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Effects and Economic Implications of Metaphylactic Treatment of Feeder Cattle with Two Different Dosages of Tilmicosin on the Incidence of Bovine Respiratory Disease (BRD) – A Summary of Two Studies

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Abstract

Two studies were conducted to evaluate the efficacy of tilmicosin for metaphylactic treatment of bovine respiratory disease (BRD), and subsequent effects on calf performance, in newly received, high-risk feedlot cattle. Calves in each study were randomly assigned to one of three treatment groups: negative control; 4.55 mg/lb body weight (BW) (10 mg/kg BW) tilmicosin (TIL10); or 9.1 mg/lb BW (20 mg/kg BW) tilmicosin (TIL20).

In Study I, calves receiving tilmicosin had lower BRD morbidity ($P<0.01$) and mortality rates ($P=0.02$) compared to controls. Furthermore, BRD morbidity was lower ($P\leq0.05$) in the TIL20 (16.8%) compared to the TIL10 (24.3%) group. Average daily gain was improved ($P<0.01$) in both tilmicosin metaphylaxis treatment groups compared to controls when deads and removals were not included in the final calculations (2.9 lb and 3.0 lb vs 2.8 lb or 1.32 kg and 1.36 kg vs 1.27 kg), as well as when deads and removals were included in the evaluation (2.7 lb and 2.8 lb vs 2.4 lb or 1.23 kg and 1.27 kg vs 1.09 kg, respectively). Calves treated metaphylactically with tilmicosin had greater economic return per pen ($P<0.01$) than did controls.

In Study II, calves in both TIL10 and TIL20 treatment groups had lower ($P\leq0.05$) morbidity compared to controls (68.5, 49.9, and 44.0% for control, TIL10, and TIL20, respectively). No significant differences in performance were observed between treatment groups.

Keywords: bovine, feedlot, BRD, metaphylaxis, tilmicosin, economic

Résumé

Deux recherches ont étudié l'efficacité de la tilmicosine pour le traitement métaphylactique du complexe respiratoire bovin (CRB) et son influence sur la performance zootechnique, chez des veaux de risque sanitaire élevé nouvellement arrivés en parc d'engraissement. On a distribué les veaux de façon aléatoire dans les trois groupes de vaccination suivants : témoins négatifs (aucune vaccination), 4,55 mg de tilmicosine par livre (10 mg/kg) de poids vif (TIL10) et 9,1 mg de tilmicosine par livre (20 mg/kg) de poids vif (TIL20).

Dans l'étude I, chez les veaux traités à la tilmicosine, le CRB a occasionné un taux de morbidité inférieur ($P\leq0.01$) et un taux de mortalité inférieur ($P=0.02$) par rapport aux veaux témoins. De plus, la morbidité due au CRB a affecté moins de veaux ($P\leq0.05$) dans le groupe TIL20 (16,8 %) que dans le groupe TIL10 (24,3 %). Les deux traitements métaphylactiques à la tilmicosine ont amélioré le gain moyen quotidien de poids par rapport aux témoins, aussi bien quand on excluait du calcul final les veaux morts et mis à l'écart (2,9 lb et 3,0 lb versus 2,8 lb, ou 1,32 kg et 1,36 kg versus 1,27 kg) que quand on les incluait dans l'évaluation (2,7 lb et 2,8 lb versus 2,4 lb ou 1,23 kg et 1,27 kg versus 1,09 kg, respectivement). Les veaux soignés par traitement métaphylactique à la tilmicosine se sont montrés plus rentables ($P<0.01$) que les témoins.

Dans l'étude II, les veaux traités aux deux doses de tilmicosine ont affiché un taux de morbidité inférieur ($P\leq0.05$) à celui des témoins (68,5 %, 49,9 % et 44,0 % pour les témoins et les veaux TIL10 et TIL20, respectivement). On n'a pas décelé de différence entre les deux groupes soignés à la tilmicosine, ni de différence significative entre les performances des veaux des trois traitements de vaccination.

Introduction

Tilmicosin,[a] a macrolide antibiotic, was approved in the United States (US) in 1992 for treatment of bovine

respiratory disease (BRD) caused by *Mannheimia haemolytica*. In 1996, it was approved for control of BRD in cattle at high risk of developing BRD. At that time, the term "metaphylaxis" was first used in the US, and is defined as treatment given to animals experiencing any level of viral or bacterial disease before clinical signs of disease appear.[10] Numerous studies have demonstrated the efficacy of tilmicosin for controlling BRD in cattle at risk of developing respiratory disease.[1-9,11]

The objective of these studies was to evaluate efficacy of tilmicosin for control of BRD in newly received, high-risk feedlot cattle utilizing 0, 4.55, or 9.1 mg/lb body weight (BW) (0, 10, or 20 mg/kg BW) tilmicosin, and subsequent effects on calf performance.

Materials and Methods

Scope of the studies

In two studies, feedlot calves at high risk of developing BRD were utilized to evaluate two dosages of tilmicosin administered metaphylactically at arrival processing. Calves were housed and fed at two commercial research feedlots with management conditions similar to commercial feedlots, except smaller pens were utilized. Calves in each treatment group were fed in the same pen.

Data were collected through harvest. Outcome variables measured included health and performance differences between controls (no metaphylaxis at arrival processing) and calves treated with 4.55 or 9.1 mg/lb BW (10 or 20 mg/kg BW) tilmicosin at processing.

Statistical analyses were conducted to determine if observed differences in health and performance variables between treatments were statistically significant. Economic differences were also calculated and statistically analyzed. In all analyses, pen was the experimental unit.

Research facilities

Study I was conducted in a commercial research facility in the Texas panhandle. Calves were housed in outdoor dirt pens constructed with pipe and cable siderail fencing. Study II was conducted in a commercial research facility in Colorado where calves were also housed in outdoor, dirt pens. In both studies, feed was delivered into permanent concrete feedbunks along the front side of the pens. Hospital facilities, similar to those found in commercial feeding facilities, were used to evaluate and treat sick cattle. Hydraulic chutes were equipped with scales to individually weigh calves. Treated calves were not housed in hospital pens, but instead were returned to their home pen immediately after treatment.

Study calves

Study I was conducted December 2006 through September 2007, while Study II was conducted November 2006 through June 2007. A total of 1,000 crossbred heifers were purchased from auction markets in Texas for use in Study I, and transported by truck to the research feedlot. Mean enrollment BW was 456 lb (207 kg) with a range of 323-585 lb (147-266 kg). For Study II, 1,045 English crossbred steers were purchased from livestock markets in Colorado. Mean enrollment weight was 584 lb (265 kg) with a range of 347-699 lb (158-318 kg). Any calf arriving at the research feedlot with signs of pre-existing BRD was not included in the studies.

Within 12 hours of arrival at the feedlot, calves in Study I were processed as follows:

- Individually numbered tag was placed in the ear
- Individual rectal temperature was taken and recorded
- Individual BW was recorded
- Modified-live infectious bovine rhinotracheitis (IBR) virus and bovine viral diarrhea (BVD) virus vaccine[b] was administered according to label instructions
- 7-way clostridial bacterin-toxoid[c] was given according to label instructions
- An autogenous bacterin[d] containing *Mannheimia haemolytica*, *Pasturella multocida*, and *Histophilus somni* antigens was administered
- A probiotic[e] feedlot drench was given orally
- Calves were treated for internal and external parasites[f]
- A growth-promoting implant[g] was administered according to label instructions

At 50 days-on-feed, Study I calves were:

- Administered a growth-promoting implant[h]
- Administered modified-live IBR virus vaccine[i]
- Treated for internal and external parasites[f]

At 148 days on study, calves were administered:

- A modified-live IBR virus vaccine[i]
- Two growth-promoting implants[j,k]

Within 36 hours of arrival at the feedlot, calves in Study II were processed as follows:

- Individually numbered tag was placed in the ear
- Individual rectal temperature was taken and recorded
- Individual BW was recorded
- A modified-live IBR virus, BVD virus, parainfluenza-3 (PI3) virus, and bovine respiratory syncytial (BRS) virus vaccine[l] was administered according to label instructions
- Treated for internal and external parasites[m]

- Administered a growth-promoting implant[n]

At 75 to 77 days-on-feed, Study II calves were administered:

- A growth-promoting implant[o]
- Modified-live IBR virus and BVD virus (types 1 and 2) vaccine[b]
- Treatment for lice[p] and internal and external parasites

In both studies, calves were additionally processed as follows:

- Tilmicosin[a] (4.55 or 9.1 mg/lb BW; 10 or 20 mg/kg BW) was administered subcutaneously (SC) to calves allotted to one of the two metaphylaxis treatment groups. Dosage was based on individual BW. Calves in the control groups did not receive tilmicosin.
- A skin sample (ear notch) was taken from each calf, and placed in formalin.

Skin samples were submitted to the Texas Veterinary Medical Diagnostic Laboratory (Amarillo) for immunohistochemical testing to identify calves persistently infected with BVDV.

Experimental design

In both studies, calves were randomly assigned to treatment during arrival processing utilizing a computer-based, random-number generator. Calves from each truckload were equally assigned to each treatment. Body weight was not used to determine treatment assignment.

Calves in both studies were assigned to one of the following treatment groups: 1) negative control group (CON); 2) metaphylactic treatment with tilmicosin at 4.55 mg/lb BW (10 mg/kg BW; TIL10); or 3) metaphylactic treatment with tilmicosin at 9.1 mg/lb BW (20 mg/kg BW; TIL20). There were four blocks, each consisting of two TIL10 pens, two TIL20 pens, and one CON pen. Cattle were allocated to 50-head pens for a total of 200 calves in the CON group and 400 calves in both the TIL10 and TIL20 treatments.

Feeding management

Calves in both studies were fed typical feedlot diets containing monensin sodium[q] and tylosin[r] on an *ad libitum* basis throughout the study. Feed was weighed upon issue to each pen. Intake was adjusted to a dry matter basis. Unconsumed feed was removed from feed bunks and weighed on harvest shipment day. Water was provided *ad libitum* via an automatic watering system.

Animal health management

Calves in both studies were observed daily by trained animal health personnel who were masked (blinded) to treatment. A five-day post-treatment evaluation period following arrival processing was observed for cattle in the TIL10 and TIL20 treatment groups. During this period, no cattle were treated for BRD except those displaying a CIS (clinical impression score) 4 or greater (Table 1) and a rectal temperature of 104°F (40°C) or higher. Cattle in the CON group were eligible for BRD treatment 24 hours after processing.

Eligible calves in all treatment groups were removed from their home pen and taken to the hospital for further evaluation if they exhibited signs of BRD and had a CIS of ≥2. Calves with a CIS ≥2 and a rectal temperature ≥104°F were treated for BRD; those with a CIS ≥2 and a rectal temperature <104°F were not treated. All calves were returned to their designated home pen after evaluation and/or treatment.

All calves diagnosed with BRD the first time were treated with enrofloxacin[s] (5.0 mg/lb or 11.0 mg/kg) administered SC. Those that experienced treatment failure or relapse for the first time were treated with

Table 1. Description of Clinical Illness Scores (CIS) used to classify a calf as sick with bovine respiratory disease (BRD).

Clinical Illness Score (CIS)	Description	Clinical appearance
1	Normal and healthy	No abnormal clinical signs.
2	Slightly ill	Mild abnormal character of respiration. Slight depression, gauntness, and nasal and/or ocular discharge.
3	Moderately ill	Moderate abnormal character of respiration. Noticeable dyspnea, gauntness, depression, nasal and/or ocular discharge.
4	Severely ill	Severe abnormal character of respiration. Pronounced dyspnea, depression, and gauntness. Nasal and/or ocular discharge.
5	Moribund	Down, near death. Open mouth breathing.

florfenicol[t] (18.2 mg/lb or 40 mg/kg) SC. Calves relapsing a second time were treated with oxytetracycline[u] (4.5 mg/lb or 10 mg/kg) SC. Calves were not eligible for retreatment for three days following the first or second treatment for BRD. Treatment outcome categories are outlined in Table 2.

Harvest management

In both studies cattle were harvested in complete blocks. Carcass traits (hot carcass weight, quality grade, and yield grade) were collected and recorded at the harvest facility.

Data collection

Individual BW were collected at arrival processing, reimplant, and study completion. Primary treatment outcome measures for all groups included BRD morbidity, mortality and chronicity rates, and mean days to onset of BRD. Performance measures included BW gain, average daily gain (ADG), and feed efficiency. Outcome measures for first-line treatment of BRD with enrofloxacin included treatment outcome (treatment success, relapse, and failure) and case fatality rate.

Economic modeling

An economic model was developed for each pen of calves. Model inputs were calf cost, health cost (metaphylaxis cost, therapy cost, cost of chronic calves, cost of dead calves), feed cost, and return. Model outputs were pen profit and mean profit per head. The following describes the valuation of each variable in the pen-level model:

- Calf cost calculated based on sum of each calf's BW multiplied by historical purchase price for the corresponding year, month, calf weight, and region.
- Health cost for each pen was calculated as the sum of the cost of the metaphylaxis program, therapeutic cost (treatment, repull, second repull, and new episode), cost of chronics, and cost of deads.
- Metaphylaxis cost = cost of tilmicosin/lb BW × total pen initial weight
- Therapy cost
  - Treatment cost = (mean initial weight × number of head treated × cost of enrofloxacin/lb of BW) + standard labor/facilities/supply charge per head treated
  - Re-pull cost = (mean initial weight × number of head treated × cost of florfenicol/lb of BW) + standard labor/facilities/supply charge per head treated
  - Second re-pull cost = (mean initial weight × number of head treated × cost of oxytetracycline/lb of BW) + standard labor/facilities/supply charge per head treated
  - New episode cost = (mean initial weight × number of head treated × cost of enrofloxacin/lb of BW) + standard labor/facilities/supply charge per head treated
- Chronic cost = (mean purchase cost × 0.75 × number of chronic calves) + (standard yardage fee × total number of days-on-feed until classified as chronic)
- Dead cost = (mean purchase cost × number of dead calves) + (standard yardage fee × total number of days-on-feed until death)
- Feed cost was calculated based on actual tons of dry matter feed consumed multiplied by feedyard's ration cost per ton of dry matter
- Gross economic return was calculated based on the sum of each calf's final BW multiplied by historical selling price for the corresponding year, month, calf weight, and region

Table 2. Bovine respiratory disease (BRD) therapy outcome categories.

BRD therapy response variable	Description
Treatment success	A calf recovered at day 3. Clinical Illness Score (CIS) =1 or CIS < initial CIS and temperature <104.0°F following antimicrobial therapy, and shows no additional signs of BRD or requires no additional therapy for BRD within 21 days of the previous BRD therapy.
Treatment failure	A calf that at three days post-treatment for BRD has a CIS greater than the initial CIS or CIS is >1 and rectal temperature is ≥104.0°F.
Relapse	A calf with an improved CIS at three days post-BRD antimicrobial treatment, but observed with signs of BRD (CIS >1) and has a rectal temperature ≥104°F within 21 days of the previous BRD therapy.
New episode	A calf diagnosed with BRD (CIS >1) and a rectal temperature ≥104°F >21 days following the previous BRD case.
Chronic/removal	A calf judged by the masked, attending veterinarian to have a debilitating health condition that prevents it from continuing with other calves on the study.

- Pen profit = return – calf cost – health cost – feed cost
- Mean profit per head = pen profit / number of calves in pen on arrival

Statistical Analysis

In both studies, pen was used as the experimental unit unless indicated otherwise. Percent mortality, morbidity, and removals on a pen basis were calculated for the control and tilmicosin treatment groups. Results were statistically analyzed using a generalized linear mixed model (GLIMMIX procedure in SAS, SAS Institute, Cary, NC). A binomial distribution with a logit link was used in the analysis. Treatment group was the only fixed effect in the statistical model. Replicate was included as a random effect. Where a statistically significant treatment effect was observed ($P \leq 0.05$), treatment groups were compared in a pair-wise fashion.

Days to first pull and temperature at processing were analyzed as described for the other health measures, but ANOVA was used to evaluate the treatment effects under the assumption of a normal distribution (MIXED procedure). Therapy responses following metaphylactic treatment with tilmicosin or the control treatment were evaluated as described above for percent mortality.

Initial BW, final BW, ADG, total weight gain, daily dry matter intake, feed conversion, and hot carcass weight were evaluated by ANOVA with treatment as a fixed effect and replicate as a random effect. ADG and total weight gain were calculated using total pen weights. Results were analyzed with and without dead animals and removals.

Quality and yield grade distributions were analyzed using the GLIMMIX procedure in SAS (calf as the experimental unit). The statistical model included treatment as the only fixed effect; replicate was included as a random effect. The multinomial distribution with a cumulative logit link was used. Percent Choice was evaluated as described above for mortality (pen as the experimental unit).

Economic parameters were analyzed with pen as the experimental unit. The data from the two study sites were analyzed separately. All values were evaluated by ANOVA (the MIXED procedure in SAS) with treatment as a fixed effect and block as a random effect. Where significant treatment effects were observed ($P \leq 0.05$), pair-wise comparisons were made. Differences between means were declared significant if $P \leq 0.05$.

Results

Study I

Bovine respiratory disease morbidity and mortality rates were significantly affected by metaphylactic treatment. Calves receiving tilmicosin had lower BRD morbidity ($P<0.01$) and mortality rates ($P=0.02$) compared to CON calves (Table 3). Furthermore, BRD morbidity was lower ($P \leq 0.05$) in the TIL20 (16.8%) compared to the TIL10 (24.3%) group. The BRD mortality rate was not different between the two metaphylaxis groups. Metaphylactic treatment had no significant effect on BRD removals, non-BRD removals, or non-BRD mortality (Table 3). Metaphylactic treatment did not affect treatment response when clinical BRD cases were treated with enrofloxacin (Table 4).

Average daily gain was improved ($P<0.01$) in calves treated metaphylactically (TIL10 and TIL20) compared to CON calves on both "deads-and-removals-out" (2.9 lb and 3.0 lb vs 2.8 lb or 1.32 kg and 1.36 kg vs 1.27 kg, Table 5) and "deads-and-removals-in" (2.7 lb and 2.8 lb vs 2.4 lb or 1.23 kg and 1.27 kg vs 1.09 kg, Table 6) evaluations. Total weight gain was greater ($P<0.01$) in both metaphylaxis treatment groups compared to the CON group on a deads-and-removals-out (Table 5) as well as a deads-and-removals-in (Table 6) basis. Calves in the tilmicosin metaphylaxis treatment groups had improved feed conversion compared to controls on a deads-and-removals-in basis ($P<0.01$; Table 6). Carcass traits were not different among the treatment groups (Tables 7 and 8).

Profit per pen, and subsequently mean profit per head, were greater ($P=0.02$) for TIL10 and TIL20 groups compared to CON (TIL10=$45.19 and TIL20=$84.61 vs CON=$-41.41, Table 9). Input variables that were different among treatment groups were metaphylaxis cost per pen ($P<0.01$), therapy cost per pen ($P<0.01$), and total return per pen ($P<0.01$, Table 9). Metaphylaxis cost was greatest in the TIL20 group ($789.84), followed by the TIL10 group at $396.20, and $0.00 for the CON group. However, therapy cost was less ($P<0.01$, Table 9) in the calves treated metaphylactically (TIL10=$491.35; TIL20=$340.96) than in CON calves ($754.62). In addition, calves treated with tilmicosin metaphylactically had at least a $4,330 greater return per pen ($P=0.02$, Table 9) than did controls.

Study II

Mean days to first pull and percent BRD morbidity were significantly affected by metaphylactic treatment ($P<0.01$, Table 10). While the number of days to first pull was significantly longer ($P=0.05$) in both tilmicosin metaphylaxis groups as compared to the control group, no difference was observed between the TIL10 and TIL20 groups. Calves in the CON group had a significantly higher BRD morbidity rate (68.5%) than calves in the TIL10 (49.9%) or TIL20 (44.0%) groups. No difference was found in other health parameters measured comparing the two metaphylaxis treatments.

The main effect of metaphylactic treatment was significant ($P \leq 0.04$) for several BRD therapy outcomes, including treatment success, treatment relapse, and new episodes of BRD (Table 11). Treatment success rate when treating BRD with enrofloxacin was higher ($P \leq 0.05$) in the TIL10 metaphylaxis group compared to the CON or TIL20 groups (72.1% vs 57.7 and 59.8%, respectively); the success rate in calves treated with enrofloxacin was not different ($P > 0.05$) between the TIL20 and CON groups. Accordingly, the percent of relapses in the TIL10 group was lower ($P \leq 0.05$) than in cattle in the CON group. Other BRD treatment outcome comparisons for cattle treated with enrofloxacin did not differ ($P > 0.05$) among treatment groups. Although the TIL10 and TIL20 groups had similar new episode rates following enrofloxacin therapy, both groups had significantly fewer ($P \leq 0.05$) percentage new episodes compared to CON cattle.

When feeding performance outcomes were evaluated on a deads-and-removals-out basis, no significant effect of treatment was noted ($P > 0.05$, Table 12). Similarly, feeding performance outcomes were not affected by treatment on a deads-and-removals-in basis ($P > 0.05$, Table 13). There were no significant differences ($P > 0.05$) in carcass characteristics between the three treatment groups (Table 14 and Table 15).

Metaphylaxis cost per pen was different among treatment groups ($P < 0.01$, Table 16). The greatest metaphylaxis cost was in the TIL20 group ($1,010.82), followed by the TIL10 group ($502.02), and the CON group ($0.00). Therapy cost was less ($P < 0.01$, Table 16) in calves treated metaphylactically (TIL20=$925.50;

Table 3. Effects of metaphylactic treatment with differing dosages of tilmicosin on morbidity, mortality, and removals–Study I.[1]

Item	CON[2]	TIL10[3]	TIL20[4]	*P*-value[5]
No. pens	4	8	8	
No. head	200	400	400	--
Mean days to first pull	13.2[a]	22.3[ab]	33.8[b]	0.02
Mean body temperature at processing, °F	102.2	102.7	103.0	0.16
Body temperature at processing ≥104.0°F, n	18	40	58	--
Body temperature at processing ≥104.0°F, %[6]	9.0	10.0	14.5	0.09
Bovine respiratory disease (BRD) morbidity, n	68	97	67	
BRD morbidity, %[6]	34.0[a]	24.3[b]	16.8[c]	<0.01
BRD mortality, n	27	30	24	
BRD mortality, %[6]	13.5[a]	7.5[b]	6.0[b]	0.02
Non-BRD mortality, n	2	5	2	
Non-BRD mortality, %[6]	1.0	1.3	0.5	0.56
BRD removals, n	7	10	6	
BRD removals, %[6]	3.5	2.5	1.5	0.33
Non-BRD removals, n	0	2	0	
Non-BRD removals, %[6]	0.0	0.5	0.0	1.00
BRD removals and mortality, n	34	40	30	
BRD removals and mortality, %[6]	17.0[a]	10.0[b]	7.5[b]	0.01
Non-BRD removals and mortality, n	2	7	2	
Non-BRD removals and mortality, %[6]	1.0	1.8	0.5	0.30
Total removals and mortality, n	36	47	32	
Total removals and mortality, %[6]	18.0[a]	11.8[ab]	8.0[b]	0.01

[1]Least squares mean.
[2]CON = negative control; calves did not receive metaphylactic treatment at processing.
[3]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[4]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[5]*P*-values are from the assessment of the overall treatment effect.
[6]Percents are reported as number of observed/total. The statistical analysis used pen as the experimental unit.
[a,b,c]Values within a row with different superscripts are significantly different at $P \leq 0.05$.

TIL10=$934.60) than in CON calves ($1,548.31).

Discussion

These studies demonstrate the value of metaphylaxis using tilmicosin to control BRD in high-risk calves, which agrees with earlier reports.[1,4,5,8,9,10,11] The overall incidence of BRD was reduced by 29% and 51% in the TIL10 and TIL20 groups compared to CON in Study I ($P<0.01$). Mortality rates from BRD were also lower in the TIL10 and TIL20 groups compared to CON ($P=0.02$). In Study II, the incidence of BRD was reduced by 27% and 36% in the TIL10 and TIL20 groups compared to CON cattle ($P<0.01$). In addition, morbidity due to BRD in the TIL20 group in Study I was lower than in the TIL10 group, although the morbidity rates in the TIL10 and TIL20 groups did not differ in Study II.

Mortality rates due to BRD were different ($P<0.01$) between calves treated metaphylactically and CON calves in Study I. Surprisingly, even with a relatively

Table 4. Response of feeder cattle metaphylactically treated with differing dosages of tilmicosin to treatment with enrofloxacin for clinical bovine respiratory disease (BRD)–Study I.

Item	CON[1]	TIL10[2]	TIL20[3]	*P*-value[4]
No. head treated (no. head which completed the 21-day evaluation)	68	97	67	
Success rate, % (n)[5]	57.4 (39)	55.7 (54)	55.2 (37)	0.98
Failure rate, % (n)[5]	8.8 (6)	10.3 (10)	7.5 (5)	0.75
Relapse rate, % (n)[5]	33.8 (23)	34.0 (33)	37.3 (25)	0.89
Second relapse rate, % (n)[5]	35.3 (24)	23.7 (23)	32.8 (22)	0.25
New episode rate, % (n)[5]	25.0 (17)	14.4 (14)	16.4 (11)	0.24
BRD mortality, % of pulled (n)[5]	29.4 (20)	23.7 (23)	26.9 (18)	0.74
Non-BRD mortality, % of pulled (n)[5]	2.9 (2)	3.1 (3)	1.5 (1)	0.82
BRD removals, % of pulled (n)[5]	10.3 (7)	10.3 (10)	9.0 (6)	0.96
Non-BRD removals, % of pulled (n)[5]	0.0 (0)	0.0 (0)	0.0 (0)	--
BRD removals and mortality, % of pulled (n)[5]	39.7 (27)	34.0 (33)	35.8 (24)	0.76
Non-BRD removals and mortality, % of pulled (n)[5]	2.9 (2)	3.1 (3)	1.5 (1)	0.82
Total removals and mortality, % of pulled (n)[5]	42.6 (29)	37.1 (36)	37.3 (25)	0.75

[1]CON = negative control; calves did not receive metaphylactic treatment at processing.
[2]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[3]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[4]*P*-values are from the assessment of the overall treatment effect.
[5]Percents are reported as number of observed/total. The statistical analysis used pen as the experimental unit.

Table 5. Effects of metaphylactic treatment with differing dosages of tilmicosin on performance of feeder cattle: deads-and-removals-out–Study I.[1]

Item	CON[2]	TIL10[3]	TIL20[4]	*P*-value[5]
Initial body weight, lb	457.3	458.4	456.4	0.80
Final body weight, lb	1176.9	1207.3	1204.3	0.07
Average daily gain, lb	2.8[a]	2.9[b]	3.0[b]	<0.01
Weight gain, lb	701.6[a]	734.2[b]	740.7[b]	<0.01
Dry matter intake, lb	16.1	16.2	16.1	1.00
Feed conversion	5.7	5.5	5.4	0.08

[1]Least squares mean.
[2]CON = negative control; calves did not receive metaphylactic treatment at processing.
[3]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[4]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[5]*P*-values are from the assessment of the overall treatment effect.
[a,b]Values within a row with different superscripts are significantly different at $P \leq 0.05$.

Table 6. Effect of metaphylactic treatment with differing dosages of tilmicosin on performance of feeder cattle: deads-and-removals-in–Study I.[1]

Item	CON[2]	TIL10[3]	TIL20[4]	*P*-value[5]
Initial body weight, lb	454.5	458.0	456.6	0.58
Final body weight, lb	965.3[a]	1065.2[b]	1106.6[b]	<0.01
Average daily gain, lb	2.4[a]	2.7[b]	2.8[b]	<0.01
Weight gain, lb	510.8[a]	607.1[b]	650.0[b]	<0.01
Dry matter intake, lb	16.0	16.1	16.1	0.96
Feed-to-gain ratio	6.7[a]	6.1[b]	5.8[b]	<0.01

[1]Least squares mean.
[2]CON = negative control; calves did not receive metaphylactic treatment at processing.
[3]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[4]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[5]*P*-values are from the assessment of the overall treatment effect.
[a,b]Values within a row with different superscripts are significantly different at $P \leq 0.05$.

Table 7. Effect of metaphylactic treatment with differing dosages of tilmicosin on hot carcass weight and percentage USDA Choice in feeder cattle–Study I.[1]

Item	CON[2]	TIL10[3]	TIL20[4]	*P*-value[5]
No. head	164	353	368	
Hot carcass weight, lb	732.9	749.2	750.2	0.11
Percent Choice (n)	35.4 (58)	32.0 (113)	35.9 (132)	0.54

[1]Least squares mean.
[2]CON = negative control; calves did not receive metaphylactic treatment at processing.
[3]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[4]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[5]*P*-values are from the assessment of the overall treatment effect.

Table 8. Effect of metaphylactic treatment with differing dosages of tilmicosin on USDA quality grade and USDA yield grade of feeder calves–Study I.

Item	CON[1]	TIL10[2]	TIL20[3]	*P*-value[4]
Quality grade:				0.87
Choice, %	35.4	32.0	35.9	
Prime, %	0.6	1.1	0.8	
Select, %	48.2	55.0	49.5	
Standard and other, %	15.9	11.9	13.9	
Yield grade:				0.27
1, %	10.4	9.9	7.3	
2, %	40.9	33.1	38.9	
3, %	38.4	45.0	39.4	
4, %	8.5	9.9	10.1	
5, %	1.8	2.0	4.4	

[1]CON = negative control; calves did not receive metaphylactic treatment at processing.
[2]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[3]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[4]Overall treatment effect based on a cumulative logit logistic regression model.

low morbidity rate, mortality was relatively high (6.0-13.5%), resulting in high case fatality rates of 23.7 to 29.4%. Calves in Study II experienced higher BRD morbidity rates than those in Study I, but mortality rates were lower.

The disparity between the BRD morbidity and mortality rates in the two studies highlights the innate differences among populations of cattle. Several factors, such as type of cattle, weather patterns, feeding management, or aggressiveness in removing calves from the pens for diagnosis, could have contributed to the differences.

Response to treatment of clinical cases of BRD with enrofloxacin (first-line therapy) was similar among treatment groups in Study I. Success rate in Study II was higher in the TIL10 group compared to the TIL20 and CON groups. Conversely, relapse rate was the lowest in the TIL10 calves. Numerous biological factors affect success rate, such as ability to mount an immune response, stress level, disease progression, and nutritional status. Nevertheless, one would not have expected significant differences in response rates in calves treated for BRD.

Cattle treated metaphylactically with tilmicosin in Study I had significantly improved feeding performance compared to CON when calculated on a deads-and-removals-in basis. Improvement in weight gain and feed conversion has been demonstrated in other studies,[1,5,8,9,11] and is likely attributed to a reduction in BRD. Numerically, TIL20 calves had the greatest feedlot performance. A similar improvement in feeding performance was not observed in Study II, although there was a numerical advantage in feeding performance in the TIL20 group. The lack of performance improvement in Study II compared to Study I and other tilmicosin metaphylaxis studies[1,5,8,9,11] could have been related to extremely high morbidity rates in Study II.

There was greater profit per pen, and subsequently profit per head, in TIL10 and TIL20 groups compared to CON calves in Study I. Metaphylactic treatment of calves resulted in an economic advantage of at least $86.60 per head. Although not significant, calves in the TIL20 group had the greatest profit per head numerically. These numerical relationships were consistent in Study II. As expected, metaphylaxis cost in both studies was greatest in the TIL20 treatment group, followed by

Table 9. Effect of metaphylactic treatment with differing dosages of tilmicosin on economic production parameters–Study I.

Item	CON[1]		TIL10[2]		TIL20[3]		*P*-value[4]
	Mean	SEM	Mean	SEM	Mean	SEM	
Calf cost, $/pen	23,382.23	147.16	23,565.90	107.48	23,489.76	107.48	0.58
Mean calf cost, $/hd	467.65	2.94	471.32	2.15	469.80	2.15	0.58
Health cost, $/pen	4,880.46	746.64	3,586.70	565.91	2,994.17	565.91	0.12
Mean health cost, $/hd	97.61	14.93	71.73	11.32	59.89	11.32	0.12
Chronic cost, $/pen	643.28	197.05	575.24	157.95	287.48	157.95	0.15
Mean chronic cost, $/hd	12.87	3.94	11.51	3.16	5.75	3.16	0.15
Death cost, $/pen	3,482.56	722.13	2,123.91	558.20	1,575.89	558.20	0.09
Mean death cost, $/hd	69.65	14.44	42.48	11.16	31.52	11.16	0.09
Metaphylaxis cost, $/pen	0.00[a]	2.63	396.20[b]	1.94	789.84[c]	1.94	<0.01
Mean metaphylaxis cost, $/hd	0.00[a]	0.05	7.93[b]	0.04	15.80[c]	0.04	<0.01
Therapy cost, $/pen	754.62[a]	73.30	491.35b[b]	52.20	340.96[b]	52.20	<0.01
Mean therapy cost, $/hd	15.09[a]	1.47	9.83b[b]	1.04	6.82[b]	1.04	<0.01
Feed cost, $/pen	19,416.03	786.29	20,917.56	609.66	21,571.35	609.66	0.07
Mean feed cost, $/hd	388.32	15.73	418.35	12.19	431.43	12.19	0.07
Return, $/pen	45,608.06[a]	1,620.06	50,329.52[b]	1,298.80	52,285.67[b]	1,298.80	<0.01
Profit, $/pen	-2,070.65[a]	1,791.06	2,259.37[b]	1,412.98	4,230.39[b]	1,412.98	0.02
Mean profit, $/hd	-41.41[a]	35.82	45.19[b]	28.26	84.61[b]	28.26	0.02

[1]CON = negative control; calves did not receive metaphylactic treatment at processing.
[2]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[3]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[4]*P*-values are from the assessment of the overall treatment effect.
[a,b,c]Values within a row with different superscripts are significantly different at $P \leq 0.05$.

the TIL10 group, and the CON. Therapy cost showed an inverse relationship, whereby the CON calves had the greatest cost and calves in the TIL20 group had the lowest cost.

Conclusions

These studies demonstrated that metaphylactic treatment with tilmicosin reduced BRD associated morbidity and tended to reduce mortality. As a result of reduced morbidity there was a trend for improved feeding performance. In addition, mean profit per head was greater in cattle receiving tilmicosin metaphylaxis in Study I.

Footnotes

[a]Micotil® 300 Injection, Elanco Animal Health, Greenfield, IN
[b]Express 3®, Boehringer-Ingelheim, St. Joseph, MO
[c]Caliber® 7, Intervet/Schering-Plough, Inc., DeSoto, KS
[d]American Animal Health, Fort Worth, TX
[e]Anipro, XF Enterprises, Inc, Amarillo, TX
[f]Ivomec®, Merial, Inc., Duluth, GA
[g]Component E-C®, Elanco Animal Health, Greenfield, IN
[h]Component TE-IH with Tylan, Elanco Animal Health, Greenfield, IN

Table 10. Effects of metaphylactic treatment with differing dosages of tilmicosin on morbidity, mortality, and removal–Study II.[1]

Item	CON[2]	TIL10[3]	TIL20[4]	*P*-value[5]
No. pens	4	8	8	
No. head	200	397	400	
Mean days to first pull	10.7[a]	19.2[b]	20.2[b]	<0.01
Mean body temperature at processing °F	101.6	101.7	101.6	0.72
Body temperature at processing ≥104.0°F, n	10	14	10	
Body temperature at processing ≥104.0°F, %[6]	5.0	3.5	2.5	0.32
Bovine respiratory disease (BRD) morbidity, n	137	198	176	
BRD morbidity, %[6]	68.5[a]	49.9[b]	44.0[b]	<0.01
BRD mortality, n	1	5	9	
BRD mortality, %[6]	0.5	1.3	2.3	0.29
Non-BRD mortality, n	2	6	3	
Non-BRD mortality, %[6]	1.0	1.5	0.8	0.60
BRD removals, n	12	10	12	
BRD removals, %[6]	6.0	2.5	3.0	0.11
Non-BRD removals, n	5	12	6	
Non-BRD removals, %[6]	2.5	3.0	1.5	0.39
BRD removals and mortality, n	13	15	21	
BRD removals and mortality, %[6]	6.5	3.8	5.3	0.36
Non-BRD removals and mortality, n	7	18	9	
Non-BRD removals and mortality, %[6]	3.5	4.5	2.3	0.25
Total removals and mortality, n	20	33	30	
Total removals and mortality, %[6]	10.0	8.3	7.5	0.59

[1]Least squares mean
[2]CON = negative control; calves did not receive metaphylactic treatment at processing.
[3]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[4]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[5]*P*-values are from the assessment of the overall treatment effect.
[6]Percents reported as number of observed/total. The statistical analysis used pen as the experimental unit.
[a,b]Values within a row with different superscripts are significantly different at $P \leq 0.05$.

[i]Titanium IBR LP, Diamond Animal Health, Inc., Des Moines, IA
[j]Component T-H, Elanco Animal Health, Greenfield, IN
[k]Component E-H, Elanco Animal Health, Greenfield, IN
[l]Jencine® 4, Intervet/Schering-Plough Animal Health, DeSoto, KS
[m]Dectomax®, Pfizer Animal Health, New York, NY
[n]Synovex® Choice, Fort Dodge Animal Health, Overland Park, KS
[o]Revalor® S, Intervet/Schering-Plough Animal Health, DeSoto, KS
[p]Elector® Pour-On, Elanco Animal Health, Greenfield, IN
[q]Rumensin®, Elanco Animal Health, Greenfield, IN

Table 11. Response of feeder calves metaphylactically treated with differing dosages of tilmicosin to treatment with enrofloxacin for clinical bovine respiratory disease (BRD)–Study II.

Item	CON[2]	TIL10[3]	TIL20[4]	*P*-value[5]
No. head treated (no. head which completed the 21-day evaluation)[1]	137 (137)	198 (197)	176 (174)	
Success rate, % (n)[6]	57.7[a] (79)	72.1[b] (142)	59.8[a] (104)	0.03
Failure rate, % (n)[6]	3.6 (5)	3.6 (7)	6.3 (11)	0.36
Relapse rate, % (n)[6]	38.7[a] (53)	24.4[b] (48)	33.9[ab] (59)	0.03
Second relapse rate, % (n)[6]	13.1 (18)	7.1 (14)	8.6 (15)	0.19
New episode rate, % (n)[6]	19.0[a] (26)	10.7[b] (21)	9.2[b] (16)	0.04
BRD mortality, % of pulled (n)[6]	0.0 (0)	2.5 (5)	5.2 (9)	0.45
Non-BRD mortality, % of pulled (n)[6]	0.7 (1)	1.5 (3)	1.1 (2)	0.79
BRD removals, % of pulled (n)[6]	8.8 (12)	5.1 (10)	5.2 (9)	0.35
Non-BRD removals, % of pulled (n)[6]	3.6 (5)	3.6 (7)	2.9 (5)	0.91
BRD removals and mortality, % of pulled (n)[6]	8.8 (12)	7.6 (15)	10.3 (18)	0.66
Non-BRD removals and mortality, % of pulled (n)[6]	4.4 (6)	5.1 (10)	4.0 (7)	0.88
Total removals and mortality, % of pulled (n)[6]	13.1 (18)	12.7 (25)	14.4 (25)	0.87

[1]Calves 2479, 2505 and 2733 did not complete the 21-day evaluation period.
[2]CON = negative control; calves did not receive metaphylactic treatment at processing.
[3]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[4]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[5]*P*-values are from the assessment of the overall treatment effect.
[6]Percents reported as number of observed/total. The statistical analysis used pen as the experimental unit.
[a,b]Values within a row with different superscripts are significantly different at $P \leq 0.05$.

Table 12. Effects of metaphylactic treatment with differing dosages of tilmicosin on performance of feeder cattle: deads-and-removals-out–Study II.[1]

Item	CON[2]	TIL10[3]	TIL20[4]	*P*-value[5]
Initial body weight, lb	587.5	582.3	587.3	0.29
Final body weight, lb	1319.0	1342.1	1341.3	0.16
Average daily gain, lb	3.59	3.73	3.70	0.09
Weight gain, lb	731.4	759.7	753.7	0.09
Dry matter intake, lb	16.9	18.0	17.5	0.12
Feed conversion	4.71	4.81	4.71	0.60

[1]Least squares mean.
[2]CON = negative control; calves did not receive metaphylactic treatment at processing.
[3]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[4]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[5]*P*-values are from the assessment of the overall treatment effect.

Table 13. Effect of metaphylactic treatment with differing dosages of tilmicosin on performance of feeder cattle: deads-and-removals-in–Study II.[1]

Item	CON[2]	TIL10[3]	TIL20[4]	*P*-value[5]
Initial body weight, lb	588.4	581.8	584.3	0.26
Final body weight, lb	1187.2	1230.3	1240.0	0.21
Average daily gain, lb	3.18	3.37	3.39	0.11
Weight gain, lb	598.8	648.5	655.7	0.14
Dry matter intake, lb	16.8	17.9	17.3	0.09
Feed to gain ratio	5.31	5.32	5.13	0.50

[1]Least squares mean.
[2]CON = negative control; calves did not receive metaphylactic treatment at processing.
[3]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[4]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[5]*P*-values are from the assessment of the overall treatment effect.

Table 14. Effect of metaphylactic treatment with differing dosages of tilmicosin on hot carcass weight and percentage USDA Choice in feeder cattle –Study II.[1]

Item	CON[2]	TIL10[3]	TIL20[4]	*P*-value
No. of head	179	364	370	
Hot carcass weight, lb	815.1	823.2	822.9	0.53
Percent choice (N)	31.8%[2] (57)	39.4 (143)	41.1 (152)	0.13

[1]Least squares mean.
[2]CON = negative control; calves did not receive metaphylactic treatment at processing.
[3]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[4]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing

Table 15. Effect of metaphylactic treatment with differing dosages of tilmicosin on USDA quality grade and USDA yield grade of feeder calves–Study II.

Item	CON[1]	TIL10[2]	TIL20[3]	*P*-value[4]
Quality grade:				0.42
Choice, %	31.8	39.4	41.1	
Select, %	55.9	56.2	52.2	
Standard, %	1.7	0.8	1.6	
No roll, %	10.6	3.6	4.9	
Condemned, %	0.0	0.0	0.3	
Yield grade:				0.93
1, %	15.2	11.3	10.8	
2, %	27.5	33.1	33.9	
3, %	40.5	42.7	40.1	
4, %	15.2	11.6	13.6	
5, %	1.7	1.4	1.6	

[1]CON = negative control; calves did not receive metaphylactic treatment at processing.
[2]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[3]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[4]Overall treatment effect based on a cumulative logit logistic regression model.

[r]Tylan®, Elanco Animal Health, Greenfield, IN
[s]Baytril®, Bayer Animal Health, Shawnee Mission, KS
[t]Nuflor®, Intervet/Schering-Plough Animal Health, DeSoto, KS
[u]Biomycin 200®, Boehringer-Ingelheim, St. Joseph, MO

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Table 16. Effect of metaphylactic treatment with differing dosages of tilmicosin on economic production parameters–Study II.

Item	CON[1]		TIL10[2]		TIL20[3]		*P*-value[4]
	Mean	SEM	Mean	SEM	Mean	SEM	
Calf cost, $/pen	29,127.29	181.36	28,713.81	128.24	28,922.23	128.24	0.20
Mean calf cost, $/hd	582.55	3.63	574.28	2.56	578.45	2.56	0.20
Health cost, $/pen	3,921.75	640.53	3,487.58	550.73	3,853.28	550.73	0.66
Mean health cost, $/hd	78.44	12.81	69.75	11.01	77.07	11.01	0.66
Chronic cost, $/pen	1,908.49	379.81	1,224.85	273.09	1,014.11	273.09	0.18
Mean chronic cost, $/hd	38.17	7.60	24.50	5.46	20.28	5.46	0.18
Death cost, $/pen	464.95	372.96	826.10	311.28	902.85	311.28	0.47
Mean death cost, $/hd	9.30	7.46	16.52	6.23	18.06	6.23	0.47
Metaphylaxis cost, $/pen	0.00[a]	4.07	502.02[b]	2.88	1,010.82[c]	2.88	<0.01
Mean metaphylaxis cost, $/hd	0.00[a]	0.08	10.04[b]	0.06	20.22[c]	0.06	<0.01
Therapy cost, $/pen	1,548.31[a]	164.03	934.60[b]	154.31	925.50[b]	154.31	<0.01
Mean therapy cost, $/hd	30.97[a]	3.28	18.69[b]	3.09	18.51[b]	3.09	<0.01
Feed cost, $/pen	16,284.39	439.37	17,612.86	310.68	17,224.99	310.68	0.08
Mean feed cost, $/hd	325.69	8.79	352.26	6.21	344.50	6.21	0.08
Return, $/pen	65,890.71	1,606.13	68,100.89	1,284.90	68,816.95	1,284.90	0.24
Profit, $/pen	16,557.28	1,964.87	18,286.65	1,647.84	18,816.45	1,647.84	0.49
Mean profit, $/hd	331.15	39.30	365.73	32.96	376.33	32.96	0.49

[1]CON = negative control; calves did not receive metaphylactic treatment at processing.
[2]TIL10 = calves were metaphylactically treated with tilmicosin at 4.55 mg/lb (10 mg/kg) BW at processing.
[3]TIL20 = calves were metaphylactically treated with tilmicosin at 9.1 mg/lb (20 mg/kg) BW at processing.
[4]*P*-values are from the assessment of the overall treatment effect.
[a,b,c]Values within a row with different superscripts are significantly different at $P \leq 0.05$.