PEER REVIEWED

Efficacy of Metaphylactic Tilmicosin for Controlling Bovine Respiratory Disease in High-Risk Northern Feeder Calves

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Abstract

The objectives of this study were to: 1) evaluate the effect of metaphylactic tilmicosin on the health and performance of high-risk northern calves, and 2) determine the efficacy of tilmicosin for treatment of bovine respiratory disease (BRD) following its use in an arrival metaphylaxis program. Four-hundred crossbred steer calves weighing an average of 601 lb (273 kg) each were purchased at livestock auctions in South Dakota and Montana, and shipped to a commercial research feedlot in northern Colorado. At processing, calves were randomly assigned to one of two treatment groups: 1) nonmedicated controls or 2) metaphylaxis with tilmicosin. Cattle assigned to the metaphylaxis group were administered tilmicosin once at label dose. Control cattle received no antibiotic at processing.

Metaphylactic use of tilmicosin at processing reduced BRD morbidity compared to controls (25.5 vs 56.5%; P < .01). Average days to first pull were greater in the metaphylaxis group (13.9 vs 9.6 days; P < .01). BRD mortality and chronic rates did not differ between treatments. When calculated on a "deads out" basis, calves receiving tilmicosin at processing gained more weight during the first 28 days (3.65 vs 3.11 lb/day; 1.66 vs 1.41 kg; P < .01), and 102 days on feed (DOF) (3.85 vs 3.67 lb/day; 1.75 vs 1.67 kg; P <.01) than control calves. At harvest (191 DOF), daily gain tended to be greater (3.42 vs 3.34 lb/day; 1.55 vs 1.52 kg; P =.10) for calves in the metaphylactic tilmicosin treatment group. There were no differences in feed intake or feed conversion between groups. Hot carcass weight tended to be greater for the calves in metaphylactic treatment group (791.5 vs 777.8 lb; 359.8 vs 353.5 kg; P = .06). Other carcass traits did not differ.

When tilmicosin was used as first treatment for calves with BRD, response rates were identical for both treatment groups (86%). No differences were observed between treatment failure (6.5 vs 4.6%; P = 0.68), first relapse (7.5 vs 9.4%; P = 0.71), second relapse (4.4 vs 2.7%; P = 0.72) or new episode (11.9 vs 10.8%; P = 0.85) rates for calves in the metaphylaxis and control groups, respectively.

In this study, metaphylactic treatment with tilmicosin at processing decreased morbidity, and increased days to first treatment for those calves that subsequently required BRD therapy. Efficacy of tilmicosin as the first line therapy for BRD following its use in an on-arrival metaphylaxis program was not compromised in this study.

Résumé

Les objectifs de cette étude étaient : (1) d'évaluer l'effet de l'administration métaphylactique de tilmicosine sur la santé et la performance de veaux nordiques d'engraissement à haut risque, et (2) de déterminer l'efficacité potentielle de la tilmicosine pour le traitement du complexe respiratoire bovin (CRB) suite à son utilisation métaphylactique dès l'arrivée des animaux. Un total de 400 bouvillons de race croisée, pesant en moyenne 273 kg (601 lb) chacun, ont été achetés dans des encans de bétail du Dakota du sud et du Montana et acheminés dans un parc d'engraissement commercial de recherche au nord du Colorado. À leur arrivée, les veaux ont été alloués aléatoirement dans l'un des

deux groupes suivants: (1) groupe témoin sans médication, et (2) groupe traité recevant une administration métaphylactique de tilmicosine. Les veaux du groupe traité ont reçu une simple administration de tilmicosine à la dose recommandée. Les veaux du groupe témoin ne recevaient pas d'antibiotique à l'arrivée.

L'administration métaphylactique de tilmicosine à l'arrivée des animaux réduisait la morbidité par rapport au groupe témoin (25.5% versus 56.5%; P < .01). Le nombre de jours moyen avant le premier traitement était plus grand dans le groupe traité (13.9 versus 9.6 jours; P < .01). Le taux de mortalité associé au CRB et les taux chroniques n'étaient pas différents entre les deux groupes. N'incluant que les animaux en vie, les veaux recevant la tilmicosine à l'arrivée gagnaient plus de poids que les veaux témoins durant les 28 premiers jours (3.65 versus 3.11 lb/jour; 1.66 versus 1.41 kg/jour; P < .01) et durant les 102 premiers jours d'engraissement (3.85 versus 3.34 lb/jour; 1.75 versus 1.67 kg/jour; P < .01). À la fin de l'engraissement (191 jours), il y avait une tendance à un gain de poids plus élevé chez les veaux traités que chez les veaux témoins (3.42 versus 3.34 lb/jour; 1.55 versus 1.52 kg/jour; P = .10). Il n'y avait pas de différence dans la prise alimentaire ou dans le taux de conversion alimentaire entre les deux groupes. La masse de la carcasse chaude était un peu plus grande dans le groupe traité que dans le groupe témoin (791.5 versus 777.6 lb; 359.8 versus 353.5 kg; P = .06). Les autres caractéristiques des carcasses étaient similaires entre les deux groupes.

Lorsque la tilmicosine était utilisée en première ligne pour le traitement des veaux avec le CRB, le taux de réponse était similaire dans les deux groupes (86%). Il n'y avait également aucune différence entre les groupes traités et témoins au niveau du risque d'échec du traitement (6.5 versus 4.6%; P = .68), du taux de première rechute (7.5 versus 9.4%; P = 0.71), du taux de seconde rechute (4.4 versus 2.7%; P = 0.72) ou du taux de nouvelle récidive (11.9 versus 10.8%; P = 0.85).

Dans cette étude, le traitement métaphylactique avec la tilmicosine dès l'arrivée des animaux a réduit la morbidité et augmenté le nombre de jours avant le premier traitement pour les veaux qui ont nécessité subséquemment un traitement contre le CRB. L'efficacité potentielle de la tilmicosine comme traitement de première ligne contre le CRB, suite à son utilisation métaphylactique lors de l'arrivée des animaux, n'a pas été compromise dans cette étude.

Introduction

Bovine respiratory disease (BRD) has a significant effect on health and performance of beef calves. Economic losses can be significant. Direct economic losses result from treatment costs, including supportive therapy, labor associated with surveillance and treatment, chronic cases marketed at a discount, and BRD-associated mortality. Indirect losses are due to reduced gain, poorer feed conversion and reduced carcass quality. In the 2000-2001 Texas A&M Ranch to Rail program, losses due to BRD were estimated to be $151.18 per head for sick cattle.[19] Metaphylactic use of tilmicosin is a well-established practice to control BRD in high-risk southeastern calves.[2,3,5,6,12,16,24,27] The purpose of this study was to: 1) determine if metaphylactic treatment with tilmicosin is a justifiable practice in auction market calves of northern US origin, and 2) determine the usefulness of tilmicosin for treatment of BRD following its use in an arrival metaphylaxis program.

Materials and Methods

Experimental design

In November 1998, four-hundred British and Continental crossbred steer calves were purchased from livestock auctions in South Dakota and Montana, and shipped to a commercial research feedlot in northeastern Colorado. These steers were considered to be at high risk for developing BRD. The average body weight of the calves when purchased was 601 lb (273 kg). Shrink during transit was 4.6%. Calves were penned at the research feedlot by truckload and allowed to rest for approximately 36 hours prior to allotment to treatment and processing. Hay and water were offered *ad libitum.* No calves were diagnosed or treated for BRD during the rest period.

At processing, calves were assigned within truckload to one of two treatment groups: 1) non-medicated control group or 2) metaphylaxis group. Randomization to treatment was done by using a computer generated complete block design based on chute order of the calves. Steers assigned to a metaphylaxis group were administered tilmicosin[a] once by subcutaneous injection in the neck at 4.55 mg/lb (10 mg/kg) body weight. Control steers received no antibiotic at processing. During processing, calves were individually weighed and uniquely identified with an ear tag. Rectal temperatures were measured and recorded. All calves were vaccinated with a modified-live virus IBR/BVD[b] vaccine, implanted[c] and treated with an endectocide[d] for internal and external parasite control. There were four replicates (50 head/pen) of each treatment.

Steers were observed daily for signs of BRD by trained feedlot personnel who were blinded to treatment. Calves with a clinical impression score (CIS) ≥ 1 (Table 1) were taken to the hospital and the rectal temperature was taken. If the rectal temperature was 104°F (40°C) or greater, the calf was treated with tilmicosin (4.55 mg/lb) and returned to its home pen. Calves with a rectal temperature less than 104°F were returned to

Table 1. Description of clinical illness scoring system.

Clinical illness score	Description	Clinical appearance
0	Normal	No abnormal clinical signs
1	Slightly ill	Mildly abnormal character of respiration. Dyspnea may be combined with some depression, gauntness, nasal and/or ocular discharges. Hair coat may be rough.
2	Moderately ill	Moderately abnormal character of respiration. Noticeable dyspnea, gauntness, depression, and nasal and/or ocular discharges. Hair coat may be rough.
3	Severely ill	Severely abnormal character of respiration. Pronounced dyspnea, depression and gauntness. Nasal and/or ocular discharges. Hair coat may be rough.
4	Moribund	Down and at the point of death. Mouth breathing.

their home pen without therapy. Calves in the metaphylaxis group were not treated prior to 48 hours after processing. Treatment failures and relapses (Table 2) were retreated with long-acting oxytetracycline[e] at 9 mg/lb (20 mg/kg) bodyweight given subcutaneously. Second relapses and new episodes (Table 2) were retreated with tilmicosin at 4.55 mg/lb.

The standard feedlot feeding protocol was used, and calves were offered finisher ration by 43 days on feed (Table 3). Monensin[f] and tylosin[g] were included in all diets. The cattle were re-implanted[h] and administered modified-live virus IBR vaccine[i] at 102 days on feed. All cattle were harvested at 191 days on feed.

Observations during the trial included rectal temperature at processing, BRD morbidity and mortality, days to first pull, response to first therapy, body weight on days 28, 102 and 191 (harvest), and dry matter consumption (pen basis). Carcass parameters, including hot carcass weight, dressing percent, marbling score, ribeye area, backfat thickness, USDA quality and yield grade, and kidney, pelvic and heart fat, were recorded at harvest. All animals that died during the trial were necropsied by the attending veterinarian (KCR).

Statistical analysis

Data were analyzed by analysis of variance using the General Linear Model procedure of SAS.[25] The model included treatment, replication, and treatment x replication as sources of variation. Prior to the analysis of variance, the pen proportions for morbidity, mortality, treatment success rate, new episodes, and treatment failure/relapse rate were re-expressed with the arcsine transformation typically used to stabilize the variance of proportions. Specifically, the transformation was the arcsine of the square root of the observed proportion in each pen. Because the number of animals included in the analysis of the treatment success and the treatment failure/relapse rates differed among pens, a weighted analysis was used to test for differences among treatment groups.

Statistical significance was declared when $P \leq .05$. Differences where $P > .05$, but $\leq .10$, were described as "approaching significance", or trends.

Results and Discussion

The BRD morbidity rate for steers in the metaphylaxis group was significantly lower than the control group (25.5 vs 56.5%; P<.01; Table 4). The magnitude of reduction in BRD morbidity is similar to that reported by other researchers.[4,5,6,12-14,17,18,23,24,28]

During the first 28 days of the study, the average days to first pull for BRD was greater in the metaphylaxis group (13.9 vs 9.6 days; P<0.1). There was no difference in respiratory mortality (1.0 vs 0.0%; P=.39) or the chronic rate (0.5 vs 0.5%) between the two groups. The non-BRD mortality rate was less in the metaphylaxis group as compared to the control group (1.0 vs 2.5%; P=.06). In the metaphylaxis group, non-BRD mortalities included one bloat and one central nervous system infection. There were five non-BRD mortalities in the control group; four bloats and one death resulting from an ascending toe abscess.

The effect of metaphylactic treatment with tilmicosin at processing on calf performance is presented in Table 5. When expressed on a "deads out" basis (i.e., data from all animals that died are removed from the performance calculations), average daily gain (ADG) during the first 28 days (3.65 vs 3.11 lb/day; 1.66 vs 1.41 kg; P <.01) and 102 days (3.85 vs 3.67 lb/day; 1.75 vs

Table 2. Therapeutic response categories.

Therapy response variable	Description
Treatment success	An animal that is fully recovered following initial antibiotic therapy period, no additional therapy required within 21 days of initial therapy.
Treatment failure	An animal that at 72 hours post initial therapy, clinical illness score (CIS) is greater than time 0 CIS, or CIS is 1 or greater and rectal temperature is ≥ 104°F (40°C).
Relapse	An animal that is deemed recovered at 72 hours post initial therapy, but is observed with signs of BRD (CIS ≥ 1), has a rectal temperature ≥ 104°F (40°C), and is ≤ 21 days from the initial therapy.
Second relapse	An animal that exhibits clinical signs of BRD within 21 days of second therapy.
New episode	An animal that is observed with signs of BRD (CIS ≥ 1), and has a recal temperature ≥ 104° F (40°C), and necessitates treatment > 21 days following the previous therapy.

Table 3. Feedlot ration composition, starter (#1) through finisher (#4).

		% in ration, as fed			
Ingredient	% DM	#1	#2	#3	#4
Alfalfa hay	88.5	46.7	29.6	17.7	10.5
Flaked corn	78.0	39.5	29.3	17.9	10.5
Molasses/steep	60.0	10.0	7.0	4.0	2.0
Starter supplement	92.7	3.8	–	–	–
High moisture corn	74.2	–	29.3	53.8	69.3
Finisher supplement	93.1	–	3.8	5.1	6.2
Fat	99.0	–	1.0	1.5	1.5
Days ration fed	–	1-23	23-33	33-43	43-191

1.67 kg; P<.01) was significantly greater for calves in the metaphylaxis group than the controls. At harvest, daily gain tended to be greater (3.42 vs 3.34 lb/day; 1.55 vs 1.52 kg; P = .10) for calves in the metaphylaxis group as compared to controls. There were no differences in dry matter intake or feed conversion between treatment groups. When performance data were calculated on a "deads in" basis (calves that died were included in performance calculations), there was no difference in final body weight, ADG or feed conversion (Table 5).

Average daily gain was determined within each treatment group for those calves that remained healthy (never treated) through 102 days on feed (DOF), and calves that were treated for respiratory disease (Table 6). Calves treated with tilmicosin at processing that remained healthy had greater ADG compared to healthy non-medicated controls (3.91 vs 3.71 lb/day; 1.78 vs 1.69 kg; P<.01). This improvement in gain of seemingly healthy calves supports the previous observation that there is significant subclinical respiratory disease in feedlot cattle.[27] Administration of tilmicosin for control of BRD may reduce the occurrence of subclinical respiratory disease, resulting in greater weight gain. Similarly, sick calves that were treated for BRD at least one time had higher average daily gain (3.72 vs 3.63 lb/day; 1.69 vs 1.65 kg; P <.01) when treated with tilmicosin at processing than non-medicated controls. Other studies have shown that morbid cattle do not gain as well as cattle that remain healthy,[1,23] which is in agreement with results shown in Table 6.

The effect of metaphylactic treatment with tilmicosin at arrival processing on carcass parameters are presented in Table 7. Hot carcass weight was 791.5 and 777.8 lb (359.8 vs 353.5 kg; P=.06) for metaphylaxis and control calves, respectively. Other carcass traits measured did not differ.

Steers treated at processing with tilmicosin that remained healthy throughout the feeding period (never treated) had heavier hot carcass weights at harvest (797.4 lb; 362.5 kg vs 778.5 lb; 353.9 kg) (P=.05) compared to healthy, non-medicated controls (Table 8). Heavier carcass weights in the tilmicosin treatment

Table 4. Effect of metaphylaxis with tilmicosin at processing on morbidity and mortality in high-risk northern calves fed to harvest.

	Treatment			
Item	Non-medicated control	Metaphylaxis	SE[a]	P-value
No. head	200	200		
No. pens	4	4		
Temperature≥ 104° F at processing (%)	2.5	3.0		
Days to first pull	9.6	13.9	.23	<.01
Respiratory morbidity				
Days 1-28 (%)	56.5	25.5	3.58	<.01
Days 29-191 (%)	5.0	4.5	1.76	.85
Therapeutic response				
Treatment success (%)	86.0	86.0	5.53	1.0
Treatment failures (%)	4.6	6.5	2.98	.68
Relapses (%)	9.4	7.5	3.20	.71
Second relapses (%)	2.7	4.4	3.02	.72
New episodes (%)	10.8	11.9	3.80	.85
Mortality				
BRD (%)	0	1.0	.71	.39
Non-BRD (%)	2.5	1.0	.35	.06
Removals				
BRD-chronics (%)	0.5	0.5	.58	1.0
Non-BRD chronics (%)	1.0	1.0	.82	1.0

[a]Standard error of the mean

group may result from a reduction in subclinical respiratory disease, resulting in better gain and therefore heavier carcasses at harvest. There was no difference in hot carcass weight between the two treatment groups in morbid calves (pulled and treated one or more times).

The second objective of this study was to evaluate the use of tilmicosin as the first-line BRD treatment following its metaphylactic use at processing. The response rate to treatment with tilmicosin as first therapy for BRD was identical (86.0%) for both the metaphylaxis and control groups (Table 4), indicating that in this study the metaphylactic use of tilmicosin at processing did not compromise its effectiveness as a subsequent first-line therapeutic for BRD. This finding has been observed in other studies.[13,16,20-23,27] Furthermore, no differences were observed in treatment failure (6.5 vs 4.6%; P=0.68), first relapse (7.5 vs 9.4%; P=0.71), second relapse (4.4 vs 2.7%; P=0.72) or new episode (11.9 vs 10.8%; P=0.85) rates between the metaphylaxis and control groups, respectively.

In this study using northern auction-origin calves, peak BRD morbidity occurred greater than seven days post-arrival (Figures 1 and 2). In spite of the significant time interval between metaphylaxis and the onset of clinical disease, the incidence of BRD was still significantly lower in calves which received tilmicosin at processing as compared to controls. Administration of tilmicosin can reduce the number of *Mannheimia haemolytica* organisms in nasal secretions for up to six days following treatment.[7,8] This suggests that fewer organisms may be available to cause infection of the calf or to infect other calves. Metaphylactic treatment at processing allows calves more time to adapt to feed before peak clinical illness occurs. As a result, calves should be in better nutritional status before peak disease challenge occurs. Improved nutritional status may correlate with improved immunity. In addition, control of BRD for several days following metaphylaxis may be associated with the accumulation of the antibiotic in alveolar macrophages and the neutrophils for at least 14 days.[9,10]

Table 5. Effect of metaphylaxis with tilmicosin at processing on feedlot performance of high-risk northern calves fed to harvest.

	Treatment			
Item	Non-medicated control	Metaphylaxis	SE[a]	P-value
Deads out:				
Initial wt (lb)	579.2	578.9	3.49	.95
Final wt. (lb)	1216.1	1231.5	3.17	<.05
Daily gain (lb)				
0-28 days	3.11	3.65	.06	<.01
0-102 days	3.67	3.85	.01	<.01
0-191 days	3.34	3.42	.03	.10
DM intake (lb)	18.8	18.8	.38	.99
Feed conversion	5.63	5.50	.10	.44
Deads in:				
Initial wt. (lb)	578.8	579.8	3.92	.88
Final wt. (lb)	1191.4	1206.5	11.20	.41
Daily gain (lb) (0-191 days)	3.21	3.29	.07	.52
Feed conversion	5.74	5.62	.14	.60

[a]Standard error of the mean

Table 6. Effect of metaphylaxis with tilmicosin at processing on average daily gain (ADG) of healthy and sick calves at re-implant (102 DOF).

	Treatment			
Item	Non-medicated control	Metaphylaxis	SE[a]	P-value
ADG (lb), healthy, never treated, (n)	3.71 (76)	3.91 (139)	.008	<.01
ADG (lb), sick, pulled and treated 1 or more times, (n)	3.63 (120)	3.72 (58)	.010	<.01

[a]Standard error of the mean

Conclusions

Results of this study suggest that metaphylactic treatment with tilmicosin at processing decreases morbidity and increases days to first treatment in high-risk northern calves. Calves treated with tilmicosin at processing had higher interim average daily gain (through day 102), and tended to have heavier hot carcass weights compared to controls. Calves treated with tilmicosin at processing, and never observed with BRD, had higher live-weight gain and heavier carcass weights compared to control calves never observed with BRD. Metaphylactic use of tilmicosin at on-arrival processing did not compromise the effectiveness of the drug as a subsequent first-line therapy for BRD in northern, high-risk calves.

Footnotes

[a]Micotil® 300, Elanco Animal Health, Indianapolis, IN 46240
[b]Bovi-Shield™ IBR/BVD, Pfizer Animal Health, Overland Park, KS 66214
[c]Component® E-S, VetLife, Ivy Animal Health, Overland Park, KS 66214
[d]Dectomax®, Pfizer Animal Health, Exton, PA 19341
[e]Bio-Mycin® 200, Boehringer Ingelheim Vetmedica, St. Joseph, MO 64506

Table 7. Effect of metaphylaxis with tilmicosin at processing on carcass parameters in high risk-northern calves fed to harvest.

	Treatment			
	Non-medicated control	Metaphylaxis	SE[a]	P-value
Hot carcass wt (lb)	777.8	791.5	3.33	.06
Dressing percentage	64.0	64.3	.15	.23
Ribeye area (sq. in.)	13.1	13.2	.07	.22
USDA yield	2.4	2.4	.05	1.0
Marbling score[b]	4.4	4.4	.07	.81
Back fat thickness (in.)	0.45	0.45	.01	.77
% KPH fat	1.98	1.98	.01	1.0
% Choice or better	66.8	65.8	3.88	.87

[a]Standard error of the mean
[b]Marbling score: 4 =small, 5 = modest

Table 8. Effect of metaphylaxis with tilmicosin at processing on hot carcass weight (HCW) of healthy and sick calves at harvest. (191 DOF).

	Treatment			
Item	Non-medicated control	Metaphylaxis	SE[a]	P-value
HCW (lb) healthy, never treated, (n)	778.5 (75)	797.4 (138)	4.12	<.05
HCW (lb) sick, pulled and treated 1 or more times, (n)	776.9 (117)	779.2 (55)	7.77	.84

[a]Standard error of the mean

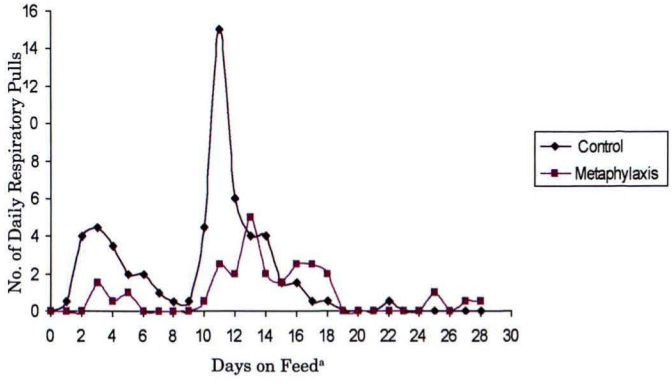

Figure 1. Effect of metaphylaxis with tilmicosin at processing on daily bovine respiratory disease pulls in northern calves during the first 28 days on feed.
[a]Day 1 = 24 hours post-processing

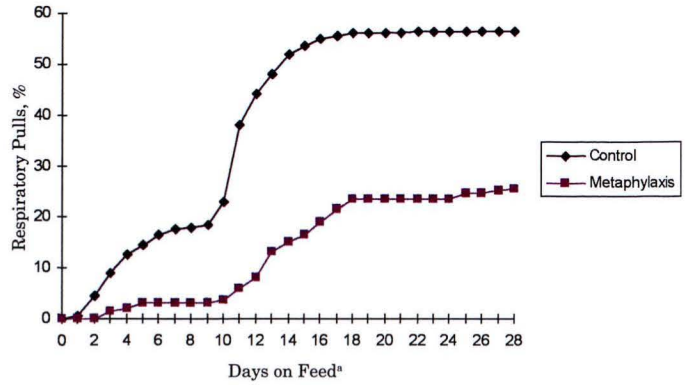

Figure 2. Effect of metaphylaxis with tilmicosin at processing on cumulative bovine respiratory disease pulls in northern calves during the first 28 days on feed.
[a]Day1 = 24 hours post-processing

[f]Rumensin®, Elanco Animal Health, Indianapolis, IN 46240
[g]Tylan®, Elanco Animal Health, Indianapolis, IN 46240
[h]Component® TE-S, VetLife, Ivy Animal Health, Overland Park, KS 66214
[i]Bovi-Shield™ IBR, Pfizer Animal Health, Exton, PA 19341

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