



Short communication

## Efficacy and productive performance of moxidectin in feedlot calves infected with nematodes resistant to ivermectin



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### ABSTRACT

Anthelmintic resistance (AR) of gastrointestinal nematodes to macrocyclic lactones is an increasingly common worldwide phenomenon limiting cattle production. This has motivated the search for alternatives, such as new active compounds, added drug synergisms, different doses, and alternate administration routes. The aim of this study was the assessment of moxidectin (MXD) performance in feedlot calves with a history of AR to ivermectin (IVM). Crossbred female calves aged 6–7 months and weighing 163 kg (SD = 34 kg) were divided into 3 groups of 35 animals each. They were assigned to the following antiparasitic treatment groups: IVM group (0.2 mg/kg IVM); MXD group (0.2 mg/kg MXD), and ricobendazole + levamisole (RBZ + LEV) group (7.5 mg/kg RBZ + 8 mg/kg LEV). On days 0, 26, and 47, fecal samples were taken and the weight of each animal was registered. Anthelmintic efficacy (by fecal egg count reduction), total weight gain (TWG) and average daily weight gain (AWG) were compared between the groups. A mixed SAS procedure was used for statistical analysis. Fecal egg count reduction 26 days post-treatment (PT) was calculated at 28% for the IVM group, 85% for the MXD group, and 99% for the RBZ + LEV group. AWGs (Standard Error) of 1.095 g (56), 1.264 g (49), and 1.340 g (52) were registered for the IVM, MXD, and RBZ + LEV groups, respectively ( $p < 0.05$ ). Coprocultures revealed that MXD more effectively reduced *Haemonchus* spp. and *Cooperia* spp. egg counts than IVM. This resulted in higher AWGs and TWGs for this group; similar results were seen for the RBZ + LEV group as well. In this study, animals treated with MXD gained about 160 more g/day than animals treated with IVM. This represents a gain of 16 USD per animal over the 47 day trial.

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### 1. Introduction

Gastrointestinal nematode (GIN) infections in calves economically affect cattle production (Kaplan, 2004). This is especially pertinent in Argentina, where 3,640,000 animals a year are fattened in feedlots (Robert et al., 2009). Fattening cycles for calves weighing 150–200 kg on arrival are short (3–4 months) (Pordomingo, 2013), meaning that even if reinfection is not possible, weight loss due to GINs can still be important (Fazzio et al., 2014).

Subcutaneous administration of macrocyclic lactones (ML), mainly ivermectin (IVM), has been widely adopted in feedlots due to the broad-spectrum activity of the drug against nematodes and arthropods. Unfortunately, the frequent use of IVM, particularly

in areas of *Rhipicephalus microplus* infestation, has increased the prevalence of GIN resistance (Fiel et al., 2005). Administration of IVM to animals infected with ML-resistant nematodes may lead to an 8.3% weight loss, requiring an extension of the fattening cycle (Fazzio et al., 2012, 2014). This has limited the use of this group of drugs, in spite of the advantages. This is particularly a problem in Argentina, where the earliest cases of ML resistance against *Cooperia* were recorded 15 years ago (Anziani et al., 2001).

Moxidectin (MXD) is a milbemycin ML. Although its mechanism of action and antiparasitic spectrum are similar to that of IVM, it does exhibit some pharmacodynamic and pharmacokinetic differences, including a better efficacy profile (Prichard et al., 2012; Lloberas et al., 2013). For example, MXD resulted in an egg count reduction of over 90% when given to Holstein calves infected with IVM-resistant *Cooperia oncophora* and *Ostertagia ostertagi* (De Graef et al., 2012); this level of activity is consistent with expectations for effective use (Wood et al., 1995). In a separate sheep trial, MXD

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was even more effective against IVM-resistant *Hemonchus contortus* (Lloberas et al., 2013). However, MXD resistance has also been documented (Anziani et al., 2001; Kaplan, 2004; Sutherland and Leathwick, 2011)

Thus, the aim of this study was to test MXD performance in feedlot calves that previously demonstrated anthelmintic resistance (AR) to IVM. To accomplish this, fecal egg count reduction and weight gain were assessed over the first 47 days of fattening in a commercial feedlot.

## 2. Materials and methods

This study was carried out from July to August 2014 in a commercial feedlot located in Marcos Paz, Buenos Aires, Argentina (−34.7968, −58.9002), a region with a mild climate. The crossbred *Bos indicus* × *Bos Taurus* female calves that were used were shipped 900 km from Esquina, Corrientes, Argentina (−30.0173, −59.5496), a subtropical climate where AR has previously been demonstrated (Fazzio et al., 2014). Cattle in this region graze together on the same fields with sheep. None of the calves used in this study had any previous record of any kind of deworming treatment, let alone MXD use.

During the first 72 h, the calves remained in pens with free access to hay and water. After 72 h, one dose of Policlostrigen®, a polyvalent clostridial vaccine (Biogénesis Bagó, Garín, Argentina), and one dose of Maxitil, a macrolide antibiotic (Biogénesis Bagó), were administered. The calves were put on a diet of corn grain, sunflower meal, and wheat bran, and were given a regular vitamin and mineral supplement. Protein and fiber content accounted for 15% and 25% of the calves' diet in the first 26 days, respectively, after which point they were transitioned to a finishing diet containing protein and fiber content of 12% and 8%, respectively.

After 72 h from the point of arrival, 105 healthy calves were randomly selected and ear-tagged. Calves were between 6–7 months old and had an average weight of 163 kg (SD = 34 kg). These calves were then immediately divided into 3 groups of 35 animals each and were treated as follows: IVM group (IVM 1%, 0.2 mg/kg subcutaneous; Ivomec®, Merial, Lyon, France), MXD group (MXD 1%, 0.2 mg/kg subcutaneous; Cydectin Alfa®, Fort Dodge Animal Health, Overland Park, USA), Ricobendazole (RBZ) + Levamisole (LEV) group (RBZ, 7.5 mg/kg subcutaneous; Axilur® PI, Intervet, Vicente Lopez, Argentina; LEV, 8 mg/kg subcutaneous; Fosfamisol® MV, Biogénesis Bagó).

Out of the 35 calves in each group, 18 were selected randomly and were individually sampled for feces on days 0, 26 and 47. The Fecal Egg Count Reduction (FECR) test was performed on day 26 due to reports of more reliable results (Das Neves et al., 2014). The eggs per gram (EPG) parameter was calculated using a modified version of the McMaster method, where each egg represents 20 eggs/g of feces (Roberts and O'sullivan, 1950). FECR was then calculated using the following formula:  $100 \times [1 - (T2/T1)]$  (Cristel and Suárez, 2006), where T2 is the EPG arithmetic mean of each group on day 26 post-treatment (PT) and T1 is the arithmetic mean of the same group on day 0. Egg reduction confidence intervals of 95% were calculated according to Coles et al. (1992). Pooled fecal cultures were carried out twice per group and per date (days 0 and 26) for third stage larvae (L3) differentiation (Van Wyk et al., 2004).

Each calf was individually weighed on days 0, 26, and 47. The EPG value, average daily weight gain (AWG), and total weight gain (TWG) over the whole study were statistically analyzed by a mixed procedure using SAS 9.1 software (Cary, USA). Random effects for each animal (experimental unit), along with the fixed effects of time (0 vs. 26 vs. 47), treatment (IVM vs. MXD vs. RBZ + LEV), and the interaction of the two, (time x treatment) were included in the analysis. The Slice option was used to detect statistical differences at

**Table 1**

Fecal egg count reduction in feedlot calves, at 26 days post-treatment with ivermectin, moxidectin or ricobendazole + levamisole.

	All genera	Cooperia Efficacy (95% CI)	Haemonchus
IVM	28% (0–69)	0% (0–51)	66% (21k86)
MXD	85% (72–92)	79% (60–89)	91% (82–95)
RBZ + LEV	99% (97–100)	100% (100–100)	100% (100–100)

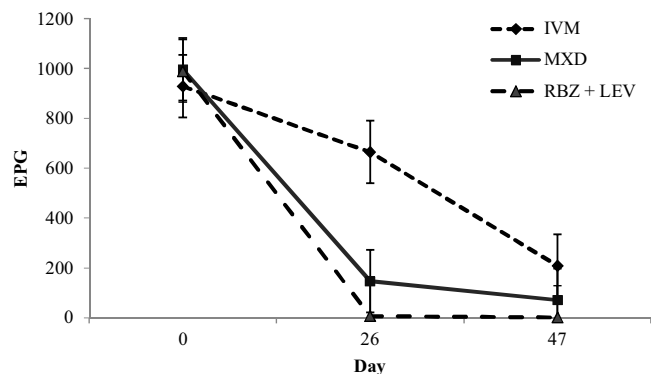
IVM: ivermectin group (0.2 mg/kg ivermectin 1%).

MXD: moxidectin group (0.2 mg/kg moxidectin 1%).

RBZ + LEV: ricobendazole + levamisole (7.5 mg/kg ricobendazole and 8 mg/kg levamisole).

CI: confidence interval.

n = 18 animals per group.



**Fig. 1.** Effect of anthelmintic treatment on fecal eggs per gram (mean per group) in feedlot calves.

IVM: ivermectin group (0.2 mg/kg ivermectin 1%).

MXD: moxidectin group (0.2 mg/kg moxidectin 1%).

RBZ: ricobendazole + levamisole (7.5 mg/kg ricobendazole and 8 mg/kg levamisole).

\*\*p-value < 0.001.

n = 18 animals per group.

each time. A p-value < 0.05 was considered statistically significant, while a value of  $0.05 \leq p < 0.10$  was seen as a tendency.

## 3. Results and discussion

FECR revealed that egg count reduction was high (99%) for the RBZ + LEV group, moderate (85%) for the MXD group, and insufficient (28%) for the IVM group (Wood et al., 1995) (Table 1). No significant difference was seen in PT EPG comparing the MXD and RBZ + LEV groups (Fig. 1).

Coprocultures revealed a relatively equal distribution of *Cooperia* and *Haemonchus* at the beginning of the experiment, but *Cooperia* predominated on day 26. The lower bound of the confidence interval calculated for day 26 PT for MXD use against *Haemonchus* is considered to be consistent with moderate activity (Wood et al., 1995) (Table 1; Fig. 2). No L3 were harvested in the RBZ + LEV group after treatment.

Differences in FECR were correlated with significant differences in TWG and AWG (Table 2, Fig. 3). This shows that the MXD and RBZ + LEV groups behaved similarly, whereas the IVM group performed more poorly. These findings are similar to those of Stromberg et al. (2012), who observed a drop in feed intake and AWG reduction in feedlot animals infected with ML-resistant *C. punctata*.

The negative effects of GIN on feedlots have been studied even before the recent rise in AR levels. Results vary depending on the antiparasitic drug used, age of the animal, and parasite burden at the beginning of the fattening period. Yet, as noted by Stockdale and Harries (1979), AWG, feed intake, and other indicators are still consistently adversely affected.

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