COMPARISON OF GAMITHROMYCIN, TILMICOSIN AND TULATHROMYCIN: METAPHYLACTIC TREATMENTS IN HIGH RISK CALVES FOR BOVINE RESPIRATORY DISEASE

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B.S., Kansas State University, 2008

A THESIS

submitted in partial fulfillment of the requirements for the degree

MASTER OF SCIENCE

Department of Clinical Sciences
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KANSAS STATE UNIVERSITY
Manhattan, Kansas

2013

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Abstract

Bovine Respiratory Disease (BRD) continues to be one of the largest animal health concerns in the cattle industry. BRD is a multifaceted group of pathogens, both viral and bacterial, that take advantage of an immune compromised calf to cause disease. This study took aim at comparing metaphylactic treatments for BRD in both the feedlot and pasture setting.

In the feedlot study, heifers (n=579, 403.7 ± 27.4 lbs) from Southwest Texas were identified as being high risk for BRD and shipped to the Clayton Livestock Research Center in Clayton, NM. Cattle were randomly allocated within truck load lots into 18 to 20 head treatment pens (30 pens; 3 treatments; 10 reps). Cattle were given one of three metaphylactic treatments based on the randomly assigned treatment for their pen within a replicate. The three antibiotic treatments administered at initial processing were: 1) Tulathromycin (2.5 mg/kg), 2) Tilmicosin (13.3 mg/kg), and 3) Gamithromycin (6.0 mg/kg). Cattle were fed a typical commercial starter diet for the first 56-60 d with a step-up ration change at day 28. At the end of the feeding period, pens were weighed and body weights recorded. Dry Matter Intake, morbidity, and mortality were recorded by CLRC personnel daily. Cattle administered tulathromycin had higher daily gains than cattle administered gamithromycin by 0.29 lbs/d ($P<.01$) and tended ($P=0.09$) have higher daily gains than cattle that received tilmicosin by 0.18 lbs/d. Tulathromycin treated cattle tended ($P = 0.12$) to have improved feed efficiency compared to gamithromycin treated cattle. Cattle that received tulathromycin (5.2%) had lower morbidity rates ($P < .02$) than tilmicosin (14.6%) and gamithromycin (12.79%) treated cattle. There were no treatment differences in dry matter intake or mortality in cattle.

For the wheat pasture study, heifers (n=120, 393.2 ± 28.6 lbs) from the same origin and risk were shipped to the CLRC and processed before being trailed to a nearby wheat pasture. Cattle were randomly assigned into three treatment groups (3 treatments, 40 reps), and were given one of three metaphylactic treatments. The three antibiotic treatments administered at initial processing were: 1) Tulathromycin (2.5 mg/kg), 2) Tilmicosin (13.3 mg/kg), and 3) Gamithromycin (6.0 mg/kg). Cattle were allowed to graze on wheat for 54 days with free-choice Hi-Pro mineral mixed with Lasalocid, an ionophore. After 54 days on wheat pasture, the cattle were trailed back to the CLRC facilities and final individual weights were recorded. Morbidity and mortality were recorded daily by CLRC personnel. No differences were identified for ADG (P=0.98), morbidity (P=0.46) or mortality (P=0.36) among the three treatment groups.

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Acknowledgements

I would first like to thank Dr. Dan Thomson, my masters advisor, for all his guidance, input, and ultimately, investment in my future. He has continued to provide opportunities for me to learn and further my career. I feel honored to have someone so distinguished in the veterinary industry to rely on for advice, both now and after I graduate.

Dr. Chris Reinhardt and Dr. Mike Hubbert have both been instrumental in helping setup and complete my M.S. research. They deserve much gratitude for their time spent teaching and guiding me towards successful writing and research methods.

Special thanks goes to DJ Rezac and Dr. Siddartha Torres-Rico for their support and insight as I pestered them with questions continuously. Their patience with an inexperienced graduate student was much appreciated.

To all the employees at the Clayton Livestock Research Center, Brett Acuna, Jim and Jonnie Sue McDonald, Lisa Blan, and Casey Murdock, I'd like to say thank you for hard-work and diligence in completing a successful research project.

Finally, thank you to all the companies that provided their products for use in this project: Cargill Sweet Bran, Pfizer Animal Health, Merial, Elanco, and Bayer.

Chapter 1 - Literature Review: Bovine Respiratory Disease

Bovine Respiratory Disease

In an extensive review article written by Griffin et al in 2010, they outlined the bacterial pathogens associated with bovine respiratory disease complex (BRDC), as well as the pathology and clinical signs associated with the disease.[1] This article lists *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni,* and *Mycoplasma bovis* as the important bacterial pathogens of BRDC. It also states that many factors, including stress, viral, and/or parasitic infections can suppress the calves' immune response and allow these bacterial pathogens to replicate. *Mannheimia haemolytica* is believed to be the main bacterial pathogen most often associated with BRDC. Clinical signs of BRDC have proven to be difficult to diagnose until many days after disease onset due to the prey response of cattle in which they mask illness to avoid detection by predators. This behavior allows cattle to mask early symptoms from feedlot personnel. Clinical signs may include nasal and ocular discharge, depression, anorexia, fever, tachypnea, and coughing.[1] More severe cases will show respiratory distress, encrusted muzzles, excessive tear production, and dyspnea. The main cause of death associated with BRDC is acute pleuropneumonia. The main pathological lesions described in this article include lungs with bilateral consolidation with firm and heavy texture. Fibrinous adhesions to the parietal and visceral pleura are observed with acute fibrinous and serofibrinous pleuritis. In chronic cases, coagulation necrosis surrounded by progressively worse pale fibrous tissue are seen. The article concludes that these four bacterial pathogens are the most significant cause of morbidity and mortality of BRDC, and a better understanding of these pathogens' virulence factors and pathogenesis, may lead to better management, therapeutics, and vaccines.[1]

A trial by Schneider et al in 2009, used treatment records and lung lesion scores to assess the impact of BRDC on performance and carcass traits. Treatment records from 5,976 animals and lung lesions from a subset number of 1,665 were used for analysis. The observed incidence rate of BRDC at the feedyard was 8.17%. Of cattle never treated for BRD 60.6% had lung lesions present after harvest; also, 74% of cattle treated at least once for BRD had lung lesions, indicating that 26% of cattle treated for BRD did not have lung lesions. Performance decreased in cattle that were treated for BRDC compared to those never treated.[2]

Economic Implications

Revisiting the study conducted by Schneider et al in 2009, economic implications of BRD were also evaluated. The results of the specific cattle, based on carcass premiums and actual price received, showed that cattle treated once, twice, or three or more times returned $23.23, $30.15, and $54.01, respectively, less than untreated cattle. Cattle not suffering from BRD were more valuable in this study ($P < 0.01$). These costs do not include the added losses due to medicine cost, labor, veterinary fees, and death loss.[2]

Brooks et al evaluated the economic effects of BRD on feedlot calves in 2011. During the backgrounding phase (initial 63 days in feedyard), heifers treated zero, once, twice, or three times had $111.12, $92.51, $59.98, and $20.62, respectively, greater net returns ($P < 0.01$) than those considered chronic (treated four or more times).[3] This finding was in agreement with a study by Fulton et al. in 2002 showing calves never treated for BRD yielded greater returns than those treated one or more times.[4]

Mean profit per head, in a study comparing metaphylactic treatments of two dosages of tilmicosin with an untreated control, revealed greater returns (P = 0.02) on both tilmicosin treatment groups (20 mg/kg dose = $84.61, 10 mg/kg dose = $45.19) than the untreated controls (-$41.41).[5] Their second study, compared identical treatment groups as in the first study but in a difference location, numerically greater returns (P > 0.05) were shown in cattle treated with metaphylactic tilmicosin (20 mg/kg dose = $376.33, 10 mg/kg dose = $365.73) than untreated controls ($331.15).[5]

Macrolide Class of Antibiotics

At the time of this study, the single dose macrolide antibiotics approved for control of BRD in feedlot cattle are: tilmicosin, tulathromycin, and gamithromycin. Macrolides belong to a class of antibiotics that contain a lactone ring in their molecular structure. Gamithromycin and tulathromycin contain 15-member rings, and tilmicosin contains a 16-member ring. Their pharmacokinetic and pharmacodynamic properties of having a high volume of distribution and being dependent on time spent above the minimum inhibitory concentration (MIC) are favorable for their metaphylactic use. A high volume of distribution allows for a smaller dose to be administered to reach a high concentration in the target tissue. Macrolides are bacteriostatic and work by invading the bacterial cell membrane and binding to the 50s ribosome subunit, preventing protein synthesis. Translocation between the 50s and 30s ribosome is interrupted, creating early detachment of incomplete peptide chains. Without these proteins essential for cell survival, the bacterium dies.[6]

Lombardi et al in 2011 studied the pharmacokinetic properties of tilmicosin. In this experiment, they used light weight and heavy weight cattle, and two dosages (10 mg/kg and 20 mg/kg). In light weight cattle receiving 10 mg/kg tilmicosin, blood concentrations reached a maximum of 0.714 μg/ml at 0.571 h post-injection. In light weight cattle receiving 20 mg/kg tilmicosin, blood concentrations reached a maximum of 1.059 μg/ml at 1.571 h post-injection. The half-life of tilmicosin in this experiment was between 30.83 and 31.15 hours across all treatment groups.[7]

In 2004, Nowakowski et al studied the pharmacokinetic properties of tulathromycin. Two studies were completed using multiple groups of cattle. Serum and lung tissue analysis was performed to determine the desired parameters. Results of both studies indicated that peak concentrations of tulathromycin were higher in the lungs (4,100 ng/g) than in plasma (approximately 500 ng/ml), and achieved these concentrations within 24 h of administration. Although the results varied among treatment groups, in the first study, the elimination half-life ranged between 58 and 99 h.[8]

Giguere et al in 2011 studied the pharmacokinetic properties of gamithromycin. They studied concentrations of gamithromycin in plasma, pulmonary epithelial lining fluid (PELF), bronchoalveolar lavage cells (BAL), and lung tissue. Results showed that the half-life of gamithromycin in the plasma of cattle was 62 h. It took gamithromycin one hour to reach a peak concentration of 0.433 μg/ml in the plasma. In the PELF, the half-life was 50.6 h, and it took 24 h to reach a peak concentration of 4.61 μg/ml. BAL cells showed a longer half-life at 125 h, and it took 24 h to reach a peak concentration of 17.8 μg/ml. Finally, after measuring gamithromycin properties in the lungs, results indicated a half-life of 93 h, and it took 12 h to reach a peak

concentration of 27.8 μg/g. These results are similar to other macrolides, as lung concentrations are much higher than plasma concentrations.[9]

These three articles measuring the pharmacokinetic properties of three of the most commonly used macrolides shows similar half-lives between tulathromycin and gamithromycin, with the half-life of tilmicosin being one half to one third shorter in duration.

Metaphylaxis

In a trial conducted in Italy in 2010 by Sgoifo Rossi et al, they compared metaphylactic treatments of gamithromycin with untreated controls, oxytetracycline, and tulathromycin. Gamithromycin treated cattle had a lower ($P < 0.0001$) morbidity rate (4.8%) than the untreated controls (34.4%). Similarly, gamithromycin treated cattle had a lower ($P < 0.0001$) morbidity rate (1.7%) than oxytetracycline treated cattle (14.5%). In their third metaphylactic trial, the morbidity rate of cattle receiving gamithromycin (9.3%) was lower ($P = 0.006$) than cattle receiving tulathromycin (14.6%).[10]

Booker et al in 2007 evaluated the efficacy of tulathromycin as a metaphylactic antimicrobial in feedlot calves. Treatment groups consisted of calves at high risk for BRD receiving tulathromycin, tilmicosin, or oxytetracycline. In this experiment, calves were followed all the way to harvest. Slaughter weight, weight gain, carcass weight, days on feed, and daily dry matter intake were significantly ($P < 0.05$) higher in calves pre-treated with tulathromycin compared to tilmicosin and oxytetracycline treated calves. No difference ($P > 0.05$) was found between treatment groups for dressing percentage. Both morbidity and mortality rates were

significantly lower ($P < 0.05$) for calves treated with tulathromycin than those treated with tilmicosin and oxytetracycline.[11]

In an attempt to evaluate the efficacy of metaphylaxis versus fever-based treatments and negative controls, Galyean et al in 1995 completed three trials with high risk calves using tilmicosin. The first two trials consisted of only two treatment groups: metaphylactic treatments with tilmicosin and no treatment. In both trials 1 and 2, no differences were found for average daily gain ($P > 0.05$) and dry matter intake ($P > 0.05$); however, mass treatment did decrease ($P < 0.01$) the prevalence of calves treated for BRD from 46.4% in controls to 0% in calves metaphylactically treated on arrival.[12] In the third trial, a third treatment group was implemented where only calves with rectal temperatures above 39.7 °C (103.5 °F) were treated with tilmicosin on arrival. Results of this trial showed increased average daily gains ($P < 0.01$) during the initial 28 day feeding period. Dry matter intake was greater ($P < 0.05$) and feed conversion was lower ($P < 0.03$) for both the metaphylaxis treatment group and calves treated based on rectal temperature when compared with the negative control group. Morbidity rates were significantly decreased ($P < 0.01$) from calves not treated (43.6%) to calves mass treated (11.9%) and calves treated based on rectal temperatures (12.9%). No differences were found between groups of mass treated calves and groups of calves on treated based on rectal temperature.[12]

Three years after the Galyean et al trial, Vogel et al in 1998 completed a similar study with high risk calves also using tilmicosin. This trial consisted of three treatment groups: 1) nonmedicated control group, 2) fever-based medicated group where calves were treated with tilmicosin if their rectal temperatures exceeded 104 °F, and 3) metaphylaxis group where all calves received tilmicosin. Results indicated that both fever-based and metaphylactic treatments with tilmicosin decreased the morbidity and mortality; as well as, increased gains, of high risk

calves when compared to the negative control treatment group. Finally, results also indicated that fever-based treatments with tilmicosin were less effective at decreasing BRD incidence than metaphylaxis.[13]

Study Objectives

Due to BRD being the most prevalent and economically costly disease in the cattle industry, it becomes important to assess the methods used to lessen its effects. With a wide variety of antibiotics available, and the growing popularity of metaphylaxis, many studies are being performed, to compare effectiveness. These two studies are aimed at comparing three popular macrolides in a specific class of calves in a specific environment when used as metaphylactic treatments for BRD. The first study aims at comparing the three macrolides on performance, feed conversion, morbidity and mortality in high risk heifers entering a feedyard. The second study compares performance, morbidity and mortality in high risk heifers being on wheat pasture.

Chapter 2 - Comparison of Gamithromycin, Tilmicosin and Tulathromycin: Metaphylactic Treatments in High Risk Calves for Bovine Respiratory Disease

Introduction

Bovine Respiratory Disease (BRD) continues to be one of the largest animal health concerns in the cattle industry.[1,2,3] Bovine Respiratory Disease is caused by a group of pathogens, both viral and bacterial, that take advantage of an immune-compromised calf to cause disease.[1] The viral pathogens include Infectious Bovine Rhinotracheitis (IBR), Bovine Respiratory Syncytial Virus (BRSV), Parainfluenza-3 (PI3), and Bovine Viral Diarrhea (BVD – Type I and II) (Griffin et al, 2010). Bacterial pathogens consist of *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus* somni, and *Mycoplasma bovis*.[1] Identifying BRD in cattle can be very difficult. Of cattle never treated for BRD, 60.6% had lung lesions present after harvest; also, 74% of cattle treated at least once for BRD had lung lesions, indicating that 26% of cattle treated for BRD did not have lung lesions.[2]

The cost of BRD to the beef industry due to death, poorer conversions, and therapy cost each year is estimated to be between $800 and $900 million.[14] As the number of treatments increased during the backgrounding phase, the net returns decreased; also, animals treated for BRD three or more times have lower average daily gain (ADG) than animals treated less than three times. Calves treated metaphylactically with tilmicosin had greater ($P < .01$) economic return than controls.[5]

Macrolides belong to a class of antibiotics that contain a lactone ring in their molecular structure. Gamithromycin and tulathromycin contain 15-member rings, and tilmicosin contains a 16-member ring. Their pharmacokinetic and pharmacodynamic properties of having a high volume of distribution and being dependent on time spent above the minimum inhibitory concentration (MIC) are favorable for their metaphylactic use. Macrolides are bacteriostatic and work by invading the bacterial cell membrane and binding to the 50s ribosome subunit, preventing protein synthesis.[6]

Two experiments were completed comparing gamithromycin, tilmicosin, and tulathromycin in both a feedyard and pasture setting. The objectives of these experiments were to compare the efficacy of the three macrolides, administered metaphylactically, on health and performance of heifers at high risk for developing BRD.

Materials and Methods

Feedyard Study

Animals

All animals were treated and handled in accordance with protocols approved by the New Mexico State University Institutional Animal Care and Use Committee (# 2011-034).

Over a 17 day period starting October 27, 2011, individual loads of heifers (n = 592, 403.3 $\pm$ 27.4 lbs) identified as being high risk (defined as comingled, long haul, and light weight calves with sale barn origin) for BRD arrived at the Clayton Livestock Research Center (CLRC) near Clayton, NM. The heifers consisted of a variety of hide colors and of mixed genetics. Each load (114-120 animals per load) was unloaded and heifers weighed individually before being placed in an arrival pen with free-choice access to long-stemmed hay, a minimal amount (< 1.0 lb/head as fed) of starter ration and ad libitum access to water. After 24-48 h rest, cattle were individually processed and placed in home pens. Within arrival group, cattle were randomly allocated into two replicates, and then randomized to one of three treatment groups (n = 18-20 animals per pen, depending on load size). Treatments were: tulathromycin[a], tilmicosin[b], and gamithromycin[c]. All arrival groups were fed for 56-60 days depending on when the weather allowed for final weights to be measured.

Treatments

Treatment groups consisted of the following: 1) tulathromycin (n = 192; 2.5mg/kg, 1.1 ml/100 lb), 2) tilmicosin (n = 193; 13.2 mg/kg, 2 ml/100 lb), 3) gamithromycin (n = 194; 6 mg/kg, 1.82 ml/100 lb). Within arrival group, cattle were randomly assigned to treatment group

as they were processed, in groups of three animals each, and placed in the appropriate sorting pen. Once sorted, each treatment group was moved to an assigned soil-surfaced pen (40 ft x 115 ft, with 36 ft bunk line; 19-20 animals/pen). Each heifer had about 22 inches of bunk space. Water was supplied to each pen with a bunk line continuous flow water tank. Pen served as the experimental unit. The study consisted of three treatments with ten replicates per treatment. During initial processing, each heifer was weighed, vaccinated for BVD (Type I and II)[d], IBR, BRSV, and PI_3[e], given a doramectin[f] injection and oral albendazole[g], and implanted with 100 mg progesterone and 10 mg estradiol benzoate[h]. Each animal received an individual identification ear tag, a tag identifying treatment assignment, and any horns, if present were tipped to approximately 2.54 cm diameter.

Feeding

Heifers were started on a receiving diet composed of 20% ground corn, 57% wet corn gluten feed[i], 18% ground corn stalks, and 5% of a supplement containing decoquinate[j] (Table 2.1). 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 5% of a supplement containing lasalocid[k] (Table 2.1). Feed was delivered to the bunks twice daily by way of an auger mixer wagon. Throughout the feeding period, cattle were offered as close to ad libitum feed as possible to minimize the amount of feed left over before the next feeding period. Cattle and feed bunks were evaluated visually 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 and for proximate analyses. In addition, at each

scheduled weigh period (d 28 and 56), residual feed was collected, weighed, and sampled for dry matter to determine dry matter intake.

Animal Health

Clinical monitoring was completed at the same time each day by trained animal health personnel. Animals were assessed daily through the end of the study based on severity of common clinical signs associated with BRD according to the following protocol. Any animal deemed as "sick" was scored as follows: 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 pulled with a combined score ≥ 3 and a rectal temperature ≥ 104°F was treated with ceftiofur crystalline free acid[l], according to label directions, and a 5 day moratorium so that no retreatment was allowed until 5 days following the original treatment. Any animal removed from the pen for treatment with a combined score ≥ 3 and a rectal temperature < 104°F was treated with enrofloxacin[m], according to label directions, and a 3 day post-treatment moratorium. Any animal removed from the pen for treatment with a combined score < 3 was not treated and was returned to its home pen. Any animal removed from the pen for treatment for a second time was treated with ceftiofur crystalline free acid as its second treatment; however, if the animal received ceftiofur crystalline free acid as its first treatment, then enrofloxacin was used as its second treatment. Sick animals were returned to their home pen following treatment.

Statistical Analysis

Individual weights at processing, pen weights at the end of the trial period, average daily pen intake, morbidity, and mortality measurements were recorded. Average daily gain was calculated as the average weight change of calves per pen divided by the length of the trial period. Feed efficiency was measured as the average dry matter intake per calf per pen divided by the average daily gain of calves per pen. Average daily gain and feed efficiency were calculated on both deads in and deads out basis across treatment groups. All data were blocked by truck load. SAS^{n} was used for statistical analysis. Initial weight, final weight, dry matter intake, average daily gain, and feed conversion were measured using mixed model analysis. Morbidity, mortality, and retreatments were analyzed using a Wilcoxon Rank-Sum Test. Differences between treatments were determined using a protected F-test with an alpha = 0.05; if the ANOVA Type III probability was ≤ 0.05, means were separated using a least squares means procedure.

Wheat Pasture Study

Animals

All animals were treated and handled in accordance with protocols approved by the New Mexico State University Institutional Animal Care and Use Committee (# 2011-034).

On October 24, 2011, a single load of heifers (n = 120, 393.2 $\pm$ 28.6 lbs) identified as being at high risk to develop BRD arrived at the Clayton Livestock Research Center (CLRC) in Clayton, NM. The heifers consisted of a variety of hide colors and of mixed genetics. The cattle were unloaded and placed in an arrival pen with free-choice access to long-stemmed hay and ad libitum access to water. After 24-48 h rest, cattle were individually processed and trailed to a 125 acre center-pivot-irrigated wheat pasture. At processing, each animal was allocated into three treatment groups (n = 40) consisting of metaphylactic treatment with either gamithromycin, tilmicosin, or tulathromycin.

Treatments

Treatments consisted of the following: 1) tulathromycin (n = 192; 2.5mg/kg, 1.1 ml/100 lb), 2) tilmicosin (n = 193; 13.2 mg/kg, 2 ml/100 lb), 3) gamithromycin (n = 194; 6 mg/kg, 1.82 ml/100 lb). Cattle were randomly assigned to treatment group and placed in temporary pens. During initial processing, each heifer was weighed, vaccinated for BVD (Type I and II), IBR, BRSV, and PI_3, given a doramectin injection and oral albendazole, and implanted with 100 mg progesterone and 10 mg estradiol benzoate. Each animal received an individual identification ear tag, a tag identifying treatment assignment, and any horns, if present were tipped to approximately 2.54 cm diameter. Once processing was completed, all treatment groups were trailed approximately one mile to the irrigated wheat pasture. The individual animal served as the experimental unit.

Feeding

Cattle were allowed to graze on irrigated wheat pasture for 54 days. Water was supplied to the pasture with six continuous flow, heated water tanks. During two instances of extreme weather (snow/cold), cattle were supplemented with bales of grass hay. Three (3) tubs of Hi-Pro® mineral (900 lbs) with lasalocid (7.2 pounds) allowed for a free-choice mineral and ionophore to promote nutrition, growth and control coccidia levels.

Animal Health

Clinical health monitoring was completed at the same time each day (approximately 0900 hrs) by trained animal health personnel. Animals were assessed daily through the end of the study based on scoring severity of common clinical signs associated with BRD as explained in the feedyard trial. Animals pulled to treat were trailed to the south end of the pasture to working corrals and chute to be assessed and treated. After treatments, animals were immediately returned to pasture.

Statistical Analysis

Data were entered into Microsoft Excel (2010) throughout the experiment. Individual weights at post-arrival processing and at the end of the trial period, morbidity, and mortality measurements were recorded. Initial weight, final weight, and average daily gain were measured using GLM procedure; morbidity and mortality were analyzed using FREQ procedure.

Results

Feedyard Study

Seven animals were removed from the feedyard study. Two were removed due to lameness; three were removed due to animal welfare concerns based on severe clinical morbidity prior to expiration of the assigned moratorium; two were severely anorectic; two were removed due to suspected polioencephalomalacia. The results indicate there were no differences ($P = 0.73$) in initial weight among treatment groups (Table 2.2). However, tulathromycin-treated calves tended ($P = 0.10$) to have greater end weight than gamithromycin treated calves (Table 2.2). There were no differences ($P = 0.20$) between treatment groups for the average dry matter intake of calves during the trial period (Table 2.2). On a deads in basis, cattle administered tulathromycin had greater ($P < 0.01$) ADG than cattle administered gamithromycin by 0.29 lbs/d and tended ($P = 0.09$) to have greater ADG than cattle that received tilmicosin by 0.18 lbs/d (Table 2.2). No differences were found between gamithromycin-treated calves and calves treated with tilmicosin. Tulathromycin treated cattle tended ($P = 0.12$) to have improved feed efficiency compared to gamithromycin treated cattle (Table 2.2), with tilmicosin-treated calves being intermediate to and not different from the other two treatments. Results for deads out analysis yielded similar results as deads in analysis (Table 2.2). Calves that received tulathromycin (5.2%) had reduced ($P < 0.02$) morbidity rates than those that received tilmicosin (14.6%) and gamithromycin (12.79%; Table 2.3). No differences were found in morbidity between tilmicosin treated calves and gamithromycin treated calves. Mortality rates were low

across all treatment groups, and there were no treatment differences (Table 2.3) for mortality or retreatment rate.

Wheat Pasture Study

One animal was removed from the study due to being removed from the pasture for three days for treatment of clinical coccidiosis.

Initial body weight did not differ by treatment (P = 0.72; Table 2.4). In contrast with the feedlot study, final weights remained similar among treatment groups (P = 0.90). Therefore, ADG did not differ (P = 0.98) among treatments. Morbidity and mortality did not differ among treatments (P = 0.46 and 0.35, respectively).

Discussion

Results from the feedyard study indicate that metaphylactically treating high risk calves with tulathromycin upon arrival provided the greatest opportunity to minimize the pathogenic effects of BRD. Results also indicated that there was no difference across all variables in calves treated with tilmicosin and calves treated with gamithromycin. No differences were noted for any variable among treatment groups in the wheat pasture study. Average daily gain for calves in all treatment groups were lower than anticipated. This may be due to adverse weather conditions (i.e. extreme cold, snow, and high winds) on two occasions with no shelter provided. Without a negative control in which to compare the antibiotics, it is not possible to tell if they were effective at mitigating BRD.

The present study found differing results versus those reported in Sgoifo Rossi et al. In that study, cattle treated with gamithromycin had a lower morbidity rate (9.3%) than tulathromycin treated cattle (14.6%).[10] However, in the present feedyard study, tulathromycin treated cattle had a lower morbidity rate (5.16%) compared to cattle treated with gamithromycin (12.79%; P = 0.02). On the other hand, the study discussed earlier by Booker et al. that compared treatments with tulathromycin and tilmicosin, found similar results as the present feedyard study.[11] Although those authors found differences between tulathromycin and tilmicosin for ADG, morbidity, and mortality, the present feedyard study only found a significant difference for morbidity, a trend for ADG, and no difference for mortality.

Results of Van Donkersgooed and Merrill (2012) showed a decrease (P = 0.01) in first-pull treatment rates for BRD in gamithromycin treated calves than in calves treated with tilmicosin.[15] In both metaphylactic and non-metaphylactic studies, treatment with either

tulathromycin or gamithromycin showed no differences across all variables when taken 150 days to closeout.[16]

In conclusion, the feedyard study found that high risk cattle treated upon arrival with tulathromycin had greater ADG than calves treated with gamithromycin with tilmicosin-treated calves being intermediate, and reduced morbidity than cattle treated with tilmicosin or gamithromycin; however, for calves being placed on wheat pasture, there were no differences for performance or health measures among the treatments used in this study.

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Table 2.1: Feedyard supplement composition. Values listed as percentage of total ration.

Supplement Ingredient	Deccox Supplement	Bovatec Supplement
Decoquinate 27.2 g/lb	0.031	0
Lasalocid 91 g/lb	0	0.015
Cargill Beefmax 510	0.045	0.045
Urea 45% Nitrogen	0.25	0.25
Limestone	1.5	1.5
Corn distillers grain	2.95	2.95
Sodium Chloride	0.2	0.2
Vitamin A/D 1000/200	0.00025	0.00025
Vitamin E-50	0.006	0.006
Total	**4.98225**	**4.96625**

Table 2.2: Feedyard average initial weights, average out weights, average dry matter intake, average daily gain, and feed efficiency for calves in each treatment group. Deads in and deads out analysis.

Treatment	Tulathromycin*	Tilmicosin*	Gamithromycin*	SE	P
Avg In Wt, lb	403.5	402.7	405.1	3.29	0.73
Avg Out Wt, lb	553.0[a]	544.3[ab]	540.1[b]	8.28	0.10
DMI, lb	12.52	12.28	11.99	0.20	0.20
ADG, lb					
Deads In	2.54[a]	2.36[ab]	2.25[b]	0.11	0.03
Deads Out	2.62[a]	2.48[ab]	2.36[b]	0.09	0.02
F:G					
Deads In	4.96	5.29	5.43	0.26	0.27
Deads Out	4.82	5.01	5.10	0.17	0.27

***** Values within a row with different superscripts are significantly different ($P < .05$).

Table 2.3: Feedyard morbidity, mortality, and retreatments per pen of each treatment group.

Treatment	Tulathromycin*	Tilmicosin*	Gamithromycin*	P
Mortality	1.02%	1.55%	1.53%	0.93
Morbidity	5.16%[a]	14.62%[b]	12.79%[b]	0.02
Retreats	0.00%	2.56%	1.50%	0.16

*Values within a row with different superscripts are significantly different ($P < .05$).

Table 2.4: Wheat pasture average initial weights, average out weights, and average daily gain for calves in each treatment group.

Treatment	Tulathromycin*	Tilmicosin*	Gamithromycin*	SE	P
Avg In Wt, lb	395.9	390.6	392.7	6.50	0.72
Avg Out Wt, lb	452.9	447.9	449.7	10.87	0.90
ADG, lb	1.07	1.08	1.06	0.13	0.98

* No significant difference found among values (P > .05).

Table 2.5: Wheat pasture morbidity and mortality rates of each treatment group.

Treatment	Tulathromycin*	Tilmicosin*	Gamithromycin*	P
Mortality				
No. of Head	2	2	5	0.35
Percentage	5.13%	5.00%	12.5%	
Morbidity				
No. of Head	2	5	5	0.46
Percentage	5.13%	12.50%	12.50%	

* No significant difference found among values (P > .05).

Appendix A - Product Index

[a]Draxxin, Pfizer Animal Health, New York, NY.

[b]Micotil, Eli Lilly and Company, Indianapolis, IN.

[c]Zactran, Merial LTD, Duluth, GA.

[d]Bovishield Gold 5, Pfizer Animal Health, New York, NY.

[e]Inforce 3, Pfizer Animal Health, New York, NY.

[f]Dectomax, Pfizer Animal Health, New York, NY.

[g]Valbazen, Pfizer Animal Health, New York, NY.

[h]Synovex C, Pfizer Animal Health, New York, NY.

[i]Sweet Bran, Cargill Inc., Blair, NE.

[j]Deccox, Pfizer Animal Health, New York, NY.

[k]Bovatec, Pfizer Animal Health, New York, NY.

[l]Excede, Pfizer Animal Health, New York, NY.

[m]Baytril 100, Bayer Animal Health, Shawnee Mission, KS.

[n]SAS, ver. 9.1.3; SAS Institute, Cary, NC.