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Efficacy of pyrantel pamoate and ivermectin paste formulations against naturally acquired *Oxyuris equi* infections in horses

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ABSTRACT

In recent years, numerous veterinary practitioners have reported anecdotal episodes in which anthelmintic treatment did not appear to deliver the expected efficacy against equine pinworms (*Oxyuris equi*). Anthelmintic resistance has not been demonstrated formally in equine pinworms, so a clinical study was designed to evaluate the efficacy of paste formulations of pyrantel pamoate or ivermectin against naturally acquired infections with *O. equi*. Twenty-one horses (>4 months to 15 years of age) with patent, naturally acquired pinworm infections were blocked by source of origin and allocated randomly to one of three treatment groups: horses ($n = 7$) assigned to Group 1 were treated orally with pyrantel pamoate paste at a dosage of 13.2 mg/kg (2× label dosage), Group 2 horses ($n = 7$) were untreated controls, and horses ($n = 7$) assigned to Group 3 were treated orally with ivermectin paste at a dosage of 200 μg/kg. Fourteen days after treatment, horses were euthanatized, necropsied, and large intestinal contents were processed for recovery of adult pinworms. In addition, duplicate 1% aliquots of intestinal contents from the cecum, ventral colon, dorsal colon, and small colon were collected, preserved, and examined for recovery and enumeration of fourth-stage larval *O. equi*. Anthelmintic efficacy against pinworms was evaluated by comparing the post-treatment worm counts of Groups 1 and 3 to those of control animals. Mean numbers of *O. equi* adults recovered postmortem were significantly decreased by both pyrantel pamoate ($P = 0.0366$) and ivermectin ($P = 0.0137$) treatment, with respective efficacies of 91.2% and 96.0%. In addition, both products demonstrated >99% efficacy against fourth-stage *O. equi* larvae. The current study demonstrated acceptable adulticidal and larvicidal efficacy of both pyrantel pamoate and ivermectin paste formulations against *O. equi* and did not support the existence of macrocyclic lactone or pyrimidine resistance in the pinworm populations evaluated.

1. Introduction

In recent years, numerous practitioners have reported putative failures of anthelmintic treatment to remove adult pinworm (*Oxyuris equi*) infections. Some perceived failures were based on persistent anal pruritus after anthelmintic treatment, but tail-rubbing can be caused by non-parasitic factors. Nonetheless, a portion of these reports included unequivocal evidence of pinworm survival, such as passage of adult worms in feces several weeks after treatment, or appearance of typical egg masses in the perianal region.

Most anecdotal reports of treatment failure have involved the repeated use of ivermectin in mature horses. The possibility of macrocyclic lactone resistance in *O. equi* has not been evaluated formally, but adult pinworms have been reported to survive treatment with ivermectin paste

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administered at the label dosage of 200 μg/kg (Reinemeyer et al., 2006a). Pinworms surviving ivermectin treatment were subsequently removed by pyrantel pamoate paste (6.6 mg/kg), suggesting that some individual nematodes within the population were not uniformly susceptible to macrocyclic lactone anthelmintics. Other researchers have recently reported the survival of ivermectin treatment by adult and larval pinworms (Lyons et al., 2009).

Anthelmintic resistance in strongyles and ascarids of horses can be detected and monitored by the use of Fecal Egg Count Reduction Testing (Coles et al., 1992). However, quantitative egg counting techniques are not applicable to *O. equi* because pinworm eggs are not routinely passed in feces. Rather, gravid females protrude from the anus and deposit eggs in a sticky film directly onto the anus and perianal skin. Aided by the host's body temperature, eggs larvate and become infective within approximately five days. Eggs flake off into the environment, and transmission is accomplished via inadvertent ingestion. The usual prepatent period of *O. equi* is 5 months (Urquhart et al., 1996).

To investigate the possibility of anthelmintic resistance in equine pinworms, a clinical study was designed to evaluate the efficacy of pyrantel pamoate or ivermectin paste formulations against naturally acquired infections with *O. equi*.

2. Materials and methods

2.1. Animals and husbandry

Twenty-one light saddle breed horses, >4 months to 15 years of age, were either born and weaned at the testing facility during 2007 and 2008, or acquired from commercial sources during 2008. Foals and mature horses were identified by uniquely numbered, plastic, leg or neck bands, respectively. Horses were housed individually in 4 m × 4 m stalls constructed of tubular metal panels. Stall flooring was packed limestone bedded with pine or hardwood shavings and sawdust. Horses were offered hay and grain daily at ~1.5% and 0.5% of body weight, respectively, divided into similar portions offered during a.m. and p.m. hours. Drinking water was provided *ad libitum* in 14-L buckets, and was replenished at least twice daily. Feces were removed daily, and stall bedding was removed and replaced at approximately weekly intervals.

2.2. Experimental design

A blinded, controlled efficacy study was implemented to determine the susceptibility of naturally acquired *O. equi* infections to pyrantel pamoate or ivermectin, administered once orally. When three or more horses were concurrently identified with patent *O. equi* infections, candidates were acclimated to experimental conditions for seven days. A physical examination of each horse was conducted by a veterinarian at the onset of acclimation (Day −7), and clinical observations of general health were conducted by trained personnel once daily throughout the acclimation and post-treatment phases of the study. On Day −1, candidates were blocked by source of origin, ranked by ascending identification number, and allocated randomly to one of three treatment groups. Anthelmintic treatments were administered orally on Day 0 by unblinded personnel. Enrolled horses were euthanized 14 days after treatment, and appropriate alimentary samples were collected for enumeration of adult and larval stages of *O. equi*.

Masking was achieved by complete separation of duties. Personnel with knowledge of treatment assignments did not determine any outcome measures (e.g., physical examinations, health observations, worm counts), and personnel who determined outcome measures were unaware of treatment assignments.

2.3. Treatments

Horses assigned to Group 1 ($n = 7$) were treated with a 19.13% paste formulation of pyrantel pamoate (Pyrantel Pamoate Paste®)[2] once orally on Day 0 at a target dosage of 13.2 mg/kg. This dosage was selected because the manufacturer of the pyrantel formulation is systematically evaluating its efficacy against various nematode targets in horses (Reinemeyer et al., 2008). Horses in Group 2 ($n = 7$) served as untreated controls, and Group 3 horses ($n = 7$) were treated with a 1.87% paste formulation of ivermectin (Eqvalan Paste®)[3] once orally on Day 0 at a target dosage of 200 μg/kg. Individual doses of both products were prepared by weight to the nearest 0.1 g, and were based on body weights measured with a certified livestock scale on the day before treatment (Day −1). Prior to administration of paste formulation, the oral cavity of each intended recipient was flushed with tap water to remove any residual hay or feed. Paste was delivered orally, over the back of the tongue, by unmasked personnel.

2.4. Parasitologic parameters

Individual fecal samples were collected from each candidate on one or more occasions and processed by means of a sucrose centrifugation flotation technique (Cox and Todd, 1962). If *O. equi* infection could not be confirmed by fecal examination, each candidate's perianal region was scraped with a tongue depressor coated with lubricant. Captured skin detritus was transferred to a glass slide and examined microscopically. Eligibility for enrollment was based on antemortem evidence of patent *O. equi* infection, using one or both laboratory methods.

Horses were euthanized and necropsied 14 days after treatment. At necropsy, the cecum, ventral colon, dorsal colon, and small colon were removed and separated. Each segment of gut was opened separately, and the contents were collected in a suitable container. The mucosal surface of each organ was rinsed with water, and the washings were combined with the contents. Additional water was added to bring the total volume of each organ to a multiple of 5 l. One percent aliquots of the contents of the cecum, ventral colon, dorsal colon, and small colon were collected

[2] Pyrantel Pamoate Paste, Teva Animal Health, Inc. (previously IVX Animal Health, Inc.).
[3] Eqvalan, Merial Ltd., Duluth, GA, USA.