RISK FACTORS OF THE BENZIMIDAZOLE RESISTANCE DEVELOPMENT IN SMALL RUMINANTS FROM BRAZILIAN NORTHEAST SEMI-ARID AREA

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Abstract

Resistance to benzimidazole anthelmintics is reported as an old and persistent problem in many parts of the world. Resistance development depends on the presence of resistance promoters and there are operational, genetic and bioecological factors. However, little is known about real impact of these factors on resistance development, they are just considered through mathematical models. The objective of this work was to determine the correlation between the presence of benzimidazole anthelmintic resistance and its promoters in small ruminant farms in Brazilian northeast semi-arid area. The work was accomplished in 25 sheep and goats farms in the state of Ceará, Brazil. The procedure used to detect anthelmintic resistant nematode was the faecal egg count reduction test. In addition, a questionnaire about management practices, infrastructure, anthelmintic usage, climate characteristics, flocks sanitary state and veterinary assistance was applied. Data were analyzed using RESO statistical program. The questionnaires were analyzed using SPSS release 8.0. In sheep farms, the prevalence of benzimidazole resistance was 88% and in goats farms, it was 87,5%. In sheep and goats farms, Haemonchus was the most prevalent genus, followed by Trichostrongylus spp. and Oesophagostomum spp. Through the questionnaires analysis it could be established correlations between the resistance development and its promoters. The treatment frequency per year and management conditions showed some correlation. The fast rotation of active principle and treatment in dry season showed a low level of correlation. The production finality, animal species, veterinary assistance, pasture rotation and treatment in rainy season showed a very low correlation with the development of anthelmintic resistance.

Key-words: resistance development; benzimidazole; sheep; goats; Brazil

Introduction

Gastrointestinal nematode infections cause high economic losses in small ruminant production (Girão et al., 1992). The control of nematodes is mainly based on the use of anthelmintics (Coop & Kyriazakis, 2001). Failures in this kind of control are the first signs of anthelmintic resistance (Sangster, 2001).

Anthelmintic resistance happens in all classes of drugs used in nematode control (Craig, 1993). Resistance to benzimidazole anthelmintics is reported as an old and persistent problem in many parts of the world (Drudge et al., 1964; Echevarria et al., 1996; Waller et al., 1996; Boersema & Pandey, 1997; Melo et al., 1998; Chartier et al., 1998; Waller et al., 1995; Terril et al., 2001). Resistance development depends on the presence of resistance promoters and the main factors are operational, genetic and bioecological (Hennon, 1993; Martin, 1997). Underdosage, treatment frequency and fast rotation of active principle are examples of operational factors (Echevarria, 1996). The number of resistant allele, frequency, dominance and interaction degree with genome will influence the resistance development (Le Jambre, et al., 1979). The size of refugia population is the bioecological factor (Prichard, 1990; Jackson, 1993). However, little is known about the real impact of these factors on resistance development, they are just considered through mathematical models (Smith, et al., 1999).

The objective of this work was to determine the correlation between the presence of benzimidazole anthelmintic resistance and its promoters in small ruminant farms in Brazilian northeast semi-arid area.

Materials and methods

Farms

The work was accomplished in 25 sheep and goats farms in the state of Ceará, Brazil, located on a semi-arid region with an annual rainfall varying from 800 to 1000 mm with an irregular distribution. The area presents two seasons: a dry one (June to December) and a rainy one (January to May). The maximum and minimum temperatures are 33°C and 23ºC, respectively.

Procedure

The procedure used to detect anthelmintic resistant nematode in this work was the faecal egg count reduction test (FECRT), as recommended by the World Association for the Advancement of Veterinary Parasitology (WAAVP) (Coles et al., 1992).

In each flock, 24 female animals were selected and randomly separated into two groups. None of the tested animals received any anthelmintic treatment for at least six weeks prior to the beginning of the study. On day 0, animals from group I received oxfendazole (Systamex ®/Coopers) orally at 5mg/kg body weight; Group II remained as untreated control.

In addition, a questionnaire about management practices, infrastructure, anthelmintic usage, climate characteristics, flocks sanitary state and veterinary assistance was applied.

Parasitologic assays

Faecal samples were collected from the rectum in treatment day and 14 days after. The samples were processed for faecal egg count (FEC) using a modified McMaster technique described by Ueno & Gonçalves (1998). A pooled faecal sample from both groups, treated and control, were harvested for 7 days at 25°C. The infective larvae identification was performed according to Georgi & Georgi (1990).

Statistic analysis

Data were analyzed using RESO statistical program (1989). Resistance was declared according to the WAAVP guidelines (Coles et al., 1992). The conditions were: efficacy was lower than 95% and the lower limit of 95% confidence interval was lower than 90%. Only one of these criteria is indicative of benzimidazole resistance. The questionnaires were analyzed using SPSS release 8.0, it was applied Qui-square test, then test exact of Fisher and Monte Carlo's method. Due to small sampling, the tendency was observed according to the contingency coefficient. Through this it was determined the correlation between the resistance factors promoters and the resistance occurrence in the studied flocks.

Results

In sheep farms, the reduction of faecal egg count varied from 0 to 100%. The prevalence of benzimidazole resistance was 88%. In goats farms, the reduction in egg faecal count varied from 2 to 96%. The prevalence of benzimidazole resistance was 87,5%. In both species, Haemonchus was the most prevalent genus, followed by Trichostrongylus spp. and Oesophagostomum spp.

The number of sheep and goats on the farms ranged from 70 to 1200 (mean 176) and from 80 to 500 (mean 220) respectively. 92% of the farms aimed at meat production and kept their animals grazing under semi-intensive conditions with night confinement. Only 28% of the farms had veterinary assistance (mean 8 visits per year). The most frequent diseases recorded were linfadenitis, miiasis and pododermatitis. 52% of the farms used pasture rotation.

All the farmers used anthelmintics, mainly benzimidazole products (52%). Generally, 2 to 3 groups of anthelmintic were used per year and its efficacy was considered good by the farmers. The mean frequency of anthelmintic treatments per year were three, ranging from 1 to 5. In 12% of the farms animals were drenched on the rainy season, in 48% on the dry season and in 40% of the properties on both seasons.

Through the questionnaires analysis there were established correlations between the resistance development and its promoters. The treatment frequency per year and management conditions showed some correlation. The fast rotation of active principle and treatment in dry season showed a low correlation. The production finality, animal species, veterinary assistance presence, pasture rotation and treatment in rainy season showed a very low correlation with development of anthelmintic resistance (Table 1).

Tab. 1. Correlation between the presence of benzimidazole anthelmintic resistance and its promoters in small ruminant properties in Brazilian northeast semi-arid area

Resistance promoters	**Contingency coefficient value***	**Aproximate significance**
Management conditions	0.485	0.021
Production finality	0.159	0.723
Animal species	0.011	0.958
Veterinary assistance presence	0.044	0.826
Rotation of active principle	0.336	0.203
Pasture rotation	0.108	0.588
Treatment frequency per year	0.442	0.195
Treatment in rainy season	0.135	0.495
Treatment in dry season	0.359	0.055

* 0 – 0.19: very low correlation; 0.20 - 0.39: low correlation; 0.40 – 0.59: some correlation.

Discussion

Benzimidazole resistance is widely distributed (Drudge et al., 1964; Waller et al., 1995; Waller et al., 1996; Chartier et al., 1998; Terril, et al., 2001). The resistance frequency reported in this survey in a semi-arid area was similar to those reported in south Brazil tropical humid region (Echevarria et al., 1996; Farias et al., 1997; Soccol et al., 1996), Scotland (Jackson, et al., 1992) and Africa (Boersema & Pandey, 1997). However, the results reported for goats were superior to those reported in northeast Brazil (Vieira & Cavalcante, 1999) and England (Hong et al., 1996). Nevertheless, the benzimidazole anthelmintics are still being widely used (Lanusse, 1996) and this fact probably causes the increase or maintenance of high resistance frequency of sheep and goats flocks in the whole world.

In relation to animals number and production purposes, sheep and goats flocks are similar as described to those Pinheiro et al. (2000) that accomplished a wide survey through questionnaires about sanitary handlings aspects in 127 properties of Ceará state. However, the management conditions differ, because in this work it prevailed the semi-intensive conditions and the percentage of farms with veterinary assistance was inferior. In relation to frequency of diseases, the results are similar to other flocks in the same state. Oliveira, et al. (1995), mention pododermatitis and ectoparasites. Therefore, the samples represent the small ruminant properties of the studied area, even if it could same not be considered appropriate for the survey purpose. This work was able to determine the variance of studied characteristics (11%) and to make possible the calculations of the valid samples valid for a general population. This data may be utilized for future studies in this area.

Benzimidazole anthelmintics are mostly used for nematode control in this area, as well as in other Brazilian northeast regions (Vieira and Cavalcante, 1999), in Denmark and France (Maingi et al, 1996; Chartier et al, 1998). However, in Mexico and Kenya, macrocyclic lactones and levamisole are the most common anthelmintics used, respectively. The treatment frequency is similar to Kenya and Mexico, but is superior to Denmark. In these countries the anthelmintic group rotation rarely exist, because anthelmintics are changed each two or three years (Torres-Acosta, et al., 2003; Maingi, et al., 1996; Maingi, et al., 1997) different from the studied area where the fast rotation of active principle is performed.

The impact study of the resistance promoter factors is rare. Generally, mathematical models are used (Barnes & Dobson, 1990), which is reference to determine management models (Sangster, 1999), however they need to be validated (FAO, 2003). Some factors clearly implicate the development and dissemination of the resistance. Among those, some factors were evidenced, even if just as a tendency: treatment frequency, fast rotation of active principle and treatment with a small refugia population. This factors were cited by Martin et al. (1981), Jackson (1993), Coles (2001), Hennon (1993) and Echevarria (1996).

The combinations of those factors could have propitiated the high frequency of the resistance alleles in population. The strategic treatment indicated for the Brazilian northeast area, determines four annual treatments, three during dry season when the refugia population is small or null (Embrapa, 1994). The two factors combined make possible the fast development of the anthelmintic resistance (Sangster, 2001).

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