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ANTIPARASITIC ACTION OF IVERMECTIN, MOXIDECTIN AND PIPERAZINE AGAINST *Parascaris* spp. IN FOALS AT SOUTHERN RIO GRANDE DO SUL, BRAZIL

(Ação antiparasitária de Ivermectina, Moxidectina e Piperazina contra Parascaris spp. em potros no sul do Rio Grande do Sul, Brasil)

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ABSTRACT

Parascaris spp. are the most dangerous parasites of foals, and their presence is related to poor growth, weight loss, colics and death after impaction or intestinal perforation. The reduction in the effectiveness of antiparasitics has become a serious threat to animal health and there is little prospect of the emergence of a new anthelmintic for horses. Therefore, the objective was to evaluate the effectiveness of active principles used in the control of ascarids in Creole foals, in a ownership located in the south of Rio Grande do Sul, Brazil. The Gordon and Whitlock technique was used on 12 samples of foal faeces that were collected on the date of administration of the antiparasitic and 14 days afterwards. The evaluation of the effectiveness of the active principles was carried out through the Faecal Egg Count Reduction Test (FECRT). All the anthelmintics used failed against *Parascaris* spp. and therefore should not be used to control infections caused by these helminths in the population studied. In addition, generalized resistance of ascarids to avermectins was observed. The results also show that other management practices should be implemented on the ownership, in an attempt to reduce infections by these helminths.

Keywords: Anthelmintic, equinoculture, horses, FECRT.

RESUMO

Parascaris spp. são os parasitas mais perigosos dos potros e estão relacionados ao baixo crescimento, perda de peso, cólicas e morte após impactação ou perfuração intestinal. A redução da eficácia dos antiparasitários tornou-se uma séria ameaça à saúde animal e há poucas perspectivas de surgimento de um novo anti-helmíntico para equinos. Portanto, objetivou-se avaliar a eficácia dos princípios ativos utilizados no controle de ascarídeos em potros crioulos, em uma propriedade localizada no sul do Rio Grande do Sul, Brasil. Foram utilizados os resultados da técnica de Gordon e Whitlock de 12 amostras de fezes de potros, que foram coletadas na data da administração do antiparasitário e 14 dias após. A avaliação da eficácia dos princípios ativos foi realizada por meio do Teste de Redução de Contagem de Ovos nas Fezes (TRCOF). Todos os anti-helmínticos utilizados falharam contra Parascaris spp. e não devem ser usados para controlar as infecções desses helmintos na população estudada, além disso, há uma resistência generalizada dos ascarídeos contra as avermectinas. Os resultados também mostram que outras práticas de manejo devem ser implementadas na propriedade, na tentativa de reduzir as infecções por esses helmintos.

Palavras-chave: *Anti-helmintíco, equinocultura, cavalos, TRCOF.*

INTRODUCTION

Equine breeding is of great importance in the Brazilian economic sector, whose market has animals with high zootechnical value and, consequently, aggregation of high financial values. At the national level, horse breeding generates approximately R$ 16 billion per year (MAPA, 2016). In Rio Grande do Sul (RS), in addition to direct activities such as work, horse

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breeding, especially the Creole horse, is related to the cultural traditions of the people in leisure (COSTA *et al.,* 2014).

Horse management in RS is mainly extensive, where the animals remain on pastures - natural or cultivated - often maintained with high animal density, increasing the propensity to intestinal parasitism and favoring constant infections due to the presence of parasites in these pastures (REINEMEYER, 2009). Problems related to endoparasitosis considerably limit the productive performance of these animals (MOLENTO, 2005).

Parascaris spp. are the most dangerous parasites of foals (REINEMEYER, 2009) and their prevalence is known to be high, generally in the range of 31-61% (AUSTIN *et al.,* 1990). May cause poor growth, weight loss, colic and death after intestinal impaction or perforation (REINEMEYER, 2009). Foals have low immunity against these nematodes and anthelmintics are the main form of parasite control (CRAIG *et al.,* 2007), which is a challenge for veterinarians and breeders.

The reduction in the effectiveness of antiparasitics has become a serious threat to health and animal production in several locations, on the other hand, there is little prospect of the emergence of a new chemical group of anthelmintics for horses. In Brazil, more specifically in the south of the country, knowledge of the level of antiparasitic resistance of *Parascaris* spp., especially in foals, is limited. Therefore, through this study, the objective was to evaluate the effectiveness of active ingredients used to control ascarids in Creole foals, in a ownership located in Pelotas, Southern of Rio Grande do Sul, Brazil.

MATERIAL AND METHODS

Collection of faeces and parasitological procedures

The study analyzed the results of diagnoses carried out during the year 2018 and which are stored in the database of the laboratory of the Study Group on Parasitic Diseases of the Faculty of Veterinary - Federal University of Pelotas. This work was approved by the Animal Experimentation Ethics Committee of the Federal University of Pelotas under registration number 7888/2017.

We used the results of feacal samples from 12 Creole foals, six males and six females, naturally infected, from an equine ownership in the city of Pelotas, located at the South of Rio Grande do Sul (31º48’8’’S; 52º24’45’’O). The ownership has an extensive management system and the antiparasitic treatment is carried out with rotation of the active ingredients.

Faecal samples were collected on the date of administration of the antiparasitic, by the veterinarian responsible for the ownership. The concentrations and doses administered were Ivermectin 1% (0.2mg/kg) at 90 days of life, Piperazine (0.35 g/kg) at 180 days, Ivermectin 2% (0.2mg/kg) at 270 days and Moxidectin (0.4 mg/kg) at 360 days of life of the animals (Tab. 01). The drugs were administered orally, according to the manufacturers' recommendations.

The samples were taken directly from the rectal ampulla of the foals with the aid of gloves and plastic bags and identified according to the name of each animal. They were placed in an isothermal box, cooled with reusable ice and sent to the laboratory for analysis. For processing, the technique of Gordon and Whitlock (1939) was used, providing the result in eggs per gram of feces (EPG). In general, samples were processed the same day, or stored at 4 ºC

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until processed the next day. After 14 days of administration of the anthelmintic, a new collection was performed in order to analyze the parasite load.

Table 01: Data on dose and active principles tested, as well as the age of the animals in which the drugs were administered in the equine population studied.

Active principles	Dose	Number of Animals	Age (days)
Ivermectina 1%	0.2mg/kg	12	90
Piperazina	0.35g/kg	12	180
Ivermectina 2%	0.2mg/kg	12	270
Moxidectina	0.4mg/kg	12	360

Anthelmintic efficacy test

To evaluate the effectiveness of the active ingredient, the Faecal Egg Count Reduction Test (FECRT) was calculated, which uses the pre- and post-treatment helminth egg count according to the formula: %FECR = (FECpre – FECpost/FECpre) x 100 (NIELSEN and REINEMEYER, 2018). Populations of *Parascaris* spp. were considered resistant when the reduction in stool egg count was <95% (MOLENTO, 2005). Only foals infected with *Parascaris* spp., with egg counts above 100 EPG, were included in this study.

Statistical Analysis

Blaker's, Sterne, Clopper-Pearson and Wilson confidence interval are calculated as described by Reiczigel, Földi, Ózsvári (2010). The authors recommend Blaker's interval for general use. The lower and upper limits of the confidence interval were calculated at 95%.

RESULTS AND DISCUSSION

The results of the FECRT test, according to the active principles used in the foals, are shown in Tab. 02. The efficacy indices of Ivermectin 1%, Piperazine, Ivermectin 2% and Moxidectin were, respectively, 31.81%, 46.76%, 44% and 48.70%.

Table 02: Means EPG pre and after treatment, and Efficacy Index (IEF) of the active principles tested against *Parascaris* spp. in the equine population studied.

Active Principles	Mean EPG Pre treatment	SD	Mean EPG after treatment	SD	IEF (%)	CI
Ivermectina 1%	600	333.91	409.09	293.10	31.81	28.70 - 35.50
Piperazina	631.81	361.43	336.36	231.39	46.76	42.89 - 50.65
Ivermectina 2%	609	315.29	341	312.90	44	40.11 - 47.97
Moxidectina	655	232.86	336	185.86	48.70	44.89 - 52.53

CI = confidence interval; SD = Standar deviation

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The striking result of this study is that absolutely all the active principles used failed against *Parascaris* spp. in the evaluated foal population. The resistance of helminths to Moxidectin stands out, since its dose is twice the dose of Ivermectin, and yet it was not successful in foals. Furthermore, for these populations of macrocyclic lactones (LMs) resistant ascarids, formulations such as benzimidazoles or piperazine could be easily administered alternatives and generally provide good efficacy (REINEMEYER, 2009), however, this did not occur with the use of piperazine.

Lyons *et al*. (2016) when evaluating the activity of Piperazine against roundworms in foals from farms in Kentucky, in the years 2014 and 2015, found satisfactory results, however, it was a little lower than expected compared to its effectiveness for many years (DRUDGE and LYONS, 1986). In the past, the typical dose rate used was 88 mg/kg, which was highly effective on roundworms. In the study by Lyons *et al*. (2016), the dose was 112mg/kg, in the present study, the dose used was three times higher (0.35g/kg = 350mg/kg) and it was still not effective, indicating parasitic resistance against the molecule.

The reduced efficacy of Ivermectin (39.3%) and Moxidectin (48.1%) against *Parascaris* spp. in foals was observed by Cooper *et al*. (2020) in Argentina and the data are like the present study. Although there are several international reports on *Parascaris* spp. resistance, the resistance status of the local nematode population is largely unknown. Monitoring the state of susceptibility or resistance in each establishment is essential for the design of control programs based on the sustainable use of anthelmintics.

The data are worrying because, among all the stages of a horse's life, the first year of age requires greater attention in terms of management and nutrition, since the foal presents an accelerated growth at this stage of its life. They can reach, by 12 months of age, up to 90% of their final height (REZENDE *et al.,* 2000; SOUZA *et al.,* 2017). In addition, it is during this period that weaning occurs (around 180 days), one of the most stressful events for the animal. As a result of stress, the foal has its immunity reduced, becoming more susceptible to the development of diseases (CAZAPAL-MONTEIRO *et al.,* 2012).

Since the 1980s, drugs of the avermectin class have been commercialized and successfully used to control nematodes in horses. In most of the global equine market, LMs are the most commonly used anthelmintics (CANEVER, 2012). There are several published studies where ivermectin has been shown to have 100% effect against adult stages of *Parascaris* spp. (DIPIETRO *et al.,* 1987; FRENCH *et al.,* 1988). Furthermore, the anthelmintic resistance of *Parascaris* spp. was considered unlikely because a large part of the population of the parasite, the long-lived eggs in the environment, are considered refuges, that is, they are not exposed to the drug and, therefore, are not selected for resistance (LIND *et al.,* 2009).

The present study clearly shows that resistance to avermectins is a problem in the population tested and could become a problem throughout the region soon, as anthelmintics are overused by many ownerships, where it is a It is common practice to administer Ivermectin for the treatment of suspected *Strongyloides* infection when foals are less than one month old. From there, frequent anthelmintic rotation is implemented and juvenile horses are often dewormed at monthly intervals until the first year of life. Many ownerships use LM at least bimonthly on juvenile horses (CRAIG *et al.,* 2007). As this group of drugs has larvicidal action against *Parascaris*, the refugee population within a host is minimized each time the drug is

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administered to an infected foal. This routinely happens whenever the interval between treatments is shorter than the prepatent period for *Parascaris* (ie, 75-80 days).

Furthermore, susceptible genotypes in the local population do not have the opportunity to reproduce whenever LM treatments are repeated at intervals shorter than the prepatent period or the egg reappearance period, thus minimizing refuges in the environment. Typical parasite control practices of juvenile horses in many breeding systems essentially constitute the exclusive and/or excessively frequent use of a single class of drugs and therefore intensively select for anthelmintic resistance (KAPLAN, 2004). Thus, the previous use of some other LM in the rest of the herd may also have caused a cross-reaction between the drugs (MOLENTO, 2004; MOLENTO *et al.,* 2008).

CONCLUSIONS

It can be concluded that none of the treatments used were effective and, therefore, they should not be used to control infections by *Parascaris* spp. in the population studied, in addition, there is a generalized resistance of ascarids against LM. They also demonstrate that other management practices should be implemented on the ownership, in an attempt to reduce infections by these helminths, which allows their full development and avoids economic losses, since the creation of juvenile horses requires updated knowledge about the biology and epidemiology of the parasites species, as well as local evidence on the anthelmintic resistance status of each herd.

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