat rate in this study. Rectal temperatures of tilmicosin treated calves were significantly (p<.01) lower than the rectal temperatures of calves in the ceftiofur treatment group.

Treatment days favored (p<.01) the tilmicosin treated group but this must be interpreted with great caution. Because tilmicosin is a single injection treatment and ceftiofur was administered a minimum of three days, a statistical bias exists.

Weight gains (Table 4) were not impressive in either treatment group. Calves treated with tilmicosin gained 0.63 pounds per day while those treated with ceftiofur had essentially no gain (p<.04). Total gains of 19 pounds and 0 pounds in the tilmicosin and ceftiofur groups, respectively, are well below projections for the 28 day receiving period. This loss of performance illustrates another major loss due to bovine respiratory disease.

Table 4. Effect of tilmicosin or ceftiofur on 28 day performance (Trial 1 and 2 combined)[a].

	Tilmicosin	Ceftiofur	Probability (p<)
Number	62	59	
Weight (lbs)			
Arrival	502	498	
Final	521	498	.07
ADG (lb)	0.63	-0.03	.04

[a]Least squares means.

It is interesting to compare the response rates of calves from the two different origins. Calves in trial 1 treated for respiratory disease with either drug showed acceptable response rates. This is similar to results seen in another Oklahoma trial.[1] Calves in trial 2 were treated during the same time period and under similar management conditions. The response rates were markedly lower, regardless of the therapy used. Also, there was a greater difference in efficacy between the two antibiotics used in the Kentucky origin calves (Trial 2). This strongly emphasizes that factors other than the antibiotic used also impact response to treatment. Calves that are stale and generally mismanaged prior to arrival are much less responsive to treatment for respiratory disease than fresh calves.

The results of this comparative study correlate well with earlier published results[2,3] from Canada.

Products Used

[a]IBR-PI$_3$, Norden Laboratories, Lincoln, NE.
[b]Ultrabac®7, SmithKline Beecham Animal Health, Exton, PA 19341.
[c]Ivomec-F®, Merck AgVet Div., Rahway, NJ 07065.
[d]Micotil® 300 Injection, Elanco Animal Health, Indianapolis, IN 46285.
[e]Naxcel®, The Upjohn Co., Kalamazoo, MI 49001
[f]Spectam® Injectable, Sanofi Animal Health, Inc., Overland Park, KS 66210. A valid veterinarian-client-patient relationship was maintained for use of this product in an extra-label manner.

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