Efficacy of nitenpyram on the treatment of tungiasis in dogs from brazilian southern amazonic region

Eficácia do nitempiram no tratamento de tungíase em cães da Amazônia meridional brasileira

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RESUMO

A tungíase é uma doença de pele zoonótica causada pela penetração da pulga fêmea de *Tunga penetrans* na pele de muitos hospedeiros mamíferos. Entre os hospedeiros, animais domésticos, sinantrópicos e silvestres servem como reservatórios. No entanto, os cães são considerados a principal fonte de infestação humana em comunidades rurais e endêmicas. O objetivo deste estudo foi avaliar a eficácia tungicida do nitempiram para o tratamento da tungíase causada por *Tunga penetrans* em cães naturalmente infestados da região amazônica brasileira. Doze cães que apresentaram de três a cinquenta e três lesões viáveis receberam uma dose de nitempiram. Os animais receberam dosagens de acordo com a recomendação do fabricante. Os critérios utilizados para determinar a eficácia do medicamento foram o número de lesões viáveis após o tratamento. Estes foram quantificados aos 3, 7 e 14 dias após o tratamento. De acordo com os resultados, a eficácia do Nitempiram foi de 92,20%, 88,07% e 66,06% nos 3, 7 e 14 dias pós-tratamento.

Palavras-chave: *Tunga penetrans*; cão; neonicotinoides

ABSTRACT

Tungiasis is a zoonotic skin disease caused by the penetration of the female flea of *Tunga penetrans* into the skin of many mammal hosts. Among the hosts, domestic, synanthropic and sylvatic animals serve as reservoirs. However, the dogs are considered the main source of human infestation in rural and endemic communities. The aim of this study was to evaluate the tungicidal efficacy of nitenpyram for the treatment of tungiasis caused by *Tunga penetrans* in naturally infested dogs from brazilian amazonic region. Twelve dogs presenting from three to fifty-three viable lesions received one dose of nitempyram. The animals received dosages according to the manufacture’s recommendation. The criteria used to determine the drug efficacy were the number of viable lesions after treatment. These were quantified at 3, 7- and 14-days post-treatment. According to the results, the efficacy of Nitempyram was 92.20%, 88.07% and 66.06% in the 3, 7 and 14-days post-treatment.

Keywords: *Tunga penetrans*; dog; neonicotinoids

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INTRODUCTION

Tungiasis, popularly known in Brazil as bicho-de-pé or bicho-do-porco, is an ectoparasitosis with one-health importance caused by *Tunga penetrans*. It is considered the smallest of the known fleas, reaching 1 millimeter in length when it reaches adulthood and it lives in sandy, hot and dry grounds (OLIVEIRA et al., 2014). Males and females are considered hematophagous, however, only the fertilized female is responsible for tungiasis (VIESTEL; DA SILVA, 2012).

The specie *T. penetrans* has a wide distribution and a high degree of specificity and occurs in the Neotropical region and sub-Saharan Africa. However, some authors have already reported in the USA, Europe and New Zealand, always having traveling people who have been infested in enzootic areas (PILGRIM, 1993; SANUSI et al., 1989; VERALDI et al., 1996).

In veterinary medicine, tungiasis is often neglected because it is self-limiting, but it is a disease that has a considerable prevalence in Brazil and is related to socioeconomic factors (VIESTEL; DA SILVA, 2012; HARVEY et al., 2017; HARVEY et al., 2019). It is usually asymptomatic, but complications can occur, such as inflammation of the region and secondary infections by pathogens, such as *Clostridium tetani*, *Staphylococcus aureus*, *Escherichia coli* and *Streptococcus* sp (GATTI et al., 2008).

Therapy for cases of tungiasis is not so explored in the literature. However, some studies have already verified potential drugs in the treatment of cases of *T. penetrans* parasitism in veterinary medicine. Studies in dogs, as performed by Klimpel et al. (2005). The authors verified the efficacy of the formulation based on imadacloprid and permethrin in parasitized dogs in the state of Ceará. In this study, the authors report an efficacy of 97.7% on the fourteenth day of treatment, maintaining efficacy above 70% in 28 days of study.

In pigs, other drugs have also been tested. Mutebe et al. (2016a) evaluated the effectiveness of a spray formulation based on Chlorpyrifos, dichlorphos and gentian violet, also obtaining efficacy in the treatment of parasitized animals. Mutebe et al. (2016b) report that as a prerequisite for the treatment of tungiasis in animals, commercially available products must be tested to validate their tungicidal efficacy, as well as to prevent new infestations by *T. penetrans* at field level.

In a recent study, Dos Santos et al. (2022) verified high efficacy in tungiasis control in dogs through the use of fluralaner-based oral antiparasitic (Isoxazolin) in a
randomized controlled trial in Bahia. This study demonstrated efficacy rates of more than 90% to three months after treatment.

Among ectoparasiticidal drugs, nitenpyram stands out due to its rapid effect. According to Chatellier (2001), the effect of nitenpyram on *Ctenocephalides felis felis* is observed between 15-30 minutes after oral administration to the host animal. Efficacy reaches between 95-100% within six hours after administration and 100% within 24 hours after treatment. According to Schenker et al. (2001); Hovdae Hoser (2002), the referred drug is safe because its absorption in the blood as well as its excretion are fast, being considered with low toxicity for mammals.

Therefore, the objective of this study is to evaluate the tungicidal efficacy in dogs naturally parasitized by *Tunga penetrans* in the southern Amazon region of Mato Grosso State, Brazil.

**MATERIAL AND METHODS**

Overview

The study was conducted by the Laboratory of Animal Health from the Universidade Federal de Mato Grosso (UFMT), Mato Grosso State, Brazil. All protocols were reviewed and approved by the Institutional Animal Care and Use Committee (CEUA # 23108.057027/2020-23). There was no control group because it was a painful wound that cause suffering to the animal, going so against the principles of animal welfare.

Animals and study design

Houses were visited in urban and rural areas to participate in the present study in order to verify the occurrence of dogs infested by *Tunga penetrans* in the Mato Grosso State, Southern Amazon Region.

For this study, 12 dogs (6 females and 4 males), between 1 and 8 years of age and from weight between 3.4–32.6 kg with short hair were used. Two days before the application of the product, all animals underwent a clinical examination to verify their health status. Throughout the study, the dogs were observed daily to monitor their general health condition.
The dogs enrolled were naturally infested with at least three tungiasis lesions. The animals were treated in Day 0 with Nitempyram (Capstar®, Novartis Animal Helath) following the manufacturer's recommendations. In relation to animals, the dogs underwent a detailed clinical evaluation to assess characteristic lesions of tungiasis. Each lesion per animal was counted, registering these injuries in a specific dermogram. Only Stage 2 and 3a lesions, as described by Eisele et al. (2003), were accounted for.

The visits were repeated on the third, seventh and fourteenth days after treatment. In these days, the animals included in the study had their bodies evaluated to account for the characteristic lesions of tungiasis by *T. penetrans* and the lesions were recorded in a specific dermogram.

Statistical analysis

The tungicidal efficacy was calculated based on the following formula:

\[
\text{Effectiveness} \, \% = \frac{\text{average of II and IIIa tungiasis lesions counted in the Day 0} \times \text{mean of tungiasis II and IIIa lesions recovered in each experimental day}}{\text{average of II and IIIa tungiasis lesions counted in the Day 0}} \times 100. \]

Statistical analysis was performed using the statistical program Bioestat 5.3. In order to evaluate the type of distribution of the data, whether para-metric or not, was chosen the Shapiro-Wilk test. According to the test, the data were non-parametric. Then, the comparison of mean values between day 0 and +3, 0 and +7, and 0 and +14 was determined using the Wilcoxon Test (Signed-Rank Test) test. The level of significance was 95% (p ≤ 0.05) (Sampaio, 2002).

RESULTS AND DISCUSSION

In visited houses the prevalence of tungiasis was high in dogs, compared to others studies (De Carvalho et al., 2003; Klimpel et al., 2005). The tungiasis lesions were mainly found along the extremities. Up to 58 tungiasis lesions were found on individual dogs. The 12 selected dogs had a total of 218 lesions prior to treatment (Table 1). On Day-0, the average of 18,17 tungiasis lesions was counted in the dogs.

On the third day post treatment, it was counted a total of 17 lesions on the dogs. The animal #3 and #4 were from the same house and they presented the higher number of lesions. It was repeated during all the experimental days. It could be explained by the
high environmental. It was a house on the rural area with a sandy yard. This characteristic ground favors the development of *Tunga* fleas as described by Oliveira et al. (2014).

The efficacy of nitenpyram in the control of tungiasis reached the high level in the third day of the study, with 92.92% of reduction in tungiasis lesions. The efficacy was decreasing during the following evaluations. The decreasing efficacy was also previewed, due to the nitenpyram excretion rate. Hovdae Hoser (2002) reported that the refereed drug is almost eliminated in 24 hours after been administrated. However, the Stage II and IIIa lesions caused by *Tunga penetrans* can remain longer. According to Eisele et al (2003), the change of lesion feature (Stage 4a and 4b) starts 48 hours after the flea death and last for 14 days.

Only in the seventh and fourteenth days it was verified new lesions sites. According to Eisele et al. (2003), the stages 3, phase of beginning hypertrophy, and stage 4, the white halo stage, became macroscopically visible. These new counted lesions can indicate the absence of nitenpyram in the animal and the presence of immature stages in the environmental.

The results presented the Nitenpyram as a possible drug for tungiasis treatment. However, the chemical control must integrate a multimodal strategy to prevent this zoonosis, such as environmental education, rural education and environmental sanitation.
Table 1: Number of *Tunga penetrans* lesions in naturally infested dogs treated with Nitenpyram over 14 days post treatment period in southern amazon region, Brazil.

<table>
<thead>
<tr>
<th>Animal ID</th>
<th>Experimental Day</th>
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<tr>
<td></td>
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<tr>
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<tr>
<td><strong>Arithmetic Mean</strong></td>
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<tr>
<td><strong>Efficacy %</strong></td>
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<tr>
<td><strong>p Value</strong></td>
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