Effects of extended-release eprinomectin on fescue toxicosis, performance, and reproduction on fall-calving beef cows

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ABSTRACT: The objective of this experiment was to evaluate effects of extended-release eprinomectin on fescue toxicosis and impacts on performance and reproduction in fall-calving beef cows. Fall-calving Angus × Simmental multiparous cows [*n* = 335; age = 5.8 ± 2.1 yr; 586.5 ± 6.0 kg body weight (BW); 5.48 ± 0.05 body condition score (BCS)] were stratified by BW, age, and BCS and randomly assigned to one of three treatments. Treatments included a spring injection of extended-release eprinomectin (SERE) on day 0, a fall injection of extended-release eprinomectin injection (FERE) on day 84, and a saline control (CON). All treatments were administered at a rate of 1 mL/50 kg BW. Prior to the experiment, all cows were treated with oral fenbendazole to minimize parasite load. Cows grazed endophyte-infected tall fescue. Hair coat score (HCS), BW, and BCS were recorded on all cattle. Fecal egg count (FEC), respiration rate (RR), horn fly and tick count, hematocrit (% packed cell volume, PCV), and serum prolactin were analyzed on a subset of cows (35/treatment). On day 194, cows were artificially inseminated (AI) and 11 d following AI were exposed to bulls for 51 d. Milk production was estimated on day 210 on a subset of 85 cow–calf pairs (28–29/treatment). There was a tendency for a treatment × time interaction ($P = 0.07$) for FEC likely driven by an increase in FEC of the CON cattle at day 126 compared to SERE and FERE. There was a tendency for a treatment × time interaction ($P = 0.06$) for cow BW, largely driven by time differences; however, there was no effect of treatment ($P = 0.84$) on BW. There was no difference ($P \geq 0.13$) in cow PCV, fly and tick count, BCS, HCS, RR, and serum prolactin throughout the experiment. Additionally, there was no difference ($P \geq 0.46$) in Julian calving date, calf birth BW, or milk production between treatments. Interestingly, heifer calves born to FERE dams tended to have greater ($P = 0.06$) weaning BW compared to heifer calves born to CON dams. In addition, there was no difference ($P \geq 0.17$) in heat patch scores, AI conception rates, or overall pregnancy rates between treatments. Extended-release eprinomectin did not impact cow growth performance, reproductive performance or fescue toxicity symptoms when grazing endophyte-infected tall fescue; however, calf weaning BW tended to be improved.

Key Words: beef cow, eprinomectin, fescue toxicosis, reproduction

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INTRODUCTION

Tall fescue covers over 14 million ha of pasture in the United States and feeds approximately 12 million beef cows (Kallenbach, 2015). However, grazing tall fescue can cause negative impacts to

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cattle, as the endophyte produces toxic ergot alkaloids, which can cause fescue toxicosis (Klotz and Smith, 2015). Symptoms of fescue toxicosis include increased respiration rates (RR), rough hair coats, reduced serum prolactin, and reduced conception rates (Porter and Thompson Jr, 1992; Roberts and Andrae, 2004). Additionally, reduced performance of calves born to dams that have grazed endophyte-infected tall fescue have been reported, such as reduced birth weights and weaning weights (Bolt and Bond, 1989).

An anthelmintic, ivermectin, has been shown to reduce some symptoms of fescue toxicosis, such as growth performance and hair coat score (HCS); however, it is a short-acting anthelmintic as it only remains effective for 28 d (Ellis et al., 1989; Bransby et al., 1993; Bransby et al., 1995). An extended-release eprinomectin anthelmintic has more recently been released on the market and is biologically active for up to 150 d (Forbes, 2013; Soll et al., 2013). Extended-release eprinomectin has been shown to be effective at reducing parasite loads and improving weight gains in growing cattle (Kunkle et al., 2013; Rehbein et al., 2013; Backes, 2016) and heifer reproductive performance (Backes, 2016). Moreover, Volk et al. (2019) reported improved reproductive performance and growth of developing heifers administered extended-release eprinomectin while grazing endophyte-infected tall fescue when parasite loads were low.

Additionally, previous research has shown no differences in cow body weight (BW) or reproductive performance when spring-calving cows were treated with extended-release eprinomectin compared to cows administered a different anthelmintic or untreated controls (Backes, 2016; Andresen et al., 2018b). To our knowledge, there is no published literature on the effects of fall-calving cows grazing endophyte-infected tall fescue when treated with extended-release eprinomectin. Therefore, the objective of this experiment was to evaluate the effects of extended-release eprinomectin on fescue toxicosis and its impacts on beef cow performance and reproduction when cattle are grazing endophyte-infected tall fescue. We hypothesized that extended-release eprinomectin would be effective in reducing the symptoms of fescue toxicosis and improving overall performance in fall-calving cows grazing on endophyte-infected tall fescue.

MATERIAL AND METHODS

Animals and Experimental Design

The Institutional Animal Care and Use Committee of the University of Illinois approved the procedures used in this experiment (protocol 16056) and followed the guidelines recommended in the Guide for the Care and Use of Agricultural Animal in Agricultural Research and Teaching (FASS, 2010).

To evaluate the effects of extended-release eprinomectin (LongRange; Boehringer Ingleheim, Duluth, GA) on cows grazing endophyte-infected tall fescue, 335 fall-calving Angus × Simmental multiparous cows [(age = 5.8 ± 2.1 yr; mean ± standard deviation, 586.5 ± 6.0 kg initial BW; initial body condition score (BCS) = 5.48 ± 0.05] were utilized at the University of Illinois Dixon Springs Agricultural Center in Simpson, IL. Cows were stratified by BW, age, and BCS and were assigned to treatment (111–112 cows/treatment) using a stratified randomized design. Cows maintained in one of three commingled groups with all treatments equally represented in each group. Treatments included: a spring extended-release eprinomectin injection (SERE), a fall extended-release eprinomectin injection (FERE), and a saline control injection (CON). All treatments were administered subcutaneously at a rate of 1 mL/50 kg BW. Any treatments not receiving extended-release eprinomectin at that time point were given saline at the same dosage. Treatments were administered on day 0 (May 25, 2016; SERE) and day 84 (August 17, 2016; FERE). Two weeks prior to experiment initiation, all cattle were administered with oral fenbendazole (Safe-guard; Merck Animal Health, Summit, NJ) so that differences between treatments could be attributed to the effect of extended-release eprinomectin on fescue toxicosis. Rainfall for 2016 was 135 cm for the research station and the previous 10 yr average was 112 cm of rainfall. The average high temperature from May to September for 2016 was 28.9 °C and the previous 10 yr average high temperature from May to September was 28.7 °C. All animals were grazing endophyte-infected tall fescue ("Kentucky-31"; 82% infected) pastures and had free choice to a mineral supplement (Renaissance Nutrition, Roaring Springs, PA; 0.16% S, 17.85% Ca, 2.99% P, 24.50% salt, 9.35% Na, 5.84% Mg, 0.06% K, 2,214 mg/kg Fe, 2,013 mg/kg Mn, 2,511 mg/kg Zn, 1,500 mg/kg Cu, 27 mg/kg Co, 36 mg/kg I, 26 mg/kg Se, 110,177 IU/kg vitamin A, 3,084 IU/kg vitamin D, 545 IU/kg Vitamin E, and 6,614 mg/kg chlortetracycline). Pasture composition and ergot alkaloid concentration are presented in Figure 1. Beginning on day 177, cows were offered free-choice hay [7.7% crude protein (CP), 75.1% neutral detergent fiber (NDF), and 44.1% acid detergent fiber (ADF)] and 1.8 kg corn distillers grains per cow per day (25.3% CP, 44.2% NDF, 11.5% ADF, and 10.5% crude fat). On day 242, cows were transitioned over 3 d to 2.7 kg corn distillers grains per cow per

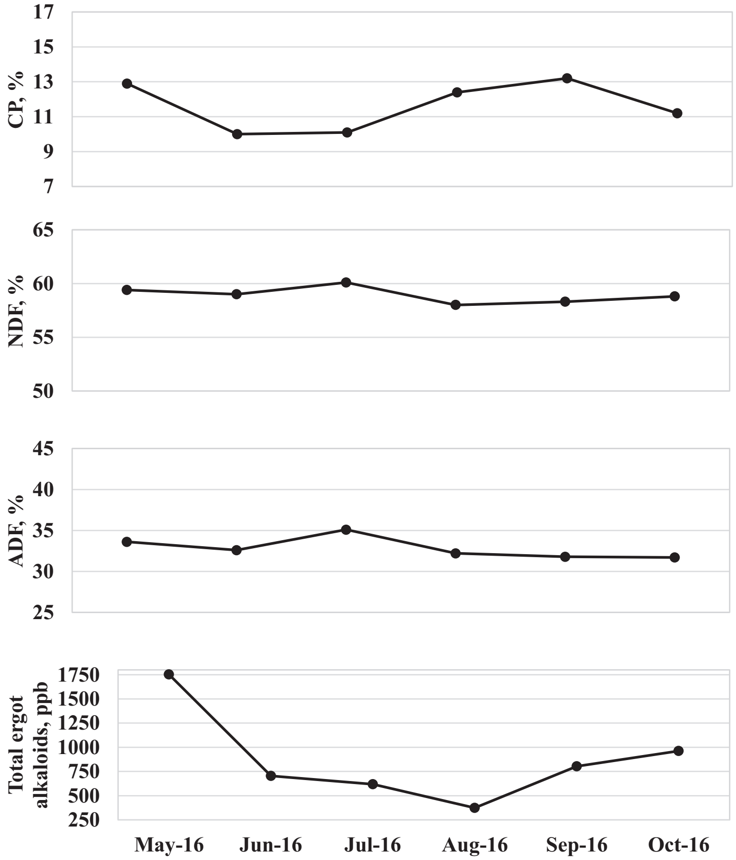

Figure 1. Forage quality [percentage CP, NDF, ADF, and total ergot alkaloids (ppb)] of endophyte-infected fescue (*Festuca arundinacea*) pastures from May 2016 to October 2016. Samples were collected as cattle rotated pastures and were composited on a monthly basis.

day and remained at this level until the end of the experiment.

Sixteen cows were removed from the experiment due to death (three SERE, five FERE, and eight CON). The authors acknowledge this is relatively high death loss and contribute to high incidence of anaplasmosis and lymphoma present in this herd. Additionally, 28 cows were removed due to late-term abortions or loss of calf (10 SERE, 9 FERE, and 9 CON). Three cows were removed from the experiment due to poor condition (one FERE and two CON) and three cows were sold (two FERE and one CON). One cow was not rebred as her calf was born too late (one SERE). All analysis included cow performance data until the date they were removed from the experiment.

Sample Collection and Analytical Procedures

Full 2 d BW measurements were collected and averaged at experiment initiation (days −1 and 0) and at the end of the experiment (days 301 and 302). Throughout the experiment, 1 d BW were recorded on days 42, 84, 126, 168, 194, and 243. Body condition scores were collected concurrent with BW and were evaluated using a 1–9 scale [emaciated = 1; obese = 9; as described by Wagner et al. (1988)] by one trained evaluator. Hair coat scores (1–5, in which 1 = slick, short coat and 5 = unshed, full winter coat) were evaluated and recorded on days −1, 42, 84, 126, and 168 by one trained evaluator.

Forage samples were collected by randomly clipping approximately 5 cm from the ground, from at least 12 different locations, within the pasture. Fescue stems were collected throughout each field by collecting the bottom 6 inches closest to the ground. Feed and forage samples were collected monthly throughout the experiment. Forage samples were dried at 55 °C for a minimum of 3 d, ground through a 1 mm screen using a Wiley mill (Arthur H. Thomas, Philadelphia, PA), and were composited for all three replicates. Ground feed and forage were analyzed for NDF and ADF using an Ankom 200 Fiber Analyzer (Ankom Technology, Macedon, NY) as well as CP (Leco TruMac, LECO Corporation, St. Joseph, MI) (Figure 1). Feed samples were also analyzed for crude fat using an Ankom XT10 fat extractor (Ankom Technology, Macedon, NY). Total ergot alkaloid analysis of forages and percent infected stems were conducted in a commercial laboratory (Agrinostics Limited, Co., Watkinsville, GA).

A subset of cows (n = 105; 35 SERE, 35 FERE, and 35 CON) were utilized for additional sampling of RR, fecal egg counts (FEC), horn fly and tick counts, hematocrit (% packed cell volume, PCV), and serum prolactin. The subset of cows was from one replicate group and the same animals were utilized throughout the experiment. To determine RR, while cattle were on pasture, two individuals simultaneously counted the number of breaths per cow in 15 s on days 2, 44, 85, 125, and 167 in the afternoon. The two observations were then averaged and multiplied by 4 to determine breaths per minute. Rectal grab samples were collected for determination of FEC per gram of feces using a modified version of the Modified Wisconsin flotation method on days −1, 42, 84, 126, and 168. After collection, fecal samples were stored at 20 °C until processed. Three grams of feces was mixed well with 15 mL of a sodium nitrate solution (Feca-Med; VetOne, MWI Animal Health, Boise, ID) and strained into a 15 mL polypropylene concial tube (Corning; Corning, NY). Samples were then centrifuged for 5 min at 725 × g. After centrifugation, tubes were filled just over the top to form a meniscus with the sodium nitrate solution and a cover glass slip (VWR VistaVision 18 × 18 mm; VWR International, Randor, PA) was placed onto the meniscus for 4 min. Cover slips were then removed and placed directly onto a microscope slide (VWR VistaVision 75 × 25 × 1 mm; VWR International, Randor, PA), which was scanned under a microscope to count the total number of eggs on the entire cover slip. Total number of eggs per 3 g of feces was recorded and then converted to eggs per gram (EPG) of feces for statistical analysis.

Fly counts were determined by taking a high resolution picture (Sony RX10 III Camera with Zeiss Vario-Sonnar 2.4–4/8.8–220 telephoto lens with approximately 20.1 working megapixels) of one side of each cow when cows were on pasture on days 1, 43, 79, and 125. To standardize the pictures, the cow's FID was visible in the picture along with the tail being still to not push flies away. After all cows were photographed, the pictures were uploaded onto a computer and the count tool in photo shop (Adobe Photoshop CC 2015, 2015.1.2 Release) was used to click each fly to count the total number of flies on the side of the cow, excluding the lower legs, head, and neck to keep the count area consistent throughout all pictures. Tick counts were determined by counting the number of ticks on both ears of the cows when they were in the chute on d −1, 42, 84, and 126.

Blood samples were collected for both serum prolactin and hematocrit (PCV) on days −1, 42, 84, 126, and 168. Blood was collected via jugular venipuncture into one 10 mL serum blood collection vacuum tube (Becton, Dickinson and Co., Franklin Lakes, NJ) and one 10 mL plasma blood collection vacuum tube with K2 EDTA (Becton, Dickinson and Co., Franklin Lakes, NJ). Blood in the serum tube was allowed to clot at room temperature before being centrifuged at 1,300 × g for 20 min at 5 °C. Serum was stored at −20 °C for subsequent prolactin analysis. Serum was analyzed for prolactin analysis via a radioimmunoassay as described by Bernard et al. (1993) at the University of Tennessee (Knoxville, TN). The intra-assay CV was 6.6% and the interassay CV was 8.1%. Hematocrit was determined using the microhematocrit procedure. Heparinized 75 mm microhematocrit capillary tubes (Fisher Scientific Co., Cat. No. 02-668-66) were filled two-thirds full with whole blood from the plasma tubes and sealed with Critoseal clay in duplicate. Samples were then centrifuged in an international microcapillary centrifuge (Model MB; International Equipment Company, Boston, MA) for 10 min and read on a microhematocrit capillary tube reader (Oxford Labware, St. Louis, MO) to determine PCV.

Within 24 hr of birth, calf birth BW was recorded. Milk production was assessed on day 210, approximately 93 ± 6 d postpartum, using the weigh-suckle-weigh (WSW) technique on a subset of 85 cow–calf pairs (28 or 29/treatment) as described by Beal et al. (1990). Only heifer calves were utilized in the WSW procedure. Steer calves were early weaned on day 201 (83 ± 6 d of age) and heifer calves were conventional weaned on day 301 (184 ± 6 d of age). Steer calf weaning weights were not recorded as they were early weaned; however, heifer calf weaning weights were collected at time of weaning (day 301).

Heat detection patches (Estrotect Heat Detectors, Rockway Inc., Spring Valley, WI) were applied to determine estrous cyclicity on day 168, approximately 26 d prior to synchronization. Heat patches were visually scored on day 194 from 1 to 4 (1 = less than half, 2 = more than half, 3 = fully activated, 4 = missing). On day 194, cattle were started in the 7 d CO-Synch + controlled internal drug release (CIDR; Pfizer Animal Health, New York, NJ) insert with timed artificial insemination (AI) protocol (Johnson et al., 2013). At 11 d following AI, cows were exposed to clean-up bulls for a 51 d breeding season. Artificial insemination pregnancy rates were collected 39 d after AI, and overall pregnancy rates were determined 97 d after AI. Pregnancy rates were determined by a trained technician via ultrasonography (Aloka 500 instrument, Hitachi Aloka Medical America, Inc., Wallingford, CT; 7.5 MHz general purpose transducer array) or rectal palpation.

Statistical Analysis

A stratified randomized design was used and cow served as the experimental unit. Body weight, BCS, HCS, RR, FEC, fly and tick counts, serum prolactin, and PCV were analyzed as repeated measures in the MIXED procedure of SAS (SAS Inst. Inc., Cary, NC) with fixed effects of treatment, pasture, time, and the interaction of treatment and time. The REPEATED statement was used to model the repeated measurements within animal for each variable and the unstructured covariance structure was used for all parameters, except FEC. After considering the Akaike and Bayesian information criterion, the compound symmetry covariance structure was used for FEC analysis. Fecal egg counts on day −1 was different between treatments, so it was included as a covariate for all FEC analysis. Additionally, FEC residuals were not normally distributed, so FEC were transformed using the Boxcox procedure of SAS. Fecal egg counts were transformed using $(FEC + 1)^{-3}$. Untransformed least square means are reported for FEC. The SLICE statement was used to separate least square means when the interaction of treatment and time was significant ($P \leq 0.05$). The MIXED procedure of SAS was also used to analyze milk production and Julian birth date with fixed effects of treatment and pasture. Calf birth weight was analyzed using the MIXED procedure of SAS with fixed effects of treatment, pasture, sire, and sex. Calf weaning weight was analyzed using the MIXED procedure of SAS with fixed effects of treatment, pasture, and sire. The GLIMMIX procedure of SAS was used to analyze reproductive performance parameters, including heat patch score (HPS), AI conception rate, and overall pregnancy rate. Significance was declared at $P \leq 0.05$ and tendencies were declared from $0.05 < P \leq 0.10$. Means reported in tables are least squares means.

RESULTS

There was a tendency for a treatment × time interaction ($P = 0.07$; Table 1) for FEC likely driven by an increase in FEC of the CON cattle at day 126 compared to SERE and FERE cattle, the first FEC sampling post-fall treatment. Moreover, there was a treatment effect ($P < 0.01$) on FEC with the CON cattle having greater FEC throughout the experiment. There was no treatment × time interaction or treatment effect ($P \geq 0.33$) on cow fly counts, tick counts, and PCV throughout the experiment.

There was a tendency for a treatment × time interaction ($P = 0.06$; Table 2) for cow BW, which was driven primarily by time differences. However, the overall effect of treatment on BW was not different ($P = 0.84$). There was no treatment × time interaction or treatment effect ($P \geq 0.13$; Tables 2 and 3) on cow BCS, HCS, RR, and serum prolactin concentration throughout the experiment.

There was no difference ($P \geq 0.46$; Table 4) in Julian calving date, calf birth BW, or milk production between treatments. Interestingly, heifer calf weaning weights tended ($P = 0.06$; Table 4) to be greater for heifer calves from FERE dams compared to heifer calves from CON dams. At the time of AI, HPS were not different ($P > 0.37$; Table 5) between treatments and there were no differences ($P \geq 0.17$) in AI conception or overall pregnancy rates.

DISCUSSION

Fescue toxicosis negatively impacts performance of cattle when they are grazing endophyte-infected tall fescue (Roberts and Andrae, 2004). Improvements in performance while still grazing endophyte-infected tall fescue have been reported when cattle were treated with ivermectin (Ellis et al., 1989; Bransby et al., 1993; Bransby, 1997). Extended-release eprinomectin, another anthelmintic in the same class as ivermectin, is biologically active for up to 150 d (Forbes, 2013). Extended-release eprinomectin has also shown improvements in heifer growth performance and reproduction when grazing endophyte-infected tall fescue but has not shown reductions in commonly known symptoms of fescue toxicosis such as HCS, RR, and prolactin concentrations (Volk et al., 2019). This current experiment was designed to assess fall-calving cow performance when treated with extended-release eprinomectin while grazing endophyte-infected tall fescue.

Control cows had increased FEC at day 126 compared to SERE and FERE cattle; however, all cattle regardless of treatment, had extremely low FEC (<1 EPG). A threshold of >200 EPG was defined by Vercruysse and Claerebout (2001), in which cattle exhibit symptoms of parasite gastroenteritis; however, a threshold for subclinical parasite load impacting weight gains has not been defined. In this

Table 1. Influence of extended-release injectable eprinomectin on cow FEC, fly count, tick count, and hematocrit

	Treatment[1]				P-value[2]		
Item	SERE	FERE	CON	SEM	Trt	Time	Trt × Time
n	35	35	35				
FEC, eggs per gram[3]					<0.01	0.03	0.07
Day −1	0.17	0.08	0.19	—	0.12		
Day 42	0.10	0.12	0.14	—	0.75		
Day 84	0.05	0.12	0.26	—	0.12		
Day 126	0.03^{a}	0.02^{a}	0.70^{c}	—	<0.01		
Day 168	0.08	0.02	0.13	—	0.18		
Fly count[4]					0.61	<0.01	0.63
Day 1	18.4	28.1	23.5	3.71			
Day 43	32.9	42.7	44.3	7.06			
Day 79	75.6	98.2	135.3	20.75			
Day 125	254.0	259.1	236.2	37.78			
Tick count[5]					0.77	<0.01	0.84
Day −1	6.0	6.0	5.7	0.78			
Day 42	1.8	1.8	1.3	0.29			
Day 84	0.3	0.3	0.3	0.11			
Day 126	0.1	0.1	0.1	0.06			
Hematocrit, % packed cell volume					0.77	<0.01	0.33
Day −1	36.9	37.1	38.1	0.47			
Day 42	36.1	36.3	36.7	0.52			
Day 84	34.7	33.7	34.8	0.58			
Day 126	31.8	31.2	30.6	0.71			
Day 168	33.3	33.1	33.3	0.68			

[a,b] Treatment means with different superscripts are different ($P < 0.01$).

[1] Treatments are defined as SERE, FERE, and CON. SERE cattle received extended-release eprinomectin injection on day 0 and FERE cattle received extended-release eprinomectin injection on day 84. Cattle not receiving an extended-release eprinomectin injection on these dates received a sterilized saline solution. All treatments were administered at a dose of 1 mL/50 kg of BW.

[2] Abbreviations are defined as treatment effect (Trt) and treatment × time effect (Trt × Time).

[3] FEC least square means are from untransformed data while the P-values are representative of the transformed data.

[4] Fly counts are reported as number of flies on one side of the animal.

[5] Tick counts are reported as the number of ticks in both ears of the animal.

current experiment, all cattle, regardless of treatment, were treated with oral fenbendazole 2 wk prior to experiment initiation. Due to the overall low FEC in this experiment, the authors hypothesize that the difference in FEC did not impact performance of the cattle.

Throughout the experiment, external parasites, including flies and ticks, were similar, regardless of treatment. Trehal et al. (2017) noted that heifers treated with extended-release eprinomectin had lesser fly counts compared to untreated or fly tagged heifers; however, treatments were not commingled among pastures. In another experiment, Andresen et al. (2018b) noted no differences in fly counts between cows treated with extended-release eprinomectin and doramectin. Fly counts were recorded on cows separated on pasture by treatment as well as pastures with treatments commingled in Andresen et al. (2018b). In this current experiment, it is important to note that all treatments were commingled on pastures. Partially treated herds have experienced reduction in horn flies in both treated and untreated cattle (Harvey and Brethour, 1983). Anemia is another symptom of internal parasite infection and can be determined using hematocrit, which measures oxygen carrying capacity of the circulatory system of the animal and dehydration level (Craig, 1988; Nordenson, 2006). Cattle experiencing anemia typically have a PCV of 24% or less (Marcotty et al., 2008). In this experiment, there was no difference between treatments in PCV and no cattle were experiencing anemia. Rosenkrans et al. (2001) described greater PCV in steers treated with a slow-release ivermectin bolus compared to cattle not treated with ivermectin bolus. Rosenkrans et al. (2001) reported PCV values numerically similar to values in this experiment. It is important to note that the experiment was only 28 d and steers were

Table 2. Influence of extended-release injectable eprinomectin on cow BW and BCS

	Treatment[1]				*P*-value[2]		
Item	SERE	FERE	CON	SEM	Trt	Time	Trt × Time
n	111	112	112				
BW, kg					0.84	<0.01	0.06
Day 0	586	587	587	6.0			
Day 42	626	623	624	6.5			
Day 84	630	624	628	6.2			
Day 126	600	592	592	6.5			
Day 168	590	586	579	7.0			
Day 194	595	591	583	6.7			
Day 243	581	579	575	7.0			
Day 302	584	587	583	6.9			
BCS					0.83	<0.01	0.19
Day −1	5.4	5.5	5.5	0.05			
Day 42	5.9	5.8	5.8	0.05			
Day 84	5.8	5.8	5.9	0.06			
Day 126	5.4	5.4	5.4	0.08			
Day 168	5.1	5.1	5.0	0.08			
Day 194	5.5	5.6	5.4	0.08			
Day 243	4.8	4.9	4.9	0.07			
Day 302	5.3	5.4	5.3	0.07			

[1] Treatments are defined as SERE, FERE, and CON. SERE cattle received extended-release eprinomectin injection on day 0 and FERE cattle received extended-release eprinomectin injection on day 84. Cattle not receiving an extended-release eprinomectin injection on these dates received a sterilized saline solution. All treatments were administered at a dose of 1 mL/50 kg of BW.

[2] Abbreviations are defined as treatment effect (Trt) and treatment × time effect (Trt × Time).

Table 3. Influence of extended-release injectable eprinomectin on cow serum prolactin, HCS, and RR

	Treatment[1]				*P*-value[2]		
Item	SERE	FERE	CON	SEM	Trt	Time	Trt × Time
n	35	35	35				
Serum prolactin, ng/mL					0.80	<0.01	0.76
Day −1	21.7	22.8	25.4	2.73			
Day 42	45.6	44.4	47.2	3.42			
Day 84	17.7	18.3	21.4	3.07			
Day 126	11.1	6.6	4.1	3.96			
Day 168	3.1	2.2	2.3	0.94			
HCS[3]					0.79	<0.01	0.90
Day −1	1.8	1.9	1.9	0.07			
Day 42	1.3	1.4	1.4	0.05			
Day 84	1.4	1.5	1.5	0.05			
Day 126	1.6	1.6	1.6	0.05			
Day 168	2.4	2.4	2.4	0.06			
RR, breaths/min					0.13	<0.01	0.29
Day 2	55.2	58.6	53.3	1.43			
Day 44	48.2	49.5	49.4	0.63			
Day 85	54.3	54.2	52.2	1.08			
Day 125	44.1	44.1	43.7	1.55			
Day 167	31.6	31.9	32.2	0.79			

[1] Treatments are defined as SERE, FERE, and CON. SERE cattle received extended-release eprinomectin injection on day 0 and FERE cattle received extended-release eprinomectin injection on day 84. Cattle not receiving an extended-release eprinomectin injection on these dates received a sterilized saline solution. All treatments were administered at a dose of 1 mL/50 kg of BW.

[2] Abbreviations are defined as treatment effect (Trt) and treatment × time effect (Trt × Time).

[3] HCS was evaluated on 1 to 5 scale, in which 1 = slick, short coat and 5 = unshed, full winter coat.

Table 4. Influence of extended-release injectable eprinomectin on cow calving date, calf birth weight, milk production, and calf weaning weight

	Treatment[1]				
Item	SERE	FERE	CON	SEM	*P*-value
Calving data					
n	98	98	102		
Calving date, Julian d	264	263	263	0.6	0.46
Calf birth weight, kg	32.9	33.2	32.3	0.86	0.61
Milk production					
n	28	28	29		
kg/d	7.1	6.8	6.5	0.43	0.65
Heifer calf weaning weight					
n	52	52	49		
kg[2]	187.0	198.3	184.5	4.88	0.06

[1] Treatments are defined as SERE, FERE, and CON. SERE cattle received extended-release eprinomectin injection on day 0 and FERE cattle received extended-release eprinomectin injection on day 84. Cattle not receiving an extended-release eprinomectin injection on these dates received a sterilized saline solution. All treatments were administered at a dose of 1 mL/50 kg of BW.

[2] Heifer calves were weaned and weighed on day 301.

Table 5. Influence of extended-release injectable eprinomectin on cow HPS and subsequent reproductive performance

	Treatment[1]			
Item	SERE	FERE	CON	*P*-value
HPS[2]				
n	97	97	96	
1—Less than half, %	2.9	3.6	5.2	0.60
2—More than half, %	6.3	9.2	6.3	0.64
3—Fully activated, %	74.4	75.3	72.0	0.87
4—Missing, %	14.4	8.2	13.5	0.37
AI conception				
n	97	96	95	
%	56.8	67.9	59.0	0.25
Overall pregnancy				
n	96	95	92	
%	91.4	97.5	93.8	0.17

[1] Treatments are defined as SERE, FERE, and CON. SERE cattle received extended-release eprinomectin injection on day 0 and FERE cattle received extended-release eprinomectin injection on day 84. Cattle not receiving an extended-release eprinomectin injection on these dates received a sterilized saline solution. All treatments were administered at a dose of 1 mL/50 kg of BW.

[2] Heat patches were visually scored at time of breeding (day 194) from 1 to 4 (1 = less than half, 2 = more than half, 3 = fully activated, 4 = missing).

housed in a barn and fed endophyte-infected hay, which may have impacted some of the stressors from fescue toxicosis (Rosenkrans et al., 2001).

There was a tendency for a treatment × time interaction for BW, largely driven by the differences in BW over time. Cow BCS was not different between treatments throughout the experiment. All cattle in the current experiment were dewormed prior to the experiment, so differences in BW due to parasite loads were not expected. However, in previous research with eprinomectin, cattle were not dewormed prior to the experiment, so some parasite load differences were reported. Andresen et al. (2018b) noted no differences in BW or BCS in cows treated with either extended-release eprinomectin or doramectin when FEC were low. However, in a case study, fall-calving cows treated with extended-release eprinomectin in the fall had greater ADG and BW change compared to cows treated with injectable ivermectin in the fall (Andresen et al., 2018a). The authors acknowledged that FEC were not recorded in the experiment, so it is difficult to know if this was influenced by parasite loads (Andresen et al., 2018a). Additionally, Backes (2016) noted no differences in BW of spring-calving cows treated with extended-release eprinomectin, oral oxfendazole, or untreated controls. Interestingly, Backes (2016) noted an improvement in BCS at 91 d posttreatment for cows treated with oxfendazole compared to cows treated with extended-release eprinomectin (5.9 BCS vs. 5.7 BCS). However, this was not different at any other time point and the authors noted that BCS was not different at the end of the treatment period and likely did not impact overall cow performance. In developing heifers, Volk et al. (2019) noted increased BW gain and BCS when heifers were treated with extended-release eprinomectin compared to control cattle. Growing heifers have additional requirements for growth compared to cows and mature animals are more resilient, which are both possible reasons for the differences between these two experiments.

Cattle grazing endophyte-infected tall fescue typically have decreased serum prolactin concentrations. Ergot alkaloids produced by the toxic endophyte can bind the D-2-dopamine receptors and disrupt the dopaminergic pathways, decreasing the prolactin concentration (Berde and Stürmer, 1978). In the current experiment, serum prolactin concentrations were similar between treatments. However, from early summer to late fall, serum prolactin concentrations decreased in all cattle. Previous literature has reported similar times of reduced serum prolactin concentrations cattle grazing endophyte-infected tall fescue (Fanning et al., 1992; Aiken et al., 2013; Stowe et al., 2013; Shoup et al., 2016). As serum prolactin was reduced, all cows in this experiment were likely experiencing fescue toxicity. Prolactin may be impacted by many different factors, including physiological factors, and can vary from animal to animal (Akers et al., 1980; Petitclerc et al., 1983). In addition, environmental factors such as day length, season, and temperature can also impact prolactin levels (Leining et al., 1979; Peters et al., 1980; Tucker et al., 1991). In addition, prolactin has been used in many other fescue toxicosis experiments to determine if animals are exposed to toxicity (Hill et al., 2000). Previous work conducted at the same research station (Stokes et al., 2018) reported an increase in prolactin levels at this same time point. In Stokes et al. (2018), ergot alkaloids also decreased from 2,088 μg/kg in May to 921 μg/kg in June. Additionally, Shoup et al. (2016) reported prolactin levels around 40–60 ng/mL in both May and July and decreased levels around 0 in October post-calving. Ergot alkaloid concentrations were only reported in October in Shoup et al. (2016) at 1,165 ug/kg. From a different research station, Hill et al. (2000) reported varying serum prolactin levels (approximately 1–10 ng/mL) from cattle grazing endophyte-infected tall fescue over four different grazing periods ranging in ergot alkaloid concentration from 373 μg/kg to 3,297 μg/kg. It is important to note that cattle in Hill et al. (2000) that were grazing endophyte-free tall fescue for the duration of the experiment with ergot alkaloid concentrations of 0 μg/kg had prolactin levels varying from 3 to 13 ng/mL over a 16 d period. These results indicate that while prolactin may help explain some of the fescue responses, it should not be the sole indicator of toxicosis, which is why we included HCS, RR, as well as performance parameters.

Other indicators of fescue toxicosis, such as increased RR and HCS, were evaluated in this experiment. Hair coat score and RR was not different between treatments. Increased HCS and RR are caused by a combination of decreased prolactin and increased vasoconstriction, which reduces blood flow and the animal's ability to dissipate heat (Finch, 1986; Porter and Thompson Jr, 1992). Volk et al. (2019) noted no differences in RR and HCS between heifers treated with extended-release eprinomectin and controls grazing endophyte-infected tall fescue. Backes (2016) noted an improvement in HCS of spring-calving cows treated with oxfendazole compared to cattle treated with extended-release eprinomectin and untreated controls at 91 d posttreatment. However, there were no differences at any other time point (Backes, 2016). Shoup et al., 2016 reported similar values for RR at similar times, while Stokes et al., 2018 reported greater RR in July and September.

Since cows were treated during gestation, calf parameters were analyzed for potential fetal programming effects. Cows treated with extended-release eprinomectin may have had improved nutritional status during crucial points of fetal development, which could have positive impacts on calf development and performance (Wu et al., 2004). Calf birth BW, calving date, and cow milk production were similar in this experiment. Calves born to dams grazing endophyte-infected tall fescue have been reported to have reduced birth weight (Bolt and Bond, 1989). Reduced milk production has also been noted in cattle grazing endophyte-infected tall fescue (Porter and Thompson Jr, 1992). However, other research did not see differences in milk production even when dams showed differences in other symptoms of fescue toxicity (Bolt and Bond, 1989; Shoup et al., 2016). If extended-release eprinomectin had been effective in alleviating some of the fescue toxicosis symptoms, specifically cow BW, BCS, and RR, it could have impacted calf birth BW, calving date, and cow milk production.

Interestingly, weaning weights tended to be greater for heifer calves from FERE dams compared to heifer calves from CON dams. If birth BW or milk production was different, it would have been expected to impact the weaning weights. The authors note the difference in weaning weight could potentially be attributed to parasite differences between the calves, although it was not assessed in this experiment. In a case study, Andresen et al. (2018a) reported a tendency for calf actual weaning weight to be greater for fall-born calves to dams treated with extended-release eprinomectin compared to calves born to dams treated with ivermectin. Age at weaning was different, so adjusted weaning weight was greater for calves born to extended-release eprinomectin dams compared to those born to ivermectin dams (Andresen et al., 2018a). The cattle in Andresen et al. (2018a) were treated in the fall, which was the last trimester of gestation for the calves. However, no data was reported on calf birth BW, calving date, and cow milk production (Andresen et al., 2018a). In another experiment, Andresen et al. (2018b) reported no difference in calf birth BW or weaning weight when cows were treated while gestating in the spring with either extended-release eprinomectin or doramectin, although milk production and calving date were not evaluated in Andresen et al. (2018b).

Conversely, Backes (2016) reported greater weaning weights for calves from spring-calving cows treated with oxfendazole compared to calves of extended-release eprinomectin dams. However, it should be noted that these were spring-calving cows and were treated prior to the calving season, so it is difficult to compare spring- and fall-born cattle weaning weight performance. Unfortunately, calf birth BW, calving date, and cow milk production were not reported in Backes (2016). More research is needed on calf performance from dams treated with extended-release eprinomectin.

Extended-release eprinomectin did not impact AI conception or overall pregnancy rate. Andresen et al. (2018b) reported no differences in AI and overall conception rates in cows treated with either extended-release eprinomectin or doramectin. However, in a case study, there was a trend for overall pregnancy rate to be greater for fall-calving cows treated with extended-release eprinomectin compared to cows treated with injectable ivermectin (Andresen et al., 2018a). However, the authors acknowledge that the case study had low number of cattle, forage type was not mentioned and FEC were not reported, so it is difficult to compare the data (Andresen et al., 2018a).

Interestingly, Backes (2016) reported a trend for greater pregnancy rate in cows treated with oxfendazole compared to cows treated with extended-release eprinomectin. It is important to note that the number of cattle included in the experiment was low and the experiment lacked replication of treatments, which potentially confounds reproductive differences in Backes (2016). In developing heifers, Volk et al. (2019) reported a greater overall pregnancy rate and a trend for greater AI conception rate when heifers were treated with extended-release eprinomectin in the spring. Volk et al. (2019) also reported improved BW and BCS of heifers treated with extended-release eprinomectin prior to breeding, which may have impacted reproductive performance.

Overall, extended-release eprinomectin did not have an impact on cow performance, reproductive performance, and fescue toxicity symptoms when grazing endophyte-infected tall fescue. However, there was a trend for calf weaning weight to be greater. Further research is needed to investigate the underlying mechanisms responsible for the trend in increased weaning weight.

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