

Effects of spring administration of extended-release eprinomectin on fescue toxicosis, performance, and reproduction of fall-born beef heifers

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ABSTRACT: The objective of this experiment was to assess the effects of eprinomectin, an extended-release injectable parasiticide, on fescue toxicosis and its impacts on beef heifer performance and reproduction. Fall-born Angus × Simmental heifers (age = 246.3 ± 22.4 d; 264.8 ± 21.1 kg body weight [BW]) were randomly assigned to one of two treatments: extended-release eprinomectin injection (ERE; *n* = 100) or control (CON; saline; *n* = 99). Treatments were administered at a rate of 1 mL/50 kg BW. Prior to experiment, heifers were dosed with oral fenbendazole to minimize parasite load. All heifers grazed endophyte-infected tall fescue as a single group and were offered a 50:50 supplement mix of corn gluten feed and soybean hulls (2.7 kg as fed per heifer per day). Body condition scores (BCS), BW, hair coat score (HCS), blood, and fecal samples were collected throughout the experiment. A subset of 40 heifers were randomly selected (20 per treatment) to assess respiration rate (RR). On d 138, heifers began a 14-d controlled internal drug release + prostaglandin synchronization protocol. Following artificial insemination (AI), heifers were exposed to five bulls for 71 d. On d 214 and 291, AI and overall pregnancy rates, respectively, were determined.

There was a treatment × time interaction (*P* < 0.01) for BW, BCS, and average daily gain (ADG). The ERE heifers had greater (*P* < 0.04) BW and BCS compared to CON heifers from d 55 and 112, respectively. In addition, ERE heifers had greater (*P* ≤ 0.04) ADG from d 0 to 56, 56 to 112, 112 to 171, and 171 to 214; however CON heifers had greater (*P* < 0.01) ADG from d 214 to 291. There was no treatment × time interaction or treatment difference (*P* ≥ 0.27) for HCS, RR, and serum prolactin concentrations. However, serum prolactin decreased (*P* < 0.01) in all heifers over time. There was a treatment × time interaction (*P* < 0.01) for fecal egg counts (FEC). The FEC did not differ (*P* ≥ 0.32) on d -1 or 55; however, ERE heifers had decreased (*P* < 0.01) FEC compared with CON heifers on d 111 (1.52 vs. 13.56 eggs per gram). The ERE heifers tended (*P* = 0.10) to have greater AI pregnancy rates (69% vs. 58%) and had greater (*P* = 0.01) overall pregnancy rates (84% vs. 68%) than CON heifers. Spring administration of extended-release eprinomectin improved BW, ADG, BCS, and AI and overall pregnancy rates in fall-born beef heifers. However, the underlying mechanism is still unclear, as there were minimal to no differences in HCS, RR, serum prolactin, and FEC.

Key words: beef heifer, eprinomectin, fescue toxicosis, reproduction

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INTRODUCTION

Tall fescue is a predominate forage found throughout the United States, occupying 14

million hectare of pasture and feeding approximately 12 million beef cows (Kallenbach, 2015). Most tall fescue is infected with an ergot alkaloid-producing endophyte, but unfortunately, once ingested, tall fescue can cause a variety of negative physiological effects to cattle (Klotz and Smith, 2015). Most symptoms of fescue toxicosis arise from vasoconstriction and can include hoof loss, increased core body temperatures, increased respiration rates (RR), decreased serum prolactin concentrations, agalactia, decreased weight gain, and poor reproductive performance (Roberts and Andrae, 2004). Overall, in the United States, fescue toxicosis costs the beef industry a staggering \$2 billion annually, with three-fourths of the losses from embryonic loss or failing to conceive (Kallenbach, 2015).

Using pharmaceutical technologies already commercially available to beef cattle producers, such as anthelmintic to reduce symptoms of fescue toxicosis, could be vastly beneficial to the entire beef industry. The anthelmintic ivermectin has been shown to alleviate heat stress and other symptoms of fescue toxicosis (Bransby et al., 1993; Bransby, 1997; Roberts and Andrae, 2004). Unfortunately, ivermectin is only biologically active within the animal for 28 d. A more recent anthelmintic on the market and in the same class as ivermectin, an extended-release eprinomectin, lasts up to 150 d. Extended-release eprinomectin has been reported to improve heifer reproductive performance (Backes et al., 2016), increase weight gains (Kunkle et al., 2013; Rehbein et al., 2013; Backes et al., 2015), and improve average daily gains (ADG) (DeDonder et al., 2015) in previous research. However, there is little research on the effects of the extended-release eprinomectin on cattle grazing endophyte-infected tall fescue (Backes, 2016) and there is no data focusing on the effects on fescue toxicosis. The objective of this experiment was to evaluate the effects of extended-release eprinomectin on fescue toxicosis and its impacts on beef heifer performance and reproduction. Our hypothesis was that extended-release eprinomectin would be effective in reducing the symptoms of fescue toxicosis and improving overall performance in heifers grazed on endophyte-infected tall fescue.

MATERIAL AND METHODS

The Institutional Animal Care and Use Committee of the University of Illinois approved the procedures used in this experiment (protocol 15097) and followed the guidelines recommended in the Guide for the

Care and Use of Agricultural Animal in Agricultural Research and Teaching (FASS 2010).

Animals and Experimental Design

To evaluate the effects of extended-release eprinomectin (LongRange; Boehringer Ingelheim, Duluth, GA) on heifers grazing endophyte-infected tall fescue, 199 fall-born, Angus × Simmental heifers (age = 246.3 ± 22.4 d; mean \pm SD, 264.8 ± 21.1 kg initial body weight [BW]) were used at the University of Illinois Dixon Springs Agricultural Center in Simpson, IL. Heifers were assigned to one of two treatments: a spring extended-release eprinomectin injection (ERE) or a control (CON) saline injection. Heifers were stratified by BW and randomly assigned to treatment. All treatments were administered on d 0, subcutaneously, at a rate of 1 mL/50 kg BW. Two weeks prior to experiment initiation, all cattle were administered oral fenbendazole (Safe-Guard; Merck Animal Health, Summit, NJ), to minimize differences in parasite load across both treatments, so authors could better attribute differences between treatments to the effect of ERE on fescue toxicosis. Throughout the experiment, heifers grazed endophyte-infected tall fescue pastures (Kentucky-31; $\geq 90\%$ infected; total ergot alkaloid concentrations June: 1917 $\mu\text{g/L}$, July: 659 $\mu\text{g/L}$, and September: 2,554 $\mu\text{g/L}$). Heifers grazed pastures (56.9% dry matter [DM], 63.9% neutral detergent fiber [NDF], 36.2% acid detergent fiber [ADF], and 10.3% crude protein [CP]) as a single group and were rotated among pastures under the discretion of trained University of Illinois personnel as determined by the visual appraisal of forage availability. Heifers were supplemented with a 50:50 mix of corn gluten feed and soybean hulls (2.7 kg as fed per heifer per day; 85.4% DM, 50.6% NDF, 28.9% ADF, 18.0% CP, and 2.2% crude fat) for the duration of the experiment and had access to free choice mineral (Renaissance Nutrition, Roaring Springs, PA; 0.16% S, 17.88% Ca as calcium carbonate, 2.99% P as monocalcium phosphate, 24.5% salt, 9.35% Na, 5.74% Mg as magnesium oxide, 0.06% K, 2,214 mg/kg Fe as iron oxide, 2,013 mg/kg Mn as manganese hydroxychloride [IntelliBond M; Micronutrients Inc., Indianapolis, IN], 2,511 mg/kg Zn as hydroxyl zinc [IntelliBond Z; Micronutrients Inc.], 1,001 mg/kg Cu as tribasic copper chloride [IntelliBond C; Micronutrients Inc.], 27 mg/kg Co as cobalt carbonate, 36 mg/kg I as calcium iodate, 26 mg/kg Se as sodium selenite, 110,178 IU/kg vitamin A, 3,084 IU/kg vitamin D, 545 IU/kg vitamin E, and 1,179 mg/kg of chlortetracycline).

Heat detection patches (EstroTECT Heat Detectors; Rockway Inc., Spring Valley, WI) were applied on d 112 to determine estrus cyclicity prior to synchronization. Heat patches were visually scored on d 138 from 0 to 3 (0 = missing, 1 = fully activated, 2 = partially activated, and 3 = not activated). At this time, heifers also began a 14-d controlled internal drug release (Pfizer Animal Health, New York, NJ) insert + prostaglandin synchronization protocol with timed artificial insemination (AI; Mallory et al., 2013). Heat detection patches were applied to determine estrus on d 168. On d 171, AI occurred and heat patches were visually scored using the same scale as described previously. On d 180, heifers were exposed to five bulls, which had all passed breeding soundness exams, for a 71 d breeding season. Conception rates to AI were determined on d 214 (43 d after AI) and overall pregnancy rates were determined on d 291 (120 d after AI). Pregnancy rates were determined by a trained technician via ultrasonography (Aloka 500; Hitachi Aloka Medical America, Inc., Wallingford, CT; 7.5 MHz general purpose transducer array) or rectal palpation.

Sample Collection and Analytical Procedures

BWs were collected 10 times throughout the experiment, with full 2-d BW measurements collected and averaged at experiment initiation (d -1 and 0), d 55 and 56, d 111 and 112, and at the end of the experiment (d 290 and 291). Throughout the experiment, 1-d BW was recorded on d 6, 13, 27, 83, 138, 171, and 214. Body condition scores (BCS) were collected concurrent with BW and were evaluated using a 1–9 scale (emaciated = 1; obese = 9; as described by Wagner et al. [1988]). Hair coat scores (HCS; 1–5, in which 1 = slick, short coat and 5 = unshed, full winter coat) were evaluated and recorded on d 0, 13, 27, 55, 83, and 112. A subset of heifers ($n = 40$; 20 ERE and 20 CON) were used to determine RR on d 1, 54, and 110. To determine RR, two individuals simultaneously counted the number of breaths per heifer in 15 s, while cattle were on pasture in the afternoon. The two observations were then averaged and multiplied by four to determine breaths per minute.

Forage samples were collected by randomly clipping approximately 5 cm from the ground, from at least 12 different locations, within the pasture. Feed and forage samples were collected monthly and composited throughout the experiment. Forage samples were dried at 55 °C for a minimum of 3 d and ground (1-mm Wiley cutting mill;

Arthur H. Thomas, Philadelphia, PA). Ground forage and feed samples 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). Feed samples were also analyzed for crude fat using an Ankom XT10 fat extractor (Ankom Technology). Fescue stems were collected in June, July, and September by randomly picking 30 stems in the pasture with only the bottom 6 inches being collected. Stems were analyzed for total ergot alkaloid concentration in a commercial lab (Agrinostics Limited, Co., Watkinsville, GA).

Rectal grab samples were collected on d -1, 55, and 111 for determination of fecal egg count (FEC) per gram of feces using a modified version of the Modified Wisconsin flotation method. After collection, fecal samples were stored at 20 °C until processed. Three grams of feces were mixed with 15 mL of a sodium nitrate solution (Feca-Med; VetOne, MWI Animal Health, Boise, ID) and strained into a 15 mL polypropylene conical tube (Corning; Corning, NY). Samples were then centrifuged for 7 minutes at $725 \times g$. After centrifugation, tubes were filled with sodium nitrate solution to form a meniscus, and a cover glass slip (VWR VistaVision 18 × 18 mm; VWR International, Radnor, PA) was placed onto the meniscus for 4 min. Coverslips were then removed and placed directly onto a microscope slide (VWR VistaVision 75 × 25 × 1 mm; VWR International), which was scanned under a microscope to count the total number of eggs on the entire coverslip. Total number of eggs per 3 g of feces was recorded and then converted to eggs per gram (EPG) of feces for statistical analysis.

Blood samples were collected for serum prolactin at four time points during the experiment (d 0, 6, 55, and 111). Blood was collected via jugular venipuncture into one 10 mL serum blood collection vacuum tube (Becton, Dickinson and Co., Franklin Lakes, NJ) and was allowed to clot at room temperature before being centrifuged at $1,300 \times g$ for 20 min at 5 °C. Serum was stored at -20 °C for subsequent prolactin analysis. Serum was analyzed for prolactin concentration via a double-antibody radioimmunoassay (Spoon and Hallford, 1989). The intra-assay coefficient of variation (CV) was 8.2% and the interassay CV was 8.9%.

Statistical Analysis

A completely randomized design was used and heifer served as the experimental unit. Body weight, BCS, ADG, FEC, HCS, RR, and blood serum

prolactin were analyzed as repeated measures in the MIXED procedure of SAS (SAS Institute Inc., Cary, NC), with fixed effects of treatment and time, and the interaction between 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, Toeplitz covariance structure was used for FEC. Fecal egg count residuals were not normally distributed, so FEC were transformed using the BoxCox procedure of SAS. FECs were transformed using $(\text{FEC} + 1)^{-1.5}$. Untransformed least square means are reported for FEC. The SLICE statement was used to separate least square means when the interaction of treatment and date was significant ($P \leq 0.05$). The GLIMMIX procedure of SAS was used to analyze reproductive performance parameters, including HPS, AI pregnancy 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 and figures are least squares means.

RESULTS

There was a treatment \times time interaction ($P < 0.01$; Table 1) for FEC. At d -1 and 55, there was no effect ($P \geq 0.32$) of ERE on FEC. However, by d 111, ERE heifers had 12.04 fewer ($P < 0.01$) fecal EPG than CON heifers.

There was a treatment \times time interaction ($P < 0.01$; Figure 1) for BW. At experiment initiation until d 27, there was no difference ($P \geq 0.11$) in heifer BW. However, at d 55, ERE heifers had 6 kg greater ($P = 0.04$) BW compared to CON heifers. Furthermore, ERE heifers had consistently heavier ($P < 0.01$) BW from d 83 until d 291 compared to CON heifers. This increase observed in heifer BW translated to ERE heifers having a treatment \times time interaction ($P < 0.01$; Table 2) for ADG. Heifer

ADG was 0.05, 0.26, 0.07, and 0.07 kg greater ($P \leq 0.04$) from d 0 to 56, 56 to 112, 112 to 171, and 171 to 214, respectively. However, CON heifers had a 0.06 kg greater ($P < 0.01$) ADG from d 214 to 291. There was a treatment \times time interaction ($P < 0.01$) for BCS (Figure 1). From d 0 to 83, there was no difference ($P \geq 0.20$) in heifer BCS. However, from d 112 to 291, ERE heifers had greater ($P < 0.01$) BCS compared to CON heifers.

There was no treatment \times time interaction or treatment effect ($P \geq 0.27$) for HCS, RR, and serum prolactin concentrations. An effect of time was observed ($P < 0.01$) as all heifers had decreased serum prolactin concentrations and HCS along with increased RR over time, regardless of treatment.

The ERE heifers tended ($P = 0.09$; Table 3) to have more patches missing than CON heifers prior to initiation of estrus synchronization protocol, whereas CON heifers tended ($P = 0.09$) to have more heat patches partially activated prior to initiation of estrus synchronization protocol. However, there was no difference ($P = 1.00$) between treatments in percent of heifers with a fully activated patch prior to initiation of estrus synchronization protocol. Heifers treated with ERE had more ($P = 0.03$) heat patches fully activated at time of AI compared to CON heifers. Heifer AI pregnancy rate tended ($P = 0.10$; Table 3) to be greater for ERE heifers in comparison to CON heifers (69% and 58%, respectively). Moreover, overall pregnancy rate was greater ($P = 0.01$; Table 3) for ERE heifers compared to the CON heifers (84% and 68%, respectively).

DISCUSSION

Cattle grazing endophyte-infected tall fescue commonly experience fescue toxicosis that negatively affects the animal's performance (Roberts and Andrae, 2004). Previous literature has shown some improvements in performance of cattle experiencing

Table 1. Influence of extended-release injectable eprinomectin on heifer fecal egg count over time

Item	Treatment ¹			P-value		
	ERE	CON	SEM	Trt	Time	Trt \times Time
<i>n</i>	100	99				
Fecal egg count, egg per gram ²				<0.01	<0.01	<0.01
d -1	0.19	0.08	—	0.32		
d 55	0.00	0.01	—	0.81		
d 111	1.52	13.56	—	<0.01		

Trt = Treatment effect; Trt \times Time = treatment by time effect.

¹CON cattle received a sterilized saline solution, and ERE cattle received injectable eprinomectin. Treatments were administered at initiation of the experiment at a rate of 1 mL/50 kg body weight.

²Fecal egg count least square means are from untransformed data whereas the *P*-values are representative of the transformed data.

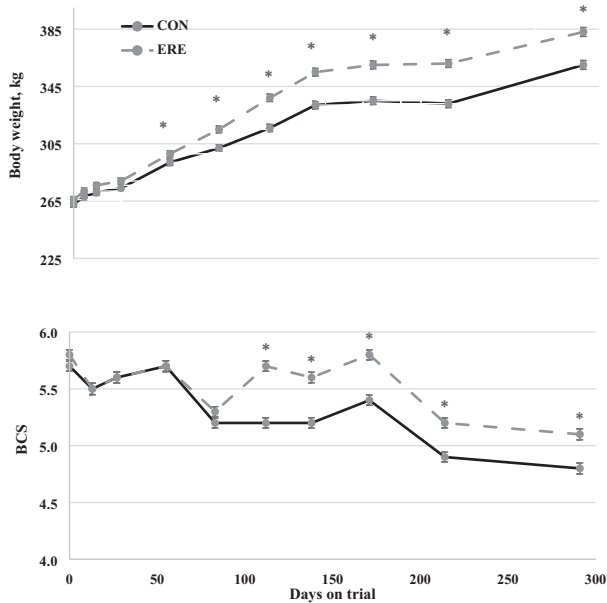


Figure 1. Effect of an extended-release injectable eprinomectin (ERE) on heifer body weight (BW) and body condition score (BCS). Control cattle received a sterilized saline solution ($n = 99$), and ERE cattle received injectable eprinomectin ($n = 100$). Treatments were administered at initiation of the experiment at a rate of 1 mL/50 kg BW. There was a treatment \times time interaction ($P < 0.01$) for BW. Heifer BW was different ($P < 0.04$) at d 55 as ERE heifers had greater BW compared to CON and this difference continued at d 83, 112, 138, 171, 214, and 291. In addition, there was a treatment \times time interaction ($P < 0.01$) for BCS. Heifer BCS was different ($P < 0.01$) at d 112, 138, 171, 214, and 291 as ERE heifers had greater BCS compared to CON heifers. *Differences ($P \leq 0.05$).

fescue toxicosis when they were treated with ivermectin; however, the potential mechanism is not well understood (Ellis et al., 1989; Bransby et al., 1993; Bransby, 1997). This experiment was designed to determine if extended-release eprinomectin, a slow release anthelmintic, also affects heifer performance when grazing endophyte-infected tall fescue.

Throughout the experiment, FEC were collected to monitor potential differences in parasite load. As an extended-release eprinomectin anthelmintic was used in this experiment, ERE heifers were expected to have minimal FEC for the duration of the experiment (Forbes, 2013). Throughout the experiment, all heifers had low FEC (< 14 EPG), which is considered a level where cattle would not show symptoms of parasite gastroenteritis. In previous literature, cattle with FEC > 200 EPG exhibit symptoms of parasite gastroenteritis; however, a threshold for subclinical parasite load that negatively affects gain has not been clearly defined (Verduyck and Claerebout, 2001). At d 111, CON heifers had greater FEC compared to ERE cattle (13.56 and 1.52 EPG, respectively). Owing to the overall minimal FEC reported throughout this experiment, the authors

hypothesized that this FEC difference did not largely influence performance parameters including BCS, BW, and ADG.

Body weights were not different from d 0 to 27, but by d 55, ERE heifers were heavier in comparison to CON heifers and maintained this increased weight throughout the remainder of the experiment. In addition, BCS was improved in ERE heifers compared to CON heifers in the latter half of the experiment, and ADG was improved in ERE heifers compared to CON heifers throughout the experiment until d 214 to 291. From d 214 to 291, CON heifers exhibited greater ADG than ERE heifers, likely as a compensatory gain, as in the previous period, CON heifers had a negative ADG. After a period of nutrient restriction, cattle compensate with a period of greater gain (Ryan et al., 1993).

Previous literature has shown that cattle treated with ivermectin have had greater BW gain compared to untreated cattle when grazing endophyte-infected pastures; however, FEC were not reported in all experiments (Ellis et al., 1989; Bransby, 1997). Ellis et al. (1989) noted that there is an added benefit of anthelmintics on animal performance greater than from parasites alone; however, a mechanism was not mentioned. In addition, Bransby et al. (1993) stated that even when FEC were low (≤ 35 EPG), cattle treated with ivermectin had increased ADG grazing endophyte-infected tall fescue compared to untreated cattle grazing endophyte-infected tall fescue. Moreover, Bransby et al. (1993) also noted that cattle treated with ivermectin while grazing endophyte-infected tall fescue had improved ADG compared to untreated cattle with similar FEC grazing low-endophyte tall fescue.

Furthermore, Backes et al. (2015) also reported improved ADG for heifers grazing endophyte-infected tall fescue when treated with ERE in comparison to heifers dosed with the combination of moxidectin and oxfendazole and untreated heifers. The ERE-treated heifers had less FEC compared to the control heifers and had similar FEC compared to the combination dosed heifers at all times except for d 84 (Backes et al., 2015). In a large experiment by Andresen et al. (2018) using 13 herds from seven states, there was no difference in BW change or ADG between cows treated with extended-release eprinomectin and doramectin. Cattle in this experiment were all treated with an anthelmintic and had low FEC (< 3 EPG), but forage source was not mentioned (Andresen et al., 2018). In the current experiment, all cattle were dosed with oral fenbendazole (Safe-Guard) 2 weeks prior to experiment initiation

Table 2. Influence of extended-release injectable eprinomectin on heifer average daily gain, hair coat score, respiration rate, and serum prolactin concentrations over time

Item	Treatment ¹			P-value		
	ERE	CON	SEM	Trt	Time	Trt × Time
<i>n</i>	100	99				
Average daily gain, kg/day				<0.01	<0.01	<0.01
d 0–56	0.57	0.52	0.017	0.02		
d 56–112	0.69	0.43	0.017	<0.01		
d 112–171	0.39	0.32	0.018	<0.01		
d 171–214	0.02	–0.05	0.023	0.04		
d 214–291	0.29	0.35	0.015	<0.01		
Serum prolactin, ng/mL				0.74	<0.01	0.72
d 0	93.18	91.08	7.637			
d 6	54.65	61.42	5.899			
d 55	49.56	51.49	3.088			
d 111	9.00	8.78	1.123			
Respiration rate, breaths per minute				0.27	<0.01	0.95
d 1	37.4	38.5	1.28			
d 54	35.8	37.6	0.87			
d 110	55.3	57.3	2.50			
Hair coat score ²				0.32	<0.01	0.90
d 0	2.4	2.4	0.10			
d 13	2.4	2.4	0.09			
d 27	2.1	2.1	0.08			
d 55	1.5	1.6	0.07			
d 83	1.5	1.7	0.06			
d 112	1.7	1.8	0.06			

Trt = Treatment effect; Trt × Time = treatment by time effect.

¹CON cattle received a sterilized saline solution, and ERE cattle received injectable eprinomectin. Treatments were administered at initiation of the experiment at a rate of 1 mL/50 kg body weight.

²Hair coat score was evaluated on a 1 to 5 scale, in which 1 = slick, short coat and 5 = unshed, full winter coat.

and FEC remained low throughout the duration of the study. Thus, the improvement in BW and BCS is likely not because of internal parasites.

Although external parasites were not evaluated in this experiment, they could be a potential explanation for the BW gain differences. Horn flies are one of the most common ectoparasites that can negatively affect animal performance (Byford et al., 1992). Previous literature has indicated extended-release eprinomectin may have some level of fly control (Vesco et al., 2015; Trehal et al., 2017); however, other studies have not noted improvements in fly control in cows (Andresen et al., 2018). In this current experiment, it is important to remember that all cattle were comingled and horn fly differences were not anticipated as partial-treated herds have seen reduction in horn flies in both treated and untreated cattle (Harvey and Brethour, 1983). Thus, the improvement in BW and BCS is likely not because of ectoparasites.

Rough hair coat, increased RR, and decreased prolactin concentrations are symptoms of fescue toxicosis. HCS, RR, and prolactin concentrations were not different in this experiment; however,

numerically, ERE heifers had decreased HCS and RR compared to CON heifers. Previous literature has also shown that cattle grazing tall fescue, that have slick hair coats, will have increased BW gain and improved BCS compared to cattle with rough hair coats (Mayberry et al., 2017). Increased RRs in cattle grazing tall fescue is associated with ergot alkaloids and vasoconstriction, which reduces blood flow and the animal's ability to dissipate heat (Finch, 1986). The RR in this experiment were consistent with other experiments at this research station (Shoup et al., 2016); however, some studies have also seen greater RR in cattle grazing tall fescue at other locations and at this research station (Osborn et al., 1992; Stokes et al., 2018).

Prolactin concentrations are typically decreased in cattle grazing endophyte-infected tall fescue as the ergot alkaloids can bind the D-2-dopamine receptors and disrupt the dopaminergic pathways (Berde and Stürmer, 1978). Serum prolactin concentrations were not different between treatments; however, from early summer to late fall, prolactin

Table 3. Influence of extended-release injectable eprinomectin on heifer heat patch scores and reproductive performance

Item	Treatment ¹		SEM	P-value
	ERE	CON		
<i>n</i>	100	99		
Heat patch score ² , %				
Prior to estrus synchronization				
0	6.0	1.0	—	0.09
1	93.0	93.0	—	1.00
2	1.0	6.0	—	0.09
3	—	—	—	—
At time of AI				
0	0	0	—	1.00
1	66	51	—	0.03
2	14	23	—	0.11
3	20	26	—	0.32
Reproductive performance				
AI pregnancy, %	69	58	—	0.10
Overall pregnancy, %	84	68	—	0.01

AI = artificial insemination.

¹CON cattle received a sterilized saline solution, and ERE cattle received injectable eprinomectin. Treatments were administered at initiation of the experiment at a rate of 1 mL/50 kg body weight.

²Heat patches were visually scored prior to breeding (d 138) and at the time of breeding (d 171) from 0 to 3 (0 = missing, 1 = fully activated, 2 = partially activated, 3 = not activated).

concentrations decreased. In previous literature, cattle grazing toxic endophyte-infected tall fescue also had experienced this seasonal effect with reduced serum prolactin levels over similar times (Fanning et al., 1992; Aiken et al., 2013; Stowe et al., 2013; Shoup et al., 2016). This indicates that all heifers, in this experiment were experiencing fescue toxicity.

Prior to estrus synchronization, percent of fully activated heat patches was not different; however, there was a tendency for CON heifers to have less patches partially activated. At the time of AI, more ERE heifers responded to the synchronization protocol as indicated by a greater percentage of patches fully activated. Moreover, there was a tendency for ERE heifers to have increased AI pregnancy rate, and overall pregnancy rate was greater compared to CON heifers. At the time of AI, more ERE heifers responded to the synchronization protocol, which likely contributed to the improved pregnancy rates of ERE heifers compared to CON heifers. The improved BW and BCS of ERE heifers at the time of breeding may have also contributed to the improved reproductive performance noted in these heifers. At the time of AI, ERE heifers had exhibited a consistently greater BCS than CON heifers, and by d 214 of the experiment CON heifer

BCS had dropped below 5.0. Previous literature states that heifers with a BCS <5 at breeding had decreased pregnancy rates compared to cattle that had a BCS >5 (Utter et al., 1994).

Andresen (2017) reported no difference in cyclicity between heifers treated with extended-release eprinomectin and injectable ivermectin. However, extended-release eprinomectin-treated heifers had greater AI and overall pregnancy rates (Andresen 2017). It is important to note that FEC were not collected in this experiment so parasite load is unknown. In addition, these cattle were not grazing endophyte-infected tall fescue and there was lack of replication as treatments were segregated by pasture, with only one pasture per treatment.

In a large experiment, using 13 herds from seven states, no differences in pregnancy rates were noted between cows treated with extended-release eprinomectin and injectable doramectin (Andresen et al., 2018). Both groups were treated with an anthelmintic and FEC reported for this experiment were low (<3 EPG); however, forage source was not reported (Andresen et al., 2018).

Backes (2016) reported that heifers grazing endophyte-infected tall fescue and were dosed with either extended-release eprinomectin or a combination of moxidectin and oxfendazole had greater number of cyclic heifers prior to the breeding season compared to untreated heifers. In addition, after synchronization with 25 mg of PGF_{2α} and a heat detection patch, heifers treated with either extended-release eprinomectin or a combination of moxidectin and oxfendazole had a greater response to synchronization as indicated by a greater percentage of activated patches compared to untreated heifers (Backes, 2016). Furthermore, extended-release eprinomectin-treated heifers tended to have greater overall pregnancy rates compared to heifers dosed with moxidectin and oxfendazole combination (Backes, 2016). However, it is important to note that control heifers had greater FEC at several times throughout the experiment, which equated to BW and BCS differences prior to the breeding season (Backes, 2016). These differences in FEC and the lack of replication across treatment potentially confounds reproductive differences noted by Backes (2016).

Overall, spring administration of extended-release injectable eprinomectin increased BW, ADG, BCS, as well as AI and overall pregnancy rates in fall-born beef heifers previously dosed with oral fenbendazole (Safe-Guard). However, there were minimal to no differences in HCS, RR, serum prolactin, and FEC. Further research is needed to

determine the underlying mechanism of extended-release eprinomectin on improving heifer performance when grazing endophyte-infected tall fescue.

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Conflict of interest statement. None declared.

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