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University of Arkansas, Fayetteville

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Evaluation of Long-Acting Eprinomectin Compared to Conventional Anthelmintics in Cow/Calf Production

A dissertation submitted in partial fulfillment
of requirements for degree of
Doctor of Philosophy in Animal Science

by

Elizabeth Ann Backes
Lincoln University
Bachelor of Science in Agriculture, 2011
University of Arkansas
Master of Science in Animal Science, 2013

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University of Arkansas

This dissertation is approved for recommendation to the Graduate Council.

_____
Dr. Jeremy G. Powell
Dissertation Director

_____
Dr. Elizabeth B. Kegley
Committee Member

_____
Dr. Thomas A. Yazwinski
Committee Member

_____
Dr. Kelly M. Loftin
Committee Member

Abstract

Experiment 1, 83, newly weaned, fall-born crossbred heifer calves were allocated randomly to 1 of 3 anthelmintic treatments: 1) control (**CON**); 2) combination pour-on moxidectin and oxfendazole (**MO**); and 3) long-acting eprinomectin (**LAE**). Two preplanned orthogonal contrast statements were used: 1) to compare CON to treated cattle; and 2) to compare OXF to LAE. Heifer BW and BCS were greater ($P \leq 0.02$) from MO and LAE on d 112, 140, 154, 168, 182 compared to CON. Heifer cyclicity, estrous detection, natural service and overall pregnancy rates were greater ($P \leq 0.02$) for MO and LAE compared to CON. Cattle fecal egg counts (FEC) were greater ($P < 0.01$) for CON compared to treated heifers and greater ($P < 0.01$) for LAE compared to MO. Concentrations of white blood cells, lymphocytes, eosinophils, basophils, red blood cells, and platelets were greater ($P \leq 0.02$) for CON compared to treated heifers. Experiment 2, 90, spring-calving cows were allocated randomly to 1 of 3 anthelmintic treatments: 1) CON; 2) oxfendazole (**OXF**); and 3) LAE. Similar contrast statements were utilized. Cow BW, BCS on d 0, 91, 146, and 228, and pregnancy rate did not differ ($P > 0.20$) between CON and treated cows. Day 14 BCS tended ($P = 0.07$) to be greater for CON compared to treated cows. Also, BCS was greater ($P = 0.01$) and hair coat score was lower ($P < 0.01$) for OXF compared to LAE on d 91. Pregnancy rate tended ($P = 0.08$) to be lower for LAE compared with OXF. Over the duration of the study, cow FEC, concentrations of white blood cells and eosinophils were greater ($P \leq 0.04$) for CON compared to treated cows. At weaning calves were administered the same anthelmintic treatment as their dams. Calf BW on d 417 and 431 were greater ($P \leq 0.03$) for treated calves compared to CON. Calf weaning weights were lower ($P = 0.03$) for LAE compared to OXF. Calf FEC and platelets were greater ($P \leq 0.02$) for CON compared to treated calves. Carcasses from CON steers had greater ($P = 0.02$)

longissimus area and lower (P=0.02) yield grade compared to carcasses from treated calves. Based on these two studies, anthelmintic treatment can improve gain and decrease FEC in cow/calf operations.

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Dedication

I would like to dedicate this doctoral dissertation to my parents, Thomas and Carol Backes. First, I want to thank you both for your loving support with every endeavor I set out to do, especially ones that have allowed me to reach this point. Without the two of you, I would not be who I am today, and for that I am so thankful. Lastly, thank you for supporting my passion and love for agriculture, I am lucky to be able to love what I do in this field on a daily basis!

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CHAPTER 1.

LITERATURE REVIEW

Internal parasites are estimated to cost the U.S. cattle industry over $3 billion annually (Bagley et al., 1998). Research has indicated that internal parasite burdens flourish in the southern states, which encompass 11.8 million beef cows or approximately 40% of the nation's beef cow inventory (USDA-NASS, 2014). Parasite burdens have been reported to decrease feed intake and alter nutrient utilization (Kunkle et al., 2013). According to the USDA-APHIS (2009), approximately 38% of beef cattle producers do not deworm calves prior to weaning; furthermore, approximately 41% of calves are not dewormed at weaning. Although, many weaned calves are not dewormed, the same report indicated that slightly under 60% of replacement heifers and cows are not dewormed more than one time a year. The primary objective of this literature review will be to describe the important nematodes affecting cattle, the immune response associated with parasitic infections, anthelmintic resistance, and conventional anthelmintic efficacies reported in beef cattle operations.

Trichostrongylus life cycle

The general life cycle of *Trichostrongylus* spps. is similar amongst species; however, there is some variation. Levine (1968) described the general life cycle. First, adult worms living within the infected animal, produce and excrete eggs in feces. In an oxygen dependent rich environment, eggs hatch approximately 1 d after excretion in feces and create what is described as a rhabditiform 1st stage larvae. The 1st stage larvae feed on microorganisms and bacteria within the feces. Next, the 1st stage larvae molts into a 2nd stage larvae in 1 to 2 d. Following

another few days, the 2nd stage molts into a strongyliform, infective 3rd stage larvae, with its cuticle unsheathed, but not detached. After development of the 3rd stage infective larvae, this stage migrates out of the feces and moves to vegetation in close proximity to the fecal mat. On vegetation, if ingested by the appropriate host (start of prepatency), the cuticle is detached in the gastrointestinal tract, and the infective 3rd stage larvae move to the targeted area within the host. Once at the appropriate location, the 3rd stage molts to a 4th stage larvae, then to a 5th stage, and lastly into adult. After it reaches the adult stage, the nematode becomes patent and releases eggs and the cycle is perpetuated (Levine, 1968).

The time from becoming an infective larvae (3rd stage) to adult occurs in various optimal temperatures based on the nematode species (Levine, 1968). Under normal circumstances and adequate moisture, temperature plays a crucial role in the ability for eggs to hatch. For most species, temperatures between 20 to 30°C are optimal for effective hatching ability (Ballweber, 2006). Once eggs hatch and larvae enter the environment, they are subject to desiccation due to extremely low or high temperatures or contact with direct sunlight (Ballweber, 2006). Stromberg and Averbeck (1999) indicated that less than 33% of larvae that develop from excreted eggs develop into infective larvae, possibly as a result of inadequate conditions for development.

General *Trichostrongylus* spps. characteristics

Trichostrongylus spps. are considered to be small, slender nematodes (Levine, 1968) that affect multiple livestock species, including most of the domestic livestock species. The most economical and detrimental parasites that affect small ruminants, cattle, and other animals are encompassed in this group (Levine, 1968). Generally, speaking, this genus is characterized as

having a small head that is absent of a buccal cavity and cervical papillae. Females deposit thin shelled eggs that are segmented prior to deposition. The female vulva is located just behind the middle of the body and usually has predominant lips. In terms of male reproductive parts, the male bursa has predominate lateral lobes and a well distinguished, symmetrical dorsal lobe, but is absent of accessory bursal membranes. However, the gubernaculum is present in most cases, and the spicules are brown in color, and are considered to be stout, stunted, and uneven (Levine, 1968).

Important cattle nematodes and associated pathogensis

Ballweber (2006), indicated that the most common parasitic infections in cattle were as a result of *Cooperia*, *Haemonchus*, *Ostertagia*, and *Trichostrongylus* species. These parasites are commonly called the HOT Complex (Ballweber, 2006). Other genera of interest include *Bunostomum*, *Nematodirus*, and *Oesophagostomum*.

Trichostrongylids are characterized as being the most important and most pathogenic nematodes in cattle. *Ostertagia ostertagi* (*O. ostertagi*) and the *Cooperia* species are of the greatest importance and occur most commonly (Levine, 1968). Pathogenesis of *Bunostomum phlebotomum* (*B. phlebotomum*) includes, irritation of skin if acquired trans-cutaneously; (Sigetwary, 1931), diarrhea, emaciation, anemia, and decreased body weight (BW) (Levine, 1968). Cattle with infections of *Cooperia* species exhibit signs of diarrhea, emaciation, enteritis, and ultimately death if the infection continues to perpetuate (Levine, 1968).

Haemonchus placei (*H. placei*), is the predominate nematode associated with blood loss in cattle. Levine (1968) reported that *H. placei* larvae and adults can suck blood from areas located on the mucosal lining. Also, *H. placei* releases an anticoagulant that damages the

infected area mucosal lining. Symptoms associated with *H. placei* include, decreased weight, bottle jaw, anemia, and weakness.

Andrews and Maldonado (1942) evaluated the pathogenesis of *Oesophagostomum radiatum* (*O. radiatum*) indicated that cattle are primarily affected during the prepatent period, thus indicating pathogenesis is a result of the larvae for this specific gastrointestinal parasite. The authors explained that after the initial infection is established, nodules are formed. These nodules are due to inflammation and irritation, and can develop into small abscesses. Within approximately 20 days, the intestinal wall becomes inflamed and edema begins to form where the nodules are located (Andrews and Maldonado, 1942). Other signs of pathogenesis of *O. radiatum* include anorexia (Bremner, 1961), dermatitis if larvae are acquired trans-cutaneously (Levine, 1968), emaciation, anemia, weakness, and severe diarrhea (Becklund, 1958).

Pathogenesis associated with *O. ostertagi* includes, anemia, edema of the submaxillary region, and emaciation (Levine, 1968). *Ostertagia ostertagi* is characterized as having three "types" of infections. Type 1 ostertagiasis represents the classical infection, where infected animals exhibit, normal signs of pathogenesis (Martin et al., 1957; Anderson et al., 1965). Pre-type 2 ostertagiasis is when early 4th stage larvae arrest in the gastrointestinal tract. However, type 2 ostertagiasis occurs when the arrested early 4th stage larvae move out of arrestment and continue to mature into adults. This stage of ostertagiasis normally occurs through the winter and spring months in the north but late summer and early fall in the south (Levine, 1968).

If present in large abundance, *T. axei* has been reported to be highly pathogenic (Andrews et al., 1954) and can cause decreased performance, such as loss of weight and appetite and weakness (Doran, 1955).

Immune response during parasitic infections

Lymphocyte activity:

Gastrointestinal infections wreak havoc on the animal's immune system, and the mechanisms behind functional immunity still remain unclear (Gasbarre et al., 2001). Currently, it is understood that parasitic infections stimulate either 1 of 2 immune responses, and both are characterized as being an antagonistic immune response (Gasbarre et al., 2001). These immune responses are indicative of Th1 or Th2 stimulation. After stimulation of either one of these two immune responses, there is a rise in cytokines that cause stimulation or inhibition of certain components of the immune system (Gasbarre et al., 2001). However, determining if either Th1 or Th2 is the dominating force behind the immune response, is dependent on which antigen presenting cell type is in the greatest quantity, the number of co-stimulatory molecules, and the type of cytokine environment (Grencis, 1996; Constant and Bottomly, 1997). Svetic et al., (1993) reported that during times of increased parasitic infections, the Th2 immune response elicited high amounts of the cytokine Interleukin 4, IgG1 and IgE antibodies, and mast cells. Similar data were reported by Finkelman et al. (1997) and Else and Finkelman (1998) who reported that Interleukin 4 and Interleukin-13 promoted protective immunity. Interferon-γ, another cytokine, is up-regulated during times of *O. ostertagi* infection.

Cattle infected with *O. ostertagi* have been reported to have abomasal tissue changes post-infection. Average lymph node size dramatically increases during these infections (Gasbarre, 1986, 1994; Canals et al., 1997), and can contribute to an increase in parasite-specific lymphocytes or lymphocytes that cannot recognize the antigen associated with the parasite (Gasbarre, 1986). Also, the production of T lymphocytes has been reported to decrease and in

return production of B lymphocytes increase in these lymph nodes (Gasbarre, 1994; Canals et al., 1997). Interferon-γ is up-regulated during times of *O. ostertagi* infection due to the increased production of lymphocytes (Canals et al., 1997; Almeria et al., 1997) and is indicative of the role Th1 and Th2 have on the immune response during times of parasitic infections (Gasbarre et al., 2001).

Immunoglobulin production:

The production of immunoglobulins also play an important role in aiding the immune response during parasitic infections. Most of the research evaluating the relationship between immunoglobulin production and parasitic infections has been evaluated in infections associated with *O. ostertagi*. Immunoglobulin E-mediated hypersensitivity has been reported to have a direct effect against gastrointestinal protection, in terms of protective mechanisms (Jarret and Miller, 1982; Miller, 1996). Currently, there is little published data reported evaluating the effects of IgE production against gastrointestinal nematodes in cattle. However, conflicting data is reported (Baker and Gershwin, 1992; Thatcher et al., 1989; Baker and Gershwin, 1993), indicating that IgE mediated responses need to be further evaluated. In terms of IgA mediated responses in naturally- or artificially-infected cattle, *O. ostertagi*-specific IgA antibodies have been reported to increase (Canals and Gasbarre, 1990; Gasbarre et al., 1993). Frankena (1987), reported that IgG_2 antibody-containing cells increased during primary and secondary infections of *O. ostertagi* and *C. oncophora*. In terms of these primary and secondary parasitic infections in calves, IgG_2 antibody-containing cells increased in the abomasa mucosa during infections as a result of *O. ostertagi* and in the small intestines as a result of *C. oncophora*. Interestingly, Kloosterman et al. (1984) reported that high IgG titers were indicative of a lower burden, that worms were shorter, and females had less ova/female and had reduced vulval flaps. With the

research presented, it can be suggested that immunoglobulin production plays a crucial role in providing a huge impact on the animal's ability to withstand parasitic infections.

Eosinophil response:

Proportions of eosinophils have been reported to increase in both the blood and in the intestinal mucosa during parasitic infections (Rothwell, 1989) and can be a direct effect of Interleukin-5 production (Korenaga et al., 1994). The mechanism behind eosinophil's role in protecting cattle against gastrointestinal parasites is still questionable. With that being said, Washburn (1984) reported that *O. ostertagi* 3rd stage populations are bound to eosinophils, although the direct effect of eosinophils on the larvae could not be determined.

Methods of evading the immune system:

Haemonchus placei is a blood sucking parasite that directly impacts the quantity of blood in the animal. Also, in some incidences, *H. placei* has been reported to inject an anticoagulant into the circulatory system which causes greater amounts of blood losses than the parasite could actually ingest and utilize for its benefit (Levine, 1968).

Ostertagia ostertagi is a parasite that causes elevated, but small lesions on the intestinal wall that can cause edema in these locations and in some incidences can cause blood clots on the lumen of the stomach (Osborne et al., 1960). Trelkeld and Johnson (1948) reported decreased survival time of red blood cells following the establishment of an *O. ostertagi* infection.

Cooperia species have been reported to cause gross lesions on the duodenum and hemorrhages on the intestinal wall, as well as thickening of the intestinal tract mucosa and serosa (Bailey, 1949). Herlich (1965) indicated that *C. pectinata* evaded the immune system via entry

of the small intestines. It was reported that lesions were reported on the duodenum section of the small intestines and can cause lesions and mild inflammation up to 3.65 meters of the duodenum.

Oesophagostomum radiatum forms small, elevated areas on the walls of the large or small intestines. While these don't cause much inflammation or irritation, the abscesses produced by *O. radiatum* fill with leukocytes. Approximately 20 days after the initial signs of infection, the intestinal wall that encompasses these abscesses become inflamed and edematous (Mayhew, 1948). *Trichostrongylus axei* is reported to cause lesions on the abomasum wall that in return, cause inflammation, corrugation of the mucosa, sloughing of the epithelium, and lymphocytic infiltration (Doran, 1955).

Anthelmintics

Anthelmintic therapy is widely used in the livestock industry. An anthelmintic is a pharmaceutical drug that is intended to paralyze or kill parasitic worms in their host (Dictionary, 2015). Through many factors, anthelmintic resistance can occur, which allows for the intended parasite to survive post-treatment. Livestock producers commonly associate this problem to the small ruminant industry; however, recently anthelmintic resistance has become an increasing concern not just locally, but world-wide in cattle.

Currently, there are three anthelmintic classes approved for use in cattle. The first class is the imidazothiazole class and includes levamisole; the benzimidazole class is the 2nd and includes anthelmintics such as, albendazole (ALB), fendbenazole (FEN), and oxfendazole (OXF), and lastly is the macrocyclic lactone class. This class is divided into two sub-classes: 1) 1st generation avermectins [ivermectin (IVM), doramectin (DOR), eprinomectin (EPM), and abamectin]; and 2) 2nd generation mibemycins [moxidectin (MOX); Edmonds et al., 2010].

Modes of actions

Imidazothiazoles

Treatment against gastrointestinal parasites using imidazothiazoles causes paraylization due to the direct cholinergic effect, which is characterized as having effects on the acetylcholine receptors of the nematodes' muscles, where it renders it inactive. Which in return decreases the parasites' ability to carry out normal function. Also, the effect on the ganglionic stimulant decreases the parasites' ability to carry out normal processes (Adams, 2001).

Benzimidazoles

Adams (2001) stated that the primary function of this drug class is that it binds to the nematode tubulin, specifically to the β-tubulin. This binding capability prevents the dimerization with the α-tubulin, which prevents the polymerization of tubulin oligomers into microtubules. Microtubules are directly related to the cellular process, such as mitosis, protein synthesis, and energy metabolism. Preventing the formation of microtubules prevents these cellular processes to be carried out.

Macrocyclic Lactones

This drug class affects the nervous system. They increase the release of γ-aminobutyric acid (GABA) from the synapse of the nervous system, which causes the opening of the GABA-gated chloride channels. This causes the chloride ions to rapidly enter the cell. When this happens, the cell has decreased resistance, and causes a slight hyperpolarization. This ultimately can cause death or expulsion of the parasite because of the interference of transmission of neural stimuli to muscles, which causes flaccid paralysis (Adams, 2001).

Resistance

Resistance is achieved when a fecal egg count reduction (FECR) test are <90%, when the anthelmintic is administered at the recommended dose. Due to the decrease in the development of new anthelmintics, resistance is on the rise and is becoming an animal health issue (Barragry, 1994). Wolstenholme et al. (2004) describe the 4 possible avenues in which drug resistance can occur: 1) change of molecular target; 2) change in metabolism that inactivates, removes, or prevents activation of the drug; 3) change in the distribution of the drug that prevents it from acquiring the activation site; and 4) amplification of target genes to prevent drug action. Briefly, the mechanism for anthelmintic resistance in the levamisole class can occur when there are changes in the receptors associated with nicotinic acetylcholine. Bezimidazole resistance is associated with mutations located on the β-tubulin isotype 1 located on the F200Y and F167Y genes or through altered metabolism. Lastly, mutations in either or both the GluCL and GABA-R genes and the overexpression of P-glycoproteins can lead to macrocyclic lactone drug resistance (Wolstenholme et al., 2004).

Imidazothiazole resistance

Parasite resistance is not well documented in the imidazothiazole class. However, there have been reported cases of levamisole resistance in cattle populations. In one study, Soutello et al. (2007), reported minimal cases of levamisole resistance in Argentinian cattle. Cattle with parasite burdens experiencing resistance to levamisole had FECR ranging from 47.4 to 73.7%; however, it is important to note, that these cases were not seen in great detail. In the parasitic resistant populations, *Cooperia* species and *H. placei* were noted to be resistant to the anthelmintic.

Benzimidazole resistance

Emphasis on evaluating benzimidazole resistance in cattle is not as well evaluated in cattle when compared to the macrocyclic lactone class. However, there have been reports that benzimidazole resistance is occurring in cattle productions world-wide. Fendbendazole has been reported to have resistant parasite populations in cattle located in Argentina (Anziani et al., 2004), Brazil (Mejia et al., 2003), and the United States (Chaudhry et al., 2014). Soutello et al. (2007) reported that cattle populations in Brazil were experiencing parasite resistant populations when ALB was administered.

In one study, Chaudhry et al. (2014) evaluated the prevalence of parasite resistance to benzimidazoles. Adult worm populations were harvested from cattle located on farms across the United States. It was determined that *H. placei* was becoming resistant to this drug class. More interestingly, it was one of the first studies to report that the mutation located on the β-tubulin isotype 1 located on the F200Y was found; however, the polymorphism located on P168 or P167 was not detected. The determination of the location of benzimidazole resistance is an important find, because it allows for a better understanding of what locations on the gene are aiding in *H. placei* becoming resistant and gives further insight to how the nematode is altering based on anthelmintic treatment. Similarly, *H. placei* resistance was reported in Argentina (Mejia et al., 2003; Anziani et al., 2004) and Brazil (Soutello et al., 2007). *Ostertagia* species were detected to have become resistant to ALB in Brazil (Suarez and Cristel, 2007) and FEN (Mejia et al., 2003). Several studies have reported a resistant population in *Cooperia* species (Mejia et al., 2003; Anaziani et al., 2004; Soutello et al., 2007), following administration of an anthelmintic from this class.

Macrocyclic lactone resistance

The macrocyclic lactone class has been reported to be the major concern for anthelmintic resistance, with the majority of the research published evaluated this resistance (Kaplan and Vidyashankar, 2012). World-wide resistance has been reported in countries such as, Argentina, Brazil, New Zealand, United Kingdom, and the United States (Anziani et al., 2001, 2004; Condi et al., 2009; Demeler et al., 2010; Edmonds et al., 2010; Fiel et al., 2001; Mejia et al., 2003). Anthelmintics such as IVM and MOX have been reported to have become less efficacious (Anziani et al., 2001; Mejia et al., 2003; Anziani et al., 2004; Soutello et al., 2007; Suarez and Cristel, 2007; Condi et al., 2009; Gasbarre et al., 2009; Edmonds et al., 2010). Gasbarre et al. (2009) evaluated the efficacy of multiple macrocyclic lactones, such as IVM, EPM, DOR, and MOX, and compared them to a negative control (CON) and ALB, using beef calves purchased at local sale barns. It was reported that MOX treated calves had the highest FECR (82%) over 14 d and pour-on EPM had the lowest FECR (42%). Also, IVM- and MOX-treated calves had the greatest percentage of worm burdens located in the small intestines. In a similar study, Anziani et al. (2001) reported that IVM-, DOR-, and MOX-treated calves had <90% fecal egg count (FEC) following anthelmintic administration.

Many species of parasites are showing resistance to macrocyclic lactones (Anziani et al., 2004; Suarez and Cristel, 2007; Condi et al., 2009; Edmonds et al., 2010). *Cooperia* species have been reported to be resistant to IVM (Fiel et al., 2001; Anziani et al., 2004; Soutello et al., 2007; Suarez and Cristel, 2007; Edmonds et al., 2010) and MOX (Condi et al., 2009). Ivermectin resistance has been shown to be prevalent in the *Ostertagia* species (Suarez and Cristel, 2007; Edmonds et al., 2010) and *H. placei* (Anziani et al., 2004; Soutello et al., 2007). Lastly, cattle treated with MOX have been reported to have resistant populations of *Oesophagostomum* species (Condi et al., 2009).

Anthelmintics of interest

Oxfendazole

Performance of cattle treated with oxfendazole.

Changes in cattle BW have been evaluated after administration of OXF (Chambers, 1985; Purvis et al., 1994; Larson, 1995; Ives et al., 2007; Walker et al., 2013), with all of the experimental procedures differing a great deal. Walker et al. (2013) evaluated the effects of various anthelmintic treatments consisting of 1) OXF given on d 0 and MOX given on d 73; 2) MOX given on d 0 and OXF given on d 73; 3) MOX given on d 0; 4) OXF given on d 0; and 5) control (CON). It was reported that initial and final shrunk BW did not differ across treatments. However, control calves had lower ADG compared with treatments 1, 2, and 4; but, did not differ from treatment 3. When evaluating BW on different collection days, it was determined that on d 31, treatment 3 had greater BW compared with CON calves. Next, on 59 days post-treatment, treatments 1, 2, and 4 had greater BW compared with CON calves, and treatment 3 was similar to CON calves. And lastly, 108 days post-treatment the OXF treated caves had the greatest BW compared with all other treatments. In two studies, Chambers (1985) and Larson (1995) evaluated the effects of OXF administration with different implants. First, Chambers (1985) evaluated the effects of the administration of zeranol and OXF. Treatments consisted of: 1) CON; 2) zeranol; 3) OXF; and 4) the combination of zeranol and OXF application. It was reported that application of either zeranol or OXF increased BW in 8-9 month old calves, with 7.4 kg, 13.7 kg, and 20.6 kg more BW produced for zeranol-, OXF-, and combination of zeranol and OXF-treated calves, respectively, when compared to CON calves. Larson (1995) evaluated the effects of administration of OXF and Synovex-C© on 2-3 mo old calves. Treatments

consisted of 1) CON; 2) OXF administered at 2-3 mo of age and at weaning; 3) implanted with Synovex-C© at 2-3 months of age; and 4) dewormed an implanted. The author reported that there was no positive impact on BW and body condition score (BCS) over the duration of the study.

Additionally, cow reproductive performance has been evaluated in cattle operations. Purvis et al. (1994), used 388 mixed breed spring-born heifers to evaluate the effects of intrarumminal administration of OXF compared to a negative control. It was reported that heifer age at puberty, first conception and overall pregnancy rates did not differ across treatments. Similarly, Larson (1995) determined that there was no effect on heifer cyclicity at the start of the breeding season, artificial and overall pregnancy rates, and pre-breeding pelvic area in heifers dewormed with OXF, implanted with Synovex-C©, or the combination of the two, compared to CON heifers.

Oxfendazole effects on fecal egg counts and coprocultures

Evaluating the effects of oral OXF (Chambers, 1979; Borgsteede and Reid, 1982; Lyons et al., 1989; Williams et al., 1997; Walker et al., 2013) or intraruminal injection of OXF (Borgsteede et al., 1982; Solcombe et al., 1989; Purvis et al., 1994) has been evaluated in cattle operations. Williams et al. (1997) evaluated the efficacy of pour-on IVM, ALB, OXF, and FEN in 10-12 month crossbred heifer calves that were obtained from a local livestock auction barn. Cattle had naturally acquired nematode infections at purchase, grazed on pasture for approximately 9 wk, and then were moved to concrete floors, where FEC were monitored over a 28 d period. It was reported that 3 days post-treatment, cattle receiving the bezimidazole treatments had lower FEC compared to IVM pour-on and CON heifers. Also, by d 7 and 15, all

heifers that were administered an anthelmintic had lower FEC compared with CON heifers. However, by d 28, IVM pour-on had the lowest FEC compared with other treatments, but the benzimidazole treatments still had FEC that were significantly lower than those of the CON heifers. Borgsteede and Reid (1982) used 27 dairy calves that had previously completed their first grazing season. Calves were allocated to 1 of 3 treatments consisting of: 1) CON; 2) oral OXF; 3) intraruminal administration of OXF. Fecal egg counts were monitored for 7 d. It was reported that FEC were lowest in the OXF treatments compared to CON; however, no differences were reported between the two routes of OXF administration.

In one study, Chambers (1979) evaluated the effects on artificial infections in Friesian calves. Prior to the initiation of study, calves were raised worm-free. Next, calves were administered 10,000 3rd stage *O. ostertagi* and 10,000 3rd stage *C. onocophora* at 2, 6, 14, and 24 days prior to anthelmintic treatment. Calves were then allocated to either an OXF or CON treatment. The authors reported that anthelmintic treatment of OXF was 76.8% efficacious against 3rd to early 4th stage *O. ostertagi,* and 87.3% efficacious against 4th stage and 98.3% efficacious against immature 5th stage and adult *O. ostertagi*. Also, it was reported that anthelmintic administration of OXF was 99% effective against all stages of *C. onocophora*. In another study, Solcombe et al. (1989) evaluated the effects of intraruminal administration of OXF in either Angus/Simmental or Angus/Hereford calves. Control calves had lower efficacy compared to treated calves. Angus/Simmental treated calves had a greater reduction in *N. helvantianus* (100%), *Strongyloides* (83%), and *Trichuris* (100%) compared to control heifers. Next, administration of OXF in the Angus/Hereford calves, had a greater reduction in *N. helvantianus* (100%), *Trichuris* (100%), and *Monieza* (100%) compared to heifers that received no anthelmintic.

Oxfendazole concentrations

Moreno et al. (2005) compared the effects of either injectable or oral administration of various anthelmintics on milk residues in second lactation Holstein cows. Treatments consisted of: 1) oral OXF; 2) oral ALB; 3) injectable ALB sulphoxide; 4) and injectable OXF, and milk was collected for 5 days post-treatment. It was reported that oral OXF reached the greatest concentration in the milk at 12 h post-treatment and was detected for up to 72 h. Also, milk residues were detected in the milk for 36 h in the injectable OXF treatment. Thus, indicating that oral administration of OXF created quicker action and lasted longer in milk compared with other routes of administration.

Moxidectin

Performance of cattle treated with moxidectin

Efficacy of MOX has been well evaluated in beef cattle (Williams et al., 1999; Yazwinski et al., 1999; Anziani et al., 2001; Elsener et al., 2001; Reinemeyer and Cleale, 2002; Williams and DeRosa, 2003; Maritorena-Diez et al., 2005; Ives et al., 2007; Powell et al., 2008; Gomes de Soutello et al., 2010; Leathwick and Miller, 2013; Walker et al., 2013; Yazwinski et al., 2013). Cattle treated with MOX have been reported to have increased BW (Williams et al., 1999; Powell et al., 2008; Walker et al., 2013) and gain performance (Williams et al., 1999; Elsener et al., 2001; Powell et al., 2008) over cattle not treated with anthelmintic or in cattle treated with IVM (Williams et al., 1999). In one study, Williams et al. (1999) used seventy-two, 9-12 month old, Brangus/Angus, steer calves to determine the effects of pour-on varieties of MOX, DOR, IVM, and EPM and compared them to a negative control. Body weights were taken on d 0, 28, 56, 84, and 112. It was reported that treated calves had greater BW and average daily gain

(ADG) on d 28, 56, 84, and 112 compared to CON calves. Also, MOX- treated calves had greater BW and ADG compared to IVM-treated cattle on all collection d. In contrast to the previously mentioned study where performance was increased, Ives et al. (2007) evaluated the effects of 3 anthelmintics on feedlot performance in auction barn bought mixed-breed steer calves. Treatments consisted of 1) DOR; 2) MOX; and 3) MOX plus OXF. Calves in this study were harvested and carcass measurements were collected. It was reported that feedlot performance, in terms of BW, dry matter intake (DMI), daily gain, and intake:gain ratio were not positively impacted by anthelmintic treatment. Similarly, animal health characteristics, such as morbidity and mortality percentages, number of rejects were not significantly reduced in cattle receiving anthelmintic treatment compared to CON calves. Quality and yield grade did not differ across treatment groups; however, when MOX was applied with OXF, hot carcass weights were greater compared to solely MOX and CON calves.

Moxidectin effects on fecal egg counts and coprocultures

There is a vast array of the effects of MOX on FEC and coprocultures in beef cattle (Williams et al., 1999; Yazwinski et al., 1999; Anziani et al., 2001; Elsener et al., 2001; Reinemeyer and Cleale, 2002; Maritorena-Diez et al., 2005; Williams and DeRosa, 2003; Ives et al., 2007; Powell et al., 2008; Leathwick and Miller, 2013; Gomes de Soutelo et al., 2010; Walker et al., 2013; Yazwinski et al., 2013). Cattle treated with MOX have been reported to have lower FEC compared to CON (Williams et al., 1999; Anziani et al., 2001; Elsener et al., 2001; Maritorena-Diez et al., 2005; Powell et al., 2008; Gomes de Souttello et al., 2010; Walker et al., 2013; Yazwinski et al., 2013) and other various anthelmintics (Williams et al., 1999) cattle. As previously mentioned in the paper by Williams et al. (1999), Brangus/Angus steer calves were administered topical formulations of MOX, DOR, EPM, and were compared to CON

calves. Seven days post-treatment, MOX-, DOR-, and EPM-treated steer calves had lower FEC compared to CON calves. Also, on d 21 post-treatment MOX had lower FEC compared to DOR- and IVM-treated calves, as well as CON cattle.

Efficacy of MOX on worm counts varies from study to study. Yazwinski et al. (1999), Reinemeyer and Cleale (2002), Williams and DeRosa (2003), and Yazwinski et al. (2013) reported higher efficacy for calves treated with MOX compared with calves receiving no anthelmintic. Similar results were reported in cattle treated to IVM (Powell et al., 2008; Yazwinski et al., 2013). Reinemeyer and Cleale (2002) evaluated the effects of pour-on MOX and injectable MOX in Holstein calves compared to CON calves. In this study, the authors evaluated the effects of anthelmintic treatment when both larvacial and adultical inoculums were experimentally administered. It was reported that MOX (either pour-on or injectable), was 100% efficacious for *O. radiatum* females and *O. radiatum* males, 98.6 to 99.2 % for *Trichuris* species, 91.8 to 99.0% for *Cooperia* species, and 95.3 to 96.1% efficacious for *Strongyloides papillosus* (*S. papillosus*), when larvacial inoculum was administered to Holstein calves. Similar results were reported when adulticidal inoculum were administered to experiment calves. Treatment with MOX reported to be 100% efficacious for *O. radiatum* females and *O. radiatum* males, 100% for female *Trichuris* species, and 100% for *C. onocophora* males. In another study, Yazwinski et al. (1999) reported that in lactating dairy cows, the application of MOX pour-on was 100% efficacious against *Ostertagia lyrata* males, *C. punctata* males, and *O. radiatum* 4^{th} stage larvae and adults. Also, treated cows had lower populations of *Ostertagia* species adult females, inhibited 4^{th} and developing L_4 *O. ostertagi* adult males, *T. axei* adults, adult *Cooperia* species females at time of harvest. Therefore, indicating that MOX is a viable anthelmintic against gastrointestinal nematodes.

Moxidectin concentrations

In one study, Sallovitz et al. (2011) compared the *in vitro* characteristics of both MOX and DOR absorption through the skin of cattle. Samples were taken from Holstein steer calves that were harvested in an abattoir in close proximity to where the study was being conducted. Next, the research team applied either DOR or MOX pour-on variations to the skin. It was reported that both anthelmintics passed through the skin for up to 72 h post-treatment. Also, when comparing DOR to MOX, DOR had a longer lag time and higher flux compared with MOX.

Imperiale et al. (2002) and Imperiale et al. (2009) evaluated the residue effects of moxidectin pour-on. First, Imperiale et al. (2002) evaluated the effects of IVM and MOX in whole milk samples. In this study, drug free milk was fortified with either anthelmintic, and abamectin was considered as the standard. It was reported that MOX had a retention time in the milk of 8.5 min, IVM at 8.1 min, and abamectin at 11.6 minutes. Also, it was determined that MOX had a 72% drug recovery in the milk, whereas IVM had 75% drug recovery. In another study, Imperiale et al. (2009), evaluated the effects of preventative allogrooming (for 5 days) versus allowed allogroming, on plasma and milk concentrations of MOX in Holstein dairy cows. It was reported that in both treatments, concentrations of MOX were recovered from 12 to 15 d post-treatment, with lower concentrations in the preventative allogrooming group. Also, the allowed allogrooming group had a shorter time to peak concentration compared with the preventative group (3 vs. 7 days, respectively). However, after the lift on preventative care was waived, milk concentrations began to rapidly increase. Thus indicating, that the standard withdrawal period required before slaughter and milk harvesting is valid.

Eprinomectin

A pour-on formulation of EPM is available in a 0.5% solution, which is effective at 0.5 mg/kg of BW (Kunkle et al., 2013), This formulation has been reported to have positive effects on both endoparasites (Shoop et al., 1996; Williams et al., 1999; Cramer et al., 2000; Dorny et al., 2000; Cringoli et al., 2003; 2004) and ecoparasites (Shoop et al., 1996). Recently, an alternative to the pour-on EPM has been released on the market. This form of EPM is a long-acting EPM that is administered at 1 mg/kg BW subcutaneously (Forbes, 2013; Kunkle et al., 2013). In this form, EPM is incorporated into a poly(D, L-lactide-co-glycolic) acid which allows for it to be slowly released in the body (Kunkle et al., 2013; Soll et al., 2013). Forbes (2013) reported that plasma concentrations of eprinomectin in the body increase after delivery of the drug, then gradually decline to approximately d 20 and remain at low levels until approximately d 70. Around d 90, the second peak of plasma concentrations increase and remain at these levels until d 120, after which they decline until approximately d 150 to160.

Performance of cattle treated with long acting eprinomectin

Long-acting eprinomectin (LAE) treatment has also been reported to increase cattle BW over a 120-d grazing period (Kunkle et al., 2013; Rehbein et al., 2013a). In one study, cattle treated with LAE achieved approximately 10 percentage units more live weight gain compared to untreated cattle (Kunkle et al., 2013).

Long-acting eprinomectin effects on fecal egg counts and coprocultures

Recently, several studies have compared effects of LAE on gastrointestinal parasite control vs untreated groups of cattle. Rehbein et al. (2013b) evaluated the effects of LAE on induced infections of developing (4^{th} stage) and adult nematodes. Cattle were inoculated with 3^{rd}

stage larvae or eggs of numerous cattle parasites with the intent that, at time of anthelmintic treatment, nematodes were either 4th stage or adults. Treatments consisted of 1) CON; or 2) LAE. Cattle were monitored for 14 to 22 days over a series of 6 studies. Therapeutic treatment of LAE against developing 4th stage pulmonary and gastrointestinal nematodes resulted in significantly lower nematode counts compared to the CON group. A 99% efficacy of LAE for the following nematodes: *Dictyocaulus viviparous* (*D. viviparous*), *B. phlebotomum*, *Cooperia curticei (C. curticei*), *C. oncophora*, *C. surnabada*, *C. punctata*, *Haemonchus contortus* (*H. contortus*), *H. placei*, *N. helvetianus*, *O. radiatum*, *Oeosphagostomum venulosum*, *Ostertagia leptospircularis* (*O. leptospircularis*), *O.ostertagi*, *Ostertagia circumcincta*, *Ostertagia pinnata*, *Ostertagia trifurcate* (*O. trifurcate*), *S. papillosus*, *T. axei*, and *Trichostrongylus colubriformis* (*T. colubriformis*) was reported. Also, LAE treated cattle had significantly lower adult nematode counts compared with the CON cattle. Similarly, it has been reported in studies evaluating the effects of LAE on naturally infected cattle with pulmonary and gastrointestinal nematodes that LAE treatment significantly reduced overall nematode counts and inhibited 4th stage larvae (Hunter et al., 2013) and stongylid eggs (Kunkle et al., 2013; Rehbein et al., 2013a). Thus, LAE has substantial effectiveness against most pulmonary and gastrointestinal parasites that affect cattle.

Duration of efficacy of long-acting eprinomectin

There is a single manuscript in the current literature determining the length of efficacy of LAE on nematode control in cattle. Soll et al. (2013) in a series of 10 individual studies, reported the use of LAE on 198 mixed breed cattle in the United States, United Kingdom, and Germany. In these studies, cattle were allocated to either a control group or an LAE group. Cattle were experimentally infected on d 100 (studies 1 & 2) and d 120 (studies 1-8) with

variations combinations of *H. contortus*, *H. placei*, *O. ostertagi/lyrata*, *O. leptospicularis*, *Ostertagia* spps. (ovine), *T. axei, T. colubriformis, C. oncophora/surnabada, C. puctata*, C. *curticei, N. helvetianus, B. phlebotomum, O. radiatum, S. papillosus*, *Trichuris* spp. (ovine) and/or *D. vivipaus* or on d 150 with *H. contortus*, *O. ostertagi/lyrata, B. phlebotomum, O. radiatum*, and *D. viviparus*. Studies 1 and 2 reported that LAE treated cattle had fewer *C. oncophora/surnabada*, *C. puctata*, and *T. axei* compared to CON. Long-acting eprinomectin treated cattle had fewer nematode counts for *H. contortus*, *O. ostertagi/lyrata, O. leptospicularis*, *T. circumcincta*, *O. trifurcata*, *T. axei, C. punctata*, *B. phlebotomum, O. radiatum*, and *D. viviparus*. Results indicated that cattle challenged at 150 d had fewer *H. contortus*, *B. phlebotomum, O. radiatum*, and *D. viviparus*. In this series of studies, the authors reported that treatment of LAE in cattle that were experimentally challenged with a variety of pulmonary and gastrointestinal nematodes resulted in a high efficacy rate for a variety of these nematodes, and that LAE can control these nematodes for up to 150 d post treatment.

Due to its long efficacy period and effectiveness, LAE may increase in popularity with cattle producers. However, due to the long-lasting effects of LAE and possible increased in use by cattle producers, possible parasitic resistance may occur and further research is warranted to determine these affects.

Conclusion

Gastrointestinal parasites cause detrimental effects on the animal's immune system and performance, and can cause huge losses for cattle operations. Therefore, treatment against gastrointestinal parasites is crucial to improving these economic traits and the well-being of infected animals. Lastly, oxfendazole, moxidectin, and long-acting eprinomectin are

commercially available anthelmintics that beef cattle producers can implement into their operation to mitigate the negative attributes of gastrointestinal parasite infections.

Chapter II.

Effects of moxidectin/oxfendazole combination and long-acting eprinomectin administration on post-weaning performance, reproductive measurements, fecal egg counts, and complete blood cell counts in fall-born replacement beef heifers

Abstract

Huge monetary losses to the United States' cattle industry are a result of internal parasites. Little current research is available evaluating the effects of anthelmintic treatment in replacement beef heifers. The objective of this study was to evaluate the effects of anthelmintic therapy on post-weaning gain performance, reproductive measurements, fecal egg counts (FEC), and complete blood cell counts in fall-born Angus and Angus × Hereford replacement heifers. Eighty-three, newly weaned, fall-born crossbred heifer calves were stratified by d -14 BW and FEC, and d of age and allocated randomly to 1 of 3 anthelmintic treatments: 1) control (n = 28; no anthelmintic administered; **CON**); 2) combination pour-on moxidectin and oxfendazole (n = 28; **MO**); and 3) long-acting eprinomectin (n = 27; **LAE**). Heifers grazed in individual treatment groups on pastures containing endophyte-infected tall fescue, for a 274-d grazing study. Anthelmintics were administered on d 0 and 154 of the study. Two preplanned orthogonal contrast statements were utilized and included: 1) to compare CON to treated cows (OXF and LAE); and 2) to compare OXF to LAE. Heifer BW and BCS were greater ($P \leq 0.02$) from MO and LAE on d 112, 140, 154, 168, 182 compared with CON. Heifer cyclicity, estrous detection, natural service and overall pregnancy rates were greater ($P \leq 0.02$) from MO and LAE compared with CON. Cattle FEC over the 274 d study were greater ($P < 0.01$) from CON compared to treated heifers and greater ($P < 0.01$) from LAE compared to MO. Concentrations of white blood cells, lymphocytes, eosinophils, basophils, red blood cells (RBC), and platelets (PLT)

were greater ($P \leq 0.02$) from CON compared with treated heifers. In the current study, anthelmintic therapy increased performance and reproductive measurements, decreased FEC and the majority of the WBC, as well as RBC, and PLT in fall-born replacement beef heifer calves over a 274 d grazing study.

Introduction

Internal parasites are estimated to cost the United States' cattle industry over $3 billion annually (Bagley et al., 1998) and have been reported to flourish in the southern states, which incorporates 11.8 million beef cows (40% of total US beef inventory; USDA-NASS, 2014). Burdens have been reported to decrease feed intake and alter metabolism (Kunkle et al., 2013). According to the USDA-APHIS (2009), approximately 38% of beef cattle producers do not deworm calves prior to weaning; furthermore, approximately 41% of calves are not dewormed at weaning. The same report indicated that slightly under 60% of replacement heifers and cows are not dewormed more than one time a yr, thus contributing to the monetary loss associated with internal parasites.

Recently, a long-acting eprinomectin (LAE) has become commercially available for beef cattle. Long-acting eprinomectin is a member of the macrocylic lactone family and is slowly released in the body (Kunkle et al., 2013; Soll et al., 2013). Forbes (2013) outlined the plasma concentrations in the body. Concentrations of LAE in the body increase rapidly after administration, then gradually decline to approximately d 20 and remain at low levels until roughly d 70. Around d 90, the second peak of plasma concentrations increase and remain at these levels until d 120, after which they decline until d 150-160. Long-acting eprinomectin has been reported to increase animal BW (Kunkle et al., 2013; Rehbein et al., 2013a) and to be

efficacious against intestinal parasites (Hunter et al., 2013; Kunkle et al., 2013; Rehbein et al., 2013a; Rehbein et al., 2013b). However, LAE has not been well evaluated in replacement beef heifers in comparison to other anthelmintics. Therefore, the objective of this study was to evaluate the effects of LAE and a combination of moxidectin/oxfendazole administration on post-weaning performance, reproductive measurements, fecal egg counts (FEC), and complete blood cells counts (CBC) in fall-born replacement beef heifers.

Materials and Methods

This study was conducted at the University of Arkansas' Stocker Cattle Receiving Unit located in Savoy, Arkansas. All methods and procedures were approved by the University of Arkansas' Institutional Animal Care and Use Committee (approval #14034) prior to the initiation of the study.

Treatment management

This study began on June 2, 2014, where 83, newly-weaned, fall-born crossbred heifers (Angus or Hereford sired; 225 ± 3.6 kg initial BW) were utilized. Heifers were processed 14 d prior to initiation of the study (weaning) to determine BW and FEC. Also, at this time heifers were branded, administered a clostridial vaccine (Ultrabac7, Zoetis, Florham Park, NJ), as well as a respiratory and reproductive vaccine (Virashield 6 + VL5HB, Novartis, Larchwood, IA). Cattle were stratified by d -14 BW and FEC, and d of age and then allocated randomly to 1 of 3 anthelmintic treatments consisting of: 1) control (*n* = 28; no anthelmintic administered; **CON**); 2) a combination of pour-on moxidectin and oral oxfendazole (*n* = 28; **MO**; Cydectin/Synanthic combination; Boerhringer Ingelheim Vetmedica Inc., Saint Joseph, MO); and 3) long-acting eprinomectin (*n* = 27; **LAE**; LongRange; Merial Limited, Duluth, GA) and anthelmintic

treatments were applied on d 0. Anthelmintics were given at a recommended dose with moxidectin administered topically along the midline of the back (0.5 mg/kg BW) and oxfendazole administered orally (4.5 mg/kg BW). Long-acting eprinomectin was administered s.c. (1 mg/50 kg BW) in the neck. A brucellosis vaccine was administered to all study heifers on d 14 of the study (June 16, 2014).

Fifty-six days prior to the initiation of the breeding season (d 84) heifers were boostered with clostridial, respiratory, and reproductive vaccines. Respective anthelmintic treatment was re-administered to heifers on d 154 of the study (14 d prior to the initiation of the breeding season). On d 158, 10 days before initiation of the breeding season, and on d 168, beginning of the breeding season, whole blood was collected via the jugular vein to determine progesterone concentrations, which were analyzed using a RIA assay (ImmuChem Coated Tube Progesterone RIA Kit; Catalog #07-270102; MP Biomedicals, Solon, OH). Progesterone concentrations were used to determine the percentage of heifers that were considered cyclic, and heifers were considered cyclic if progesterone concentrations were $\geq$ 1 ng/mL, on either collection d (d -10 or 0 of the breeding season). On d 168, each heifer was administered 25 mg of $PGF_2\alpha$ (Lutalyse; Zoetis; Florham Park, NJ) and equipped with an Estrotect patch (Rockway Inc., Spring Valley, WI). Estrous detection was monitored for 10 d, and if estrous was detected via activated Estrotect patch, heifers were artificially inseminated (AI) by a single technician within 24 h post-estrous detection. Heifers that did not display estrous within 7 d were re-administered 25 mg of $PGF_2\alpha$ and estrous detection was monitored for 3 d, and if estrous was detected heifers were AI. Five days later, 1 fertile bull was placed in each treatment group for a 52-d breeding season. Rectal ultrasound was conducted on d 234 following the breeding season to determine AI

pregnancy rates and repeated on d 274 of the study to determine natural service (NS) pregnancy rates.

Animal management

Heifers were offered a corn-gluten supplement daily, at 1% BW and had access to 10.1-ha pastures that consisted of predominately endophyte-infected tall fescue [*Lolium arundinaceum* (Schreb.) Darybysh] and grazed by individual treatment groups for the duration of the study. When forage became limiting, supplemental hay was offered. At the end of the 274-d grazing period, heifers that were confirmed pregnant were commingled into 1 group and grazed on similar pastures on the same farm of origin, until calving.

Sample collection

Body weights and BCS (1 = emaciated; 9 = obese; Wagner et al., 1988) were recorded on d 0, 14, 28, 84, 112, 140, 154, 168, 182, 234, and 274. Hair coat scores (1 = slick, short summer coat; 5 = full winter hair coat; Gray et al., 2011) were recorded on d 0, 14, 28, and 84. Approximately 1 mo prior to the initiation of calving season, heifers were weighed to determine pre-calving body weight. Within 24 h of birth, calves were tagged, tattooed, sex was determined (bulls were banded), and weights was recorded. Also at this time, an udder score was recorded for each dam according to the Beef Improvement Federation (BIF; 2010), where udder suspension and teat size were determined using a 1 to 9 scale (udder suspension: 1 = very pendulous: 9 = very tight and teat size: 1 = very large: 9 = very small). Under these guidelines, udder scores were determined using the weakest quarter and were taken by a single, trained observer.

Heifer FEC and CBC were taken on d 0, 14, 28, 84, 154, 168, 182, 234, and 274. Fecal egg counts were processed according to the Yazwinksi et al. (1994) method. Briefly, stronglye egg counts were counted and recorded for each animal on each sampling d. Fecal samples were analyzed using a direct centrifugation fecal flotation procedure that allows for high specific gravity to concentrate strongyle eggs from 1 g of fecal sample. Samples were then analyzed to determine the amount of strongyle eggs present in the sample and counts were recorded. Blood samples were collected from the jugular vein into determine CBC using a K2 EDTA collection blood tube. Blood cell counts were determined using a Cell-Dyn 3700 SL machine (Abbott GmbH & Co., Wiesbaden, Germany).

Statistical Analyses

Performance measurements: Body weights, BCS and HCS, calf birth weights, and udder scores were analyzed using PROC MIXED of SAS (SAS Inst. Inc., Cary, NC). Heifer was considered the experimental unit. Calf sire and calf sex were included in the random statement to remove sire variation in calf birth weights. Two orthogonal contrast statements were used: 1) to compare CON to treated heifers; and 2) to compare MO to LAE. All data are reported as least squares means.

Reproductive measurements: Heifer cyclicity, estrous detection, AI, NS, and overall pregnancy rates, and calving rates were analyzed using the GENMOD of SAS. Heifer was considered the experimental unit, and the aforementioned contrast statements were utilized.

Fecal egg counts and complete blood cell counts: Fecal egg counts were log transformed [Y = log10 (x + 1)] prior to analysis and then were converted and reported as geometric means (GM). Fecal egg counts and CBC were analyzed using PROC MIXED for repeated measures of analysis, with heifer considered the experimental unit. The repeated measurement was sampling

d. Interactions between sampling d and treatment were included in the original model; however, if no interaction was detected ($P \geq 0.10$), they were removed from the model and only the main effects were reported. If a treatment × sampling d was detected, the means within a day were separated using an F-protected *t*-test. The aforementioned contrast statements were utilized for FEC and CBC. All data are reported as least squares means. Significant differences were considered when $P \leq 0.05$ and differences referred to as tendencies were those having a *P*-value between 0.05 and 0.10.

Results and Discussion

Heifer performance is outlined in Table 1. Heifer BW did not differ ($P \geq 0.84$) between treatments on d 0, 14, or 28. On d 84, heifer BW tended ($P = 0.06$) to be heavier for MO and LAE compared to CON heifers. On d 112, MO-and LAE-treated heifers had greater ($P < 0.01$) BW compared to CON, furthermore, LAE-treated heifers tended ($P = 0.10$) to have greater BW compared to MO-treated heifers. Heifer BW on d 140, 154 and 182 were greater ($P \leq 0.01$) for MO- and LAE-treated heifers compared to CON, and LAE-treated heifers had greater ($P = 0.03$) BW compared to MO-treated heifers. Long-acting eprinomectin- and MO-treated heifers tended ($P \leq 0.08$) to be heavier compared to CON; however, LAE-treated heifers were heavier ($P \leq 0.04$) compared to MO-treated heifers on d 168 (start of the breeding season) and 274. On d 234, heifer BW was not different ($P = 0.26$) between CON and treated heifers; however, LAE-treated heifers had greater ($P < 0.01$) BW compared to MO-treated heifers. Average daily gain did not differ ($P \geq 0.14$) amongst treatment groups on d 0 to 14, 112 to 140, 154 to 168, and d 234 to 274. Heifer ADG on d 14 to 28 was greater ($P < 0.01$) for LAE-treated heifers compared to MO-treated heifers, but did not differ ($P = 0.65$) between CON and treated heifers. Moxidectin/oxfendazole combination and LAE heifers had greater ($P \leq 0.01$) ADG compared to

CON on d 28 to 84, and overall (d 0 to 274), furthermore, LAE had greater ($P \leq 0.01$) ADG compared to MO on these sampling d. Treated heifers had greater ($P = 0.03$) ADG compared to CON heifers, but ADG did not differ ($P = 0.62$) from LAE- and MO-treated heifers on d 140 to 154. Average daily gain was greater ($P < 0.01$) for CON compared to treated heifers on d 182 to 234, also ADG was greater ($P < 0.01$) for LAE-treated heifers compared to MO-treated heifers. Lastly, ADG on d 84 to 112, and 168 to 182 was greater ($P \leq 0.03$) for treated heifers compared to CON; however, ADG did not differ ($P \geq 0.62$) between MO and LAE. Overall ADG was greater ($P = 0.01$) for treated heifers compared to CON heifers; furthermore, overall ADG was greater ($P < 0.01$ for LAE-treated heifers compared to MO-treated heifers.

Body condition score followed a similar pattern as heifer BW and did not differ ($P \geq 0.46$) on d 0, 14, or 28 across treatments. Heifer BCS was greater ($P \leq 0.04$) for MO- and LAE-treated heifers compared to CON on d 84, 112, 140, 154, 182, and 234; however, did not differ ($P \geq 0.15$) between MO and LAE on each respective sampling d. Body condition score on d 168 and 274 was greater ($P \leq 0.04$) for treated heifers compared to CON heifers and LAE had greater ($P < 0.01$) BCS compared to MO-treated heifers. Hair coat scores did not differ ($P > 0.05$) across treatments on any sampling d. Based on this study, heifer BW, BCS, and ADG can be improved over a 274-d grazing study, following administration of a combination of pour-on moxidectin and oral oxfendazole or long-acting eprinomectin. Our data agrees with one study that utilized seventy-two, 9 to 12 mo old, Brangus/Angus steer calves, and anthelmintic treatments consisting of: moxidectin (MXD), doramectin (DOR), ivermectin (IVM), and eprinomectin (EPM), and indicated an improvement ($P < 0.05$) in BW in treated-steers over a 122-d study compared with CON steers (Williams et al., 1999). Walker et al. (2013) utilized weaned steer and heifer calves to evaluate the effects of 1) oxfendazole (OXF) administered on d

0 and MXD on d 73; 2) MXD administered on d 0 and OXF administered on d 73; 3) OXF administered on d 0; 4) MXD administered on d 0, and compared them to a negative control. It was reported that final BW did not differ across anthelmintic treatments; however, ADG was impacted by anthelmintic administration, with calves receiving combinations of MXD and OXF, and OXF on d 0 having improved ADG compared to CON cattle. Alternatively, Ives et al. (2007) reported that administration of MOX in combination with OXF, and MOX alone did not improve feed-lot gain performance in mixed-breed steers compared to administration of DOR. In one study evaluating the effects of LAE on cattle performance, Kunkle et al. (2013) reported cattle BW was increased by approximately 10% in cattle treated with LAE compared to CON animals.

In regards to progesterone concentrations taken on d 158 and 168, fewer ($P < 0.01$) CON heifers were considered cyclic compared with treated heifers (11 vs. 65%, respectively; Table 2). Similarly, estrous detection was greater ($P < 0.01$) for treated heifers compared to CON (43 vs. 11%, respectively). Artificial insemination conception rates tended ($P = 0.08$) to be greater for CON compared to treated heifers (100 vs. 46%, respectively). Lastly, NS (75 vs 44%) and overall (80 vs. 50%) conception rates were greater ($P \leq 0.01$) for treated heifers compared to CON. Heifer cyclicity (67 vs. 63%), detected estrous (39 vs. 48%), AI conception rates (36 vs. 54%), and NS conception rates (67 vs. 85%) did not differ ($P \geq 0.15$) between MO- and LAE-treated heifers. However, overall pregnancy rates tended ($P = 0.10$) to be greater for LAE-treated heifers compared to MO-treated heifers (71 vs. 89%, respectively). Conflicting data has been reported evaluating the effects of anthelmintic therapy on reproductive performance. Loyacano et al. (2002) and Stromberg et al. (1997) reported that treatment against gastrointestinal nematodes can positively impact reproductive performance; while Purvis et al.

(1994), Zajac et al. (1991), Ryan et al. (1999), and Larson (1995) reported no advantageous effects on reproductive performance post anthelmintic therapy. Based on the current study, improved heifer gain performance, most likely as a result of the decrease in parasitic infections, prior to the initiation of the breeding season can positively impact heifer reproductive performance as reported by the increase in overall pregnancy rates in long-acting eprinomectin and in a combination of pour-on moxidectin and oral oxfendazole compared to control. It is important to note that while AI conception rates tended to be greater for control heifers compared with treated heifers, only 3 heifers were artificially inseminated compared to 11 heifers in the treated groups, thus implying that BW at the beginning of breeding season plays an important role in dictating reproductive cyclicity and likelihood of pregnancy in yearling heifers. Pre-calving BW did not differ ($P = 0.88$) between CON and treated heifers; however, LAE-treated heifers were heavier ($P < 0.01$) compared to MO-treated heifers, with pre-calving weights averaging 431, 414, and 451 kg for CON, MO, and LAE, respectively. Calving rates (percentage of heifers that calved/heifer exposed) were 42, 57, and 81 % for CON, MO, and LAE, respectively. The percentage of heifers that calved were greater ($P = 0.01$) for treated heifers compared to CON heifers; likewise, LAE-treated heifers had a greater ($P = 0.04$) calving rate compared to MO-treated heifers. Calf birth weights were similar ($P = 0.35$) across treatments and average birth weights ranged from 25 to 27 kg. Udder suspension tended to be greater ($P = 0.07$) from treated heifers compared with CON; however, did not differ ($P = 0.45$) between MO and LAE. Teat size did not differ ($P = 0.36$) amongst anthelmintic treatments.

Over the 274-d grazing season, FEC were greater ($P < 0.01$) for CON compared to treated heifers (Table 3). Also, MO had lower ($P < 0.01$) overall FEC compared to LAE (7 vs. 11, respectively). A treatment × day interaction was detected ($P \leq 0.05$) for FEC, which

indicated that CON heifers had the highest FEC on day 28 and 84 of the study compared to all other treatment and day combinations, with mean FEC for CON reaching 144 and 164 eggs/g, respectively. Treatment against gastrointestinal parasites has been well evaluated. Decreased FEC following administration of MXD (Williams et al., 1999; Anziani et al., 2001; Elsener et al., 2001; Maritorena-Diez et al., 2005; Powell et al., 2008; Gomes de Soutello et al., 2010; Walker et al., 2013; Yazwinski et al., 2013), OXF (Borgsteede and Reid, 1982; Williams et al., 1997), and LAE (Hunter et al., 2013; Kunkle et al., 2013; Rehbein et al., 2013a; 2013b) have been reported. Similar data were reported in the present study, with FEC being drastically reduced for treatment of MO and LAE over the 274-d study. Heifers treated with MO had the lowest FEC on d 14 and 168, which implies that approximately 14 d after administration, MO was the most efficacious against gastrointestinal nematodes. As previously mentioned, Forbes (2013) evaluated the efficacy length for LAE and determined that on d 150 to 160, plasma concentrations of eprinomectin decreased to low levels, indicating that it would no longer be efficacious for controlling internal parasites. In the present study, when evaluating how LAE compared to data reported by Forbes (2013), our study agrees with data reported, through the first 154 d. Fecal egg counts decrease to 4, 8, 6, eggs/g on d 14, 28, and 84 post-treatment, and then begin to rise on d 154. Also, on 168, which is 14 d post-anthelmintic treatment (2nd administration), fecal egg counts again decrease from 17 eggs/g to 5 eggs/g. However, on d 182 (28 d post-treatment) and 234 (81 d post-treatment) FEC increased to 19 and 29 eggs/g, respectively. On d 274 (120 d post-treatment), FEC decreased again to 6 eggs/g suggesting that 2 consecutive administrations of LAE can lead to different outcomes for FEC in heifers grazing on pasture, when compared to data reported by Forbes (2013).

The effects of anthelmintic therapy on complete blood counts over the 274-d study are outlined in Table 4. Concentrations of white blood cells (WBC), lymphocytes (LYM), eosinophils (EOS), basophils (BAS), red blood cells (RBC), and platelets (PLT) and the neutrophil:lymphocyte ratio (N:L) were greater ($P \leq 0.02$) for treated cattle compared to CON. Also, BAS were greater ($P = 0.01$) for MO compared to LAE and concentrations of platelets were greater ($P < 0.01$) for LAE compared to MO. Concentrations of monocytes (MON) and neutrophils (NEU) did not differ ($P \geq 0.54$) across treatments. A day effect was detected ($P < 0.01$) for WBC, LYM, and MON (Table 5). White blood cell concentrations were greatest on d 28 (10.5 K/μL) of the study compared to all other times and lowest on d 154, 168, and 274. Lymphocytes were greatest ($P < 0.01$) on d 0 and 14 compared to all other collection d. Day 84 had the least ($P < 0.01$) concentration of MON compared to other collection days. A treatment × day interaction was detected ($P \leq 0.01$) for NEU, with concentrations of NEU being greatest from all heifers on d 182, CON and LAE heifers on d 28, and MO-treated heifers on d 0 (Table 6). A treatment × day interaction was detected ($P < 0.01$) for N:L, with all heifers on d 14 having the lowest ratio compared to all other treatment and d combinations. Also, a treatment × day interaction was detected ($P < 0.01$) for EOS, with CON heifers having the highest concentration of EOS on d 182, 234, and 274. Basophils also reported a treatment × d interaction ($P < 0.01$), with LAE-treated heifers on d 28 having the greatest concentration of BAS compared to all other treatment and d interactions. Lastly, a PLT treatment × day interaction was detected ($P < 0.01$). Control and MO heifers had greater proportions of PLT on d 28 and CON on d 84. The differences reported in the CBC, could indicate that the CON heifers' elevated immune response was combating the elevated gastrointestinal parasite

infections, with CON heifers exhibiting a greater concentration of most of the white blood cells over the 274-d grazing period.

CONCLUSION

In conclusion, treatment against gastrointestinal nematode infections in replacement beef heifers can improve gain performance and reproductive performance. Anthelmintic therapy also decreased overall FEC in treated heifers, which implies that a combination of pour-on moxidectin and oral oxfendazole or long-acting eprinomectin can decrease the overall parasite burden over the grazing season. Body weights and overall conception rates were increased for LAE-treated heifers compared to MO-treated heifers. Therefore, utilization of LAE in replacement beef heifers may increase overall herd production.

Table 1. Gain Measurements of Fall-Born Heifers Treated With Either Moxidectin/Oxfendazole Combination or Long-Acting Eprinomectin Over a 274-d Grazing Period

Item	Treatments[a]			SEM[b]	*P*-Value		
	CON	MO	LAE			CON vs TREATED	OXF vs LAE
BW, kg							
d 0	225	225	226	5.4	0.98	0.93	0.90
d 14	228	228	229	5.4	0.99	0.94	0.91
d 28	234	233	237	5.3	0.84	0.88	0.57
d 84	263^{y}	269^{xy}	282^{x}	6.0	0.06	0.08	0.11
d 112	274^{f}	288^{ef}	302^{e}	6.1	<0.01	<0.01	0.10
d 140	289^{g}	304^{fg}	322^{e}	6.2	<0.01	<0.01	0.03
d 154	295^{f}	304^{ef}	324^{e}	6.5	<0.01	0.01	0.03
d 168	301^{f}	307^{f}	327^{e}	6.8	0.02	0.06	0.04
d 182	317^{f}	331^{f}	352^{e}	6.8	<0.01	<0.01	0.03
d 234	354^{f}	349^{f}	378^{e}	7.1	0.01	0.26	<0.01
d 274	373^{f}	372^{f}	409^{e}	8.4	<0.01	0.08	<0.01
ADG, kg/d							
d 0 to 14	0.23	0.23	0.22	0.075	0.99	0.93	0.93
d 14 to 28	0.43^{ef}	0.34^{f}	0.56^{e}	0.065	0.03	0.65	<0.01
d 28 to 84	0.51^{g}	0.65^{f}	0.81^{e}	0.035	<0.01	<0.01	<0.01
d 84 to 112	0.39^{f}	0.68^{e}	0.71^{e}	0.044	<0.01	<0.01	0.62
d 112 to 140	0.54	0.57	0.72	0.074	0.18	0.25	0.14
d 140 to 154	0.41^{x}	0.00^{y}	0.08^{y}	0.140	0.10	0.03	0.67
d 154 to 168	0.44	0.21	0.21	0.063	0.60	0.31	0.99
d 168 to 182	1.15^{f}	1.71^{e}	1.83^{e}	0.191	0.03	<0.01	0.66
d 182 to 234	0.72^{e}	0.36^{g}	0.51^{f}	0.034	<0.01	<0.01	<0.01

Table 1. Gain Measurements of Fall-Born Heifers Treated With Either Moxidectin/Oxfendazole Combination or Long-Acting Eprinomectin Over a 274-d Grazing Period (Cont.)

Item	Treatments[a]			SEM[b]	*P*-Value	CON vs TREATED	OXF vs LAE
	CON	MO	LAE				
ADG, kg/d							
d 234 to 274	0.46	0.56	0.77	0.110	0.14	0.13	0.18
Overall	0.54[f]	0.54[f]	0.66[e]	0.021	<0.01	0.01	<0.01
BCS[c]							
d 0	5.1	5.1	5.1	0.06	0.99	0.97	0.96
d 14	5.1	5.2	5.1	0.07	0.46	0.21	0.93
d 28	5.0	5.0	5.0	--	1.00	1.00	1.00
d 84	5.2[f]	5.4[ef]	5.5[e]	0.09	0.03	0.01	0.32
d 112	5.1[y]	5.2[xy]	5.3[x]	0.07	0.10	0.04	0.43
d 140	5.6[f]	5.8[ef]	5.9[e]	0.08	0.04	0.02	0.36
d 154	5.4[f]	5.6[ef]	5.7[e]	0.10	0.05	0.02	0.32
d 168	5.7[f]	5.8[f]	6.3[e]	0.11	<0.01	<0.01	<0.01
d 182	5.4[f]	5.7[e]	5.9[e]	0.09	<0.01	<0.01	0.15
d 234	5.8[f]	6.0[ef]	6.3[e]	0.12	0.02	0.01	0.26
d 274	5.3[f]	5.4[f]	5.8[e]	0.09	<0.01	0.04	<0.01
HCS[d]							
d 0	4	4	4	0.1	0.57	0.92	0.30
d 14	4	4	4	0.1	0.38	0.17	0.83
d 28	3	4	3	0.1	0.68	0.41	0.76
d 84	3	3	3	0.1	0.98	0.74	0.87

[a] CON = control; MO = moxidectin/oxfendazole combination; and LAE = long-acting eprinomectin.
[b] SEM = pooled SEM.
[c] 1 to 9 scale; 1 = emaciated; 9 = obese (Wagner et al., 1988).
[d] HCS = hair coat score; 1 to 5 scale; 1 = slick, summer coat; 5 = full winter hair coat (Gray et al., 2011).
[e-g] Means within a row without common superscript differ ($P \leq 0.05$).
[x-y] Means within a row without common superscript tended ($P \leq 0.10$) to differ.

Table 2. Reproductive Measurements of Fall-Born Beef Heifers Treated With Either Moxidectin/Oxfendazole Combination or Long-Acting Eprinomectin Over a 274-d Grazing Period

Item	Treatments[a]			SEM[b]	*P*- Value[c]		
	CON	MO	LAE			CON vs TREATED	MO vs LAE
Reproductive performance							
Cyclicity, %[d]	11	67	63	--	<0.01	<0.01	0.70
Estrous detection, %	11	39	48	--	<0.01	<0.01	0.50
AI, %	100	36	54	--	0.08	0.03	0.39
NS, %[e]	44	67	85	--	0.01	<0.01	0.15
Overall, %[f]	50	71	89	--	<0.01	<0.01	0.10
Pre- and post-calving measurements							
Pre-calving BW, kg	431[i]	414[j]	451[i]	12.7	0.01	0.88	<0.01
Calving rate, %	93	80	92	--	0.01	0.01	0.04
Calf birth weight, kg	25	27	25	1.4	0.35	0.48	0.18
Udder suspension[g]	7	8	8	0.3	0.13	0.07	0.45
Teat size[h]	7	8	8	0.4	0.36	0.21	0.59

[a] CON = control; MO = moxidectin/oxfendazole combination; and LAE = long-acting eprinomectin.
[b] SEM = pooled SEM.
[c] Reproductive performance and calving rate were analyzed using GENMOD; heifer BW, calf birth weight, udder suspension, and teat size were analyzed using PROC MIXED.
[d] Cyclicity was achieved if progesterone concentrations were > 1 ng/mL on either d -10 or 0 of the breeding season (d 158 or 168, respectively).
[e] NS = Natural service pregnancy rate.
[f] Overall = Overall pregnancy rate.
[g] 1 to 9 scale; 1 = very pendulous; 9 = very tight (BIF, 2010).
[h] 1 to 9 scale; 1 = very large; 9 = very small (BIF, 2010).
[i- j] Means with a row without common superscript differ ($P \leq 0.05$).

Table 3. Fecal Egg Count (Geometric Means; GM) Treatment × d Interaction of Fall-Born Beef Heifers Treated With Either Moxidectin/Oxfendazole Combination or Long-Acting Eprinomectin Over a 274-d Grazing Period

Item	Treatments[a]			SEM[b]	*P*-Value		
	CON	MO	LAE			CON vs TREATED	MO vs LAE
Overall FEC, GM[c]	24[d]	7[f]	11[e]	0.0	<0.01	<0.01	<0.01
d 0	35[i]	23[ij]	26[ij]	--			
d 14	67[h]	1[m]	4[l]	--			
d 28	144[g]	5[kl]	8[k]	--			
d 84	164[g]	80[h]	6[kl]	--			
d 154 (re-treat)	15[jk]	10[k]	17[j]	--			
d 168	12[jk]	1[m]	5[kl]	--			
d 182	7[kl]	7[kl]	19[ij]	--			
d 234	6[kl]	11[jk]	29[ij]	--			
d 274	6[kl]	5[kl]	6[k]	--			

[a] CON = control; MO = moxidectin/oxfendazole combination; and LAE = long-acting eprinomectin.

[b] SEM = pooled SEM.

[c] FEC = fecal egg counts.

[d-f] Means within a row without common superscript differ ($P \leq 0.05$).

[g-m] Means without common superscript differ ($P < 0.05$).

Table 4. Blood Cell Parameters of Fall-Born Beef Heifers Treated With Either Moxidectin/Oxfendazole Combination or Long-Acting Eprinomectin Over a 274-d Grazing Period

Item	Treatments[a]			SEM[b]	*P*-Value	CON vs TREATED	MO vs LAE
	CON	MO	LAE				
White blood cells K/µL	10[c]	9[d]	9[d]	0.5	<0.01	<0.01	0.69
Neutrophils, K/µL	2.4	2.4	2.5	0.07	0.54	0.42	0.44
Lymphocytes, K/µL	6.2[c]	5.5[d]	5.4[d]	0.20	<0.01	<0.01	0.69
Neutrophil:Lymphocyte	0.45[d]	0.51[c]	0.53[c]	0.018	<0.01	<0.01	0.42
Monocytes, K/µL	1.02	1.02	0.99	0.028	0.64	0.67	0.40
Eosinophils, K/µL	0.21[c]	0.10[d]	0.07[d]	0.012	<0.01	<0.01	0.15
Basophils, K/µL	0.12[c]	0.11[c]	0.09[d]	0.007	<0.01	<0.01	0.01
RBC, M/µL	8.87[c]	8.69[d]	8.75[cd]	0.05	0.02	0.01	0.33
Platelets, K/µL	445[c]	414[d]	417[cd]	10.8	0.08	<0.01	<0.01

[a] CON = control; MO = moxidectin/oxfendazole combination; and LAE = long-acting eprinomectin.
[b] SEM = pooled SEM.
[c-d] Means within a row without common superscript differ ($P \leq 0.05$).

Table 5. White Blood Cell Count Time Effect of Fall-Born Beef Heifers Treated With Either Moxidectin/Oxfendazole Combination or Long-Acting Eprinomectin Over a 274-d Grazing Period

	Date[a]									
Item	0	14	28	84	154	168	182	234	274	SEM[b]
WBC, K/µL[c]	10.29^{fg}	9.69^{g}	10.50^{f}	9.35^{g}	8.57^{h}	8.40^{h}	10.46^{fg}	9.72^{g}	7.85^{h}	0.271
LYM, K/µL[d]	6.5^{fg}	6.9^{f}	6.2^{g}	5.7^{gh}	4.9^{h}	4.5^{h}	5.6^{gh}	6.0^{g}	5.1^{h}	0.23
MON, K/µL[e]	1.03^{fg}	1.04^{fg}	1.06^{fg}	0.86^{h}	1.09^{fg}	1.16^{f}	1.05^{fg}	1.00^{g}	0.79^{h}	0.049

[a] White blood cell parameters were estimated on d 0, 14, 28, 84, 154, 168, 182, 234, 274 of the study.

[b] SEM = pooled SEM.

[c] WBC = white blood cells.

[d] LYM = lymphocytes.

[e] MON = monocytes.

[f-h] Means within a row without common superscript differ ($P \leq 0.05$).

Table 6. Treatment × d Interaction on Complete Blood Cell Counts of Fall-Born Beef Heifers Treated With Either Moxidectin/Oxfendazole Combination or Long-Acting Eprinomectin Over a 274-d Grazing Period

	Treatments[a]		
Item	**CON**	**MO**	**LAE**
Neutrophils, K/µL			
d 0	2.2^{ed}	3.1^{bc}	2.4^{d}
d 14	1.4^{e}	1.8^{e}	1.7^{e}
d 28	3.2^{bc}	2.9^{c}	3.1^{bc}
d 84	2.6^{cd}	2.7^{cd}	2.7^{cd}
d 154	2.5^{cd}	2.4^{d}	2.2^{de}
d 168	2.0^{de}	2.5^{cd}	2.7^{c}
d 182	3.5^{b}	3.2^{bc}	3.5^{b}
d 234	2.4^{d}	2.1^{de}	2.5^{cd}
d 274	1.8^{e}	1.3^{e}	1.7^{e}
Neutrophil:Lymphocyte			
d 0	0.39^{d}	0.58^{bc}	0.48^{cd}
d 14	0.21^{e}	0.35^{de}	0.31^{de}
d 28	0.51^{cd}	0.50^{cd}	0.56^{c}
d 84	0.47^{cd}	0.50^{cd}	0.51^{cd}
d 154	0.50^{cd}	0.66^{bc}	0.51^{cd}
d 168	0.44^{cd}	0.67^{bc}	0.71^{b}
d 182	0.67^{bc}	0.63^{bc}	0.69^{bc}
d 234	0.44^{cd}	0.37^{d}	0.63^{bc}
d 274	0.43^{cd}	0.37^{d}	0.41^{cd}
Eosinophils, K/µL			
d 0	0.13^{de}	0.05^{e}	0.09^{e}
d 14	0.09^{e}	0.05^{e}	0.03^{e}
d 28	0.06^{e}	0.02^{e}	0.02^{e}
d 84	0.10^{de}	0.08^{e}	0.05^{e}
d 154	0.17^{cd}	0.10^{de}	0.05^{e}
d 168	0.24^{cd}	0.06^{e}	0.08^{e}
d 182	0.36^{b}	0.15^{de}	0.10^{de}
d 234	0.44^{b}	0.16^{d}	0.06^{e}
d 274	0.37^{b}	0.25^{c}	0.22^{cd}
Basophils, K/µL			
d 0	0.102^{ef}	0.131^{e}	0.088^{ef}
d 14	0.116^{ef}	0.066^{f}	0.072^{ef}
d 28	0.067^{f}	0.065^{f}	0.549^{b}
d 84	0.054^{f}	0.051^{f}	0.054^{f}
d 154	0.096^{ef}	0.132^{de}	0.076^{ef}
d 168	0.387^{c}	0.243^{d}	0.189^{d}
d 182	0.097^{ef}	0.085^{ef}	0.080^{ef}
d 234	0.109^{ef}	0.111^{ef}	0.081^{ef}

Table 6. Treatment × Day Interaction on Complete Blood Cell Counts of Fall-Born Beef Heifers Treated With Either Moxidectin/Oxfendazole Combination or Long-Acting Eprinomectin Over a 274-d Grazing Period (Cont.)

	Treatments[a]		
Item	**CON**	**MO**	**LAE**
d 274	0.082[ef]	0.111[ef]	0.071[f]
Platelets, K/µL			
d 0	493[de]	527[d]	551[d]
d 14	429[e]	516[d]	540[d]
d 28	732[b]	711[bc]	623[cd]
d 84	655[bc]	643[c]	546[d]
d 154	377[e]	211[fg]	360[ef]
d 168	287[f]	207[fg]	245[fg]
d 182	519[d]	475[de]	474[de]
d 234	269[f]	245[fg]	256[fg]
d 274	245[fg]	191[g]	163[g]

[a] CON = control; MO = moxidectin/oxfendazole combination; and LAE = long-acting eprinomectin.
[b-g] Means without common superscript differ ($P \leq 0.05$).

Chapter III

Evaluation of oxfendazole and long-acting eprinomectin administration on gain and reproductive performance, fecal egg counts, and complete blood cell counts in spring-calving cows and their calves

Abstract

Cattle performance, feed intake and utilization, and reproductive performance can be decreased as a result of gastrointestinal nematode infections; however, current research is limited in regard evaluating the effects of various anthelmintic regimens in spring-calving cow operations. The objective of this study was to evaluate the effects of various anthelmintics administered to spring-calving cows and their calves on gain and reproductive performance, fecal egg counts (FEC), and complete blood cell counts. Ninety, spring-calving cows were allocated randomly to 1 of 3 anthelmintic treatments consisting of: 1) control (n = 30; no anthelmintic administered; **CON**); 2) oral oxfendazole (n = 30; **OXF**); and 3) long-acting eprinomectin (n = 30; **LAE**), and received treatment prior to calving. Cows and their calves rotationally grazed in individual treatment groups until weaning. At weaning and on d 417, calves were administered the same anthelmintic treatment as their dams and grazed by individual groups for 203 d, after which they were separated by sex. Heifers remained on the farm of origin and steers were transported to West Texas A & M Research Feedlot. Animal was considered the experimental unit and two preplanned orthogonal contrast was used: 1) to compared CON totreated cattle; and 2) to compare OXF to LAE. Cow BW, BCS on d 0, 91, 146, and 228, and pregnancy rate did not differ ($P \geq 0.20$) between CON and treated cows. Day 14 BCS tended (P

= 0.07) to be greater for CON compared to treated cows. Also, BCS was greater (P = 0.01) and HCS was lower (P < 0.01) for OXF compared to LAE on d 91. Pregnancy rate tended (P = 0.08) to be lower for LAE compared to OXF. Over the duration of the study, cow FEC, white blood cells and eosinophils were greater ($P \leq 0.04$) for CON compared to treated cows. Calf BW on d 417 and 431 and were greater ($P \leq 0.03$) for treated calves compared to CON calves. Calf weaning weights were lower (P = 0.03) for LAE compared to OXF. Calf FEC and platelets were greater ($P \leq 0.02$) for CON compared to treated calves. Heifer reproductive performance did not differ (P = 0.50) amongst treatments. Carcasses from CON steers had greater (P = 0.02) longissimus area and lower (P = 0.02) yield grade compared to carcasses from treated calves. Therefore, in this study, anthelmintic administration did not increase cow performance or steer carcass measurements but did improve calf post-weaning gain performance.

Introduction

Lawrence and Ibarbura (2009) evaluated the economic effects of gastrointestinal nematode control in beef cattle and reported that there was a 34% decrease in the break-even price for cattle that did not receive anthelmintic treatment. This decrease in monetary worth was valued at $165/hd. Also, Bagley et al. (1998) reported that gastrointestinal nematode infections can cost the United States' cattle industry approximately $3 billion annually. Decreases in gain performance (Chambers, 1985; Kunkle et al., 2013; Perry and Randolph, 1999; Purvis et al., 1994; Rehbein et al., 2013a; Walker et al., 2013; Williams et al., 1997; Williams et al., 1999) and lowered feed intake and nutrient utilization (Kunkle et al., 2013), as well as poor reproductive performance (Loyacano et al., 2002; Stromberg et al., 1997) have been reported when anthelmintic administration has not been utilized.

Recently, a long-acting eprinomectin (LAE) has become commercially available for beef cattle to control gastrointestinal nematode infections. The drug is a member of the macrocylic lactone family, and Soll et al. (2013) and Forbes (2013) indicated that LAE is slowly released in the body which can control gastrointestinal nematode infections for up to 150 to 160 d. Little research is published evaluating the effects of LAE on performance and fecal egg count reductions in beef cattle; however, improved cattle performance (Kunkle et al., 2013; Rehbein et al., 2013a) and parasite control (Forbes, 2013; Hunter et al., 2013; Kunkle et al., 2013; Rehbein et al., 2013a; Rehbein et al., 2013b; Soll et al., 2013) have been reported. However, the effects of LAE compared to other conventional anthelmintics have not been well evaluated. Therefore, the objective of this study was to evaluate the effects of LAE compared to oxfendazole on gain and reproductive performance, fecal egg counts, and complete blood cell counts in spring-calving cows and their calves.

Materials and Methods

This study took place at the University of Arkansas-Division of Agriculture Livestock and Forestry Research Station, located in Batesville, Arkansas and West Texas A & M University, located in Canyon, Texas. Prior to the initiation of the study, all methods and procedures were approved by the University of Arkansas' Institutional Animal Care and Use Committee (approval #14023).

Treatment management

On January 8, 2014, Charlois × Hereford, spring-calving cows (n = 90; 563 ± 8.1 kg BW) were processed to determine BW, BCS, and fecal egg count (FEC). Cows were stratified by BW, BCS, and FEC and were allocated randomly to 1 of 3 anthelmintic treatments consisting of: 1) control (*n* = 30; **CON**; no anthelmintic); 2) oral oxfendazole (*n* = 30; **OXF**; Synanthic;

Boehringer Ingleheim Vetmedica, Inc. Saint Joseph, MO); and 3) long-acting eprinomectin (*n* = 30; **LAE**; LongRange; Merial Limited, Duluth, GA), on February 13, 2014 (d 0; 4 d before the initiation of calving season). Anthelmintics were administered on d 0, at the labeled dose with OXF administered orally (4.5 mg/kg BW) and LAE administered s.c (1 mg/50 kg BW) in the neck to respective cows. At this time, a clostridial vaccine (Ultrabac 7, Zoetis, Florham Park, NJ) was administered.

Animal Management

Cow management

Cows and their calves rotationally grazed by individual treatment groups on 2.4-ha mixed grass pastures, consisting of predominately endophyte-infected tall fescue [*Lolium arundinaceum* (Schreb.) Darybysh; **E+**], in groups of 14 or 15 pairs, from February to October. During the calving season (February to April) cattle were supplemented with soyhull pellets 2.7 kg/d. Calves born to dams on study were processed near birth to determine birth weight, sex (bulls were surgically castrated), and all calves were tagged and tattooed. On d 71, prior to the initiation of the breeding season (April, 25, 2014) cattle were administered a reproductive and respiratory vaccine (Pyramind 10; Boehringer Ingleheim Vetmedica, Inc.). Beginning on d 91 (May 15, 2014), one fertile bull was placed in each group of animals for a 60-d breeding season. Cows were processed on d 228 to determine pregnancy by collecting serum from each cow. Serum was placed on ice and shipped for pregnancy determination (BioPryn; Moscow, ID).

Cow sample collection

Cow BW, BCS, FEC and complete blood cell counts (CBC) were taken on d 0, 14, 91, 146, and 203 of the study. Cattle BCS was determined using the protocol outlined by Wagner et al. (1988; 1 = emaciated; 9 = obese). Hair coat shedding scores (HCS) were evaluated and

determined on d 0, 91, and 146 of the study according to the Gray et al. (2011) protocol, which is a 1 to 5 scale, where 1 = slick, short, summer hair coat and 5 = full winter coat. Fecal egg counts were processed according to the Yazwinski et al. (1994) method. For CBC, approximately 6 mL of whole blood was collected from the jugular vein into a vacuum collection tube containing K2 EDTA, and were evaluated using a Cell-Dyn 3700 SL machine (Abbott GmbH & Co., Wiesbaden, Germany).

Calf management

Prior to weaning, calves were administered a respiratory vaccine (Virashield 6; Elanco, Greenfield, IN) and were revaccinated at weaning. On d 228 (weaning), calves were fenceline weaned over a 14-d weaning period, in respective dam treatment groups, on E+ based pastures. At weaning, calves were administered a labeled dose of the same anthelmintic treatment as their dams. Following the weaning period, calves grazed on dormant bermudagrass (*Cynodon dactylon*). Following the grazing phase on bermudagrass, cattle were moved to E+ pastures, and remained on respect pastures for the duration of the study. On d 417, calves were re-administered their respective anthelmintic treatment, again at a recommended dose. Calves were separated by sex on d 431. Heifers grazed in individual treatment groups from this point further. Steers were commingled into one group for 48 d and were shipped to the West Texas A & M Research Feedlot, located in Canyon, Texas.

Calf Samples collection

Heifers and steers were processed on d 146, 228 (weaning), 242, 327, 417 (retreat), and 431 to determine BW, BCS and FEC. Hair coat scores were evaluated on d 417 and 431. Whole blood was collected to determine CBC from each calf on d 228, 242, 327, and 417 of the study.

Heifer management

On d 431, heifers were administered a respiratory and reproductive vaccine (Virashield 6 +VL 5). Beginning May 15, 2015 (d 456), one fertile bull was placed in each treatment group of heifers for a 59-d breeding season. Following the breeding season, cattle were processed (d 522) to determine post-breeding BW, BCS, FEC, and CBC. Heifers were processed on d 559 to determine BW and whole blood was collected to determine pregnancy rate. At calving, calves were processed to determine birth weights, sex (bulls were surgically castrated), and all calves were tagged and tattooed.

Steer management

Upon arrival at the West Texas A & M Research Feedlot, steers were divided into a light and heavy block within each anthelmintic treatment. Steers were fed a common feedlot ration and bunks were evaluated daily to determine feed allowances using the slick bunk method. Within block, once visual estimation of backfat thickness, approximately 1.27 cm, was determined, cattle were transported to Amarillo, Texas (Tyson Fresh Meats, Inc.) for harvest. Upon harvest, carcass measurements were determined by a trained observer located at the meat processing plant.

Statistical analyses

Performance measurements: Body weights, BCS, HCS, calf birth weights, and carcass measurements were analyzed using PROC MIXED of SAS (SAS Inst. Inc., Cary, NC), with animal being the experimental unit. To remove variation in cow performance, calving date was included in the random statement to insure that differences reported were not as a result of cows calving at different times. Calf sex and sire were included in the random statement when analyzing calf birth weights to remove variation between calf sex and sire. Carcass quality grade was analyzed using PROC GENMOD. Two preplanned orthogonal contrast statements were

utilized and included: 1) to compared CON to treated cows (OXF and LAE); and 2) to compare OXF to LAE. All treatment means were reported as least squares means.

Reproductive measurements: Calving rates, from both cows and heifers, were analyzed using PROC GENMOD with animal being considered as the experimental unit. The previously mentioned orthogonal contrast statements were utilized to evaluate differences.

Fecal egg counts and complete blood cell counts: Prior to analysis, FEC were log transformed [Y = log10 (x + 1)] and reported as geometric means (GM). Fecal egg counts and CBC were analyzed using PROC MIXED for repeated measures of analysis. Sampling day was considered the repeated measure and animal was considered the experimental unit. Interactions between treatment and sampling day were included in the original model; however, if no interaction was detected ($P \geq 0.10$), they were removed from the model and only effects of treatment were reported. If a treatment × sampling day interaction was detected, means were separated using an F-protected *t*-test. The aforementioned contrast statements were utilized to evaluate differences. All data are reported as least squares means. Differences reported as significant are those exhibiting $P \leq 0.05$ and tendencies exhibited *P*-values between 0.05 and 0.10.

Results and Discussion

Cow performance, fecal egg counts, and complete blood cell counts

Eight cows were removed from study due to lack of calving (3 from CON; 3 from OXF, and 2 from LAE), therefore, data presented will account for 82 cows. Cow performance over the 228 d grazing period is outlined in Table 7. Spring-calving cow BW on d 0, 91, 146, and 228 did not differ ($P \geq 0.20$) across anthelmintic regimes, with cow BW on d 228 being 567, 574, and 572 kg, for CON, OXF, and LAE, respectively. However, BW tended ($P = 0.07$) to be greater

for CON cows compared to OXF- and LAE-treated cows, on d 14. Total gain over the duration of the study tended ($P = 0.07$) to be greater for OXF- and LAE-treated cows compared to CON cows, but did not differ ($P = 0.54$) amongst OXF and LAE. Also, ADG was greater ($P = 0.05$) for CON on d 0 to 14 compared to treated cows; however, ADG tended ($P = 0.09$) to be greater for treated cows compared to CON on d 14 to 91. Long-acting eprinomectin-treated cow ADG tended ($P = 0.08$) to be lower on d 14 to 91 compared to OXF-treated cows. Average daily gain was greater ($P < 0.01$) for LAE-treated cows compared to OXF-treated cows on d 91 to 146; however, ADG was similar ($P = 0.75$) between CON and treated cows. Also, ADG on d 146 to 228 was greater ($P < 0.01$) for treated cows compared to CON, but did not differ ($P = 0.38$) between OXF- and LAE-treated cows. Lastly, overall ADG (d 0 to 228) tended ($P = 0.07$) to be greater for treated cows compared to CON.

Body condition scores followed a similar pattern as cow BW, where BCS did not differ ($P \geq 0.36$) amongst anthelmintic treatments on d 0, 146, and 228. However, BCS tended ($P = 0.10$) to be greater for OXF-treated cows compared to LAE-treated cows, but did not differ ($P = 0.96$) between treated cows compared to CON cows on d 14 of the study. Finally, cow BCS on d 91 was greater ($P = 0.01$) for OXF compared to LAE; however, did not differ ($P = 0.96$) for CON compared to treated cows. This study disagrees with previous research reported by Kunkle et al. (2013) and Rehbein et al. (2013a) which evaluated cattle of various ages and stages of production and reported that BW was increased during the grazing season compared with the negative control. While there were improvements reported in terms of BW, ADG, and BCS throughout the study, it is important to keep in mind that BW and BCS were not improved at the end of the study period for the cows, which conflicts with other data reported. Cow HCS on d 0 (February 13) and 146 (July 9) did not differ ($P \geq 0.61$) amongst treatments. However, HCS on

d 91 was lower ($P < 0.01$) for OXF-treated cows compared to LAE-treated cows, but did not differ ($P = 0.39$) between CON and treated cows. As to be expected, cattle HCS decreased by May overall. The improvement in BCS reported in the OXF-treated cows, may have been a result of the decrease in HCS.

Cow conception rates in the subsequent breeding season (May to July), did not differ ($P = 0.59$) for CON cows compared to treated cows; however, conception rates tended ($P = 0.08$) to be greater for OXF compared to LAE cows. Conception rates were 77, 81, and 61%, for CON, OXF, and LAE respectively. Conception rates reported agree with previous work outlined by Larson (1995), which reported that conception rates were not increased in cattle administered intrarumminal of OXF compared to control cattle. It is important to remember that cows in this present study were rotated through pastures that consisted of predominately E+. In a study where similar pastures were grazed, Caldwell et al. (2013) reported that calving rates from spring calving cows were 44 and 80%, for cattle with full vs limited access to E+, respectively. Although, LAE tended to have lower conception rates compared to OXF-treated cattle, they were all greater compared to cattle with complete access to E+ reported by Caldwell et al. (2013) and OXF-treated and CON cow conception rates were similar to that of those with limited access to E+.

Effects of anthelmintic treatment on FEC over the 228 d grazing study are described in Table 8. Fecal egg counts for the duration of the grazing period were greatest ($P < 0.01$) for CON compared ti treated cows. Also, FEC were greater ($P < 0.01$) for LAE-treated cows compared to OXF-treated cows over the duration of the grazing period. Cow mean FEC averages were 2.4, 1.5, and 2.1, eggs/g for CON, OXF, and LAE, respectively. While differences arose from anthelmintic therapy, mean FEC remained low for the duration of the

study, which may have been due in part to the cows on a rotational grazing program. Allowing the cattle to be moved to fresh pasture when forage became limiting, can decrease a cow's opportunity to acquire infective 3rd stage larvae. A treatment × day interaction ($P < 0.01$) was detected for FEC. Fecal egg counts were the greatest on d 228 for LAE compared to all other treatment and d combinations. As to be expected, FEC was the lowest on d 14 for OXF- and LAE-treated cows and on d 91 for OXF-treated cows, with mean FEC averaging 1.0, 1.2, and 1.1, eggs/g respectively. Forbes (2013) outlined the duration of efficacy for LAE. It was reported that LAE increases rapidly post-administration and decreases to low levels around d 25 and remains at these levels until approximately d 70. On approximately d 90, plasma concentrations of LAE being to rise resulting in a second peak, which remains at these levels until d 120. After d 120, plasma concentrations begin to decrease through d 150 to 160. In the present study, LAE-treated cows exhibited a decrease in FEC until d 146 mimicking the duration of efficacy length reported by Forbes (2013). However, by 228, FEC exhibited by cows treated with LAE had increased to their highest levels throughout the study for all treatment and sampling day combinations. Data from the current study agrees with previous work completed that reported FEC was decreased in cattle treated with OXF (Chalmers, 1979; Borgsteede and Reid, 1982; Williams et al., 1997; Walker et al., 2013) compared to cattle that were not treated with an anthelmintic.

Effect of anthelmintic therapy on CBC over the 228 d grazing period is outlined in Table 9. Concentrations of white blood cells (WBC) were greater ($P = 0.04$) for CON compared to treated cows, furthermore, WBC were greater ($P < 0.01$) for OXF-treated cows compared to LAE-treated cows. Long-acting epriomectin-cows had greater ($P = 0.02$) concentration of neutrophils (NEU) compared to OXF; however, NEU did not differ ($P = 0.67$) from treated cows

compared to CON cows. Lymphocytes (LYM) tended ($P = 0.08$) to be greater for CON cows compared to treated cows, also, OXF had greater ($P < 0.01$) LYM compared to LAE. Inversely, the neutrophil:lymphocyte ratio (N:L) tended ($P = 0.06$) to be greater for treated cows compared to CON cows, and likewise, LAE had a lower N:L ($P < 0.01$) compared to OXF. Control cows had greater ($P = 0.01$) eosinophils (EOS) compared to treated; furthermore, EOS were greater ($P < 0.01$) for OXF compared to LAE. Differences reported for EOS could be as a result of the increase in parasitism depicted by FEC, which may indicate that EOS were trying combat the parasitic infections reported. Eosinophils are characterized as being activated during the late-phase of an inflammatory response (Abbas et al., 2015). Concentration of basophils (BAS) did not differ ($P = 0.83$) for CON compared to treated; however, BAS tended ($P = 0.06$) to be greater from OXF compared to LAE. Concentrations of monocytes (MON), red blood cells (RBC), and platelets (PLT) did not differ ($P \geq 0.30$) amongst treatments. A treatment × day interaction was detected ($P = 0.03$) for WBC, where all treatments on d 14 and CON on d 0 had the greatest concentration of WBC (Table 10). Also, CON, OXF, and LAE on d 0 and 146, as well as LAE-treated cows on d 91 had the greatest concentration of NEU, as depicted by the treatment × day interaction ($P < 0.01$). Long-acting eprinomectin-treated cows had the greatest N:L on d 91 compared to all other treatment and sampling day combinations (treatment × day interaction; $P < 0.01$). Lastly, a treatment × day interaction was detected ($P < 0.01$) for concentrations of EOS, were OXF-treated on d 91 had a greater concentration of EOS compared to all other treatment and sampling d combinations. Also, a treatment × day tendency ($P = 0.09$) indicated that CON and OXF-treated on d 14 tended to have the greatest proportions of BAS compared with all on other treatment and sampling day combinations (data not shown).

Calf performance, fecal egg counts, and complete blood cell counts

Starting on d 146, calves from dams who had been treated with OXF tended ($P = 0.10$) to have greater BW compared to calves from dams who had been treated with LAE, but BW did not differ ($P = 0.77$) for CON calves compared to calves whom dams were treated (Table 11). On d 228, average weaning weights (WW) were 239, 252, and 235 kg for CON, OXF, and LAE, respectively. Calf WW on d 228 was greater ($P = 0.03$) from OXF calves compared to LAE calves; however, WW did not differ ($P = 0.52$) from CON calves compared to calves from dams that were treated with an anthelmintic. At weaning (d 228), calves were administered the same anthelmintic that their dams received. Following anthelmintic administration, calf BW was increased in OXF- and LAE-treated calves. Calf BW on d 242 and 327 (14 and 98 post-treatment, respectively) tended ($P \leq 0.09$) to be greater for OXF- and LAE- treated calves compared to calves that did not receive anthelmintic treatment. Also, on d 417 (anthelmintics were re-administered) and 431 calf BW was greater ($P \leq 0.02$) for treated calves compared to CON calves. Calve total gain was greater ($P < 0.01$) from treated calves compared to CON calves, and tended ($P = 0.06$) to be greater for LAE-treated calves compared with OXF. Calf ADG was greater ($P \leq 0.01$) on d 228 to 242 and 417 to 431 for treated calves compared to CON calves. Also, on d 228 to 242 calf ADG was greater ($P < 0.01$) for LAE-treated calves compared to OXF-treated calves; however, ADG was the inverse of that on d 417 to 431, where OXF-treated calves had greater ($P < 0.01$) ADG compared to LAE-treated calves. Anthelmintic treatment did not positively impact ADG from d 242 to 327, with all treatments having similar ($P = 0.30$) ADG. Oxfendazole- and LAE-treated calves tended ($P = 0.08$) to have greater ADG compared to CON, and LAE had greater ($P = 0.01$) ADG compared OXF from d 327 to 417. Furthermore, overall ADG was greater ($P < 0.01$) for treated calves compared to CON calves, and treatment with LAE tended ($P = 0.06$) to increase ADG compared to OXF administration.

Overall calf ADG (d 228 to 431) averaged 0.36, 0.42, and 0.47 kg/d for CON, OXF, and LAE, respectively. These results agree with those reported by Walker et al. (2013), which indicated that cattle treated with an anthelmintic had greater performance compared to untreated cattle. In that study, weaned fall-born steers and heifers were allocated to 1 of 5 treatments consisting of: 1) oral oxfendazole given on d 0 followed by moxidectin on d 73; 2) moxidectin on d 0 and oral oxfendazole on d 73; 3) moxidectin given on d 0; 4) oxfendazole on d 0; 5) control, and were followed for a 108 d post-treatment grazing period. Treated cattle had greater overall ADG and greater BW on d 31, 59, and 108 of the study compared to CON cattle. Similar differences were not reported for BCS or HCS, with respected measurements not differing on any collection day.

The effects of anthelmintic administration on FEC in calves are outlined in Table 12 and followed a similar pattern as reported by their dams. However, as to be expected, calves averaged a higher FEC compared with their dams over a 203 d grazing period. For the duration of the grazing period, CON calves had greater ($P < 0.01$) FEC compared with treated calves, and LAE-treated calves exhibited greater ($P < 0.01$) FEC compared to OXF- treated calves. Mean FEC averaged, 64, 17, and 28 eggs/g for CON, OXF, and LAE calves respectively. A treatment × day interaction was detected ($P < 0.01$) for FEC. Fecal egg counts were greatest on d 327 (which was 99 d post-weaning and anthelmintic administration) for CON calves compared to all other treatment and day combinations, with FEC reaching 306 eggs/g. The second highest FEC was reported by OXF-treated calves on d 327, averaging 200 eggs/g. The lowest FEC over the 203 d grazing period was reported by OXF-treated cows on d 242 and 431, with mean FEC decreasing to 2 and 3 eggs/g. The decreases in FEC reported in the OXF-treated calves 14 d post-anthelmintic treatment followed a similar pattern as depicted by their dams. In regards to the LAE-treated calves, 14-d post treatment, FEC did not decrease. Furthermore, 99-d post

treatment FEC for LAE reached their highest values over the duration of the study. According to Forbes (2013), blood plasma concentrations of LAE release a second wave into the body near d 90, theoretically resulting in a decrease in FEC; however, this was not the case. The results of the current study could indicate possible anthelmintic resistance occurring in cattle treated with LAE; however, further research is warranted to evaluate these discrepancies.

The concentrations of calf NEU, MON, EOS, BAS, and the N:L did not differ ($P \geq 0.24$) across treatments (Table 13). However, concentrations of WBC, LYM, and RBC were greater ($P \leq 0.02$) for OXF-treated calves compared with LAE-treated calves; however, did not differ ($P \geq 0.26$) from CON compared to treated calves. Lastly, PLT were greater ($P = 0.01$) for CON compared with treated, also OXF-treated calves had greater ($P = 0.05$) PLT compared to LAE-treated calves. Neutrophils were greatest on d 417 for CON calves and lowest for CON calves on d 327 as depicted by the treatment × day interaction ($P = 0.01$; data not shown).

Heifer performance, reproductive measurements, and complete blood cell counts

Heifer BW on d 522, 559 (at pregnancy check), ADG from d 522 to 559, BCS and FEC on d 522 did not differ ($P \geq 0.21$) across treatments (Table 14). Similarly, pregnancy rate and calving rate (percentage of cows that calved/cow exposed) did not differ ($P \geq 0.32$) between treatments. Pregnancy rates were 79, 85, and 94 % and calving rates were 79, 85, and 87% for CON, OXF, and LAE heifers, respectively. Similar calving rates were reported by Purvis et al. (1994), indicating that calving rates were not increased in spring-born heifers administered OXF intrarumminally compared to heifers not receiving OXF. Birth weights from calves born from study heifers did not differ ($P = 0.99$) across treatments and averaged 34 to 36 kg.

Anthelmintic administration did not impact ($P \geq 0.20$) concentrations of LYM, N:L, MON, EOS, BAS, and PLT on d 522. Concentrations of WBC were greater ($P = 0.05$) and RBC

were greater ($P = 0.04$) for OXF-treated heifers compared to LAE-treated heifers; however, were similar ($P \geq 0.13$) from CON and treated calves. Similar results were reported for concentrations of NEU, where LAE tended ($P = 0.07$) to be lower compared to OXF, but did not differ ($P = 0.78$) across CON heifers compared to treated heifers.

Steer carcass measurements

Steer carcass HCW, marbling, and 12th rib fat thickness (FT) were similar ($P \geq 0.45$) across anthelmintic regimens (Table 15). Kidney, pelvic, and heart fat percentage was similar ($P = 0.69$) for carcasses from CON compared to treated calves; however, tended ($P = 0.06$) to be greater in carcasses of OXF-treated compared to LAE-treated steers. Longissimus muscle area (LMA) was greater ($P = 0.02$) and yield grade (YG) was lower ($P = 0.02$) for carcasses from CON steers compared to treated steers; however, LMA and YG did not differ ($P \geq 0.81$) between OXF- and LAE-treated steers. Although, LMA and YG differed between CON and treated steers, the percentage of carcasses that graded Choice and Select did not differ ($P = 0.63$); likewise, percentages did not differ ($P = 0.71$) between OXF- and LAE-treated steers. Percentages of carcasses that graded Select were 38, 43, and 50% and percentages of carcasses that graded Choice was 62, 57, and 50% for CON, OXF, and LAE, respectively. Carcass quality measurements in the current study disagree with previous work completed by Ballweber et al. (2000) and MacGregor et al. (2001) who utilized various anthelmintic treatments in feeder steers. Ballweber et al. (2000) evaluated the effects of fenbendazole plus topical fenthion treatment at the initiation of the grazing season and prior to the entry of feedyard and ivermectin-sustained released bolus at the beginning of the grazing season and compared them to a negative control. It was reported that carcasses from treated cattle had greater HCW, and lower YG compared to carcasses from control cattle. Secondly, MacGregor et al. (2001) reported that quality grade was

improved in carcasses from steers fed to finish after administration of doramectin upon arrival to the feed yard. There was a 5% increase in carcasses that graded choice compared to a 5% decrease in carcasses that graded select. Also, as to be expected, FT was not improved in cattle administered anthelmintic treatments, due to the cattle being fed to a desired level of finish. However, in the present study, cattle that were not administered an anthelmintic had a greater LMA and lower YG, therefore due to no differences being reported for quality grade, the monetary value associated with the decrease in yield grade may not be positively impacted.

Conclusion

To our knowledge, this is one of the only studies that compares the effects of administration of long-acting eprinomectin, oxfendazole and a negative control evaluating progeny gain performance, reproductive measurements, and complete blood cell counts, as well as carcass performance. From this study, cows treated with an anthelmintic exhibited improved ADG compared to controls; however, reproductive performance was not improved. Also, calves born from dams that received no anthelmintic had decreased performance post-weaning, and increased overall FEC during the grazing period; however, these factors did not affect carcass measurements. Therefore, anthelmintic administration exhibited benefits in calf gain performance; however, it did not impact reproductive performance or carcass measurements. Results indicate that in a rotational grazing system, administration of long-acting eprinomectin compared to oral oxfendazole and a negative control may not increase overall cow reproductive performance, but may improve cow ADG and post-weaning calf gain.

Table 7. Performance Measurements of Spring-Calving Cows Treated Prior to Calving With Either Oxfendazole or Long-Acting Eprinomectin

Item	Treatments[a]			SEM[b]	*P*-Value[c]		
	CON	OXF	LAE			CON vs TREATED	OXF vs LAE
BW, kg							
d 0	574	561	554	14.2	0.57	0.33	0.69
d 14	604	573	570	14.8	0.20	0.07	0.88
d 91	557	551	530	14.8	0.41	0.37	0.32
d 146	570	554	557	15.2	0.71	0.42	0.86
d 228	567	574	572	14.7	0.96	0.81	0.93
Total gain, kg	0.09	12.27	18.13	6.800	0.17	0.07	0.54
ADG, kg/d							
d 0 to 14	1.88	0.94	1.29	0.36	0.13	0.05	0.44
d 14 to 91	-0.57^{y}	-0.33^{x}	-0.51^{xy}	0.078	0.07	0.09	0.08
d 91 to 146	0.25^{g}	0.06^{h}	0.50^{f}	0.067	<0.01	0.75	<0.01
d 146 to 228	-0.01^{g}	0.23^{f}	0.18^{f}	0.110	<0.01	<0.01	0.38
Overall	0.00	0.05	0.08	0.030	0.17	0.07	0.54
BCS[d]							
d 0	5.6	5.7	5.6	0.09	0.89	0.95	0.63
d 14	5.8	5.9	5.8	0.059	0.25	0.96	0.10
d 91	5.8^{fg}	5.9^{f}	5.7^{g}	0.06	0.04	0.96	0.01
d 146	5.9	5.9	5.9	0.04	0.36	0.92	0.15
d 228	5.8	5.7	5.7	0.11	0.68	0.39	0.86

Table 7. Performance Measurements of Spring-Calving Cows Treated Prior to Calving With Either Oxfendazole or Long-Acting Eprinomectin (Cont.)

Item	Treatments[a]			SEM[b]	*P*-Value[c]		
	CON	OXF	LAE			CON vs TREATED	OXF vs LAE
HCS[e]							
d 0	4.9	5.0	4.9	0.03	0.61	0.60	0.40
d 91	2.8[f]	1.7[g]	3.5[f]	0.24	<0.01	0.39	<0.01
d 146	2.7	2.6	3.0	0.24	0.63	0.70	0.38
Pregnancy Rate, %	77	81	61	--	0.18	0.59	0.08

[a] CON = control; OXF = oxfendazole; and LAE = long-acting eprinomectin.

[b] SEM = pooled SEM.

[c] Cow BW, ADG, total gain, BCS, and HCS were analyzed using PROC MIXED; Pregnancy Rate was analyzed using GENMOD.

[d] 1 to 9 scale; 1 = emaciated; 9 = obese; (Wagner et al., 1988).

[e] HCS = hair coat score; 1 to 5 scale; 1 = slick, summer coat; 5 = full winter hair coat; (Gray et al., 2011).

[f-h] Means within a row without common superscript differ ($P \leq 0.05$).

[x-y] Means within a row without common superscript tended ($P \leq 0.10$) to differ.

Table 8. Fecal Egg Count (Geometric Means; GM) Treatment × Day Interaction of Spring-Calving Cows Treated Prior to Calving With Either Oxfendazole or Long-Acting Eprinomectin

Item	Treatments[a]			SEM[b]	*P*-Value		
	CON	OXF	LAE			CON vs TREATED	OXF vs LAE
FEC, GM[c]	2.4^{d}	1.5^{e}	2.1^{d}	0.03	<0.01	<0.01	<0.01
d 0	2.6^{gh}	2.5^{gh}	2.8^{gh}	--			
d 14	2.9^{g}	1.0^{i}	1.2^{i}	--			
d 91	1.5^{hi}	1.1^{i}	1.6^{hi}	--			
d 146	2.5^{gh}	1.5^{hi}	1.4^{hi}	--			
d 228	2.4^{gh}	1.9^{h}	5.5^{f}	--			

[a] CON = control; OXF = oxfendazole; and LAE = long-acting eprinomectin.
[b] SEM = pooled SEM.
[c] FEC = fecal egg counts.
[d-e] Means within a row without common superscript differ ($P \leq 0.05$).
[f-i] Means without common superscript differ ($P < 0.05$).

Table 9. Complete Blood Cell Counts of Spring-Calving Cows Treated Prior to Calving With Either Oxfendazole or Long-Acting Eprinomectin Over the 228 d Grazing Period

Item	Treatments[a]			SEM[b]	*P*-Value		
	CON	OXF	LAE			CON vs TREATED	OXF vs LAE
White blood cells K/µL	6.6[c]	6.6[c]	6.1[d]	0.07	<0.01	0.04	<0.01
Neutrophils, K/µL	2.08[x]	2.01[y]	2.22[x]	0.067	0.08	0.67	0.02
Lymphocytes, K/µL	3.195[c]	3.197[c]	2.745[d]	0.1038	<0.01	0.08	<0.01
Neutrophil:Lymphocyte	0.87[d]	0.85[d]	1.17[c]	0.062	<0.01	0.06	<0.01
Monocytes, K/µL	0.7	0.7	0.7	0.06	0.30	0.99	0.12
Eosinophils, K/µL	0.5[c]	0.6[c]	0.3[d]	0.03	<0.01	0.01	<0.01
Basophils, K/µL	0.086	0.094	0.080	0.0166	0.18	0.83	0.06
Red blood cells, M/µL	6.8	6.6	6.7	0.10	0.30	0.14	0.61
Platelets, K/µL	205	193	197	30.5	0.70	0.42	0.77

[a] CON = control; OXF = oxfendazole; and LAE = long-acting eprinomectin.

[b] SEM = pooled SEM.

[c-e] Means within a row without common superscript differ ($P \leq 0.05$).

[x-y] Means within a row without common superscript tended ($P \leq 0.10$) to differ.

Table 10. Treatment × Day Interaction on Blood Parameters of Spring-Calving Cows Treated Prior to Calving With Either Oxfendazole or Long-Acting Eprinomectin

	Treatments[a]		
Item	**CON**	**OXF**	**LAE**
White blood cell, K/µL			
d 0	7.11[bc]	6.99[c]	6.63[c]
d 14	7.78[b]	7.48[bc]	7.58[bc]
d 91	5.70[d]	6.37[cd]	5.58[d]
d 146	6.81[c]	6.89[c]	5.46[d]
d 228	5.68[d]	5.23[d]	5.19[d]
Neutrophil, K/µL			
d 0	2.6[b]	2.4[bc]	2.5[b]
d 14	1.3[d]	1.2[d]	1.8[c]
d 91	2.2[c]	2.0[c]	2.6[b]
d 146	2.6[b]	2.6[b]	2.2[bc]
d 228	1.7[cd]	1.9[c]	1.9[c]
Neutrophil:Lymphocyte			
d 0	0.8[de]	0.8[de]	0.8[de]
d 14	0.3[d]	0.3[d]	0.5[d]
d 91	1.4[c]	1.0[d]	2.2[b]
d 146	1.1[cd]	1.1[cd]	1.1[cd]
d 228	0.7[de]	1.0[d]	1.2[cd]
Eosinophils, K/µL			
d 0	0.44[d]	0.47[d]	0.39[de]
d 14	0.34[de]	0.27[e]	0.20[e]
d 91	0.68[c]	1.0[b]	0.43[de]
d 146	0.64[cd]	0.71[c]	0.23[e]
d 228	0.66[c]	0.56[cd]	0.44[d]

[a] CON = control; OXF = oxfendazole; and LAE = long-acting eprinomectin.
[b-e] Means within a row without common superscript differ ($P \leq 0.05$).

Table 11. Post-Weaning Performance Measurements of Spring-Born Calves Treated With Either Oxfendazole or Long-Acting Eprinomectin At Weaning and 189 d Post-Weaning

Item	Treatments[a]			SEM[b]	*P*-Value[c]		
	CON	OXF	LAE			CON vs TREATED	OXF vs LAE
BW, kg							
d 91	108	110	104	4.5	0.38	0.84	0.18
d 146	164	170	161	5.9	0.26	0.77	0.10
d 228 (weaning)	239^{xy}	252^{x}	235^{y}	7.4	0.09	0.52	0.03
d 242	235	250	245	7.7	0.13	0.06	0.46
d 327	254^{xy}	272^{x}	260^{xy}	8.7	0.09	0.09	0.16
d 417 (retreat)	296^{xy}	315^{x}	312^{xy}	10.6	0.08	0.02	0.68
d 431	313^{f}	339^{e}	330^{ef}	12.3	0.01	<0.01	0.29
Total Gain	73	86	95	7.8	<0.01	<0.01	0.06
ADG, kg/d							
d 228 to 242	-0.31^{f}	-0.12^{f}	0.64^{e}	0.125	<0.01	<0.01	<0.01
d 242 to 327	0.23	0.24	0.18	0.040	0.30	0.67	0.13
d 327 to 417	0.47^{f}	0.47^{f}	0.56^{e}	0.030	<0.01	0.08	0.01
d 417 to 431	1.13^{f}	1.65^{e}	1.30^{f}	0.120	<0.01	<0.01	<0.01
Overall	0.36^{f}	0.42^{e}	0.47^{e}	0.038	<0.01	<0.01	0.06
BCS[d]							
d 228	6	6	6	0.0	1.00	1.00	1.00
d 242	6	6	6	0.0	1.00	1.00	1.00
d 327	6	6	6	0.0	1.00	1.00	1.00
d 417	7	7	7	0.0	1.00	1.00	1.00
d 431	7	7	7	0.0	1.00	1.00	1.00

Table 11. Post-Weaning Performance Measurements of Spring-Born Calves Treated With Either Oxfendazole or Long-Acting Eprinomectin At Weaning and 189 d Post-Weaning (Cont.)

Item	Treatments[a]			SEM[b]	*P*-Value[c]		
	CON	OXF	LAE			CON vs TREATED	OXF vs LAE
HCS[e]							
d 417	5	5	5	1.1	0.38	0.48	0.23
d 431	5	5	5	0.1	0.35	0.92	0.15

[a] CON = control; OXF = oxfendazole; and LAE = long-acting eprinomectin.

[b] SEM = pooled SEM.

[c] 1 to 9 scale; 1 = emaciated; 9 = obese; (Wagner et al., 1988).

[d] HCS = hair coat score; 1 to 5 scale; 1 = slick, summer coat; 5 = full winter hair coat; (Gray et al., 2011).

[e-g] Means within a row without common superscript differ ($P \leq 0.05$).

[x-y] Means within a row without common superscript tended ($P \leq 0.10$) to differ.

Table 12. Fecal Egg Count (Geometric Means; GM) Treatment × Day Interaction of Spring-Born Calves Treated With Either Oxfendazole or Long-Acting Eprinomectin At Weaning and 189 d Post-Weaning

Item	Treatments[a]			SEM[b]	*P*-Value		
	CON	OXF	LAE			CON vs TREATED	OXF vs LAE
FEC, GM[c]	64.0[d]	16.9[f]	27.8[e]	0.04	<0.01	<0.01	<0.01
d 228 (weaning)	49[j]	20[kl]	21[kl]				
d 242	88[i]	2[m]	13[l]				
d 327	306[g]	200[h]	64[ij]				
d 417 (retreat)	22[k]	45[j]	42[j]				
d 431	36[j]	3[m]	24[k]				

[a] CON = control; OXF = oxfendazole; and LAE = long-acting eprinomectin.
[b] SEM = pooled SEM.
[c] FEC = fecal egg counts.
[d-f] Means within a row without common superscript differ ($P \leq 0.05$).
[g-m] Means without common superscript differ ($P \leq 0.05$).

Table 13. Complete Blood Cell Counts of Spring-Born Calves Treated With Either Oxfendazole or Long-Acting Eprinomectin At Weaning and 189 d Post-Weaning

Item	Treatments[a]			SEM[b]	*P*-Value	CON vs TREATED	OXF vs LAE
	CON	OXF	LAE				
White blood cells K/µL	8.9[c]	9.2[c]	7.9[d]	0.26	<0.01	0.26	<0.01
Neutrophils, K/µL	1.9	1.8	1.8	0.06	0.24	0.32	0.18
Lymphocytes, K/µL	5.97[c]	6.32[c]	5.15[d]	0.254	<0.01	0.46	<0.01
Neutrophil:Lymphocyte	1.38	1.73	1.36	0.194	0.31	0.49	0.16
Monocytes, K/µL	0.88	0.83	0.81	0.038	0.40	0.21	0.61
Eosinophils, K/µL	0.14	0.14	0.13	0.017	0.61	0.60	0.40
Basophils, K/µL	0.06	0.06	0.06	0.005	0.57	0.70	0.33
Red blood cells, M/µL	9.8[c]	9.9[c]	9.6[d]	0.15	0.04	0.31	0.02
Platelets, K/µL	662[c]	626[e]	563[d]	22.8	<0.01	0.01	0.05

[a] CON = control; OXF = oxfendazole; and LAE = long-acting eprinomectin.

[b] SEM = pooled SEM.

[c-e] Means within a row without common superscript differ ($P \leq 0.05$).

Table 14. Performance of Spring-Born Heifer Calves Treated With Either Oxfendazole or Long-Acting Eprinomectin At Weaning and 189 d Post-Weaning

Item	Treatments[a]			SEM[b]	*P*-Value[c]		
	CON	OXF	LAE			CON vs TREATED	OXF vs LAE
BW, kg							
d 522	359	377	380	10.0	0.27	0.11	0.80
d 559	372	388	387	9.9	0.44	0.20	0.93
ADG, kg/d					0.09	0.52	0.03
d 522 to 559	0.36	0.31	0.19	0.070	0.21	0.22	0.23
BCS[d]					0.09	0.09	0.16
d 552	7	7	7	1.0	1.00	1.00	1.00
Fecal egg counts, GM					0.01	<0.01	0.29
d 522	6	11	9	0.1	0.50	0.27	0.64
Pregnancy rate, %	79	85	94	--	0.45	0.32	0.42
Calving rate, %	79	85	87	--	0.39	0.53	0.82
Calf birth weight, kg	34	36	34	25	0.99	0.99	0.95
Complete blood cell counts, d 522							
White blood cells, K/µL	6.9[y]	8.2[x]	7.2[y]	0.37	0.06	0.13	0.05
Neutrophils, K/µL	2.6	2.9	2.4	0.02	0.20	0.78	0.07
Lymphocytes, K/µL	3.4	4.5	3.5	0.39	0.14	0.20	0.11
Neutrophil:Lymphocyte	0.9	0.7	0.8	0.36	0.52	0.39	0.43
Monocytes, K/µL	0.7	0.7	0.7	0.07	0.85	0.66	0.75
Eosinophils, K/µL	0.4	0.2	0.4	0.07	0.19	0.24	0.14
Basophils, K/µL	0.1	0.1	0.1	0.02	0.33	0.14	0.71
Red blood cells, M/µL	8.9[x]	8.9[x]	7.5[y]	0.50	0.06	0.23	0.04
Platelets, K/µL	199	222	162	34.9	0.47	0.87	0.23

[a] CON = control; OXF = oxfendazole; and LAE = long-acting eprinomectin.

[b] SEM = pooled SEM.

[c] Heifer BW, ADG, BCS, Fecal egg counts, complete blood cell counts, and calf birth weights were analyzed using PROC MIXED; Pregnancy and calving rates were analyzed using GENMOD.

[d] 1 to 9 scale; 1 = emaciated; 9 = obese; (Wagner et al., 1988).

[x-y] Means within a row without common superscript tended ($P \leq 0.10$) to differ.

Table 15. Carcass Measurements By Spring-Born Calves Treated With Either Oxfendazole or Long-Acting Eprinomectin At Weaning and 189 d Post-Weaning

Item	Treatments[a]			SEM[b]	*P*-Value[c]		
	CON	OXF	LAE			CON vs TREATED	OXF vs LAE
HCW, kg	404	420	411	9.1	0.45	0.30	0.49
Marbling	310	307	312	10.1	0.92	0.96	0.70
12th rib fat thickness, cm	1.4	1.5	1.5	0.09	0.78	0.65	0.57
Longissimus muscle area, cm^2	104[x]	96[y]	95[y]	3.1	0.08	0.02	0.81
KPH, %	2.1	2.1	1.9	0.11	0.15	0.69	0.06
Yield Grade	2.5[y]	3.1[x]	3.1[x]	0.20	0.07	0.02	0.96
Select, n (%)[d]	5 (38)	6 (43)	6 (50)	--			
Choice, n (%)[d]	8 (62)	8 (57)	6 (50)	--			

[a] CON = control; OXF = oxfendazole; and LAE = long-acting eprinomectin.

[b] SEM = pooled SEM.

[c] Percentage of carcasses that graded Choice and Select were determined using GENOMD; All other carcass measurements were analyzing using PROC MIXED.

[d] Percentage of carcasses from CON steers compared to carcasses from treated steers that graded Choice or Select did not differ ($P = 0.63$); Percentage of carcasses from OXF-treated steers compared with carcasses from LAE-treated steers that graded Choice and Select did not differ ($P = 0.71$).

[x-y] Means within a row without common superscript tended ($P \leq 0.10$) to differ.

CONCLUSION

Based on the results in experiment 1, treatment with anthelmintics can improve heifer gain and reproductive performance. Also, improvement in BW and ADG occurred and overall pregnancy rates tended to improve with LAE compared to MO-treated heifers. In experiment 2, the use of anthelmintics reported minimal differences in terms of gain performance in cows. However, post-weaning performance was improved when an anthelmintic was administered. Results of this study indicate that in a rotational grazing system, administration of long-acting eprinomectin compared to a conventional anthelmintic and negative control may not increase cow performance, but may improve post-weaning calf performance, without improving reproductive measurements or carcass quality.

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UNIVERSITY OF ARKANSAS

Office of Research Compliance

MEMORANDUM

TO: Dr. Jeremy Powell

FROM: Craig N. Coon, Chairman
Institutional Animal Care and Use Committee (IACUC)

DATE: August 8, 2014

SUBJECT: IACUC APPROVAL
Expiration date: August 31, 2016

The Institutional Animal Care and Use Committee (IACUC) has APPROVED your modification to protocol 14034: *Performance and reproductive measurements by fall-born heifer calves under various anthelmintic treatments*

In granting its approval, the IACUC has approved only the information provided. Should there be any further changes to the protocol during the research, please notify the IACUC in writing(via the Modification form) prior to initiating the changes. If the study period is expected to extend beyond August 31, 2016 you can request another extension via a modification form submitted at least 14 days prior to that date, or submit a new protocol. By policy the IACUC cannot approve a study for more than 3 years at a time.

The IACUC appreciates your cooperation in complying with University and Federal guidelines involving animal subjects.

CNC/aem

cc: Animal Welfare Veterinarian

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UNIVERSITY OF ARKANSAS

Office of Research Compliance

MEMORANDUM

TO: Jeremy Powell

FROM: Craig N. Coon, Chairman
Institutional Animal Care and Use Committee

DATE: FEBRUARY 7, 2014

SUBJECT: IACUC APPROVAL
Expiration date: August 31, 2015

The Institutional Animal Care and Use Committee (IACUC) has APPROVED protocol 14023:
"Evaluation of various anthelmintic treatments on performance of spring-calving cows and their calves."
You may begin this study immediately.

In granting its approval, the IACUC has approved only the protocol provided. Should there be Any changes to the protocol during the research, please notify the IACUC in writing (via the Modification form) prior to initiating the changes. If the study period is expected to extend beyond August 31, 2015 you must submit a MODIFICATION. By policy the IACUC cannot approve a study for more than 3 years at a time.

The IACUC appreciates your cooperation in complying with University and Federal guidelines for involving animal subjects.

CNC/aem

cc: Animal Welfare Veterinarian

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