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Long-Acting Moxidectin for the Control of Gastrointestinal Nematodes in Preweaned Beef Calves in Tropical Areas

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Abstract

Gastrointestinal nematodes (GINs) in beef calves in the preweaning period can be an underestimated problem, and an adequate control program can result in increased productivity. In the current scenario of anthelmintic resistance, clinical studies with highly effective molecules with a prolonged period of action can contribute to the development of technologies applied in the field. The objective of this study was to evaluate the effects of a 10% moxidectin formulation (10%MOX), administered to calves aged 4–5 months, in the control of gastrointestinal nematodes and weight gain until the time of weaning. The study was divided into 2 stages. The first stage was carried out on a farm, with a randomized block design based on fecal egg counts (FEC), live weight, number of calvings of the mother, breed of the calves, and pickets. In the second stage, the study was repeated on 10 other farms, following a completely randomized design, to confirm the results obtained in the first stage. In all experiments there was a treated group and a placebo group. In the first stage, the effectiveness of 10%MOX in the FECRT performed on the 38th day post-treatment was 98.49%, and the treated animals still had lower FEC averages and a 9.4 kg increase in weight at weaning compared to those from the placebo group. In the second stage, the average increase in weight gain was 6.1 kg, confirming the results of the first stage. The study demonstrated effective control of GINs and improvement in the productive performance of calves treated in the preweaning phase, using 10% moxidectin.

Keywords: cattle, gastrointestinal nematodes, weight gain, control

1. Introduction

Gastrointestinal nematodes (GINs) are among the biggest causes of economic loss in beef cattle farming worldwide, due to their direct action and also the expenses generated with control attempts (Knox et al., 2012; Van Der Voort et al., 2013; Grisi et al., 2014). In Brazil, GINs incur an annual economic impact of approximately US$7.11 billion, taking into account only the reduction in the productive performance of affected animals (Grisi et al., 2014).

The strategic control of GINs in weaned stocker beef calves in Central Brazil currently consists of treating animals from weaning up to 18–24 months of age. This is considered the animal category with higher susceptibility to GINs, and it consequently represents a higher financial loss (Bianchin et al., 1996). Heckler et al. (2016) evaluated the effects of anthelmintic treatment in animals in the growing phase, concluding that animals that were treated 3 times a year, even when the effectiveness of the drug used was below the recommended, obtained greater weight gain than animals that were treated twice or not at all. This strategic control scheme resulted in an economic return of US$14.3 to US$49.96, depending on the economic scenario and the productivity obtained (Conde et al., 2019). Weight gain in the growing phase of treated animals was also observed in studies carried out in the United States (Walker et al., 2013) and in Argentina (Suarez et al., 2016).

Initially, verminosis in calves in the preweaning period was not considered of great importance, and it was believed that through the treatment of cows in the pre-calving period, there would be an effect on the control of parasitism in calves, because the cows were considered the sources of contamination of the pastures. On this basis, the treatment of calves was not recommended (Bianchin et al., 1987). However, a more recent study carried out with beef cattle in Brazil showed that fecal worm egg count (FEC) per gram in the preweaning category was higher than in other categories, making this category more vulnerable to infection by GINs (Martins, 2018).

Under tropical conditions, the treatment of preweaning calves and cows during the suckling period was evaluated by Catto et al. (2005), who did not observe any effect of the treatment of cows on the weight of the calves; however, the calves treated at 4–5 months of age showed greater weight gain. In this study, ivermectin (IVM) was used, and the effect of a conventional formulation was also compared to that of a long-acting (IVM-LA) agent, noting that only IVM-LA resulted in an average increase in weight gain in calves of 7.1 kg compared to the control group. A similar result was obtained with IVM-LA in calves at 4–6 months, but under different epidemiological conditions, with gains of 22.7 and 12.4 kg in the period of 84–100 days of evaluation (Rehbein et al., 2016).

In these two studies, an increase in weight gain in calves treated with IVM-LA at 4–6 months was proven, with high efficacy greater than 94% up to the 70th DPT. However, in Brazil and other countries, IVM, even at higher concentrations, is no longer showing satisfactory efficacy due to the phenomenon of resistance (Borges et al., 2015), while moxidectin (MOX) may still be effective against these ivermectin-resistant populations (Soutello et al., 2007, Fazzio et al., 2014). A study in Argentina clearly shows the advantage of MOX treatment in calves infected by a population of ivermectin-resistant GINs, with weight gains of 15.7 kg and 23.5 kg in calves treated with IVM and MOX, respectively (Canton et al., 2020).

The aim of this study was to evaluate the effects of 10% moxidectin formulation on the control of gastrointestinal nematodes and on the performance of calves treated in the preweaning period.

2. Method

This study was carried out on 11 commercial farms dedicated to the production of beef cattle, and divided into 2 stages. The first stage was developed in a randomized block design based on fecal worm egg count (FEC) per gram, live weight, number of calvings of the dam, breed of calves, and pickets. In the second stage, the study was repeated in 10 different locations, in different Brazilian states, following a completely randomized design, to confirm the results obtained in the first stage.

2.1 First Stage

2.1.1 Location and Animals

In a farm located in the city of Bela Vista, state of Mato Grosso do Sul, Brazil, 202 animals aged between 3 and 5 months, fixed-time artificial insemination products, and offspring of multiparous Nellore cows were used, with the latter having been mated with bulls of the Nellore and Angus breeds, all evenly distributed between treatments. The study animals were kept together with their mothers.

2.1.2 Pickets

Five area repetitions, called Pickets 12, 15, 21, FP, and LA, were used. Pickets 12, 15, 21, and LA were formed by *Brachiaria brizantha* cv. *Marandu*, and the FP picket by *Brachiaria humidicola* cv. *Llanero*. All animals received mineralized salt and fresh water ad libitum.

2.1.3 Treatment

The 202 animals were divided into 2 groups according to a randomized block design, considering the FEC factors, weight, breed, and number of calvings of the dam and bull, in each of the 5 area repetitions. Treatments were randomly assigned within each block: Treatment 1: Moxidectin 10% (10%MOX), 1,000 μg/kg, in a single dose injected subcutaneously at the base of the right ear, as recommended by the manufacturer; Treatment 2: Placebo (saline solution—0.9% NaCl—injected subcutaneously in the injection triangle).

Treatment was carried out on day D0, after allocation of the animals to the groups according to the randomization plan.

2.1.4 FEC Counts, Coproculture, and Weight Gain Assessment

Parasitism by GINs was assessed on the day of treatment (D0) and on the day of weaning of the animals (D120), which was performed in stages according to the age of the animals. Individual stool samples were collected directly from the rectal ampoule, transported under refrigeration to the Laboratory of Parasitic Diseases/FAMEZ/UFMS for FEC counts using the modified Gordon & Whitlock (1939) technique, with 1:25 sensitivity. Pools per group were made from these same samples for stool cultures to determine the genera of nematodes present (Roberts & O'Sullivan, 1950). Stool cultures were performed in triplicate in each of the 5 area replicates to determine the nematode genders present in the animals participating in the study. To identify the 3rd instar larvae (stage) (L3), the taxonomic criteria described by Keith (1953) and Ueno and Gonçalves (1998) were used. A pool of fecal samples from the animals collected on days zero, on D38, and on the weaning date was made for each group in each repetition area.

To assess the efficacy of 10%MOX, a fecal egg count reduction test (FECRT) was performed on the 38th day after treatment according to Coles et al. (1992). For this, tests were performed in 2 replicates of each area, with 24 and 59 animals selected from each area. The effectiveness was calculated using the following mathematical equation: Efficacy (%) = [1-(T2/C2)]x100, where T2: mean FEC of the treated group in the posttreatment sampling and C2: mean FEC of the control group in the posttreatment sampling. Lower and upper limits of efficacy at the 95% confidence interval were also calculated.

Weight gain was evaluated by weighing the animals individually on the day of treatment (D0) and on the weaning days (D120), calculating the average weight gain and the average daily gain.

2.2 Second Stage

Another 10 clinical studies were carried out on commercial farms distributed in 4 different geographic regions of Brazil (Table 1), where 686 calves were randomly distributed between the groups treated with 10%MOX and the placebo group, with application of saline solution.

Table 1. Geographic location of farms, number of animals in each group, and animal characteristics in clinical studies evaluating the weight gain of calves treated with 10%MOX in the preweaning period

State/Region	**Age**	**Sex**	**Number of placebo animals**	**Number of animals treated**
Goiás/Midwest	NI	M/F	52	63
Mato Grosso/Midwest	4 months	M/F	45	46
Mato Grosso/Midwest	4–5 months	M	3	28
Minas Gerais/Southeast	3–4 months	NI	19	23
Minas Gerais/Southeast	6–8 months	NI	41	40
Pará/North	4–5 months	M	56	55
Rio Grande do Sul/South	NI	M	21	24
São Paulo/Southeast	5–6 months	NI	23	28
São Paulo/Southeast	4 months	M	19	27
São Paulo/Southeast	NI	M/F	36	37

NI – Not informed; M – Male; F – Female

Individual weighing of the animals and collection of feces for evaluation of FEC were carried out on days zero (treatment) and on weaning days (approximately D120).

2.3 Statistical Analysis

Data were analyzed considering the initial weight of the animals as a covariate and the random effects of genetic group, month of birth, and management lot. The SAS University PROC GLIMMIX (SAS Institute Inc., Cary, CA) procedure was used. A significance level of 5% was considered.

The results of FEC counts (log-transformed), weight, and weight gain were subjected to factorial analysis of variance (two-way ANOVA) and Sidak's multiple comparisons test, to verify differences between groups at the significance level of 5% using GraphPadPrismversion 6.0 for Windows (GraphPad Software, San Diego, California, USA, www.graphpad.com).

3. Results

3.1 First Stage

The efficacy of 10%MOX evaluated in the 38th DPT through FECRT in batches 21 and LA was 98.78% and 98.21%, respectively, with an average efficacy of 98.49% (Table 2).

Table 2. Test of reduction in the FEC of calves treated with 10%MOX before weaning, kept in pickets 21 and LA

Batch 21		
	pre-FEC	post-FEC
Treated (n = 11)	78.3	2.3
control (n = 13)	100.0	186.5
	Efficacy	**98.78%**
	IC95%	95–100%
Batch LA		
	pre-FEC	post-FEC
Treated (n = 25)	304.3	4.0
control (n = 24)	259.8	224.0
	Efficacy	**98.21%**
	IC95%	93–100%

FEC counts were influenced by time and treatment factors. In both groups, there was a significant reduction in the means of FEC in calves between day zero (3–5 months of age) and the time of weaning (8 months of age) (Figure 1 and Table 3).

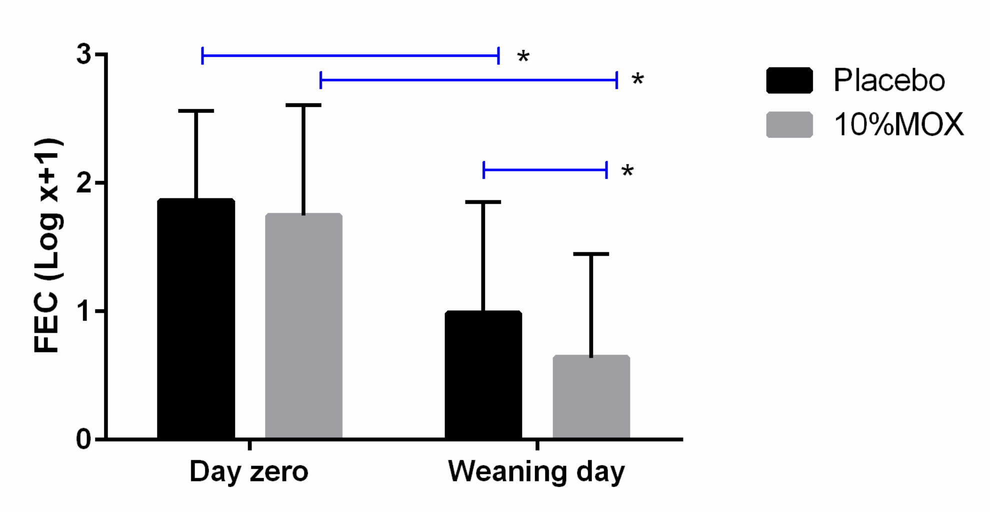

Figure 1. Mean of log-transformed FEC values of calves treated before weaning with 10%MOX and control group. *statistical difference ($P < 0.05$) by Sidak's multiple comparison test

In addition to the reduction in mean FEC at weaning, in the group of calves treated with 10%MOX, there was a higher percentage of animals with negative stool analysis (56.8%) than in untreated calves (36%) (Table 3).

Table 3. Number of animals with negative stool analysis at 3–5 months of age (day zero) and on the day of weaning

Group	Animals with FEC = 0/total animals	
	Treatment day	Weaning day
Treated	15/102	58/102
	14.7%	56.8%
Placebo	10/100	36/100
	10.0%	36.0%

In pooled stool cultures of animals in the placebo group on D0, there was a predominance of the genus *Cooperia* spp, followed by *Haemonchus* spp. and *Oesophagostumum* spp. In the control group on the weaning day and in the group treated on D0 and on the weaning day, there was a predominance of the genus *Haemonchus* spp., followed by *Cooperia* spp. and *Oesophagostomum* spp. No larvae of the genus *Trichostrongylus* spp. were observed in any of the groups, at any time during the study (Figure 2).

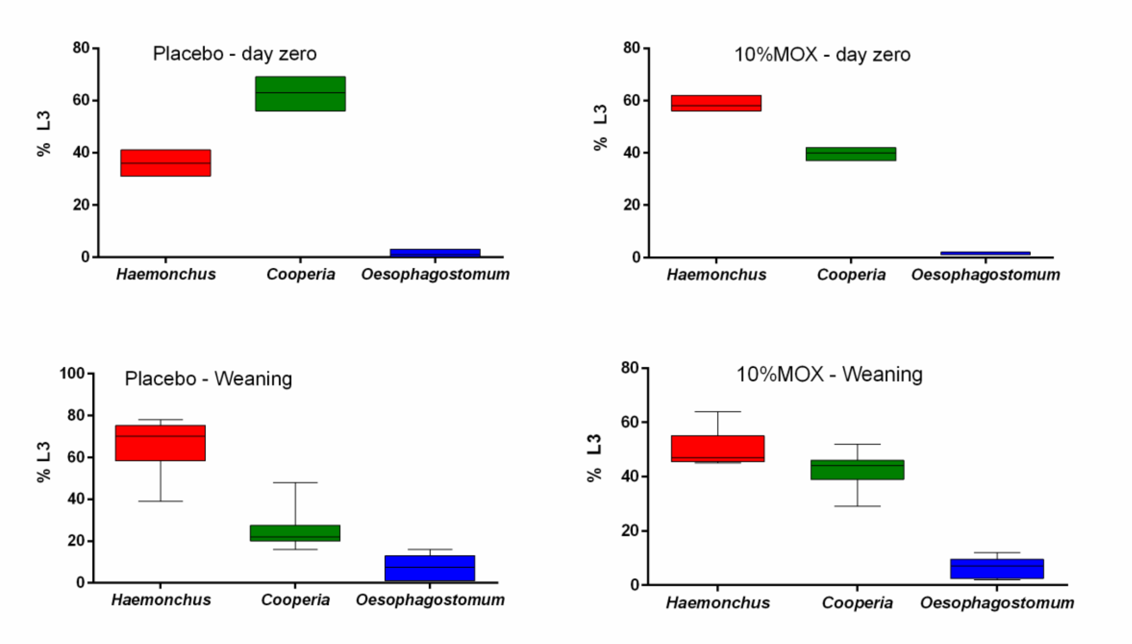

Figure 2. Boxplot, with quartiles (1st, 2nd, 3rd, and 4th) and medians, of the percentage of larvae of each genus recovered in fecal cultures

The effect of the treatment of beef calves at 3–5 months on weight at weaning was significant ($P < 0.05$) and resulted in a difference of 9.4 kg between the treated group and the placebo group (Table 4 and Figure 3). Treated animals showed an increase in daily gain of 82 grams compared to the control group (Table 4 and Figure 4).

Table 4. Least squares means and standard errors of the means of the weaning weight, mean daily gain, and initial and weaning FEC of calves treated with 10%MOX before weaning and control group

Variable	Control	10%MOX	*P*-Value
Zero day weight (kg)	134 ± 23.7	134 ± 23.8	0.943
Weaning weight (kg)	203.5 ± 21.1	212.9 ± 21.1	< 0.001
Average daily gain (kg/d)	0.515 ± 0.091	0.597 ± 0.091	< 0.001
zero day FEC	133 ± 81.9	130 ± 81.6	0.892
weaning FEC	33.7 ± 4.32	18.7 ± 4.21	< 0.001

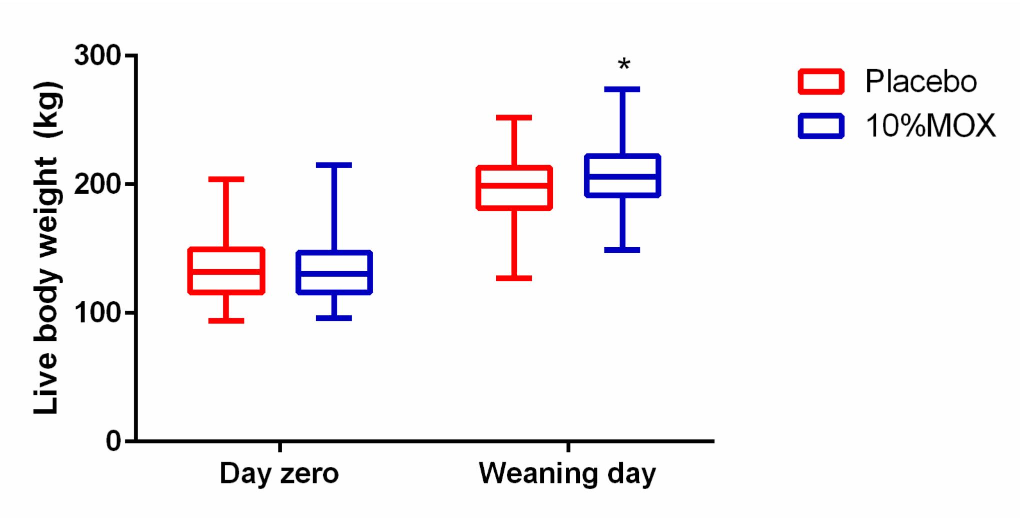

Figure 3. Boxplot, with quartiles (1st, 2nd, 3rd, and 4th) and medians, of the final live weight of calves treated with 10%MOX before weaning and placebo group. *statistical difference by Sidak's multiple comparisons test

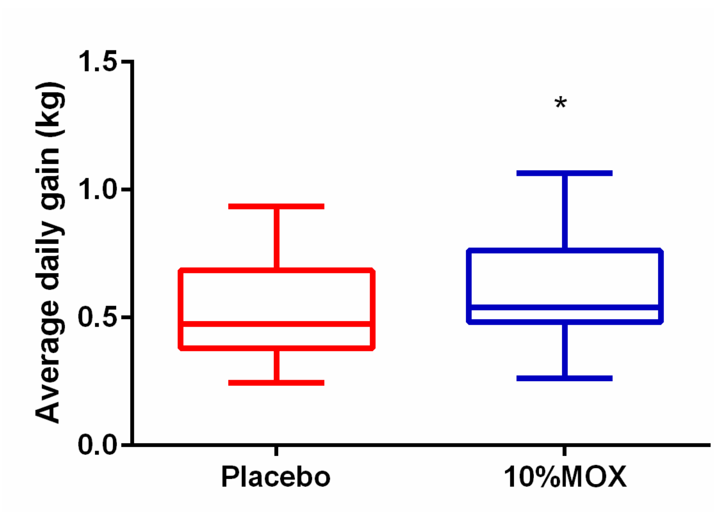

Figure 4. Boxplot, with quartiles (1st, 2nd, 3rd, and 4th) and medians, of the final average daily gain of calves treated with 10%MOX before weaning and placebo group. *statistical difference by Sidak's multiple comparisons test

3.2 Second Stage

In the other 10 clinical studies carried out in the second stage, the calves treated with 10%MOX showed an increase in 6.1 kg ($P < 0.001$) in live weight at weaning compared to the control group. Mean FEC counts at weaning in calves treated with 10%MOX were lower ($P < 0.05$) than in untreated calves (Table 5). In these clinical studies, it was not possible to perform FECRT until the 38th DPT.

Table 5. Means of FEC and weight on the day of treatment, at 4–6 months of age, and on the weaning day (D120) in beef calves in 10 clinical studies

Variable	Moxidectin 10%	Placebo
Initial live weight (kg)	145.73 ± 10.44[a]	146.10 ± 10.45[a]
Final live weight (kg)	221.90 ± 7.28[a]	217.09 ± 7.29[b]
Average weight gain (kg/animal)	75.75 ± 0.82[a]	69.64 ± 0.86[b]
Initial FEC (eggs/g)	287.48 ± 101.54[a]	331.29 ± 102.51[a]
Final FEC (eggs/g)	244.72 ± 122.23[a]	356.48 ± 123.55[b]

4. Discussion

The efficacy percentage found in this study, with an average of 98.49%, shows that the population of gastrointestinal nematodes parasitizing the animals was susceptible to moxidectin, according to the criteria defined by Coles et al. (2006). This result is similar to that reported in Brazil and other countries, where moxidectin remains effective (Soutello et al., 2007; Almeida et al., 2013, Fazzio et al., 2014).

In both stages of the study, treated and untreated animals were kept in the same area, along with their dams and untreated calves, which, according to Reinemeyer (1992), can lead to an underestimation of the effect of the treatment on the weight gain of the treated animals, because they were exposed to the same level of infection. However, this may not be an experimental error; in a study carried out by Heckler et al. (2016) in the state of Mato Grosso do Sul, Brazil, rearing animals were evaluated and the treated and control groups were allocated to different pastures, and there was no difference between the count of larvae in the pastures in the groups, leading to the conclusion that there was no difference in the potential of infection in treated and control animals.

In the current study, the decrease in FEC observed in both groups (treated and control) in the first stage is different from that described for this category in beef calves in the Brazilian cerrado region (Catto et al., 2005). At weaning, an increase in the susceptibility of calves to verminosis is expected, a result that was observed in the second stage, when there was an increase in the FEC of animals belonging to the control group. However, higher FEC means in the preweaning category were also found by Martins (2018) and reinforce the relevance of anthelmintic treatment in this animal category.

Another factor that influenced the FEC counts was the anthelmintic treatment with 10%MOX in calves aged 3–5 months, with a significant reduction ($P < 0.05$) compared to the control group; this difference was observed in both stages of this study. Similar results have been reported in calves treated between 3 and 6 months with long-acting ivermectin, showing significantly lower mean FEC 84–120 days later, when compared to the control group (Catto et al., 2005; Rehbein et al., 2016).

Neves (2017) described an increase in the weight gain of animals treated during the preweaning phase, when compared to untreated animals kept under the same rearing system; however, in this study, treatments were performed every 28 days, which has little commercial applicability because it increases the expense of anthelmintics and considerably increases the burden of animal handling. On the other hand, the present study showed similar results, with the use of only one treatment, at 3–5 months of age for calves, using a long-acting anthelmintic; this protocol would facilitate animal handling and use in the field and aim to wean heavier calves.

Treatment with 10%MOX did not affect the percentage distribution of the GIN genera found in the animals of the first stage of the study, a desirable result, as it indicates that resistance selection pressure has not occurred or favored any genus. This result is different from that found by Condi et al. (2009), who reported a proportional increase in L3s of *Oesophagostomum* spp. in the stool cultures of calves treated with moxidectin.

In the current study, animals treated with 10%MOX in both stages showed greater weight gain and a significantly higher average daily gain than the control group. This result supports what was described by Catto et al. (2005), who observed greater weight gain in calves treated with long-acting ivermectin, when compared to animals that received 1% ivermectin and also animals that did not receive treatment. The effect of anthelmintic treatment on the weight of calves at weaning, even if it is only 6.1 kg (second stage) or 9.4 kg (first stage), may not have the consequence of shortening the production cycle in later stages of rearing and finishing, but it certainly results in a greater economic return for the breeding farms, for which the price of weaned calves is based on live weight.

5. Conclusion

The study showed effective control of gastrointestinal verminosis and an improvement in the productive performance of calves treated in the preweaning phase, therefore indicating the use of the drug in a single application in animals aged 3–5 months.

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