Resistance of bovine gastrointestinal nematodes to four classes of anthelmintics in the semiarid region of Paraíba state, Brazil

Resistência de nematódeos gastrintestinais de bovinos à quatro classes de anti-helmínticos no semiárido do Estado da Paraíba, Brasil

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Abstract

The effectiveness of four anthelmintic classes on cattle gastrointestinal nematodes in the semi-arid region of Paraíba State, Brazil, was evaluated. Twenty farms were used, testing 40 animals in each one, totaling 800 animals. Cattle were divided into four groups composed with ten animals: I, treated with albendazole sulfoxide 15%; II, treated with ivermectin 1%; III, treated with closantel 25%; IV, treated with levamisole hydrochloride 7.5%. All treatments were administered subcutaneously. For the Fecal Egg Count Reduction Test (FECRT), individual fecal samples were collected on days 0 and 14, and sent for analysis of egg count per gram of feces (EPG) and larval cultures. It was observed that multiresistance was present in 95% (19/20) of the farms. Resistance to ivermectin and albendazole was observed in 95% (19/20), to closantel in 75% (15/20) and to levamisole in 20% (4/20). The most used management system was semi-intensive (75%; 15/20) and the ivermectin was the most reported drug for controlling helminths (65%; 13/20). It was concluded that the anthelmintic resistance of bovine gastrointestinal nematodes is high in the semi-arid of Paraíba State, Brazil, with multiresistance observed mainly to ivermectin, albendazole and closantel.

Keywords: Antiparasitics, helminthiasis, multiresistance, ruminants.

Resumo

Avaliou-se a eficácia de quatro classes de anti-helmínticos sobre nematódeos gastrintestinais de bovinos na região semiárida da Paraíba, Brasil. Foram utilizadas 20 fazendas, sendo testados 40 animais em cada uma, totalizando 800 animais. Os bovinos foram distribuídos em quatro grupos compostos por dez animais: I, tratado com sulfóxido de albendazol 15%; II, tratado com ivermectina 1%; III, tratado com closantel 25%; IV, tratado com cloridrato de levamisole 7,5%. Para o Teste de Redução da Contagem de Ovos Fecais (TRCOF), amostras fecais individuais foram coletadas nos dias 0 e 14 e enviadas para análises de contagem de ovos por grama de fezes (OPG) e coproculturas. Observou-se que a multirresistência estava presente em 95% (19/20) das fazendas. Foi observada resistência à ivermectina e ao albendazol, em 95% das fazendas (19/20); ao closantel, em 75% (15/20) e ao levamisole, em 20% (4/20). O sistema de manejo mais utilizado foi o semi-intensivo (75%; 15/20) e a ivermectina foi o fármaco mais relatado para controle de verminose (65%; 13/20). O gênero de helminto mais prevalente foi Haemonchus spp. (76,7%). Conclui-se que é alta a resistência anti-helmíntica por nematódeos gastrintestinais de bovinos no Semiárido da Paraíba, Brasil, com multirresistência observada principalmente à ivermectina, ao albendazol e ao closantel.

Palavras-chave: Anti-parasitários, helmintoses, multirresistência, ruminantes.
Introduction

Brazil stands out among the milk and beef-producing countries, with the fastest-growing agribusiness in the world. This country finished 2020 with a record final balance of US$ 87.7 billion, which contributed positively and decisively to the total trade balance (Kreter et al., 2021). In this country, the profitability of livestock activities can be significantly reduced by the effects of parasites, which affect the welfare and productivity of cattle. Infections with gastrointestinal nematodes have an annual economic impact of 7.11 billion dollars (Grisi et al., 2014).

The main genera of nematodes that parasitize cattle are *Haemonchus* spp., *Trichostrongylus* spp., *Cooperia* spp., belonging to the *Trichostrongylidae* family; *Oesophagostomum* sp., belonging to the *Strongylidae* family; *Strongyloides* sp., to the *Strongyloides* family; and *Trichuris* spp., to the *Trichuridae* family. In cattle, the parasitic infection occurs under ideal temperature and humidity conditions, and transmission occurs during the ingestion of pasture contaminated with infective larvae, which, in the animal's gastrointestinal tract, become adults, reaching reproductive maturity, reproducing and eliminating their eggs in the environment through feces (Bowman, 2010; Neves, 2014). This cycle is completed around 28 to 35 days. However, the infecting larvae can remain in the environment for a few months (Taylor et al., 2013). Usually, cattle nematode infections are mixed, in which more than one species parasitizes the same animal (Fávero et al., 2020). The absence of adequate anthelmintic control can lead to significant losses, which gives rise to decreased food intake, gastrointestinal disorders and impaired animal development, leading to death in extreme cases (Cezar et al., 2008; Almeida et al., 2020).

To avoid losses relating to helminth infections, the main means of control is through use of chemical compounds with a broad spectrum of activity, mainly comprising macrocyclic lactones, benzimidazoles, imidazothiazoles and salicylanilides (Taylor et al., 2013; Silva et al., 2017; Ramos et al., 2020). Most of the time, these are administered without applying any technical criteria for drug selection, in an empirical and indiscriminate manner. This has additional implications for the effectiveness of anthelmintic treatments, since it causes the emergence and dissemination of parasitic resistance (Neves et al., 2014; Geurden et al., 2015. Ramos et al., 2018; 2020).

The resistance of bovine gastrointestinal nematodes to most drugs available on the market has become an emerging problem worldwide (O'Shaughnessy et al., 2014; Rose et al., 2015; Berk et al., 2016; Lobayan et al., 2017; Baiak et al., 2019). In several countries, there are high rates of resistance, such as in New Zealand (Leathwick & Luo, 2017), Australia (Bullen et al., 2016), Germany, Belgium and Sweden (Demeler et al., 2009), Sudan (Mohammedsalih et al., 2021), United States (Gasbarre, 2014) and Argentina (Cristel et al., 2017). In Brazil, there have been reports of resistance to benzimidazoles (Ramos et al., 2020; Fávero et al., 2020), macrocyclic lactones (Neves et al., 2014; Borges et al., 2015; Ramos et al., 2020), imidazothiazoles (Neves et al., 2014; Ramos et al., 2020) and salicylanilides (Silva et al., 2017; Ramos et al., 2020).

In the semiarid region of Brazil, information about the effectiveness of anthelmintics is scarce. Therefore, the objective of the present study was to obtain more information on anthelmintic resistance in cattle in the semiarid region of the state of Paraíba, northeastern Brazil. The efficacy of injectable formulations of albendazole sulfoxide, ivermectin, closantel and levamisole hydrochloride was evaluated in naturally infected cattle in 20 farms from 20 different municipalities across the state of Paraíba.

Material and Methods

Ethical approval and location of the study

This study was approved by our institution’s research ethics committee, under registration number 23000.000663.2019-81.

It was carried out in the semi-arid region of the state of Paraíba, northeastern Brazil. This area forms part of the Caatinga biome. Its rains are irregular and are concentrated in the months from January to May, with average annual precipitation between 250 and 800 mm. The average maximum temperature is 32 °C and the average minimum temperature is 20 °C. There are high rates of evaporation and the relative humidity of the air is around 70% (IBGE, 2019).

Fecal samples were collected between January and December 2020, on 20 cattle farms that had herds of more than 40 animals, with a history of problems with nematode control or indiscriminate anthelmintic use, and on which the cattle had not been dewormed for at least 90 days. Each farm was located in a different municipality, as shown in Figure 1.
Diagnosis of anthelmintic resistance

On each farm, 40 naturally infected animals were used, of both sexes, aged between four months and eight years, regardless of breed. These 40 animals had an egg count per gram of feces (EPG) ≥ 150. Subsequently, the animals were identified individually through ear tags and were randomly distributed into four groups composed of ten animals each: group I, treated with albendazole sulfoxide 15% (3.4 mg / kg) (Agebendazol®, Agener União); group II, treated with ivermectin 1% (0.2 mg / kg) (Ivomec®, Boehringer Ingelheim); group III, treated with closantel 25% (5 mg / kg) (Taitec®, Calbos); group IV, treated with levamisole hydrochloride 7.5% (3.75 mg / kg) (Ripercol®, Zoetis). Prior to the treatments, all animals underwent weight estimation by means of a weighing tape (Fita Torácica para Pesar Gado®, MultitecAgro). All treatments were performed as a single dose, administered subcutaneously after previous antisepsis of the application site, in accordance with the manufacturers’ recommendations.

Fecal samples were collected individually and directly from the rectal ampoule, on the same day, before the anthelmintic treatment (day 0) and 14 days after (day 14) (FAO, 2004). Subsequently, these were placed in plastic bags, labeled, kept refrigerated in an isothermal box and promptly sent to the Veterinary Parasitology Laboratory (VPL) of the Instituto Federal da Paraíba (IFPB), Sousa, Paraíba, for analysis.

EPG counts were performed by a McMaster modified technique (Gordon & Whitlock, 1939), with a sensitivity of 50 EPG. Larval cultures (Roberts & O'Sullivan, 1950) were carried out per group and per collection, from a pool of samples. However, when the mean EPG was zero in a given group on day 14, larval cultures were not performed. Were used eggCounts package version 2.3, which is a “R” package developed to analyze faecal egg count reduction using Bayesian hierarchal models (Wang & Paul, 2018). The percentage efficacy was calculated, along with the lower (L95) and upper (U95) 95% confidence limits. The models are tailored for a variety of practical situations, including individual treatment efficacy, zero inflation, small sample size and potential outliers (Wang et al., 2018).
Anthelmintic resistance of cattle nematodes

The anthelmintic resistance status was interpreted using the method described by Lyndal-Murphy et al. (2014), and based on the World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines on anthelmintic resistance (Coles et al., 1992), considering the EPG reduction percentage and the upper and lower 95% confidence limits:

- **Efficacious (E):** percentage reduction and upper 95% confidence limit above 95% and lower 95% confidence limit above 90%.
- **Confirmed anthelmintic resistance (R):** percentage reduction and upper 95% confidence limit below 95% and lower 95% confidence limit below 90%.
- **Suspicion of resistance (S):** neither of the above criteria fulfilled.

Epidemiological questionnaire

A structured epidemiological questionnaire was used at the farms visited, to collect information about the rearing system (extensive, intensive or semi-intensive), number of animals, type of herd exploitation, average daily milk production, deworming strategy, drugs used, frequency of drug use, routes of administration, use of endectocides and movements of animals (purchase and/or sale).

Results

The arithmetic mean (AM), minimum and maximum faecal egg counts before and after treatment, the percentage efficacy calculated based on AM, along with the lower (L95) and upper (U95) 95% confidence limits per anthelmintic and per farm are shown in Tables 1-4. Multidrug resistance was observed in 95% (19/20) of the farms evaluated in this study. Among these farms, 5% (1/20) showed resistance to one drug, 20% (4/20) to two drugs, 60% (12/20) to three drugs and 15% (3/20) to all four of the drugs evaluated (Tables 1-4). Anthelmintic resistance to ivermectin and albendazole was detected in 95% (19/20) of the herds, closantel in 75% (15/20) and levamisole in 20% (4/20) (Table 5).

In larval cultures, presence of five genera of gastrointestinal helminths was observed. These were predominantly *Haemonchus* spp. (76.7%), which was most prevalent in all larval cultures, followed by *Trichostrongylus* spp. (13.2%), *Oesophagostomum* sp. (8.5%), *Cooperia* spp. (1.1%) and *Strongyloides* sp. (0.5%) (Table 6).

It was observed that the management system most used was semi-intensive (75%; 15/20), followed by extensive (20%; 4/20) and intensive (5%; 1/20). Dairy farms were the most frequent type among the farms studied (40%; 8/20), followed by mixed farms (35%; 7/20) and beef farms (25%; 5/20). The number of cattle per farm ranged from 45 to 600 animals and the average daily milk production ranged from zero (beef herds) to 1700 liters.

Among the active ingredients most reported by the farmers for controlling worms, ivermectin was cited as the only drug used in 65% (13/20) of the farms, followed by doramectin (20%; 4/20), which are both in the group of macrocyclic lactones. In addition, ivermectin, doramectin and moxidectin were administered alone or in association also for controlling *Rhipicephalus microplus* and/or *Haematobia irritans* on 95% (19/20) of the farms. Levamisole was mentioned in 15% (3/20) of the farms, used separately on one farm, in association with ivermectin on another and in association with ivermectin and doramectin on the third. There was no report of previous use of albendazole or closantel.

Anthelmintics were administered by means of injection on 100% of the farms. This took place in the entire herd at least once a year, mostly during the rainy season (January to May), on 75% (15/20) of the farms. On the remaining 25% (5/20) of the farms, this was only done when verminosis was suspected and, in these cases, administration was individual.

Discussion

In the semiarid region of northeastern Brazil, the present study was the first to test the anthelmintic efficacy of four distinct pharmacological groups against bovine gastrointestinal nematodes. Multiresistance was found in 19/20 herds tested. The phenomenon of multidrug resistance was also observed by Ramos et al. (2018, 2020) in...
Anthelmintic resistance of cattle nematodes

The results regarding ivermectin demonstrated that anthelmintic resistance was present on 95% (19/20) of the farms, with 36.5% of efficacious mean for FECR. In São Paulo, Soutello et al. (2007) and Neves et al. (2014) detected anthelmintic resistance in 92% (23/25) and 100% (10/10), respectively, of cattle herds evaluated, after treatment with this drug. Ramos et al. (2020), in Rio Grande do Sul, also detected resistance on all the farms examined (7/7).

In Argentina, resistance to ivermectin was seen on 93.5% (58/62) (Lobayan et al., 2017) and 100% (4/4) (Cristel et al., 2017) of the cattle farms evaluated.

In line with the lower efficacy rates of ivermectin, it was observed that macrocyclic lactones, especially avermectins, were the drugs most used for anthelmintic treatments on the farms studied, similarly to what had been observed in other studies (Pereira, 2011; Suarez & Cristel, 2014). Soutello et al. (2007) and Ramos et al. (2018, 2020) stated that the higher rate of resistance to ivermectin, compared with other drugs, was probably related to its frequent use, and to its easy availability and ease of acquisition by farmers. Use of this drug has also been reported for controlling ticks (R. microplus) and horn flies (H. irritans), which indiscriminately boosts its use in cattle.
Anthelmintic resistance of cattle nematodes

Table 2. The arithmetic mean (AM), minimum (Min) and maximum (Max) faecal egg counts before (pre) and after (post) treatment of 10 animals per farm with Albendazole Sulfoxide 15% (ALB) on the 20 farms (1-20) in the semiarid region of Paraíba state, Brazil. The percentage (%) efficacy calculated based on the arithmetic group mean is provided, along with the lower (L95) and upper (U95) 95% confidence limits. The anthelmintic resistance status (Status) is provided as confirmed anthelmintic resistance (R) or suspicion of resistance (S).

| Farm | ALB Pre | ALB Post | Efficacy |
|------|---------|----------|----------|
|      | AM | Min | Max | AM | Min | Max | % | L95 | U95 | Status |
| 1    | 340 | 150 | 1950 | 145 | 0 | 650 | 57.8 | 42.3 | 78.7 | R       |
| 2    | 155 | 150 | 250 | 100 | 0 | 150 | 36.1 | 0 | 73.2 | R       |
| 3    | 355 | 150 | 1150 | 225 | 50 | 500 | 35.7 | 0 | 78.9 | R       |
| 4    | 160 | 150 | 300 | 160 | 0 | 450 | 0 | 0 | 0.17 | R       |
| 5    | 160 | 150 | 450 | 40 | 0 | 350 | 77.2 | 66.1 | 94.4 | R       |
| 6    | 300 | 150 | 500 | 160 | 0 | 600 | 42.1 | 0 | 83.1 | R       |
| 7    | 150 | 150 | 250 | 80 | 0 | 200 | 50.3 | 37.2 | 78.9 | R       |
| 8    | 155 | 150 | 210 | 90 | 0 | 150 | 42.1 | 0 | 77.2 | R       |
| 9    | 250 | 150 | 300 | 30 | 0 | 100 | 88.3 | 71.2 | 92.0 | R       |
| 10   | 185 | 150 | 500 | 185 | 0 | 1050 | 0 | 0 | 0.3 | R       |
| 11   | 200 | 150 | 350 | 65 | 0 | 100 | 67.9 | 61.2 | 91.1 | R       |
| 12   | 315 | 150 | 1100 | 65 | 0 | 200 | 78.7 | 70.4 | 89.0 | R       |
| 13   | 285 | 150 | 650 | 210 | 0 | 600 | 29.1 | 0 | 69.3 | R       |
| 14   | 245 | 150 | 900 | 160 | 0 | 550 | 22.6 | 0 | 70.1 | R       |
| 15   | 265 | 150 | 1300 | 10 | 0 | 100 | 97.7 | 87.2 | 100.0 | S       |
| 16   | 195 | 150 | 300 | 75 | 0 | 100 | 62.3 | 50.7 | 88.2 | R       |
| 17   | 420 | 150 | 2900 | 45 | 0 | 150 | 88.3 | 79.2 | 93.2 | R       |
| 18   | 165 | 150 | 250 | 165 | 0 | 400 | 0 | 0 | 0.21 | R       |
| 19   | 205 | 150 | 400 | 65 | 0 | 150 | 71.2 | 36.4 | 94.1 | R       |
| 20   | 855 | 150 | 4900 | 135 | 0 | 450 | 81.9 | 54.3 | 89.8 | R       |

herds, thus generating greater pressure for selection and dissemination of resistant alleles in parasite populations (Graef et al., 2013; Neves et al., 2014; Vilela et al., 2020). These actions can promote faster development of drug resistance (Leathwick & Luo, 2017).

For albendazole, anthelmintic resistance was also observed on 95% (19/20) of the farms, with 51.5% of efficacious mean for FECR. Ramos et al. (2020) obtained similar values for the FECR (49.8%) and detected resistance to this drug on all the farms evaluated (7/7). On the other hand, Soutello et al. (2007) detected anthelmintic resistance on only 20% (5/25) of the farms examined, with an average FECR of 75.9%. In Sudan, Mohammedsalih et al. (2021) reported that a reduction (< 90%) in the effectiveness of albendazole on bovine gastrointestinal nematodes had occurred.

Resistance to closantel was observed on 75% (15/20) of the farms, with 55.8% of efficacious mean for FECR, which was similar to the results obtained by Ramos et al. (2020), of 55.2%, and Silva et al. (2017), of 45.45%. However, Bushra et al. (2019) and Maqbool et al. (2018) found reductions of 94.44% and 100%, respectively, in India. In the present study, despite the observed resistance, no use of this drug was reported in the herds. According to Neves (2014), the low use of closantel among cattle may be due to the fact that most products sold are for oral use, thus limiting the possibility of administering them to cattle.
Resistance to levamisole was observed on 20% (4/20) of the farms. Similar results regarding resistance to this drug were reported by Ramos et al. (2020), of 28% (2/7), and Bullen et al. (2016), of 25% (5/20), in Australia. In the present study, levamisole demonstrated the highest efficacious mean (93.1%). Efficacious status was obtained on 55% (11/20) of the farms. The good efficacy of this drug in the herds tested may have resulted of its low selection pressure, as it was not used frequently by the farmers, such that it was only mentioned on 15% (3/20) of the farms.

The *Haemonchus* was the most prevalent parasite genus in all larval cultures, both before and after treatments. This has also been reported in several other studies evaluating bovine gastrointestinal nematodes (Borges et al., 2015; Lobayan et al., 2017; Silva et al., 2017; Ramos et al., 2020). This nematode probably acquires resistance faster due to its high biotic potential and great genetic variability. In addition, it harbors the allele that causes decreased susceptibility to a drug (Blackhall et al., 1998; Chaudhry et al., 2015). *Haemonchus placei* is the species that is considered most relevant in cattle (Borges et al., 2015; Santos et al., 2015). It causes gastric hemorrhagic lesions, due to its high capacity for hematophagy (Taylor et al., 2013).

Visual estimation of the animals’ weight was the practice generally used by the farmers. According to Leathwick & Luo (2017), this can be reflected in inefficiency of the treatment, given that doses below or above those recommended

### Table 3

The arithmetic mean (AM), minimum (Min) and maximum (Max) faecal egg counts before (pre) and after (post) treatment of 10 animals per farm with Closantel 25% (CLO) on the 20 farms (1-20) in the semiarid region of Paraiba state, Brazil. The percentage (%) efficacy calculated based on the arithmetic group mean is provided, along with the lower (L95) and upper (U95) 95% confidence limits. The anthelmintic resistance status (Status) is provided as efficacious (E), confirmed anthelmintic resistance (R) or suspicion of resistance (S).

| Farm | CLO | Pre | Post | Efficacy | L95 | U95 | Status |
|------|-----|-----|------|----------|-----|-----|--------|
|      | AM  | Min | Max  | AM       | Min | Max |        |
| 1    | 210 | 150 | 750  | 70       | 0   | 250 | 67.2   |
| 2    | 150 | 150 | 150  | 100      | 0   | 200 | 31.7   |
| 3    | 170 | 150 | 250  | 25       | 0   | 100 | 86.9   |
| 4    | 180 | 150 | 250  | 40       | 0   | 50  | 77.6   |
| 5    | 345 | 150 | 1900 | 25       | 0   | 200 | 91.1   |
| 6    | 266.7| 150| 600 | 11,1 | 0  | 50 | 94.3 |
| 7    | 165 | 150 | 350  | 35       | 0   | 200 | 79.6   |
| 8    | 190 | 150 | 550  | 65       | 0   | 300 | 66.6   |
| 9    | 240 | 150 | 1050 | 295      | 0   | 1000| 0      |
| 10   | 150 | 150 | 150  | 150      | 0   | 200 | 0      |
| 11   | 155 | 150 | 200  | 155      | 0   | 250 | 0      |
| 12   | 535 | 150 | 1550 | 295      | 0   | 600 | 47.2   |
| 13   | 220 | 150 | 600  | 195      | 0   | 350 | 12.3   |
| 14   | 490 | 150 | 1200 | 85       | 0   | 250 | 88.2   |
| 15   | 210 | 150 | 350  | 15       | 0   | 50  | 96.1   |
| 16   | 185 | 150 | 500  | 90       | 0   | 600 | 47.3   |
| 17   | 300 | 150 | 800  | 165      | 0   | 1150| 49.1   |
| 18   | 245 | 150 | 600  | 170      | 0   | 300 | 32.2   |
| 19   | 375 | 150 | 1700 | 15       | 0   | 50  | 98.8   |
| 20   | 230 | 150 | 750  | 110      | 0   | 500 | 50.7   |
Anthelmintic resistance of cattle nematodes

Table 5. The number of farms with efficacious (E), confirmed anthelmintic resistance (R) or suspicion of resistance (S) for Ivermectin 1% (IVM), Albendazole Sulfoxide 15% (ALB), Closantel 25% (CLO) and Levamisole Hydrochloride 7.5% (LEV), and the percentage of efficacious mean (EM%) of the anthelmintics on cattle gastrointestinal nematodes in the semiarid region of Paraíba state, Brazil.

| Treatment   | N animals | N farms | EM (%) | R   | S   | E   |
|-------------|-----------|---------|--------|-----|-----|-----|
| IVM         | 200       | 20      | 36.5   | 19  | 1   | 0   |
| ALB         | 200       | 20      | 51.5   | 19  | 1   | 0   |
| CLO         | 200       | 20      | 55.8   | 15  | 3   | 2   |
| LEV         | 200       | 20      | 93.1   | 4   | 5   | 11  |
| Total       | 57        | 10      | 13     |     |     |     |

by the manufacturers might be estimated. In addition, most of the farmers (75%; 15/20) used anthelmintics at the beginning of the rainy season. However, if the animals are treated and transferred to clean pastures, or if they are treated during the dry season, resistance can develop quickly, even if the animals receive few annual treatments.
Table 6. Percentage (%) of cattle gastrointestinal nematodes by genus and farm recovered from larval cultures before (pre) and after (post) anthelmintic treatments with Ivermectin 1% (IVM), Albendazole Sulfoxide 15% (ALB), Closantel 25% (CLO) and Levamisole Hydrochloride 7.5% (LEV) in the semi-arid region of Paraíba state, Brazil.

| Farms | IVM | ALB | CLO | LEV |
|-------|-----|-----|-----|-----|
|       | 1   | 2   | 3   | 4   |
|       | 5   | 6   | 7   | 8   |
|       | 9   | 10  | 11  | 12  |
|       | 13  | 14  | 15  | 16  |
|       | 17  | 18  | 19  | 20  |
| Pre  | H   | 84  | 91  | 85  | 75  | 71  | 94  | 50  | 72  | 80  | 75  | 100 | 89  | 51  | 82  | 80  | 62  | 74  | 90  | 100 | 80  |
| T    | 10  | 6   | 9   | 16  | 14  | 4   | 40  | 13  | 18  | 25  | 0   | 3   | 49  | 0   | 4   | 23  | 4   | 5   | 0   | 19  |
| O    | 6   | 3   | 0   | 6   | 11  | 0   | 10  | 11  | 2   | 0   | 0   | 1   | 0   | 18  | 16  | 15  | 22  | 5   | 0   | 1   |
| C    | 0   | 0   | 6   | 3   | 3   | 2   | 0   | 3   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| S    | 0   | 0   | 0   | 0   | 0   | 1   | 0   | 1   | 0   | 0   | 0   | 7   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| Post | H   | 94  | 74  | 78  | 95  | 97  | 61  | 93  | 75  | 98  | 70  | 60  | 100 | 81  | 85  | 76  | 95  | 74  | 74  | 94  | 58  |
| T    | 6   | 7   | 12  | 3   | 2   | 34  | 7   | 8   | 2   | 30  | 30  | 0   | 1   | 5   | 18  | 2   | 6   | 21  | 4   | 42  |
| O    | 0   | 9   | 5   | 2   | 1   | 5   | 0   | 17  | 0   | 1    | 0   | 0   | 18  | 16  | 3   | 20  | 5   | 2   | 0   |
| C    | 0   | 0   | 5   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| S    | 0   | 10  | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 10  | 0   | 0   | 0   | 0   | 0   | 0   | 0   |

|       | 1   | 2   | 3   | 4   |
|       | 5   | 6   | 7   | 8   |
|       | 9   | 10  | 11  | 12  |
|       | 13  | 14  | 15  | 16  |
|       | 17  | 18  | 19  | 20  |

with anthelmintics (Martin et al., 1981; Papadopoulos et al., 2001). Therefore, management methodologies and strategies should be designed to keep parasites in refugia in herds, thereby prolonging the effectiveness of current anthelmintics and preserving susceptible nematode genotypes (Berk et al., 2016).
Movement of animals without previous knowledge of the clinical history was a common practice reported by all the farmers. Moreover, no investigations or parasitological examinations were conducted on newly acquired animals. Both of these practices contribute to dispersion of resistant nematode populations. Bullen et al., (2016) suggested that, without prior knowledge of the farm's anthelmintic resistance status, movement of dairy cattle constitutes a considerable risk with regard to introduction of anthelmintic resistance on unaffected farms.

In addition, through PCR, Ramos et al. (2020) demonstrated the presence of co-infections of species of *Haemonchus* spp. that affect different cattle and sheep that share pastures. This matter deserves further study and may explain the high rates of anthelmintic resistance found on the farms studied, especially in relation to the drugs albendazole and closantel. Although no previous use of these drugs was reported in the herds evaluated, they are widely used among small ruminants and anthelmintic resistance to them in the semi-arid region of Paraíba has already been reported (Lima et al., 2010; Silva et al., 2018).

To optimize the effectiveness of anthelmintics in populations of multidrug-resistant nematodes, Ramos et al. (2016) suggested that combinations of two drugs belonging to different chemical groups should be used. However, they stressed the importance of conducting anthelmintic efficacy tests in order to choose the chemical groups to be used, as well as introduction of control measures for gastrointestinal worms within the management of cattle. Acquisition of cattle without adequate sanitary management before or after transporting them needs to be avoided. This is especially important in relation to acquisition from farms on which grazing combined with goats and/or sheep is practiced: this can be considered to be a critical point regarding worm control. Chaudhry et al. (2015) reported the first genetic confirmation of hybridization between *H. contortus* and *H. placei* in the field, thus increasing the possibility of inter-species transmission of anthelmintic resistance mutations.

**Conclusion**

It was concluded that the anthelmintic resistance of bovine gastrointestinal nematodes in the semi-arid region of Paraíba, northeastern Brazil, is high. Multidrug resistance was observed on almost all the farms evaluated, especially in relation to the drugs ivermectin, albendazole and closantel. Levamisole was considered to be the drug with the best anthelmintic efficacy. It can be suggested that the sanitary management of cattle herds in the semi-arid region should be adapted so as to avoid mass deworming without applying technical criteria. Moreover, animals should only be transported after a parasitological diagnosis has been made, especially in the case of acquisition from farms with a history of problems regarding worm control and from farms use pastures intercropped between cattle and small ruminants.

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