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Small strongyle infection: Consequences of larvicidal treatment of horses with fenbendazole and moxidectin

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Abstract

The study was undertaken to evaluate adverse effects of larvicidal treatment in horses naturally infected with cyathostomins. Out of 24 ponies kept on pasture, four animals were housed in September and anthelmintically cured to serve as worm-free controls (group C-0). The others were housed in December. Eight animals each were treated 8 weeks later with 5 × 7.5 mg/kg fenbendazole (FBZ) or 1 × 0.4 mg/kg moxidectin (MOX). Four animals remained untreated (group C-i). Two, 4, 6 and 14 days after the end of treatment two animals of each of the treated groups were necropsied together with group C-0 and C-i animals. Infected animals before treatment showed weight loss, eosinophilia, increased plasma protein and globulin contents. Treatment was followed by weight gain and temporal plasma protein and globulin increase. Proportions of $CD4^+$ and $CD8^+$ T lymphocytes in the peripheral blood did not differ between the groups before treatment but dropped significantly temporally after FBZ treatment. Group C-0 was worm-free at necropsy. Group C-i animals contained variable numbers of luminal and tissue cyathostomins. Histological sections showed larval stages in the lamina propria und submucosa surrounded by macrophages. Either treatment was effective against luminal parasites and reduced the number of larvae in the bowel wall beginning 4–6 days after FBZ and 6–14 days after MOX treatment. Histologically, as a first reaction after FBZ application T lymphocytes accumulated around morphologically intact L4 in the submucosa. Subsequently T lymphocytes associated with eosinophils infiltrated the submucosa. Parasites became enclosed by granulomas with eosinophils adhering to and invading the larvae which started to disintegrate on day 4. Later on, particularly on day 14 inflammation extended into the mucosa and was frequently associated with ulcerations. Third stage larvae in general and L4 in the lamina propria, however, seemed not to be affected until day 14 and even then, parasites did usually not generate extensive inflammation. After MOX treatment severe morphologically detectable alterations of tissue larvae could not be observed earlier than day 14. Different from FBZ treatment, larvae disintegrated and were obviously resorbed without causing severe inflammation in the gut wall. In conclusion treatment with either drug was efficacious against tissue larvae of cyathostomins but there may be different clinical consequences: in contrast to

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MOX effects, killing of larvae due to FBZ was associated with severe tissue damage, which clinically may correspond to reactions caused by synchronous mass emergence of fourth stage larvae, i.e., may mimic larval cyathostominosis.

Keywords: Horse; Larval cyathostominosis; Larvicidal treatment; Adverse effects; Fenbendazole; Moxidectin; T lymphocytes; Histopathology

1. Introduction

Small strongyles were underestimated as pathogens of the horse for a long time but are meanwhile considered the most important helminths in equines. They represent a relatively heterogenous group of nematodes consisting of more than 50 species, the most important of them belonging to cyathostomins, a subfamily of Strongylidae (Lichtenfels et al., 1998). The pathogenic stages are the larvae which develop in the mucosa and submucosa of the large intestine. A particular pathogenic factor is a synchronous reactivation of hypobiotic larvae and a subsequent mass emergence of fourth stage larvae into the gut lumen, which may be initiated by a variety of epidemiological risk factors in late winter and spring (e.g., Giles et al., 1985; Lyons et al., 1994; Reid et al., 1995). It is associated with severe inflammation of the intestinal wall and extended mucosal lesions (Ogbourne, 1978; Murphy and Love, 1997). Consequences may be a massive loss of liquids and proteins into the gut and the entrance of bacterial enterotoxins into the tissue. The clinical picture of this ''larval cyathostominosis'' is highly variable and intra vitam diagnosis is often difficult (Giles et al., 1985; Lyons et al., 1994; Klei and French, 1998; Abbott, 1998). Chemotherapeutic measures are not always effective, particularly not in severe cases. Nevertheless drugs of choice are at present fenbendazole (FBZ: Klei et al., 1997; Di Pietro et al., 1992; Duncan et al., 1998) and moxidectin (MOX: Monahan et al., 1996; Eysker et al., 1997; Bauer et al., 1998; Bairden et al., 2001). However, there is an ongoing debate on the real benefit of such drug applications since it was reported in a number of cases that horses developed clinical symptoms of larval cyathostominosis within a short period of time after treatment. It was suggested that according with Gibson (1953) and Smith (1976) the treatment might result in reactivation of hypobiotic tissue stages of the parasites by removing adult parasites or killed larvae would induce heavy inflammation of the intestinal wall, both mimicing larval cyathostominosis (see Mair, 1993; Reilly et al., 1993; Reid et al., 1995; Murphy et al., 1997a,b). Up to date, however, there are no real proofs for these suggestions.

The present study aimed to analyse consequences of anthelmintic treatment in larval cyathostomin infections in detail. Naturally infected horses were examined before and after treatment with FBZ and MOX applying a variety of clinical-chemical and histopathological techniques. The study revealed evidence for tissue damage by degenerating larvae particularly after FBZ treatment and suggests differences in the immunological response after treatment with the two drugs.

2. Material and methods

2.1. Animals and treatment

Twenty-four ponies (12 males, 12 females; various breeds including mixed breeds) at an age of 6–9 months, which were supposed to be naturally infected with cyathostomins after paddock grazing were used in the study. The animals derived from various farms. Body weights of the animals ranged from 39 to 128 kg.

The animals were divided by chance into 10 groups: groups C-0 and C-i with 2 males and 2 females each, groups FBZ 2, FBZ 4, FBZ 6, FBZ 14 with 2 male animals each and groups MOX 2, MOX 4, MOX 6, MOX 14, each with 2 female animals.

Group C-0 was determined to serve as worm-free control. Animals were treated orally with 1 mg/kg ivermectin (Ivomec®, Merial) in early September, housed and treated 12 days later orally with 0.5 mg/kg MOX (Cydectin®, 0,1% suspension Fort Dodge). A third treatment with 20 mg/kg FBZ (Panacur® paste, Intervet) daily on five subsequent days started 2 days later.