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Progress Report No. 113

Comparison of Gamithromycin, Tilmicosin and Tulathromycin: Metaphylactic Treatments in High Risk Calves for BRD

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Introduction

Bovine Respiratory Disease Complex (BRDC) 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. 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). Vaccines are currently available to help minimize the susceptibility of feedlot calves to these viruses. Bacterial pathogens consist of *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis.* These four pathogens are opportunistic, as they can be isolated from most cattle, but replicate and cause disease in a stressed animal. Identifying BRD in cattle can be very difficult. Many producers and animal health personnel have implemented scoring techniques to try and place an objective measure on the morbidity of cattle.

According to a study by Schneider et al. (2009), 60.6% of cattle never treated for BRD had lung lesions present. Common associated signs include anorexia, depression, fever, and respiratory signs, such as coughing, tachypnea, dyspnea, nasal discharge, etc. (Taylor et al., 2010). Also, 74% of cattle treated at least once for BRD had lung lesions, indicating that 26% of cattle treated, did not have lung lesions. Management practices have been proven to help reduce the incidence of BRD in feedlot cattle, such as decreasing comingling, preconditioning, early castration, nutrition, and biosecurity (Smith, 2010).

Economics play a large part in the importance of BRD mitigation. The return on steers harvested that remained healthy was $87.60 greater than those treated for BRD (Smith, 2010). The cost of BRD due to death, poorer conversions, and treatments each year is estimated to be between $800 and $900 million dollars (Chirase and Greene, 2001). In a study by Brooks et al. (2011), results indicated as number of treatments increased during the backgrounding phase, the net returns decreased. Also, animals treated for BRD three or more times yielded a lower ADG than animals treated less than three times. The cost of gain was significantly lower in animals treated once or never versus those treated two or more times. In another study, comparing the economic implications of metaphylactic treatment of feeder cattle with Tilmicosin, results showed calves treated metaphylactically had greater economic return per pen than did controls.

Currently, there are three macrolide antibiotics marketed for use as metaphylaxis (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 pharmaco-dynamic 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. Having 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 (Ahrens, 1996).

The objective of this experiment was to compare the effects of three metaphylaxis antibiotics on health and performance of heifers at high risk for BRD.

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Experimental Procedures

This study was approved by the New Mexico State University IACUC (# 2011-034). Through a two and a half week period starting October 27, 2011, single loads of heifers (n = 592, 403.3 ± 27.4 lbs) identified as being high risk for BRD arrived at the Clayton Livestock Research Center (CLRC) in Clayton, NM. Each load (114 to 120 head) was unloaded and weighed before being placed in an arrival pen with fresh feed (hay and starter ration) and water. After a minimum of 24 hours rest, cattle were individually processed and placed in home pens. At processing, each load was allocated into two (2) sets of three (3) treatment groups (n = 18 to 20 depending on load size) consisting of metaphylactic tulathromycin, tilmicosin, and gamithromycin. Each heifer was weighed, vaccinated for BVD (type I and II), IBR, BRSV, and PI3, given a dormectin injection and oral albendazole, and implanted with 100 mg progesterone and 10 mg estradiol benzoate. Each animal received an individual ID tag, a treatment tag, and any horns were tipped if present.

Cattle were assigned a treatment group using a systematic random design and placed in the appropriate sorting pen. Once sorted, each treatment group was moved to an assigned soil-surfaced pen (40 ft × 115 ft, with 36 ft bunk line; 19 to 20 head per pen). Water was supplied to each pen with a bunk line continuous flow water tank. Cattle restraint was conducted in a tub and snake with a Silencer hydraulic chute designed for cattle processing. Treatments consisted of the following: 1) tilmicosin (193 head; 13.2 mg/kg, 2 mL/cwt), 2) gamithromycin (194 head; 6 mg/kg, 1.82 mL/cwt), 3) tulathromycin (192 head; 2.5mg/kg, 1.1 mL/cwt). The pen served as the experimental unit. The antibiotics used were tilmicosin (Micotil, Elanco Animal Health), gamithromycin (Zactran, Merial Animal Health), and tulathromycin (Draxxin, Pfizer Animal Health). The study consisted of three (3) treatments with 10 reps per treatment.

Heifers were started on a receiving diet composed of 20% ground corn, 57% sweet bran, 18% corn stalks, and 5% of a supplement containing Deccox. Dietary energy concentrations were increased through day 28 using a 2-ration (starter diet and finisher diet) transition system. The finisher diet was composed of 52% sweet bran, 30% ground corn, 13% corn stalks, and 5% of a supplement containing Bovatec. 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 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 calculate dietary dry matter and for proximate analyses. In addition, at each scheduled weigh period (d 28 and 56), feed was collected, weighed, and sampled for dry matter to calculate dry matter intake.

Daily clinical monitoring was completed by trained animal health personnel. Every effort was made to ensure that monitoring occurred at the same time daily. Animals were assessed daily through the end of the study based on the DART method. Any animal deemed as "sick" was scored as follows: **depression** (0 = normal, 1 = mildly depressed, 2 = moderately depressed, 3 = severely depressed), **anorexia** (BCS; 0 = normal, which was 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 and/or depth of respiration, 2 = labored; as 1, but open mouth breathing and/or neck extension, 3 = severe; as 2, but severe grunting and/or thumping). Any animal pulled with a combined score ≥ 3 and a rectal temperature > 104°F was treated with Ceftiofur (Excede, Pfizer Animal Health) according to label directions, and a 5 day pull/treatment moratorium. Any animal pulled with a combined score ≥ 3 and a rectal temperature < 104°F was treated with Enrofloxacin (Baytril 100, Bayer) according to label directions, and a 3 day pull/treatment moratorium. Any animal pulled with a combined score < 3 was not treated and returned to its home pen. Any animal pulled for a second time was treated with Excede as its second treatment. If the animal received Excede as its first treatment, then oxytetracycline (Biomycin 200, Boehringer Ingelheim Vetmedica) was used as its second treatment.

Data were inputted into Microsoft Excel (2010) throughout the experiment. 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 measured 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 measured for both deads in and deads out across treatment groups. SAS (v. 9.1.3; SAS Institute, Cary, NC) 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 retreatment were analyzed using a Wilcoxon Rank-Sum Test.

Results and Discussion

The results indicate that there was no difference (P = 0.73) in initial weight among treatment groups (Table 1). However, there was a significant difference (P = 0.10) in end weight between the tulathromycin treated calves and gamithromycin treated calves (Table 1). Dry matter intake was measured as the average intake per calf per pen. No

significant difference (P = 0.20) was found between treatment groups for the average dry matter intake of calves during the trial period (Table 1). For deads in, cattle administered tulathromycin had higher (P < 0.01) daily gains than cattle administered gamithromycin by 0.29 lbs/d and tended (P = 0.09) to have higher daily gains than cattle that received tilmicosin by 0.18 lbs/d (Table 2). No difference was 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). Feed efficiency between calves treated with tulathromycin and those treated with tilmicosin indicated no difference. The same results were found between tilmicosin treated calves and gamithromycin treated calves. Results for deads out analysis yielded similar results as deads in analysis (Table 2). Morbidity rates were calculated as the percentage of calves that required treatment after the initial metaphylactic treatments. Calves that received tulathromycin (5.2%) had lower (P < 0.02) morbidity rates than tilmicosin (14.6%) and gamithromycin (12.79%) treated calves (Table 3). No difference was found in morbidity between tilmicosin treated calves and gamithromycin treated calves. Measurements of mortality were recorded as percentage of deaths due to respiratory disease per pen. Mortality rates were low across all treatment groups, which resulted in no differences (Table 3). Retreatment was measured as the percentage of calves per pen that required treatment more than one time after the initial metaphylactic treatment. There were no retreatments in calves initially treated with tulathromycin, and a very small percentage in both tilmicosin and gamithromycin treated calves (Table 3).

Results from this study indicate that 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. A study conducted by Hanzlicek et al. (2011), showed similar results in calves treated with tulathromycin versus gamithromycin treated calves. Both studies followed calves for 56 days. A non-metaphylactic study measuring the effects of treatment with both tulathromycin and gamithromycin showed no effect across all variables when taken 150 days to closeout (Torres et al, 2011). This is the only study to date that includes the flex-dose tilmicosin as a treatment group. Further studies are warranted to compare these antibiotics to closeout and compare carcass characteristics.

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Studies by Hanzlicek et al. (2011) and Torres et al. (2011) are yet to be published.

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Table 1: Average initial weights, average out weights, and average dry matter intake for calves in each treatment group. All values measured in pounds. Values within a row with different superscripts are significantly different (P < .05).

	Treatment				
Item	**Tulathromycin**	**Tilmicosin**	**Gamithromycin**	SE	P
Avg In Wt	403.50	402.67	405.12	3.29	0.73
Avg Out Wt	552.97[a]	544.34[ab]	540.11[b]	8.28	0.10
DMI	12.52	12.28	11.99	0.20	0.20

Table 2: Average daily gain and feed efficiency for calves in each treatment group. Deads in and deads out analysis. Average daily gain calculated by taking the average weight change per calf per pen divided by the length, in days, of the trial period. Feed efficiency measured by taking the average dry matter intake per calf per pen divided by the average pounds gained. Values within a row with different superscripts are significantly different (P < .05).

	Treatment				
Item	Tulathromycin	Tilmicosin	Gamithromycin	SE	P
ADG					
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

Table 3: Morbidity, mortality, and retreatment per pen of each treatment group. Values calculated as percentage per pen. Values within a row with different superscripts are significantly different (P < .05).

	Treatment			
Item	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
Retreatment	0.00%	2.56%	1.50%	0.16

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