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 (95% CI = 2.27 to 2.46) greater 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, BRO, cattle, feedlot, high-risk, metaphylactic treatment

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

Para les genisses 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.

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
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 consider­
ations 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%), BRO
protocols approved by the New Mexico State University Insti­
tutional Animal Care and Use Committee (#2011-034); Beef
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Cattle
Materials and Methods
Cattle
All cattle were treated and handled in accordance with
protocols approved by the New Mexico State University Insti­
tutional 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,ab parainfluenza-3,ab
and bovine respiratory syncytial virus,ab doramectin injectable and oral albendazole,4 and implanted
with 100 mg progesterone and 10 mg estradiol benzoate.5
Horns were tipped to approximately 1 inch (2.54 cm) di­
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/head. 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 metaphylac­
tic 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 in­
jected 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); 2) tilmicosin phosphate (TIL; 6 mg/lb (13.2 mg/kg);
193 calves); or 3) gamithromycin (GAM; 2.72 mg/lb (6 mg/
kg); 194 calves).6 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. Indi­
vidual 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,18 ground
corn stalks, and 5% of a supplement containing decoquinate.1
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.6 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 sub­
sequent 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

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and a rectal temperature ≥ 104 °F (40 °C) was treated with ceftiofur crystalline free acid, 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, 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. 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 a pen means basis as a randomized complete block design and analyzed using the PROC MIXED procedure of SAS. Treatment (TRT) was included in the model as a fixed effect 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). Morbidity 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. reported that economic losses associated with BRD were primarily due to loss of ADG, death loss, and raleers (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 tilmicosin or tulathromycin was reported.

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

| 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†           | 2.54a | 2.36ab| 2.25b | 0.105|    |
| Deads-out†          | 2.62a | 2.48b | 2.36b | 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. evaluated the effect of metaprophylactic treatment of high-risk calves on health performance. Calves treated with tilmicosin had lower morbidity and mortality rates and improved ADG, suggesting that metaprophylactic treatment of respiratory disease in high-risk calves had a significant economic return compared to non-treated controls.

Sgoifo Rossi et al. reported that cattle treated metaprophylactically with gamithromycin had a lower morbidity rate (9.3%) than calves treated with tulathromycin (14.6%). 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 metaprophylactic 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. Torres et al. compared both metaprophylactic and non-metaprophylactic treatment with either tulathromycin or gamithromycin, and reported no differences in cattle performance or health characteristics when administered 150 days prior to closeout.

Booker et al. evaluated the efficacy of metaprophylactic tulathromycin in feedlot calves, and reported reduced morbidity and mortality in tulathromycin-treated calves and improved ADG compared to those treated with tilmicosin. In the present study, there was a significant reduction in morbidity in calves treated with tulathromycin compared to those treated metaprophylactically 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 metaprophylactic 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**

* Bovishield® Gold 5, Zoetis, New York, NY
* Inforce 3, Zoetis, New York, NY
* Dectomax®, Zoetis, New York, NY
* Valbavet®, Zoetis, New York, NY
* Synovex C, Zoetis, New York, NY
* Draxxin®, Zoetis, New York, NY
* Micotil®, Elanco Animal Health, Greenfield, IN
* Zactran®, Merial LTD, Duluth, GA
* Sweet Bran, Cargill Inc., Blair, NE
* Deccox®, Zoetis, New York, NY
* Bovatec®, Zoetis Animal Health, New York, NY
* Excede®, Zoetis, New York, NY
* Baytril® 100, Bayer Animal Health, Shawnee Mission, KS
* SAS, ver. 9.1.3, SAS Institute, Cary, NC

**References**


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

<table>
<thead>
<tr>
<th>Item</th>
<th>Treatment</th>
<th>RR</th>
<th>95% CI</th>
<th>P-value</th>
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<td>Number of cattle</td>
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<tr>
<td>192</td>
<td>193</td>
<td>194</td>
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</tr>
<tr>
<td>Mortality</td>
<td></td>
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<tr>
<td>2 (1.0%)</td>
<td>3 (1.5%)</td>
<td>0.67</td>
<td>-3.34-2.34</td>
<td>0.72</td>
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<tr>
<td>2 (1.0%)</td>
<td>3 (1.6%)</td>
<td>0.67</td>
<td>-3.36-2.31</td>
<td>0.71</td>
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<tr>
<td>3 (1.6%)</td>
<td>3 (1.5%)</td>
<td>1.01</td>
<td>-2.81-2.86</td>
<td>0.99</td>
</tr>
<tr>
<td>Morbidity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st treatment</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>10 (5.2%)</td>
<td>25 (12.8%)</td>
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<td>9.30-19.95</td>
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</tr>
<tr>
<td>10 (5.2%)</td>
<td>28 (14.6%)</td>
<td>0.36</td>
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<td>5 (2.6%)</td>
<td>-</td>
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<tr>
<td>5 (2.6%)</td>
<td>3 (1.5%)</td>
<td>1.68</td>
<td>-1.23-3.35</td>
<td>0.35</td>
</tr>
</tbody>
</table>

*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)


