Resistance of *Haemonchus contortus* to monepantel in sheep: first report in Espírito Santo, Brazil

Resistência de *Haemonchus contortus* ao monepantel em ovinos: primeiro relato no Espírito Santo – Brasil

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**Abstract**

The objective of this study was to provide the first report of resistance of *Haemonchus contortus* to monepantel in sheep in Espírito Santo. The study was conducted in a property with history of monepantel use since 2014 and register of low efficacy in studies conducted over the past few years with fecal egg count reduction test. Lambs born on the property (males and females aged approximately 100 days) were selected and after eggs per gram of feces (EPG) analysis on fecal samples, these were divided into two groups: a group treated with monepantel (2.5 mg / Kg) and a control group without anthelmintic treatment. Seven days later, the animals were euthanized to recover parasites from the gastrointestinal tract. The efficacy of the treatment was 61.35% against *H. contortus*, thus proving that anthelmintic resistance to monepantel was present.

**Keywords:** Anthelmintic resistance, control, nematode, ruminants.

**Resumo**

O objetivo deste estudo foi fornecer o primeiro relato de resistência de *Haemonchus contortus* ao monepantel em ovinos no Espírito Santo. O estudo foi conduzido em uma propriedade com histórico de uso de monepantel, desde 2014, e registro de baixa eficácia em estudos conduzidos nos últimos anos, utilizando-se testes de redução de contagem de ovos por grama de fezes (OPG). Cordeiros nascidos na propriedade (machos e fêmeas com idade aproximada de 100 dias) foram selecionados e, após contagem de OPG, foram divididos em dois grupos: um grupo tratado com monepantel (2,5 mg / Kg) e um grupo controle, sem tratamento com anti-helmíntico. Após 7 dias, os animais foram eutanasiados para a recuperação dos parasitos no trato gastrointestinal. O tratamento apresentou eficácia de 61,35% para *H. contortus*, comprovando que a resistência anti-helmíntica ao monepantel foi presente.

**Palavras-chave:** Anti-helmíntico, controle, nematoide, ruminantes.
Gastrointestinal helminthic infections are the main cause of economic losses in sheep farming systems, in addition to decreasing animal welfare. The genus *Haemonchus* is among the main gastrointestinal helminth found in some regions of Brazil and especially in sheep. The species *Haemonchus contortus* causes enormous damage to sheep industry, being considered a limiting factor for this economic activity (Albuquerque et al., 2017; Claerebout et al., 2020; Starling et al., 2017).

Indiscriminate use of anthelmintic drugs to control helminthic infections without selection criteria commonly generates resistance of these parasites to the drugs used. This problem has been proven in several regions of Brazil in relation to *Haemonchus* spp. In the southeastern region of Brazil, Almeida et al. (2010) found *Haemonchus* resistant to albendazole, closantel, levamisole, moxidectin, organophosphate and ivermectin. Other reports of resistance to ivermectin, albendazole, levamisole and moxidectin has been published (Veríssimo et al., 2012; Nunes et al., 2013).

Monepantel, an aminoacetonitrile derivative, is a drug that was developed with the objective of controlling nematodes in ruminants. However, there are already records of populations of gastrointestinal nematodes that are resistant to monepantel, in several countries. In New Zealand, Scott et al. (2013) reported the presence of resistance of *Trichostrongylus colubriformis* to monepantel. In Uruguay, Mederos et al. (2014) confirmed the presence of resistance of *H. contortus* to this drug. In Brazil, there have been some reports of monepantel-resistant populations of *Haemonchus* spp. (Albuquerque et al., 2017; Mallmann et al., 2018; Martins et al., 2017) and also *Trichostrongylus colubriformis* (Cintra et al., 2016).

The objective of the present study was to confirm the presence of a *H. contortus* population resistant to monepantel in a sheep farm in Espírito Santo. The farm herd was monitored by fecal egg count reduction test (FECRT), through eggs per gram of feces (EPG) and fecal cultures, throughout 2015, 2017 and 2019, to identify the predominant nematode groups and determine the effectiveness of the anthelmintics used, as described by Coles et al. (1992).

For the study, 20 lambs born on the property were subjected to two fecal collections, on days -10 and -2 before treatment, to ascertain the counts of EPG by means of the McMaster technique (Gordon & Whitlock, 1939). The fecal samples of the animals were collected and send to the Parasitology Laboratory of the Veterinary Hospital of the Agricultural Sciences Center, Federal University of Espírito Santo (HOVET-CCAE-UFES), where they were immediately processed.

From among these 20 selected lambs, after analyzing the results from the tests on days -10 and -2, 14 lambs (five males and nine females) from industrial crosses (White Dorper x Santa Inês), with an average age of 100 days, average initial weight of 17.5 kg and EPG > 1000, were selected (Table 1). This selection was made in accordance with the recommendations of the World Association for the Advancement of Veterinary Parasitology (WAAVP) (Coles et al., 2006). These lambs were divided into two groups containing seven animals each: the first group received treatment and the second was the non-treated control group.

The animals were weighed on a mechanical scale in order to calculate the volume of the anthelmintic to be administered to each lamb. The drug used in the treatment was monepantel (Zolvix®, Novartis) at a dose of 2.5 mg / Kg orally, which was administered in accordance with the manufacturer's recommendations on day 0.

After seven days of deworming, the animals were euthanized with the use of previous anesthesia with xylazine and general anesthesia with sodium thiopental followed by potassium chloride. The necropsy was performed by...
The larvae that emerged from the fecal cultures showed morphological characteristics typical of Trichostrongylidae larvae, with 87% of *Haemonchus* spp. and 13% of *Oesophagostomum* spp. larvae.

In the abomasum, *H. contortus* was found in both groups, with an average of 379 (± 191) specimens in the treated group and 980 (± 1412) in the control group, without significant difference between group means (p = 0.896). For *H. contortus*, the drug efficacy was 61.35%.

In the small intestine, the cestode *Moniezia* spp. was found in both study groups, and in the large intestine, the helminths *Oesophagostomum columbianum* and *Trichuris* spp. were found. *O. columbianum* presented in average 10 (± 17) and 47.1 (± 79) parasites in the treated and control groups, respectively, showing an efficacy of 78.8%. The low levels of efficacy may be attributed to the lack of indication of the product for the control of *Oesophagostomum*.

**Table 1.** Randomized distribution of sheep naturally infected by gastrointestinal nematodes, with formation of a treatment group and a control group based on individual mean values of eggs per gram of feces (EPG) in examinations performed on of days -10 and -2.

<table>
<thead>
<tr>
<th>Group</th>
<th>Animal</th>
<th>Weight (Kg)</th>
<th>EPG</th>
<th>Mean¹</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>TREATED</td>
<td>527</td>
<td>13.5</td>
<td>5733</td>
<td>2548.6</td>
<td>1585.5</td>
</tr>
<tr>
<td></td>
<td>151</td>
<td>13.0</td>
<td>3949</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>565</td>
<td>20.0</td>
<td>3388</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>87</td>
<td>17.5</td>
<td>2466</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>556</td>
<td>18.0</td>
<td>1877</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>229</td>
<td>19.5</td>
<td>1488</td>
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</tr>
<tr>
<td></td>
<td>93</td>
<td>16.0</td>
<td>1322</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CONTROL</td>
<td>122</td>
<td>18.0</td>
<td>4433</td>
<td>2093.2</td>
<td>1320.3</td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>13.0</td>
<td>3699</td>
<td></td>
<td></td>
</tr>
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<td>630</td>
<td>14.5</td>
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<td>47</td>
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<td>1433</td>
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</tr>
<tr>
<td></td>
<td>572</td>
<td>18.5</td>
<td>677</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹geometric mean.
Increasingly, studies evaluating the effectiveness of antiparasitic drugs have shown reductions in the effectiveness of the main drugs available, such as monepantel (Zolvix®, Novartis), which is the drug with anthelmintic activity that has more recently come onto the market (Bartley et al., 2019; Ploeger & Everts, 2018). The greatest concern regarding the reduction in the effectiveness of these drugs is in relation to *H. contortus*, the main nematode species in sheep farming (Albuquerque et al., 2017; Claerebout et al., 2020; Starling et al., 2017).

In order to understand the mechanisms that lead to the condition of parasite resistance, many studies have been developed with the aim of defining the main risk factors for this condition. It has been noted that indiscriminate treatment together with frequent use of different active ingredients leads to onset of the resistance within a short period of time (Lamb et al., 2017; Rose et al., 2015).

According to the historical survey on the farm of this study, the animals had received approximately 15 treatments with monepantel (Zolvix®, Novartis), as management against helminths, over the 18 months preceding this study. Frequent suppressive treatment with anthelmintics such as monepantel quickly leads to parasite resistance, due to rapid selection of resistant populations (Albuquerque et al., 2017; Lamb et al., 2017; Rose et al., 2015).

The history of anthelmintics used on this farm and the poor effectiveness of the deworming management implemented demonstrate that excessive use of anthelmintics, together with the lack of specific criteria for treatment and absence of any strategic control program have led to a progressive selection, from 2015 to 2019, of a monepantel-resistant *H. contortus* population. Mallmann et al. (2018) highlighted the same postulates as determining factors for selection of resistant populations of *H. contortus*.

This result demonstrates that gastrointestinal nematodes should not be controlled solely through the use of anthelmintics. A set of preventive measures should be used, while always seeking to reduce the predisposing factors for the emergence of parasitic resistance. A large number of studies addressing this topic have now presented this viewpoint (Besier, 2012; Cintra et al., 2016; Starling et al., 2017).

Another important factor to be taken into account is the periodic evaluation of the herd's by fecal examination in order to determine the degree of infection. From these values, selection criteria for the treatment of animals at the “trigger level” can be created, as described by Besier (2012). Thus, the number of treatments performed and the rotation of anthelmintics on the properties reduced, delaying the establishment of resistant populations.

The presented results demonstrate the presence of a monepantel resistant population of *H. contortus* in sheep from Espírito Santo, Brazil

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**References**


Haemonchus contortus resistente a monepantel


