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Research paper

Efficacy of major anthelmintics for reduction of fecal shedding of strongyle-type eggs in horses in the Mid-Atlantic region of the United States

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ABSTRACT

In the last decade there have been numerous reports of anthelmintic resistant cyathostomins in many parts of the world. The objective of the present study was to evaluate the efficacy of the commercially available anthelmintics against cyathostomin egg shedding in the Mid-Atlantic region of the United States. A total of 989 horses from 67 different farms located in southeastern Pennsylvania, northern Delaware, and northeastern Maryland were treated with fenbendazole, oxibendazole, pyrantel pamoate, ivermectin, or moxidectin at their recommended dosages. Fecal egg count reduction testing was used to determine the efficacy of each anthelmintic on those horses with fecal egg counts of ≥200 eggs per gram on the day of treatment (272 horses). Decreased efficacy (reduction of strongyle-type fecal egg counts by less than 90%) was found for fenbendazole, oxibendazole, and pyrantel pamoate, with only 6%, 21% and 43% of horses showing reductions of greater than 90%, respectively. The macrocyclic lactones showed high efficacy in all horses sampled in this study. The decreased anthelmintic efficacy detected in this study adds further evidence for the existence of resistant cyathostomins throughout much of the eastern United States. Findings from this study can be used to create a more sustainable approach for parasite control programs.

1. Introduction

There are more than 50 identified species of cyathostomins that infect the gastrointestinal tracts of grazing equids worldwide (Lichtenfels et al., 1998). These parasites are considered the most important gastrointestinal helminths to infect horses since they often compromise 95–100% of the total worm burden (Nielsen, 2012). Most horses harboring large numbers of cyathostomins show no signs of clinical disease; however, infections comprising encysted cyathostomin larvae can cause significant pathology, ranging from sub-clinical enteropathies to severe gastrointestinal damage resulting in diarrhea, colic, and hypoalbuminemia in heavily infected animals, a condition known as cyathostominosis (Love et al., 1999; Lyons et al., 2000). Although, measuring fecal egg counts is the most frequently used method of evaluating cyathostomin burdens in horses in clinical practice, there is no direct linear correlation of the strongyle fecal egg or larval count number with the actual worm burden, and currently there is no antemortem method to assess the number of encysted cyathostomins (Nielsen et al., 2010).

Regular anthelmintic treatment is necessary for protection against this parasitic infection because immunity against cyathostomins is slow to develop and incomplete (Klei and Chapman, 1999). Horse owners in most developed countries have unrestricted access to safe, inexpensive, easily administered commercially available anthelmintics for this purpose. But use of this medication in an intensive calendar-based regime is believed to have exerted high selection pressures on the parasite populations for resistance (Kaplan, 2002). The earliest reports of thiabendazole resistance in cyathostomins in the United States were published in the early 1960s, and since then widespread resistance to other commercially available benzimidazoles has been shown in over 21 countries (Drudge and Lyons, 1965; Lyons et al., 1999). Resistance to fenbendazole has been reported from multi-farm prevalence studies to

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be 75% or greater in England, Europe, Brazil, and the Southeastern United States (Fisher et al., 1992; Repeta et al., 1993; Ihler, 1995; Craven et al., 1998; Varady et al., 2000; Kaplan et al., 2004; Traversa et al., 2012; Canever et al., 2013; Lester et al., 2013). Although, not as prevalent, pyrantel-resistant cyathostomins have also been reported in Norway, Denmark, France, Brazil and the Southeastern United States (Ihler, 1995; Craven et al., 1998; Kaplan et al., 2004; Traversa et al., 2012; Canever et al., 2013). In contrast, until recently the macrocyclic lactones (also referred to as the avermectin/milbemycin drug class) showed no evidence of decreased efficacy. But now several reports of decreasing cyathostomin egg reappearance periods for ivermectin and moxidectin on isolated farms have emerged (Lyons et al., 2008; Rossano et al., 2010; Traversa et al., 2012; Canever et al., 2013). There is great concern that the development of avermectin/milbemycin (AM) resistance could evolve into the current situation affecting small ruminants with a high prevalence of avermectin-resistant *Haemonchus contortus* in sheep and goats worldwide, as well as AM-resistant parasites in cattle (Fleming et al., 2006; Howell et al., 2008; Edmonds et al., 2010).

Anthelmintic resistance evolves slowly over many years and can therefore remain clinically inapparent until its later stages when there is therapeutic failure with persistent clinical signs (Sangster, 1999). Since infection with cyathostomins rarely results in clinical disease specific testing must be performed in order to detect resistance as therapeutic failure would be difficult to recognize (Vidyashankar et al., 2012). Currently, only direct in vivo measurements that evaluate anthelmintic efficacy can be used to infer the existence of resistance (Kaplan, 2002, 2009). Fecal egg count reduction testing offers the most practical method for detection of changes in anthelmintic efficacy on farms and allows for continued surveillance for resistant strongyle populations.

If a more sustainable approach for parasite control programs is to be instituted, further studies must be performed to determine whether cyathostomin resistance is widespread throughout the United States, or a regional phenomenon based on management practices and/or other factors. The objective of the present study was to evaluate the efficacy of five anthelmintic drugs against cyathostomin egg shedding in horses from the Mid-Atlantic region of the United States using the fecal egg count reduction test.

2. Materials and methods

2.1. Horses

Horses of various breeds on 67 different farms in Pennsylvania (Delaware and Chester County), Maryland (Cecil County), and Delaware (Newcastle County) were evaluated for inclusion in this randomized, blinded, prospective study between April of 2008 and October of 2010. The farms were located within or close to the University of Pennsylvania's New Bolton Center Field Service's practice range. Farm types included breeding, training, pleasure, boarding and combinations of these categories. Owners provided written or oral consent for their horses to be used for the study, and the owners or barn managers completed a questionnaire for each horse included in the study. The questionnaire provided information regarding the signalment and use of the horse, as well as the frequency of deworming, the most recent anthelmintic used, whether all of the horses on the farm were dewormed at the same time, the number of hours each horse spent on pasture, and the stocking density of the pasture to which each horse was exposed. All horses sampled for the study were not treated with an anthelmintic for at least 8 weeks prior to testing. At the time of anthelmintic treatment, fecal samples were collected from the rectum of each horse or fresh feces were obtained from the stall floor, then each individual horse was randomly assigned to one of five treatment groups, including fenbendazole[1] (5.0 mg/kg), oxibendazole[2] (10 mg/kg), pyrantel pamoate[3] (6.6 mg/kg), ivermectin[4] (0.2 mg/kg), and moxidectin[5] (0.4 mg/kg). All anthelmintics were administered orally in a paste formulation by a veterinarian or technician, and dosages for each horse were determined after estimating weight by use of a weight tape. After a total of 400 horses had been sampled for the study (70 of which had been treated with moxidectin), the administration of moxidectin was discontinued in order to increase the number of horses available with high fecal egg counts for evaluation of the efficacy of the four other anthelmintic types. This study was approved by the Institutional Animal Care and Use Committee of the University of Pennsylvania.

2.2. Fecal egg count method

A modified McMaster technique was used with a detection limit of 25 eggs per gram (EPG) of feces for counting strongyle-type eggs (Zajac and Conboy, 2012). Two 2-chamber slides were counted using a dilution of 2 g of feces to 30 mL zinc sulfate solution (specific gravity of 1.2). The final number of eggs counted in four chambers was multiplied by 25 to give the EPG. Horses met the inclusion criteria for our experimental group if the strongyle fecal eggs counts (FEC) were greater than or equal to 200 EPG. For these horses fecal samples were then taken 10–14 days after treatment in similar fashion. For purposes of the analysis and reporting of this data all strongyle-type eggs in feces were considered to be from cyathostomins. This was done based on records from the Pathology Service at the University of Pennsylvania's New Bolton Center Widener Hospital for Large Animals, which has noted no large strongyles in the last 8 years in a total of 2262 necropsies performed on horses primarily stabled in the Mid-Atlantic region of the United States (unpublished data). The possibility exists that there were small numbers of large strongyle eggs in some of the fecal samples collected during this study, but the authors' assumption was that these numbers would have minimal impact on the statistical results. All FEC were performed by the same parasitologist and parasitology technician at the University of Pennsylvania's Department of Parasitology, who were blinded to sample data.

2.3. Fecal egg count reduction test

Fecal egg count reduction (FECR) tests were performed on 258 horses from 47 different farms that met the inclusion criteria of greater than or equal to 200 EPG to evaluate the efficacy of fenbendazole, oxibendazole, pyrantel pamoate, ivermectin and moxidectin. Percentage reductions were calculated for each horse according to the recommendations of the World Association for the Advancement of Veterinary Parasitology (WAAVP) for estimation of anthelmintic efficacy using the following formula (Coles et al., 1992):

$$\left(\left[\frac{\text{pre} - \text{treatment EPG} - \text{post} - \text{treatment EPG}}{\text{pre} - \text{treatment EPG}}\right] \times 100\right)$$

Mean values for percentage FECR were then calculated for each anthelmintic group, as well as the effective percentage (the percentage of horses that experienced a greater than 90% reduction in FEC after treatment) for each anthelmintic. When fecal egg counts

[1] Panacur®, fenbendazole paste 10% (100 mg/g) Intervet Inc, Millsboro, Del.
[2] Anthelcide® EQ, oxibendazole 22.7%, Pfizer Animal Health, NY, NY.
[3] Strongid® Paste, pyrantel pamoate (180 mg/mL) 23.6 g, Pfizer Animal Health, NY, NY.
[4] Eqvalan®, ivermectin paste 1.87%, Merial Limited, Duluth, GA.
[5] Quest® Gel, moxidectin (20 mg/mL), Fort Dodge Animal Health, NY, NY.