Acta Veterinaria-Beograd 2022, 72 (1), 16-29
UDK: 636.09:615.28.035
636.2.09:616.995.132
DOI: 10.2478/acve-2022-0002

Research article

MOXIDECTIN: A VIABLE ALTERNATIVE FOR THE CONTROL OF IVERMECTIN-RESISTANT GASTROINTESTINAL NEMATODES IN BEEF CATTLE

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(Received 11 August 2021, Accepted 08 March 2022)

The increasing prevalence of anthelmintic resistance in cattle especially for avermectins, is a challenge for controlling parasites in some herds. Thus, field studies demonstrating the increase in productivity by the use of anthelmintic formulations, even when a suboptimal treatment (efficacy below 95%), can contribute to the development of gastrointestinal nematodes control programs in beef cattle. The objective of the present study was to evaluate the anthelmintic efficacy and productive performance in pasture-raised beef calves, treated with macrocyclic lactones. A Split plot in time randomized block design was used to assess weight gain and reduction in fecal egg count (FECs) of treatments: 1% moxidectin (1% MOX), ivermectin (IVM) and abamectin (ABM) (2.25% IVM+1.25% ABM), 4% IVM, 3.15% IVM and placebo. For the evaluation of FECs and weight gain of the animals, individual samples were collected seven days before treatment and, +14, +30, +56, +91 and +118 days post-treatment (DPT). The efficacies in the 14th DPT were: 72.3% (1% MOX) , 22.1% (4% IVM) , 22% (2.25% IVM + 1.25% ABM) and 0% (3.15% ivermectin) . 1% MOX was the only treatment that resulted in a significant increase in weight gain of the animals compared to the placebo group after 118 days of treatment, with a difference of 7.6 kg. Therefore, MOX remains a viable alternative for the control of helminths resistant to avermectins and still capable of resulting in significant productive gains, even with an efficacy below 95%.

Key words: Anthelmintic, macrocyclic lactones, resistance, ruminants

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INTRODUCTION

Gastrointestinal nematodes (GINs) in cattle are an important cause of economic losses [1,2], as infected animals develop more slowly and produce less; the production cycle is longer and the slaughter rate reduced. Economic estimates indicate that GINs infection is responsible for a loss of about seven billion dollars a year [3] and 445.10 million dollars a year [4] in Brazil and in Mexico, respectively. However, the determination of the impact of GINs on productive performance is still flawed, as it depends on several factors such as the breed and age of the host, nutritional status, parasite species, parasite load [5], system of production (intensive, extensive and semi-extensive) and, in addition, the efficacy of the anthelmintic used.

Control of GINs is mainly based on treating animals with anthelmintics. Macrocyclic lactones (MLs), since the beginning of commercialization in the 1980s, initially with ivermectin, have been used to control parasites in an excessive manner and without alternating chemical groups in Brazil, due to their antiparasitic activity against both nematodes and arthropods (endectocides), relative low cost, ease of application and wide margin of safety [6]. As a result of indiscriminate use, the problem related to ivermectin resistance in bovine parasites can be considered ubiquitous today [7].

Anthelmintic resistance to avermectins is present in cattle in Brazil, as verified in several regions of the country [6,8,9]. In view of this scenario, there are limited options for GINs. Consequently, antiparasitic resistance represents an addition to the impact of GINs, which is not yet known and is probably underestimated in tropical areas [10].

Despite the widespread situation of resistance to avermectins, efficacy studies with *in vitro* [11] and *in vivo* [6,12] methodologies, and evaluation of weight gain in feedlot [13] have shown differences in relation to resistance for different MLs. Moxidectin (MOX), administered at the therapeutic dose in ruminants, has been shown to be effective against many ivermectin-resistant nematode species [14].

Despite *in vitro* and *in vivo* evidence of better performance of MOX for the control of avermectin-resistant GINs, there is no data to demonstrate the effects of MOX on performance traits in pasture-raised animals in a tropical environment, fed on pastures of low nutritional value and in an extensive system, a predominant condition on farms in the intertropical region.

Considering the current scenario of anthelmintic resistance and the need for more information regarding the productivity of cattle treated with MOX, the aim of this study was to comparatively evaluate MOX, ivermectin (IVM) and a combination of avermectins (ivermectin + abamectin) in relation to anthelmintic efficacy and productive performance in Nellore cattle raised on pasture and infected with IVM-resistant GINs.

MATERIALS AND METHODS

Location

The study was carried out on a commercial beef cattle farm, located in the municipality of Ribas do Rio Pardo, Mato Grosso do Sul, Brazil (20°35'26.3"S 54°01'48.3"W), between November 2019 to March 2020, totaling 118 days of experiment. During the study, the animals were kept on pasture under the same environmental conditions and the facilities used in the experiment met the basic principles of ambience and well-being. The pastures consisted of *Brachiaria decumbens*, with the maintenance of an average stocking rate of 1AU/Ha. All animals received mineral salt supplementation with a non-protein nitrogen source (Zoofós Nitro 300), with an average consumption of 130 g/animal/day throughout the experimental period. Fresh water was freely supplied from drinking fountains.

Animals

Cattle in good general health condition, verified by a veterinarian familiar with the species, not treated with anthelmintic formulations in the 90 days prior to the beginning of the experiment and aged between 12 and 15 months were selected. Initially, the group of individuals submitted to the screening evaluation consisted of 400 animals. From the initial group of 400 animals, only 300 were used for the study (165 males and 135 females), as they had the desirable characteristics for the study: being of the Nellore breed; aged between 12 and 15 months; weighed between 150 and 210 kg; eggs per gram count (EPG) ≥ 25; healthy; good nutritional status and with numerical identification. All calves were born from heifers inseminated at a fixed time with semen from the same bull.

Anthelmintics

The following anthelmintics were used for the treatments: Cydectin – 1% Moxidectin (1% MOX) (Zoetis Saúde Animal Ltda) at a dose of 1mL/50 kg, corresponding to 200 μg/kg; Solution 3.5% – 2.25% Ivermectin and 1.25% Abamectin (2.25% IVM+1.25%ABM) (MSD Animal Health) at a dose of 1mL/50 kg, corresponding to 700 μg/kg; Master LP – 4% Ivermectin (4% IVM) (Ouro Fino Saúde Animal Participações SA) at a dose of 1 mL/50 kg, corresponding to 800 μg/kg; Ivomec Gold – 3.15% Ivermectin (3.15% IVM) (Boehringer Ingelheim) at a dose of 1mL/50 kg, corresponding to 630 μg/kg and saline solution for the treatment of animals in the Placebo group (Halex Star) at a dose of 1ml/50kg.

Experimental design

The 400 animals initially evaluated were divided into two lots of 200 animals each, according to sex (male and female), each group in a different paddock. The 300 animals that were selected were distributed into five experimental groups (33 males and 27 females per group, n=60) according to a randomized block design, taking into

account the weight and EPG at seven days before treatment (D-7), picket and sex. The following treatments were randomly assigned within each formed block: treatment 1: 1% MOX; treatment 2: 2.25% IVM + 1.25% ABM; treatment 3: 4% IVM; treatment 4: 3.15% IVM and treatment 5: placebo group (physiological solution NaCl 0.9%).

Treatment was carried out on day D0 by subcutaneous route and in a single dose, after distribution of the animals in each of the groups. The weights obtained on D-7 were used to calculate the dose of treatment for each animal. The doses administered followed the recommendations of each of the manufacturers. The animals remained divided into two paddocks after treatment, with the males staying in one paddock and the females in another. Thus, in each paddock there was the same number of animals from each of the experimental groups. All animals that were excluded from the experiment, but remained in the experimental lots to adjust the stocking rate, were treated with the combination of 2.25% IVM + 1.25% ABM.

After treatment, three animals were excluded from the study for health reasons. To maintain the initial homogeneity of weight and EPG, animals in the other groups belonging to the same block were excluded. Thus, the study was concluded with 57 animals in each group (n=57), 26 females and 31 males.

Due to the high infestation by *Haematobia irritans* on D-0, all the animals in the study, as well as their contacts, received a mosquito-based earring impregnated with 6g diazinon.

On day +56 post-treatment, due to the increase in weight of the animals and the reduction in the supply of pasture, the lots, males and females, were randomly divided into two other lots each, so as to obtain two lots of females and two lots of males, which were each transferred to a different paddock. In each of the new paddocks there was the same number of animals from each of the different experimental groups and the stocking rate of 1AU/ha was maintained. The forage composition of the new paddocks, food supplementation and water availability, as well as the environmental conditions were kept similar.

Weight gain assessment

To assess the weight gain of the animals, individual weightings were performed on days -7, +30, +56, +91 and +118 post-treatment. The live weight gain (LWG) was also calculated by the difference in weight between the weights per period ($LWG=P_X-P_{D-7}$), where Px represents the weight on the evaluation date X and P_{D-7} the weight on the day D-7, and the average daily gain (ADG) from the division of the LWG by the number of evaluation days (ADG=LWG/EP), where EP represents the experimental period in days up to the date of the considered experimental date.

Evaluation of the anthelmintic activity

GINs infection was assessed in conjunction with weight gain assessment (days-7, +30, +56, +91 and +118 post-treatment). Individual stool samples were collected directly

from the rectal ampoule, transported under refrigeration to the Laboratory of Parasitic Diseases/FAMEZ/UFMS and submitted to FECs [15] with sensitivity 1:25.

Stool cultures were carried out for each treatment [16] in order to determine the nematode genera present in each experimental group. To carry out the stool cultures of each of the experimental groups, an aliquot of feces from each animal belonging to the group was collected and then the group aliquots were used to compose a pool of samples, which was used to carry out the stool culture. The recovered larvae (L3s) were classified according to the taxonomic criteria [17].

Statistical analysis

The therapeutic efficacy and residual efficacy of the anthelmintic formulations used were evaluated from the Fecal egg reduction test at the different evaluation dates, according to Coles et al. (1992), through the following mathematical equation: *Efficacy (%)= [1-(T2/C2)]x100*, where T2 represents the mean EPG of the treated group in the post-treatment sampling and C2, the mean EPG of the control group in the post-treatment sampling of the same date. For the evaluation of therapeutic efficacy, performed from D+14 post-treatment, only the 15 animals with the highest EPG counts on D-7 of each group were selected. To calculate the residual efficacy, data from all animals in the groups on days 30, 56, 91 and 118 post-treatment (DPT) were considered.

The FECs were submitted to the D'Agostino normality test (α=0.05) and as they did not present normal distribution, they were Log transformed and then, the normalized FECs data and the LWG and ADG values were submitted to factorial analysis of variance (Two-way ANOVA), followed by Tukey's multiple comparisons post test to verify differences between groups at the 95% significance level, using GraphPadPrismversion 6.0 for Windows (GraphPad Software, San Diego, California, USA, www.graphpad.com).

RESULTS

The therapeutic efficacy of all endectocides evaluated in the fecal egg count reduction test (FECRT), carried out on the 14th DPT, was less than 95% (Table 1). MOX 1% was the most effective endectocide (72.3%), followed by 4% IVM (22.1%), 2.25% IVM + 1.25% ABM (22%) and 3.15% IVM (0%), and it was the only one that caused a significant reduction in egg count ($P<0.05$) in relation to the Placebo group and the other treatments on the 14th DPT (Table 1). On the 30th DPT, the group treated with 1% MOX still had a lower mean ($P<0.05$) than the Placebo and 3.15% IVM groups (Figure 1), with an efficacy of 56.3%. Furthermore, it was the treatment that resulted in the largest number of animals (19/57) with a negative FEC in the 118th DPT. Mean FECs were significantly influenced by treatments and also by time, so that overall FECs increased on day 30 and returned to baseline levels on 118th DPT (Figure 1).

Table 1. Fecal egg count reduction test, EPG means and FEC negative calves

Treatment		Effectiveness (%) Trial date					
		-7	14*	30	56	91	118
Moxidectin 1%	Average	175a	207a	133a	253a	238a	138a
	Dev. Pad.	188	114	142	400	310	212
	Negative	0	NR	10	12	14	19
	Effectiveness (%)		72.3	56.3	3.5	0.0	0.0
Ivermectin 3.15%	Average	180a	928b	302b	259a	179a	163a
	Dev. Pad.	212	477	361	375	267	211
	Negative	0	NR	7	9	16	11
	Effectiveness (%)		0.0	0.7	1.2	12.1	0.0
Ivermectin 4%	Average	172a	580b	250ab	239a	198a	142a
	Dev. Pad.	194	296	313	314	268	194
	Negative	0	NR	7	6	16	15
	Effectiveness (%)		22.1	18.0	8.9	2.8	0.0
Ivermectin 2.25% + abamectin 1.25%	Average	178a	580b	196ab	215a	159a	145a
	Dev. Pad.	233	307	244	255	202	189
	Negative	0	NR	6	10	7	11
	Effectiveness (%)		22	36	18	22	0
Control	Average	170a	745b	304b	262a	204a	137a
	Dev. Pad.	183	491	636	547	291	170
	Negative	0	NR	4	10	13	8

*For the calculation of efficacy at D+14, only the 15 animals with the highest EPG counts were selected. **different letters in the same column indicate statistical difference (P<0.05) by Tukey's multiple comparison test.

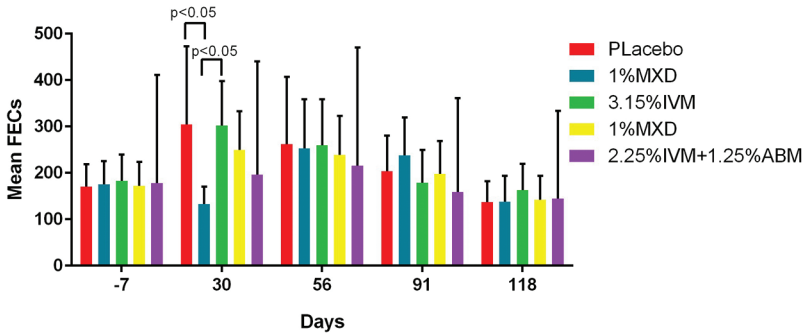

Figure 1. EPG means of endectocide-treated calves in the rearing phase, and placebo group. *p<0.05 statistical difference by Tukey's multiple comparison test.

In the stool cultures of animals in the placebo and treated groups, there was a predominance of the genus *Cooperia* followed by *Haemonchus* and *Oesophagostomum* during almost the entire study, except in some groups on D+30 and in all groups on D+118, when there was a predominance of *Haemonchus* sp. (Figure 2). No larvae of *Trichostrongylus* sp. were observed.

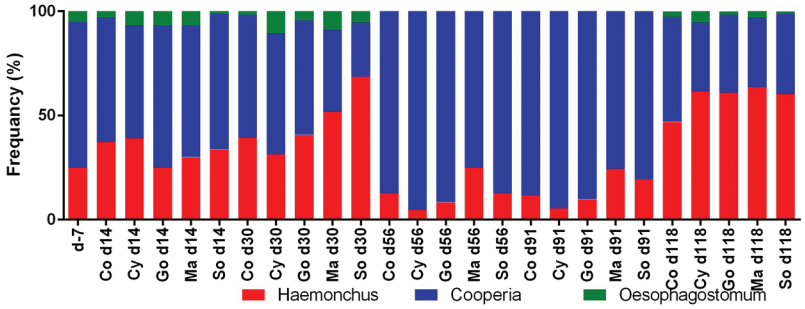

Figure 2. Frequency of gastrointestinal nematode genera recovered in fecal pool stool cultures in each group by experimental date. Co: Control, Cy: Moxidectin 1%, Go: Ivermectin 3.15%, Ma: Ivermectin 4%, So: Ivermectin 2.25% + abamectin 1.25%.

1% MOX was the only drug that resulted in a significant increase ($p<0.05$) in the weight gain of the animals compared to the Placebo group after 118 days of treatment, with a difference of 7.6 kg (Table 2 and Figure 3). The effect of 1% MOX on the significant increase in weight gain was observed from the 56th DPT. In relation to the other products, 1% MOX had higher averages ($P<0.05$) of weight gain in the 118th DPT, resulting in differences of 6 kg in relation to 3.15% IVM and 4% IVM and of 5.9 kg compared to 2.25% IVM + 1.25% ABM (Table 2 and Figure 3).

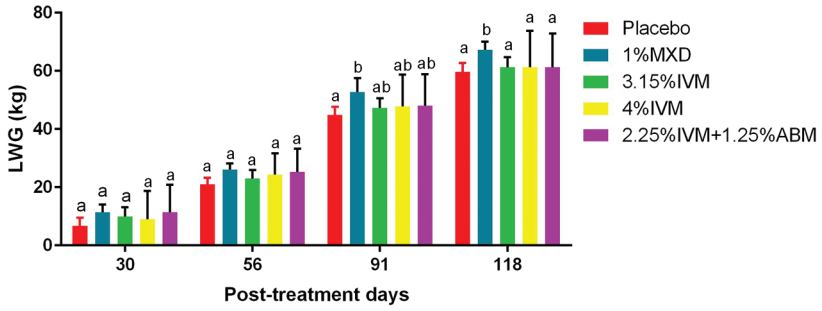

Figure 3. Mean live weight gain (LWG) of endectocide-treated calves in the rearing stage.
**different letters on the same date indicate statistical difference ($P<0.05$)
by Tukey's multiple comparison test.

Table 2. Averages of weight, live weight gain (LWG) and average daily gain (ADG) of calves in the rearing phase, treated with endectocides and placebo group.

		Control	Moxidectin 1%	Ivermectin 3.15%	Ivermectin 4%	Ivermectin 2.25% + abamectin 1.25%
Weight	d-7	187.2	187.8	187.8	187.6	187.0
	d30	193.9	199.1	197.7	196.6	198.4
	d56	208.2	213.8	210.8	211.9	212.2
	d91	232.0	240.5	235.1	235.3	239.0
	d118	246.8	253.2	249.1	249.2	248.5
LWG	d30	6.7a	11.3a	9.9a	9.0a	11.4a
	d56	21.0a	26.1a	22.9a	24.4a	25.3a
	d91	44.9a	52.7b	47.3ab	47.8ab	48.1ab
	d118	59.6a	67.2b	61.2a	61.2a	61.3a
ADG	d30	0.182a	0.307a	0.268a	0.244a	0.308a
	d56	0.334a	0.414a	0.364a	0.387a	0.401a
	d91	0.458a	0.538b	0.483ab	0.487ab	0.491ab
	d118	0.477a	0.538b	0.490a	0.490a	0.491a

*different letters in the same line indicate statistical difference ($P<0.05$) by Tukey's multiple comparison test.

DISCUSSION

In the present study, 1% MOX showed percentages of efficacy, residual efficacy and average weight gain higher than those of the other evaluated macrocyclic lactones: ivermectin (IVM) in high concentration formulations and the combination of IVM with ABM. The superiority of 1% MOX was demonstrated in animals infected with *Cooperia* sp. and *Haemonchus* sp. resistant to IVM, considering the greater efficacy in FECRT, weight gain and greater daily weight gain in cattle as well.

These results are in agreement with the results observed in other *in vivo* studies that have already demonstrated the better activity of MOX in relation to IVM, to control GINs in cattle [6,8,12,13], especially when diagnosed with IVM-resistant helminths. Studies with *in vitro* methodologies on larval stages have also shown differences between MOX and IVM in relation to resistance in *Cooperia* sp. [11] and to phenotypic and gene expression responses in *Caenorhabditis elegans* [18] after exposure to MOX and IVM. However, resistance levels for MOX (effectiveness between 60% and 90%) have already been reported [6,19,20], as we observed in this study, in which the effectiveness of MOX was equal to 72.3% on D+14.

Studies evaluating the anthelmintic efficacy of MOX against resistant populations to other drugs contribute to the knowledge of the phenotypic status of resistance,

however, it is also relevant to demonstrate that anthelmintic treatment results in an increase in animal performance. Superior performance of MOX in relation to IVM in the weight gain of cattle was previously verified only in animals kept in a feedlot system in Argentina [13], in a balanced nutritional plan that differs greatly from the nutritional plan of pasture-raised beef calves, that was evaluated in this study.

The effect of anthelmintic formulations, with different levels of efficacy, on the performance of beef cattle was evaluated [10], being observed that endectocides with efficacy of 0% and 48.2% did not result in a significant increase in the weight gain of beef calves, while a formulation with 84% efficacy resulted in a significant gain of 11.85 kg. In another study carried out in Argentina, anthelmintics with three levels of anthelmintic efficacy were evaluated: IVM was highly ineffective (42%), MOX moderately ineffective (67%) and the combination IVM + ricobendazole was highly effective (99%), with increases in weight gain from day zero of 15.7, 23.5 and 38.8 kg, respectively [20]. In this study, the 1%MOX showed efficacy of 72.3%, which is within the effectiveness range of 67% to 84% described in the aforementioned articles and which can still result in a significant increase in the weight gain of the treated animals.

Even though the suspension of the use of formulations with efficacy below 95% is recommended, the serious scenario of anthelmintic resistance in some cattle herds [6,21] may make it necessary to use formulations with intermediate efficacy, but which still result in increased productivity. An indication of this new view on anthelmintic efficacy for farm animals is the concept of resistance proposed by the World Association for the Advancement of Veterinary Parasitology (WAAVP), considering its definition as a reduction in efficacy that was previously above 95% for values below 80% [22].

The reasons why MOX has superior efficacy in controlling IVM-resistant helminths and results in better animal performance, whether in feedlot or pasture systems as we observed in this study, are not entirely clear. In the present study, the effect of MOX on the performance of cattle can be attributed to the better control of parasitism by gastrointestinal helminths in relation to other treatments, however, non-antiparasitic effects cannot be ruled out [23]. As non-antiparasitic effects are not known, they will not be discussed. What seems to be clear is that differences in plasma disposition are insufficient to explain differences in efficacy, suggesting that pharmacodynamic differences may account for the better effect of MOX and structural differences between lactones, and that they are associated with different interactions with receptors and membrane proteins, may be key factors for a more coherent explanation [14].

The chemical structure of drugs interferes with the type of chemical bond (hydrogen bonds, Van der Waals bonds, for example) between the drug and the receptor, changing the binding affinity and avidity. Considering the structural differences that are observed between IVM and MOX, such as the absence of the disaccharide portion at C13 of the macrocyclic ring, the presence of the methoxime fraction at C23 and the observation of an oleofinic side chain at C25 of MOX, it can be inferred that the

interaction between MOX and the chlorine receptor bound to the glutamate (GluCl) of nematodes will be different from the interaction observed between IVM and the same receptor, however, the level and avidity of interaction between MOX, IVM and the receptor are not yet known [24].

As a consequence of the structural differences between avermectins and milbemycins, differences in response in helminths exposed to MOX and IVM can be observed, as in the experimental model *C. elegans*. In this case, the β subunit of GluCl, which is encoded by the *glc*-1 gene, seems to play a very important role in MOX action, while it does not influence IVM action [18]. Eight different subunits for GluCl in *C. elegans* have already been reported and it is suggested that these subunits may contribute differently to the action of avermectins and milbemycins, and the same may occur in parasitic helminths. The different phenotypes of *C. elegans* demonstrate that the structure of the receptor and its location along the nervous system of helminths can influence the effect of the drug [18].

In addition, other receptors, ion channels linked to amino acids, about which little is known, can interact with MOX, some more strongly than others. The diversity of ion channels and the diversity of subunits observed in GluCl among different helminth species may be responsible for differences in behavior between avermectins and milbemycins at their site of action, which could also be one of the reasons for the better performance of MOX. However, one should be very cautious with statements, as the specificity of the different lactones for each of the different GluCl subunits is not known [24], not to mention the occurrence of the other channels.

P-gps are membrane glycoproteins that are characterized as mechanisms of resistance of parasitic helminths to anthelmintic drugs. They perform the efflux of drugs characterized as substrates, freeing helminths from the toxic concentrations of these drugs. Lactones are good substrates and activate the P-gps transport activity of nematodes [25]. However, it is suggested that the different substituents of the chemical structure are involved in modulating the stimulatory effect and binding affinity, not only the sugars, but also the other peripheral substituents [25,26]. In this way the different lactones can also interact differently with the P-gps.

MOX, an aglycone lactone, has a lower affinity for P-gp compared to IVM. IVM is a substrate and inhibitor of P-gp efflux activities [24]. A 10-fold higher concentration of MOX compared to IVM is required for the same retention effect of rhodamine 123 (standard P-gp substrate that is used in assays to evaluate the efflux activity of this glycoprotein) in the intracellular medium and reduce of ATPase activity are observed. MOX has a higher octanol:water partition coefficient than IVM, which translates into greater lipophilicity for MOX, determining greater partitioning in lipid membranes and less interaction with P-gp. Partitioning is a mandatory step for the interaction of substrates with P-gp [26].

The relationship between lactones and P-gps is not restricted to receptor-ligand interaction and modulation of receptor activity, but there is also an influence of lactones

on the level of expression of these glycoproteins in the membrane of helminth cells. In *Haemonchus contortus* IVM is capable of inducing greater expression of Hco-P-gp-2 than MOX and ABA [14], as it has greater affinity for this glycoprotein. Hco-Pgp-2 is expressed in the pharynx of the parasite and has a greater role in modulating the intracellular concentration of avermectins than of MOX. Therefore, overexpression of Hco-Pgp-2 in IVM-resistant nematodes, for example, has greater relevance in reducing the effectiveness of these drugs [27]. Furthermore, IVM was implicated in the induction of overexpression of five different P-gps in *H. contortus* (A; B; C; D and E) of six P-gps studied in an IVM-resistant isolate, while MOX was implicated in the induction of only two P-gps (C and E) in the same isolate [28].

Differences in the interaction between avermectins and MOX with Hco-Pgp-9.1, Hco-Pgp-2 and Hco-Pgp-16 may also help to explain the lower rate of resistance to MOX compared to IVM and other avermectins in *H. contortus*, given the lower interaction of MOX with these glycoproteins [27], which may also occur in *Haemonchus placei*, due to phylogenetic proximity.

Thus, there is abundant evidence that MOX and avermectins interact differently with P-gps, and the overexpression of these glycoproteins in typically resistant isolates reduces the effectiveness of avermectins, but has less of an effect on MOX [27], which could also support evidence that resistance to MOX occurs, but is less frequent and slower than in IVM, despite continuous and long-term use [24].

In general, the molecular mechanisms of resistance are poorly understood, in part due to the complexity of the helminth genome, however, it is believed that the control of resistance (from alterations in any way in receptors, efflux mechanisms and metabolism) are polygenic and that macrocyclic lactones are affected differently by the combination of genes involved in each case. In certain situations, cross-resistance between IVM and MOX can also be observed, but in most situations it is possible to observe significantly greater resistance to IVM [27].

In summary, MOX is still an alternative to assist in the control of avermectin-resistant helminth isolates and can be considered a good candidate to compose a combination with a new anthelmintic [27] or even with anthelmintics already present. existing drugs that maintain good efficacy, such as levamisole [6].

Some characteristics of MOX reinforce its use for the control of helminth isolates resistant to IVM and other avermectins, such as: high potency against isolates resistant to IVM due to structural singularities that result in different interaction with GluCl and P-gps; high lipophilicity; low interaction with membrane transporters (P-gps); high clinical safety; low ecotoxicity; low risk of neurotoxicity; potential to be used in different routes of administration; possibility of use in combination with other anthelmintics [27], provided that the first principles for the composition of a good combination are respected.

Moxidectin showed greater therapeutic efficacy in the control of *Haemonchus* sp. and *Cooperia* sp. resistant to ivermectin and the combination of ivermectin and Abamectin.

Furthermore, it was the only anthelmintic that resulted in a significant increase in weight gain and daily weight gain of Nellore cattle raised on pasture. Therefore, moxidectin proved to be a still viable alternative for the control of helminths resistant to avermectins and still capable of producing significant productive gains, even with an efficacy close to 70%.

Acknowledgements

The authors appreciate the contribution of students and workers from Federal University of Mato Grosso do Sul, Zoetis Animal Health for the financial support and assistance, and the CRA farm.

Authors' contributions

DGLB collected the data, performed the formal analysis and drafted the manuscript. MHC, CCTC and MGF collected the data. EM conceived the study. FAB participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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MOKSIDEKTIN: ODRŽIVA ALTERNATIVA ZA KONTROLU GATROINTESTINALNIH NEMATODA REZISTENTNIH NA IVERMEKTIN KOD TOVNIH GOVEDA

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Sve veća prevalencija rezistencije na antihelmintike kod goveda, posebno na avermektine, predstavlja u nekim stadima izazov za kontrolu parazita. Terenske studije pokazuju povećanje produktivnosti upotrebom anthelmintičkih formulacija, čak i pri neoptimalnom tretmanu (efikasnost ispod 95%), koji može doprineti razvoju programa kontrole gastrointestinalnih nematoda kod goveda. Cilj ove studije bio je da se proceni anthelmintička efikasnost i produktivni učinak kod teladi uzgajane na pašnjacima, a tretiranih makrocikličnim laktonima. Za procenu povećanja telesne težine i smanjenja broja fekalnih jaja (FEC) korišćena je "split analiza" u vremenski randomizovanom blok dizajnu: 1% moksidektin (1% MOKS), ivermektin (IVM) i abamektin (ABM) (2,25% IVM+1,25 % ABM), 4% IVM, 3,15% IVM i placebo. Za procenu FEC-a i povećanja telesne težine životinja, pojedinačni uzorci su sakupljeni sedam dana pre tretmana i +14, +30, +56, +91 i +118 dana posle tretmana (DPT). Efikasnost 14. DPT je bila: 72,3% (1% MOKS), 22,1% (4% IVM), 22% (2,25% IVM + 1,25% ABM) i 0% (3,15% ivermektin). 1% MOKS je bio jedini tretman koji je rezultirao značajnim povećanjem telesne težine životinja u poređenju sa placebo grupom nakon 118 dana lečenja, sa razlikom od 7,6 kg. Stoga, MOKS ostaje održiva alternativa za kontrolu helminta otpornih na avermektine i još uvek sposoban da rezultira značajnim produktivnim dobicima, čak i pri efikasnosti ispod 95%.