Veterinary Parasitology 202 (2014) 45–48

Contents lists available at ScienceDirect

Veterinary Parasitology

journal homepage: www.elsevier.com/locate/vetpar

Efficacy of a novel topical combination of fipronil, (S)-methoprene, eprinomectin and praziquantel against feline urinary bladder worm (*Capillaria plica*) infection

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ARTICLE INFO

Keywords:
Capillaria plica
Eprinomectin
Praziquantel
Nematodes
Cat

ABSTRACT

Infection with urinary capillarid bladder worms has been observed in cats worldwide. Although considered as generally causing no or little harm, infection with urinary capillarids may be associated with clinical disease which requires an appropriate treatment including the use of anthelmintics. Therefore, the efficacy of a novel topical combination formulation of fipronil 8.3% (w/v), (S)-methoprene 10% (w/v), eprinomectin 0.4% (w/v), and praziquantel 8.3% (w/v) (BROADLINE®, Merial) was evaluated against urinary capillarids in naturally infected cats. Sixteen European Short Hair cats (5 male, 11 female) with capillarid eggs in their urine pre-treatment were included in the study. At the time of treatment, the cats were approximately ten months to eight years old and weighed 1.6–3.6 kg. Cats were ranked based on decreasing bodyweight and then randomly allocated within replicates of two animals to one of the treatment groups. Each cat in the treated group received one topical application of the combination product at the minimum therapeutic dose of 0.12 mL/kg body weight delivering 10 mg fipronil + 12 mg (S)-methoprene + 0.5 mg eprinomectin + 10 mg praziquantel per kilogram of body weight while the cats allocated to the control group remained untreated. For parasite recovery, identification and count, cats were euthanized humanely 14 days after treatment. All untreated cats harboured *Capillaria plica* in their urinary bladders (range 4–12), while no capillarids were recovered from the eight treated cats. Thus, the efficacy of the novel topical combination against *C. plica* was 100%. All cats accepted the treatment well based on post-treatment observations and daily observations thereafter. No adverse events or other health problems were observed during the study.

1. Introduction

Urinary bladder *Capillaria* spp. infections of carnivores are reported to occur worldwide in wild canids as primary hosts but also in wild cats (*Felis silvestris*) and domestic cats (*Felis catus*). Information on the occurrence of urinary capillarids in domestic cats from Europe, the Americas, Australia and Japan is available through post-mortem surveys (e.g., Wagner, 1936; Zdun, 1937; Erlich, 1938; Zebrowska, 1961; Waddell, 1968; Haralampides, 1978; Butterworth and Burton, 1980; Thienpont et al., 1981; Wilson-Hanson and Prescott, 1982; Fujinami et al., 1983; Santa Cruz and Lombardero, 1987; Raschka et al., 1994; Schuster et al., 1997; Dieffenbacher, 2007; Krone

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http://dx.doi.org/10.1016/j.vetpar.2014.02.038

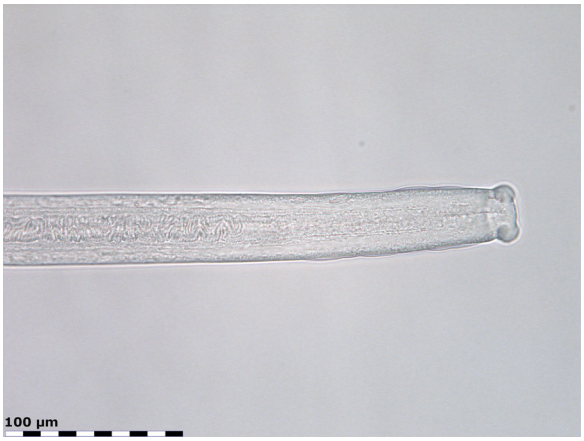

Fig. 1. Anterior extremity of a male *Capillaria plica*. ©Merial.

et al., 2008) and only recently through reports of clinical cases (Finnerup, 1986; Linden et al., 1986; Bédard et al., 2002; Dantas et al., 2008; Whitehead, 2009; Pagnoncelli et al., 2011; Rossi et al., 2011). The literature refers to three urinary capillarids occurring in cats: *Capillaria* (syn. *Pearsonema*) *feliscati*, *C.* (*P.*) *plica* and *C. travassoi*. It is, however, not clear whether those parasites are distinct species or just phenotypes of one species (Bowman et al., 2002).

Apart from anecdotal reports of disease outbreaks in farmed foxes (e.g., Volkmar, 1930; Schmid, 1934; Petrov and Borovkova, 1942), urinary capillarids reportedly cause little pathology with no pathological findings related to capillarid infections of the lower urinary tract in the majority of infected dogs and cats, presumably related to a low worm burden. However, published case reports on cats suggest an association of urinary capillariosis with clinical signs including abdominal pain, fever, urinary incontinence, dysuria, straining and cystitis requiring an appropriate symptomatic treatment but also the use of anthelmintics as causative treatment (Finnerup, 1986; Linden et al., 1986; Dantas et al., 2008; Whitehead, 2009; Pagnoncelli et al., 2011; Rossi et al., 2011).

As the treatment of urinary capillarid infection in cats was based previously only on reports published on the use of various anthelmintics in individual cases, the study reported here was conducted to evaluate the therapeutic efficacy of a novel topical combination formulation of fipronil 8.3% (w/v), (S)-methoprene 10% (w/v), eprinomectin 0.4% (w/v), and praziquantel 8.3% (w/v) (Broadline®,[1] Merial) against urinary capillarids in cats (Fig. 1).

2. Materials and methods

The study design was in accordance with the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) – GL7, "Efficacy of Anthelmintics: General Requirements" (Vercruysse et al., 2001), VICH GL20 "Efficacy of Anthelmintics: Specific Recommendations for Felines" (Vercruysse et al., 2002), and the "World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines for evaluating the efficacy of anthelmintics for dogs and cats" (Jacobs et al., 1994). The study was conducted in compliance to VICH GL9, entitled *Good Clinical Practice* and in compliance with local animal welfare legislation and was approved by an Independent Animal Care and Use Committee. All personnel involved in collecting efficacy and safety data were blinded to the treatment assigned to the animals.

2.1. Experimental animals

The study was conducted in Albania with 16 short haired cats. The cats weighed 1.6–3.6 kg prior to treatment (Day −3) and were approximately ten months to eight years old (Table 1). The animals were individually housed during the entire study and acclimated to the study facilities for seven days prior to treatment. The environmental conditions were identical for all animals in the study.

2.2. Selection of animals based on pre-treatment urine examination

The selection criterion for inclusion of cats in the study was the presence of a patent infection with urinary capillarids as confirmed by the demonstration of *Capillaria* eggs in urine samples collected during the acclimation period. Urine samples were collected from sedated cats five days prior to treatment by gentle bladder expression, and the urine sediment was examined microscopically for *Capillaria* eggs.

2.3. Experimental design

The study utilized a randomized block design based on pre-treatment body weight. Replicates of two cats each were formed sequentially based on decreasing pre-treatment body weights. Within replicates, cats were randomly allocated to treatments: one to the untreated (control) group and one to the group treated with Broadline®. The treatment was applied at the minimum therapeutic dose of 0.12 mL/kg body weight (fipronil [10 mg/kg], (S)-methoprene [12 mg/kg], eprinomectin [0.5 mg/kg], praziquantel [10 mg/kg]) directly on the skin in the midline of the neck, between the base of the skull and the shoulder blades in a single spot once on Day 0. All cats were observed hourly for four hours post-treatment and thereafter once daily until end of the study for health problems or adverse events. Fourteen days after treatment, all cats were humanely euthanized and necropsied, and the nematodes in the urinary bladder were counted.

2.4. Parasite recovery and count

Nematode counts were made on total urinary bladder contents, including parasites recovered from the epithelium of the bladder. The content of each urinary bladder

[1] Broadline® is a trademark of Merial; all other marks are the property of their respective owners.