PEER REVIEWED

Comparison of tulathromycin, tilmicosin, and gamithromycin for metaphylactic treatment of high-risk calves for control of bovine respiratory disease

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Abstract

Cross-bred heifer calves (n = 579; initial bodyweight 404 ± 27.4 lb; 183.3 ± 12.4 kg) were utilized in a randomized, complete block design to compare 3 different antibiotics for control of bovine respiratory disease (BRD) in light-weight feeder heifers. Cattle originated from southeast Texas and were shipped approximately 700 miles (1125 km) to the Clayton (New Mexico) Livestock Research Center. Heifers were randomly allocated off the truck into 30 pens, and administered 1 of 3 metaphylactic treatments at initial processing: 1) tulathromycin (TUL; 1.13 mg/lb (2.5 mg/kg)); 2) tilmicosin (TIL; 6 mg/lb (13.3 mg/kg)); or 3) gamithromycin (GAM; 2.72 mg/lb (6.0 mg/kg)). Heifers administered TUL had 0.29 lb (0.13 kg) greater (95% CI = 2.27 to 2.46) average daily gain than cattle administered GAM. Cattle administered TUL had a lower (5.2%; 95% CI = 1.2 to 9.1) morbidity rate than calves in the TIL (14.6%; 95% CI = 6.7 to 22.5) and GAM (12.79%; 95% CI = 7.7 to 17.9) groups. There were no differences in DMI or mortality in cattle between treatments.

Key words: bovine respiratory disease, BRD, cattle, feedlot, high-risk, metaphylactic treatment

Résumé

Des génisses de race croisée (n = 579; poids initial 404 ± 27.4 lb) ont été utilisées dans un plan d'expérience avec blocs aléatoires complets afin d'évaluer l'effet de trois différents types d'antibiotiques utilisés pour le traitement métaphylactique du complexe respiratoire bovin (CRB) chez les génisses de faible poids à leur arrivée dans le parc d'engraissement. Les bovins provenaient du sud-est du Texas et ont été transportés sur une distance d'approximativement 700 milles au *Clayton Livestock Research Center* (CLRC; Clayton, NM). À leur sortie du camion, les génisses ont été distribuées au hasard dans 30 enclos et ont reçu un traitement métaphylactique parmi les trois suivants : 1) Tulathromycine (TUL; 2.5 mg/kg), 2) Tilmicosine (TIL; 13.3 mg/kg) et 3) Gamithromycine (GAM; 6.0 mg/kg). Il y avait une augmentation du gain quotidien de 0.29 lb (I. C. 95% = 2.27, 2.46) chez les génisses qui recevaient le traitement TUL plutôt que le traitement GAM. Le taux de morbidité était moins élevé chez les génisses pour le traitement TUL (5.2%) (I. C. 95% = 1.2, 9.1) que pour les traitements TIL (14.6%; I. C. 95% = 6.7, 22.5) et GAM (12.79%; I. C. 95% = 7.7, 17.9). Le traitement n'a pas influencé la prise alimentaire journalière de matière sèche ou la mortalité.

Introduction

Bovine respiratory disease (BRD) continues to be one of the most significant animal health concerns in the cattle industry.[3,6,9] The cost of BRD to the beef industry due to death, poorer feed conversion, and treatment costs is estimated to be more than $3 billion/year.[15] Bovine respiratory disease in feedlot cattle is a multifactorial disease caused by a wide group of pathogens, both viral and bacterial, that take advantage of immunocompromised cattle.[6] Respiratory pathogens and a compromised innate respiratory defense mechanism due to environmental and management stressors contribute to the development of BRD, which in most cases is diagnosed within the first 3 weeks after arrival.[7] Data from the National Animal Health Monitoring System (NAHMS) from 1994, 1999, and 2011 reported that BRD deaths increased during each survey, 1.03% to 1.42% to 1.60%, respectively.[8]

Identifying and mitigating BRD in cattle can be difficult due to the increased susceptibility to BRD in high-risk cattle. One management option to minimize respiratory disease is treat at-risk calves utilizing antimicrobial metaphylaxis. A feedlot survey conducted in 2011, which included approximately 82.1% of all fed cattle in US feedlots, estimated that 21.3% of all cattle entering the feedlot received metaphylaxis treatment, while only 10.4% received metaphylaxis in 2001. More specifically, 92.6% of feedlots with a capacity of 8,000

or more head used metaphylaxis in cattle weighing less than 700 lb (318 kg) to control BRD, compared to 45.0% of feedlots surveyed with a capacity from 1,000 to 7,999 head.[14]

Criteria used to determine the use of antimicrobial metaphylaxis to control BRD in feedlots can be based on several factors, depending on feedlot preference; however, the 2 primary criteria listed as very important considerations in a 2011 feedlot survey were a known history of no previous vaccinations against respiratory pathogens (74.3%) and overall appearance of cattle (74.1%). Other reasons listed were source of cattle (auction market; 66.7%), BRD in calves received from same source previously (64.2%), long shipping distance (56.4%), season of the year (33.3%), and arrival weight (27.1%).[14] The primary antimicrobials used for metaphylaxis reported by feedlots surveyed were tilmicosin (57.6 ± 5.5%), followed by tulathromycin (45.3 ± 5.5%), ceftiofur (39.7 ± 4.3%), oxytetracycline (17.4 ± 4.5%), florfenicol (9.2 ± 3.3%), and gamithromycin (4.3 ± 2.5%).[14]

The objective of this study was to compare the efficacy of treating newly received, high-risk feedlot calves at arrival processing with gamithromycin, tulathromycin, or tilmicosin as metaphylactic treatments on health and performance characteristics.

Materials and Methods

Cattle

All cattle were treated and handled in accordance with protocols approved by the New Mexico State University Institutional Animal Care and Use Committee (#2011-034); Beef Quality Assurance guidelines were followed.

A total of 579 cross-bred heifer fall placed calves (initial bodyweight 404 ± 27.4 lb; 183.3 ± 12.4 kg) were used in a randomized, complete block design to evaluate the effects of 3 different metaphylactic treatments for BRD in high-risk calves upon arrival at the feedlot. Cattle originated from southeast Texas and were shipped approximately 700 miles (1125 km) to the Clayton Livestock Research Center in Clayton, NM. Cattle were delivered in 5 individual loads (114 to 120 head/load) over a 17-day period. The heifers were classified as high-risk because they were light-weight, auction origin, commingled, and were hauled > 8 hr. Upon arrival, heifers were weighed individually before being placed in an arrival pen. Cattle were offered free-choice long-stemmed hay, a minimal amount (< 1.0 lb (0.45 kg)/head as fed) of starter ration, and ad libitum access to water for the first 24 to 48 h.

After 24 to 48-h rest, heifers were individually weighed, vaccinated against type I and type II bovine virus diarrhea,[a] infectious bovine rhinotracheitis virus,[a,b] parainfluenza-3,[a,b] and bovine respiratory syncytial virus,[a,b] dewormed with doramectin[c] injectable and oral albendazole,[d] and implanted with 100 mg progesterone and 10 mg estradiol benzoate.[e] Horns were tipped to approximately 1 inch (2.54 cm) diameter. Each animal received an individual identification ear tag and a tag identifying treatment assignment. Heifers were housed by treatment in soil-surfaced pens (40 ft x 115 ft; 12 x 35 m) with 36 ft (11 m) of bunk line, providing approximately 22 inches (50 cm) of bunk space/hd. Water was supplied to each pen with a bunk-line, continuous-flow water tank.

Within each truckload of calves, heifers in groups of 3 were randomly assigned to receive 1 of the 3 metaphylactic treatments during processing, with groups of 3 heifers receiving the same treatment, and sorted by into pens by treatment. Persons administering metaphylactic treatments were blinded to treatment. The study antimicrobials were injected subcutaneously in the neck per label dosage and site of administration recommendations. Experimental treatments were: 1) tulathromycin (TUL; 1.13 mg/lb (2.5 mg/kg); 192 calves);[f] 2) tilmicosin phosphate (TIL; 6 mg/lb (13.2 mg/kg); 193 calves);[g] or 3) gamithromycin (GAM; 2.72 mg/lb (6 mg/kg); 194 calves).[h] Cattle were randomized into 5 blocks with 3 treatment groups within each block, and 10 replicates/treatment. Thirty pens were filled with approximately 19 to 20 heifers; a total of 579 cattle were used in this study. Individual weights were recorded on d 0, and pen weights were recorded at the end of the trial on d 56 to 60. Pen served as the experimental unit.

Heifers were initially fed a receiving diet composed of 20% dry-rolled corn, 57% wet corn gluten feed,[i] 18% ground corn stalks, and 5% of a supplement containing decoquinate.[j] Dietary energy concentrations were increased through day 28 using a 2-ration (starter diet and grower diet) transition system. The grower diet was composed of 30% ground corn, 52% wet corn gluten feed, 13% ground corn stalks, and a supplement (5%) containing lasalocid.[k] Feed was delivered to the bunks twice daily utilizing an auger-mixer wagon. Throughout the feeding period, cattle were offered feed ad libitum with an attempt to minimize the amount of feed left over before the next feeding period. Feed bunks were evaluated twice each day (morning and early afternoon) to determine the quantity of feed to offer each pen for the subsequent feeding. Weekly feed samples were obtained from randomly selected bunks to determine dietary dry matter content. In addition, at each scheduled weigh period (d 28 and 56), residual feed was collected, weighed, and sampled for dry matter content to determine DMI.

Animal health

Heifers were checked at the same time each day by trained animal health personnel that were blinded to treatments. Calves were evaluated according to the following protocol: depression (0 = normal, 1 = mildly depressed, 2 = moderately depressed, 3 = severely depressed); anorexia (rumen fill; 0 = normal (at pen average or above), 1 = slightly below pen average, 2 = moderately below pen average, 3 = severely below pen average); and respiratory (0 = normal, 1 = compromised – increased rate or depth of respiration, 2 = labored – as 1, but open mouth breathing or neck extension, 3 = severe – as 2, but severe grunting or thumping). Any animal removed from the pen with a combined morbidity score ≥ 3

and a rectal temperature ≥ 104 °F (40 °C) was treated with ceftiofur crystalline free acid,[l] according to label directions, with a 5-day post-treatment interval so that no retreatment was allowed until 5 days following the original treatment. Any animal removed from the pen for treatment with a combined morbidity score ≥ 3 and a rectal temperature < 104 °F (40 °C) was treated with enrofloxacin,[m] according to label directions, and a 3-day post-treatment moratorium. Calves removed from the pen for treatment with a combined score < 3 was not treated and was returned to its home pen. Calves removed from the pen for treatment a second time were treated with ceftiofur crystalline free acid or enrofloxacin, depending on the first treatment. Sick animals were returned to their home pen following treatment. Calves were removed from the study if severe clinical illness occurred prior to expiration of the designated post-treatment moratorium.

Statistical analysis

Average daily gain, average daily pen feed intake, morbidity, and mortality measurements were evaluated on a pen means basis as a randomized complete block design and analyzed using the PROC MIXED procedure of SAS.[n] Treatment (TRT) was included in the model as a fixed effect and pen (PEN) was included in the model as a random effect. Average daily gain and feed efficiency were calculated on both deads-in and deads-out basis across treatment groups, and pen was the experimental unit. Means were generated with the LSMEANS statement and separated using the PDIFF function when the F-statistic was significant ($P < 0.05$). Morbidity, mortality, and retreatments were analyzed using a Wilcoxon Rank-Sum Test.

Results and Discussion

Seven calves were removed from the study: 2 were removed due to lameness, 3 because of animal welfare concerns based on severe clinical signs of disease prior to expiration of the assigned post-metaphylaxis moratorium, and 2 head were removed due to neurological signs.

Heifer performance is shown in Table 1. There were no differences ($P > 0.05$) in dry matter intake or feed efficiency between treatment groups. Heifers administered TUL had greater ($P < 0.05$) ADG compared to GAM treated heifers. There was no difference in ADG between GAM and TIL treated heifers ($P > 0.05$), nor any difference in ADG between TUL and TIL treated heifers.

Calves that received TUL had a lower ($P < 0.05$) morbidity rate (5.2%) than those treated metaphylactically with TIL (14.6%) or GAM (12.79%) (Table 2). Morbidity rates of calves treated with TIL or GAM did not differ ($P > 0.05$). Mortality was low ($P > 0.05$) across all treatment groups, 1.02, 1.55, and 0.53% for TUL, TIL, and GAM groups, respectively. Risk ratios comparing treatments for morbidity and mortality are reported in Table 2. Calves administered TUL at processing were 0.36 times less likely to experience BRD and 0.67 times less likely to die compared to TIL-treated calves. Similarly, TUL-treated calves were 0.40 times less likely to suffer BRD and 0.67 times less likely to die compared to GAM-treated calves. Calves treated with TIL were 1.13 times more likely to become ill, but had the same risk ratio for mortality as GAM-treated calves. There were no retreatments in the TUL group; however, calves in the TIL group that were retreated for the second time were 1.68 times more likely to get sick compared to calves that were retreated with GAM.

Results from this study indicate that metaphylactic treatment of high-risk heifer calves with TUL upon arrival at the feedyard provided the greatest opportunity to minimize the pathogenic effects of BRD. Results from this study also suggest a similar response in calves treated with TIL as in calves treated with GAM. Average daily gain for calves in all treatment groups was lower than expected, possibly due to adverse weather conditions (i.e., extreme cold, snow, and high winds) on 2 occasions during the trial. Since a negative control was not included in the study, it was not possible to determine the economic benefit of metaphylaxis; however, Tennant et al[11] reported that economic losses associated with BRD were primarily due to loss of ADG, death loss, and railers (culls). In that report, animals metaphylactically treated with tilmicosin or tulathromycin had greater ADG ($P = 0.03$; +4.8%) compared to animals not treated, but no difference in ADG between tilmiocosin or tulathromycin was reported.[11]

Table 1. Least squares means* illustrating the effects of metaphylactic treatments on animal performance of newly received, high-risk feedlot calves.

	Treatment			
Item	**TUL‡**	**TIL§**	**GAM¶**	**SEM‖**
Initial weight, lb	403.5	402.7	405.1	3.295
Final weight, lb	553.0	544.3	540.1	8.283
DMI, lb	12.52	12.28	11.99	0.198
ADG, lb				
Deads-in†	$2.54^{a,x}$	$2.36^{a,b,y}$	$2.25^{b,x,y}$	0.105
Deads-out†	2.62^{a}	$2.48^{a,b}$	2.36^{b}	0.089
Feed:gain				
Deads-in	4.96	5.29	5.43	0.257
Deads-out	4.82	5.01	5.10	0.165

*Least squares treatment means

†Means within a row without a common superscript of a,b,c are different ($P < 0.05$) or a common superscript of x,y,z demonstrates a tendency ($P < 0.10$)

‡TUL = tulathromycin (Draxxin®, Zoetis, New York, NY) administered at 1.13 mg/lb (2.5 mg/kg)

§TIL = tilmicosin (Micotil®, Elanco Animal Health, Greenfield, IN) administered at 6 mg/lb (13.3 mg/kg)

¶GAM = gamithromycin (Zactran®, Merial Ltd, Duluth, GA) administered at 2.72 mg/lb (6.0 mg/kg)

‖Standard error of the least squares mean

Similarly, Corbin et al[5] evaluated the effect of metaphylactic treatment of high-risk calves on health performance. Calves treated with tilmicosin had lower morbidity and mortality rates and improved ADG, suggesting that metaphylactic treatment of respiratory disease in high-risk calves had a significant economic return compared to non-treated controls.[5]

Sgoifo Rossi et al[10] reported that cattle treated metaphylactically with gamithromycin had a lower morbidity rate (9.3%) than calves treated with tulathromycin (14.6%).[8] Contrarily, in the present study, tulathromycin-treated cattle had lower morbidity (5.16%) compared to cattle treated with gamithromycin (12.79%; $P = 0.02$). Van Donkersgoed and Merrill compared tilmicosin and gamithromycin for metaphylactic treatment of BRD in feeder steers, and reported a decrease ($P = 0.01$) in the first-pull treatment rate for BRD in gamithromycin-treated calves compared to those calves treated with tilmicosin.[15] Torres et al compared both metaphylactic and non-metaphylactic treatment with either tulathromycin or gamithromycin, and reported no differences in cattle performance or health characteristics when administered 150 days prior to closeout.[12]

Booker et al[2] evaluated the efficacy of metaphylactic tulathromycin in feedlot calves, and reported reduced morbidity and mortality in tulathromycin-treated calves and improved ADG compared to those treated with tilmicosin.[2] In the present study, there was a significant reduction in morbidity in calves treated with tulathromycin compared to those treated metaphylactically with tilmicosin or gamithromycin, but no difference in mortality. Average daily gain among calves treated with tulathromycin was higher than in those treated with gamithromycin, but similar to the ADG among calves treated with tilmicosin.

Conclusion

High-risk calves treated upon arrival with TUL had greater ADG than calves treated with GAM. In addition, calves that received metaphylactic treatment with TUL had lower morbidity rates than those treated with TIL and GAM. There were no differences in DMI or mortality between treatment groups.

Endnotes

[a]Bovishield® Gold 5, Zoetis, New York, NY
[b]Inforce 3, Zoetis, New York, NY
[c]Dectomax®, Zoetis, New York, NY
[d]Valbazen®, Zoetis, New York, NY
[e]Synovex C, Zoetis, New York, NY
[f]Draxxin®, Zoetis, New York, NY
[g]Micotil®, Elanco Animal Health, Greenfield, IN
[h]Zactran®, Merial LTD, Duluth, GA
[i]Sweet Bran, Cargill Inc., Blair, NE
[j]Deccox®, Zoetis, New York, NY
[k]Bovatec®, Zoetis Animal Health, New York, NY
[l]Excede®, Zoetis, New York, NY
[m]Baytril® 100, Bayer Animal Health, Shawnee Mission, KS
[n]SAS, ver. 9.1.3, SAS Institute, Cary, NC

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Table 2. Comparative effects of metaphylactic treatments on mortality, morbidity, and retreatments in newly received, high-risk feedlot calves.

	Treatment					
Item	**TUL***	**TIL†**	**GAM‡**	**RR**	**95% CI**	***P*-value**
Number of cattle	192	193	194			
Mortality	2 (1.0%)		3 (1.5%)	0.67	-3.34-2.34	0.72
	2 (1.0%)	3 (1.6%)		0.67	-3.36-2.31	0.71
		3 (1.6%)	3 (1.5%)	1.01	-2.81-2.86	0.99
Morbidity						
1st treatment	10 (5.2%)		25 (12.8%)	0.40	9.30-19.95	0.05
	10 (5.2%)	28 (14.6%)		0.36	-0.17-10.48	0.02
		28 (14.6%)	25 (12.8%)	1.13	7.47-18.11	0.62
2nd treatment	0 (0.0%)		3 (1.5%)	-	-3.79-0.79	0.19
	0 (0.0%)	5 (2.6%)		-	-4.85-0.27	0.03
		5 (2.6%)	3 (1.5%)	1.68	-1.23-3.35	0.35

*TUL = tulathromycin (Draxxin®, Zoetis, New York, NY) administered at 1.13 mg/lb (2.5 mg/kg)
†TIL = tilmicosin (Micotil®, Elanco Animal Health, Greenfield, IN) administered at 6 mg/lb (13.3 mg/kg)
‡GAM = gamithromycin (Zactran®, Merial Ltd, Duluth, GA) administered at 2.72 mg/lb (6.0 mg/kg)

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