Comparison of the effects of LONGRANGETM and DECTOMAXTM on grazing performance and parasite burden in stocker cattle

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ABSTRACT

The efficacy of a single injection of an extended-release formulation of eprinomectin (LONGRANGETM) was evaluated against a single injection of doramectin (DECTOMAXTM) in 520, castrate male, crossbred feeder steers grazing native grass in the Flint Hills region of Kansas. Animals were randomly assigned to one of two treatment groups: extended release eprionmectin (LONGRANGE,TM 50mg/mL) or injectable doramectin (DECTOMAX,TM 10mg/mL), and were then allocated to one of nine different grazing units. Animals were weighed individually and a rectal fecal samples were collected from a randomly selected 25% of the study animals on study day 0 and at the end of the study (day 76).

Initial body weight was not significantly different between treatments (P = 0.89): eprinomectin, 622 lbs and doramectin, 623 lbs. The final body weight of cattle recieveing eprinomectin was nummerically greater than doramectin at 819 and 796 lbs, respectively (P = 0.11). Cattle recieveing eprinomectin had a statistically signifincant higher average daily gain (2.59 lbs / day) than those recieveing doramectin (2.27 lbs / day) prior to pasture turnout (P = 0.02). No statistical differences in fecal egg counts were noted between treatment groups at treatment allocation (day 0, P = 0.71), nor at the conclusion of the study (day 76, P = 0.87). The extended-release eprinomectin (LONGRANGETM) administered prior to pasture turnout resulted in increased average daily gain as compared to those cattle recieving

doramectin (DECTOMAXTM) in this study.

INTRODUCTION

Gastrointestinal nematode burden is among the most economically deletrious causes of parasitism affecting cattle grazing temperate grasslands. Cattle transported to the Flint Hills region of the United States for the grazing season are often burdened by parasites on arrival due to the geographical location of their source of origin and managment conditions, and therefore, may be subjected to a continued exposure to infective larvae in the environment. Numerous studies have shown a significant positive association between the use of anthelmintics and cattle growth rate and performace over the grazing season.[1-5] Additionally, production benefits from the use of sustained release anthelmintics have been demonstrated.[6,7]

Eprinomectin is a highly effective semisynthetic anthelmintic of the avermectin family. The topical formulation has been a mainstay in strategic gastrointestional deworming protocols in cattle due to it's persistent activity.[8] An eprinomectin extended-release injection (ERI) formulation was recently developed by Merial to prolong the beneficial effects of it's parasiticidal acitvity. When dosed at 1 mg/kg subcutaneously, the pharmacokinetics are such that there is an early peak of active ingredient avalibility in the plasma within 4 days of adminstration and a second peak occurs again around 90-120 days post dosing.[9]

Eprinomectin ERI has shown a consistent and efficacious endectocidal effect against larvae and eggs of gastrointestinal nematodes in naturally occuring challenge conditions, and has also been associated with a signigicant improvement in weight gain when compared to a placebo control.[10] However, additional investigation is warranted to ascertain the effects of eprinomectin ERI versus a postive control. To that end, the objective of this study was to determine the effects on nematode burden and production benefits of eprinomectin ERI versus a single injection of doramectin.

MATERIALS AND METHODS

Animals

Five-hundred twenty, castrate male, crossbred feeder steers were sourced from auction markets in the midwest and shipped via a commercial transportation line to the the Test Site (Veterinary & Biomedical Research Center Ranch; Manhattan, KS). Animals were randomly assigned to one of two treatment groups; Eprionmectin ERI (LR, LONGRANGE, 50mg/mL) or injectable doramectin (DECT, DECTOMAX, 10mg/mL), and then allocated to one of nine different grazing units. Treatment groups were homogenous within grazing unit. Animals were weighed individually, and rectal fecal samples were collected from a randomly selected 25% of the study animals on study day 0 and again on study day 76.

Management

This study protocol was reviewed and approved by the Instituional Animal Care and Use Commitee of Veterinary & Biomedical Research Center, Inc.

On study day 0, cattle were weighed individually and administered a steriod implant (Revalor-G; Merck Animal Health; Summit, NJ) and identificated with a uniquely numbered dangle ear tag. Animals randomly selected for fecal samples were given an additional uniquely numbered Fecal ID dangle ear tag crossreferenced with the Individual ID dangle ear tag. Cattle were randomly assigned to treatment via a randomization schedule generated by Midwest Veterinary Services, Inc (Oakland, NE) Quality Assurance personnel. Animals were allocated to treatment in a 2.5:1 ratio of LR to DECT, respectively.

Treatment was comprised of either eprinomectin ERI injected subcutanesouly at the rate of 1mg/kg of body weight (LR) or doramectin injected subcutaneously at the rate of 200 mcg/kg (DECT). Pasture units were filled sequnentially and pairwise by treatment to headcounts resulting in a similar stocking densitiy. All animals within a pasture unit belonged to the same treatment group. Animals were moved overland

as a group to their assigned pasture unit after initial processing. On study day 76, cattle were moved overland as a group from their assinged pasture unit to the processing area where they were they were weighed fecal samples were collected. Scale accuracy was verified on each weigh day utilizing scale check weights to be within 5% of the known weight value.

Fecal Samples

Rectal fecal grab samples were collected at random from 25% of the study population according to a randomization schedule generated by the Quality Assurance Unit of Midwest Veterinary Services, Inc. Samples were collected and stored in accordance with internal standard operating procedures. In brief, 5-10 grams of fresh feces were removed using a double-gloved hand from the rectum while the animal was restrained. The outer glove, containing the fecal sample, was removed and placed into a whirl pack, sealed, and placed on ice-packs in a cooler for trasnport to the laboratory for processing. A clean, exam glove, free from any fecal matter was used for each animal.

A McMaster's egg per gram technique was performed due to the difficulty to accurately count high numbers of eggs. For the McMaster egg count, 3 grams of feces was mixed with 15 mL of water and poured through a strainer. The strained material was centrifuged in a 15-mL centrifuge tube at 1,500 rpm for approximately 2 minutes. Next, the sediment was mixed in 10 mL of flotation solution in a beaker and another 32 ml of flotation solution was added. The mixture was then stirred and a portion was collected via transfer pipette and added to a McMaster slide, where it was read at 100X magnification on a compound microscope. The McMaster slide has two engraved grids; all eggs seen within both grids were counted with the total number multiplied by 50 to give an egg per gram count.

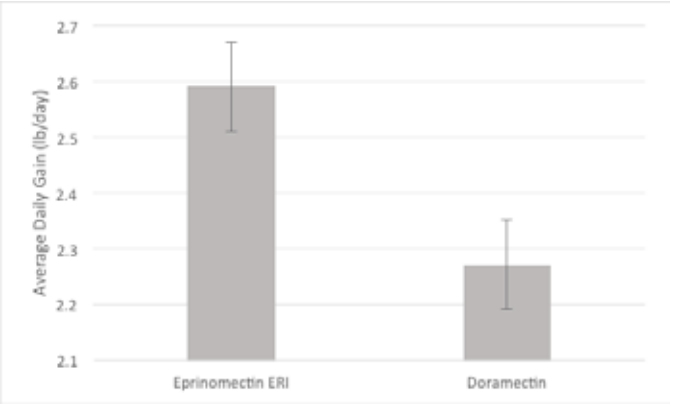
Procedures for fecal processing for Nematode propagation involved moistening fecal bags with added vermiculite to a consistency such that a ball can be formed with the mixture. The bags were mixed thoroughly and spread on date stamped stainless steel bread trays at a depth less than 2 inches deep throughout with three to five, 3-inch air slits for aeration. Trays were incubated at room temperature (70-72˚F) for 10-14 days. Fecal culture samples were broken up and placed into Baerman funnels lined with moistened muslin cloth and connected to glass tubes with rubber tubing. The funnels were left undisturbed for 8-10 hours in order to allow the L3 larvae to migrate through the tubing into the glass tubes.

Worms were transferred to beakers where dilute HCl was mixed with sediment to kill any free living soil nematodes, bacteria, or fungi. A Whatman #4 funnel apparatus, filter paper, and 50 µ mesh was connected to a vacuum flask and the larval suspension poured over the apparatus for larval collection. Larvae migrated overnight into the collection device and were removed from the supernatant. Identification and enumeration were performed by using a standard dilution method, counting the number of larvae in 100 or 200 µL on a slide by use of a microscope and calculated to the number of larvae in 1 mL.

Statistical Analysis and Data Management

Performance related variables were analyzed using the Mixed procedures of SAS (SAS Version 9.3, SAS Institute, Cary, NC) including a fixed effect for treatment. Statistical analysis used pasture level results as the analyzed variable. Fecal egg counts were analyzed using nonparametric analysis and hypothesis testing conducted utilizing the Wilcoxon Rank Sum test. Descriptive statistics were caluated for coproculture results. Fecal egg counts were transformed to the natural logarithim + 1 (Williams mean) for analysis. Average daily gain was calculated as inital weight subtracted from final weight, divided by the number of grazing days. Individual level measurements were averaged by pasture utilizing Proc Means before hyptohesis testing and the pasture was treated as the experimental unit for analysis

Figure 1. *Bar graph comparison of average daily gain (lb/day) in stocker cattle grazing native grasses on the Flint Hills of Kansas. Cattle were administered either extended release injectable eprinomectin or doramectin prior to pasture turnout. (P = 0.02)*



purposes since animals were randomized to treatment and systematically assigned to pasture as they were presented to the chute based on a predetermined patsure fill order. Significance was declared at $P \leq 0.05$.

RESULTS

Treatment, pasture, and head count data may be viewed in Table 1. Initial weight (622 and 623 lbs for LR and DECT, respectively; SE = 7.8, P = 0.89) and final weight (819 and 796 lbs for LR and DECT, respectively; SE = 9.5, P = 0.11) was not significantly different between treatment groups. However, a significant effect was detected between treatment groups for average daily gain (2.59 and 2.27 for LR and DECT, respectively; SE = 0.08, P = 0.02). Day 0 and Day 76 fecal egg counts were not significantly different for either treatment.

Least square means, their respective standard errors, and Type III Fixed Effect P-values can be viewed in Table 2 for body weight and average daily gain. Intial body weight was not significantly different between treatments (P=0.89); LR, 622 lbs and DECT, 623 lbs. The final body weight of

Table 1. *Summary of treatment, pasture, and fecal sampling data for crossbred feeder steers treated with either extended release injectable eprinomectin (LR) or injectable doramectin (DECT) before grazing native flint hills range.*

Pasture ID	Treatment	Head Count	No. of Fecal Samples[1]	No. Pooled Coproculture Samples[2]
16	LR	55	14	2
14	DECT	65	17	3
15	LR	55	14	2
12	LR	110	28	3
33	DECT	25	7	1
32	DECT	30	8	1
17	LR	120	30	3
24	DECT	25	7	1
22	LR	35	9	1
Total	-	520	134	17

[1]*Number of fecal samples collected at initial processing based on a random 25% of study population sampling procedure.*
[2]*Number of pooled individual coproculture samples from each pasture unit.*

Table 2. *Summary of performance data for crossbred feeder steers treated with either extended release injectable eprinomectin (LR) or injectable doramectin (DECT) before grazing native flint hills range for a 76 day period beginning on 02MAY2014.*

Item	Treatment			
	LR	DECT	SE	*P*
Initial Weight, lbs.	622	623	7.8	0.89
Final Weight, lbs.	819	796	9.5	0.11
ADG, lbs.[1]	2.59	2.27	0.08	0.02
DOP[2]	76	76	-	-
[1]Average Daily Gain				
[2]Days on Pasture				

Table 3. *Fecal Egg Counts for crossbred feeder steers treated with either extended release injectable eprinomectin (LR) or injectable doramectin (DECT) before grazing native flint hills range for a 76 day period beginning on 02MAY2014.*

Treatment	Mean Eggs per Gram of Feces[1]	
Pasture ID	Day 0	Day 76
LR	143	1
12	411	2
15	25	0
16	93	0
17	10	0
22	17	0
DECT	135	1
14	118	0
24	14	0
32	50	7
33	393	0
Grand Total	141	<1

[1]No significant difference between treatments within each respective sampling day was detected (P > 0.70)

LR was nummerically greater than DECT at 819 and 796 pounds, respectively (P = 0.11). Cattle recieveing LR had a statistically signifincant higher average daily gain (2.59 lb/day) than those recieveing DECT (2.27 lb/day) prior to pasture turnout (P = 0.02), displayed graphically in Figure 1.

No statistical differences in fecal egg counts were noted between treatment groups at treatment allocation (day 0, P = 0.71) nor at the conclusion of the study (day 76, P = 0.87). Raw mean fecal eggs counts by pasture and treatment may be viewed in Table 3. Qualatative results from pooled coproculutre analysis may be viewed in Table 4.

DISCUSSION

The objective of this study was to compare both the production effects and nematode burden in stocker cattle administered either

Table 4. *Pooled coproculture results for crossbred feeder steers treated with either extended release injectable eprinomectin (LR) or injectable doramectin (DECT) before grazing native flint hills range for a 76 day period beginning on 02MAY2014.*

Day 0							Day 76			
Pool #	Pasture	Trt	Trichostrongylus spp.	Cooperia spp.	Haemonchus spp.	Nematodirus spp.	Trichostrongylus spp.	Cooperia spp.	Haemonchus spp.	Nematodirus spp.
1	12	LR	+	+	+	+	+	-	+	-
2	12		+	+	+	-	-	-	+	-
3	12		+	+	+	-	-	-	+	-
4	14	DECT	-	-	+	+	-	-	+	-
5	14		-	+	+	+	-	-	+	-
6	14		-	+	+	-	+	-	+	-
7	15	LR	+	-	+	-	-	-	+	-
8	15		+	-	+	-	-	-	+	-
9	16	LR	+	+	-	-	-	-	+	-
10	16		+	-	+	-	-	-	+	-
12	17	LR	+	-	-	-	-	-	+	-
13	17		+	-	+	-	-	-	+	-
14	17		-	-	-	-	+	-	+	-
15	22	LR	-	-	+	-	-	-	+	-
16	24	DECT	+	-	-	-	-	-	+	-
17	32	DECT	+	-	-	-	+	-	+	-
11	33	DECT	-	-	-	-	-	-	+	-
Positive Pastures (%) LR			82	36	73	9	18	0	100	0
Positive Pastures (%) DECT			33	33	50	33	33	0	100	0

eprinomectin ERI or doramectin at the begining and end of a grazing period in the Flint Hills region of Kansas. It is evident that there was parasitism in both treatment groups on study day 0 as can be appreciated in Tables 3 and 4. Eprinomectin ERI and doramectin treated cattle had very low egg counts at the end of the study. There were no statistical differences in eggs per gram of feces nor in the pooled coproculture results between treatments. However, cattle administered LR had a significantly higher ADG than those cattle receiving DECT. This suggests an effect of LR on performance that was not accounted for in this study by standard fecal egg counts and coproculture.

Study day 76 pooled coproculture resulted in 100% positive samples for Haemonchus spp across treatments and pastures. This finding is unique compared to similar studies utilizing eprinomectin ERI against a negative control.[10,11] One potential explanation for this finding could be due to differences in study timing, with this current study ending at 76 days post-dosing and other similar studies concluding at 120 days post-dosing. The observation of a significant performance advantage in favor of eprinomectin ERI compared to opposing treatments, despite the abscence of readily apparent diffferences in parasite load is not isolated to the current report, however. In a comparison of eprinomectin ERI to vehicle treated controls, Kunkle et al. reported a significant difference in weight gain between treatments despite very low egg counts at day 0 and day 120 of their studies.[12]

Similar to other studies,[1,10,12] the reduced shedding of nematode eggs from cattle treated both with eprinomectin ERI and doramectin in this study serves another large benefit, reducing pasture contaimination and subsequent parasite challenge in following grazing seasons.

Several previous reports have shown eprinomectin ERI as an efficacous anthelmintic as compared to untreated controls.[10-12] To the authors‘ knowledge, this current report is the first of its kind to compare eprinomectin ERI to a positive control.

There are some acknowledged limitations of this study design as compared to previous similar reports; the short duration of this study (76 days) and the lack of negative controls do not allow an assessment of pasture parasite challenge load. The second peak of eprinomectin in the plasma is expected around 70 days post dosing. This study ended at 76 days post-dosing, which might lead one to conclude that the second peak of eprinomectin was just occuring and the full production benefits of this ERI might not have been fully recognized in this study. It is important to note that differences in production outcomes are conservative due the analysis. Weight gain data and average daily gain were analyzed on a pasture level basis. This will underestimate the effect on individual animals.

With respect to FEC, traditional statistical analysis have been performed by log transformation of results and analysis by ANOVA. The non-parametric analysis used in this study is a conservative method that is less likely to detect differences. The dramatic decrease in FEC show that both products were effective in this study. Additionally, without the use of negative controls, it is not possible to judge the parasite challenge provided by each pasture through monitoring of tracer cattle as described in previous studies.[10-12]

In conclusion, eprinomectin ERI demonstrated itself a safe and effective anthelmintic that increased productivity as compared to doramectin in this study.

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