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Short communication

Efficacy and persistent activity of moxidectin against natural *Muellerius capillaris* infection in goats and pathological consequences of muelleriosis

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ABSTRACT

The effect of moxidectin against natural *Muellerius capillaris* infection in goats was evaluated in this study. Long-acting moxidectin at a single dose of 1 mg kg^{-1} body weight was administered to an entire flock ($n = 10$) of goats. The individual faecal larval count reduction was applied as an indicator of treatment efficacy. A significant reduction (>98%) in larval counts was observed in all surveyed animals 14 days after drug administration. Moxidectin demonstrated persistent activity in this study; the mean faecal larval count reduction was 99.1% ± 1.8 on day 77 of the treatment. Macroscopic abnormalities and histological changes in the lungs of two infected goats were evident during the post-mortem examination. The pathological consequences of *M. capillaris* infection were observed even three months after parasite elimination. The results of this study indicate that moxidectin is a highly effective anthelmintic agent for the control of muelleriosis in goats. This drug provides animals with fifteen weeks of protections against *M. capillaris* reinfection.

1. Introduction

Muellerius capillaris is a cosmopolitan parasite of the lung parenchyma of domestic sheep, goats and many wild ruminants (Levine, 1980). The prevalence of this nematode is very high in grazing goats in many parts of the world. Muelleriosis in domestic small ruminants is often overlooked because this infection is usually asymptomatic or subclinical. However, goats are sensitive to *M. capillaris,* and this parasite is more pathogenic and persists longer in goats than in sheep. Decreasing productivity in goats could be considered a consequence of muelleriosis (Bliss and Greiner, 1985). Treatment of muelleriosis is complicated. Anthelmintic treatment reduces small lungworm fecundity; however, it does not eliminate all adult nematodes from the host. Benzimidazole drugs are only moderately effective against *M. capillaris* in goats (McCraw et al., 1981; Helle, 1986); even ivermectin is not fully effective in the treatment of muelleriosis (McCraw and Menzies, 1986, 1988). Geurden and Vercruysse (2007) reported the complete elimination of *M. capillaris* faecal larval counts in goats for a period of six weeks after the pour-on application of eprinomectin at the dose rate for cattle. Because the use of conventional anthelmintics in the treatment of muelleriosis in goats is not sufficiently effective in the long term and there is only limited information on this topic, the efficacy of a long-acting moxidectin formulation against natural muelleriosis was evaluated in the present study. Moxidectin has been shown to be highly effective against small lungworm infection in sheep (Papadopoulos et al., 2004). It is, however, unclear if its effect against *M. capillaris* would be similar in goats, since there is yet to be a study aimed at proving such an effect. The second objective of our survey was to assess the effect of *M. capillaris* on lung tissue after treatment.

2. Materials and methods

In July 2013, several animals from a goat flock, kept for demonstrational/educational purposes at the Czech University of Life Sciences Prague, displayed respiratory disease symptoms. A coprological examination revealed small lungworm infection in all goats of the flock. All of the adult (ten cross-breed) goats from the flock were incorporated into this study. Moxidectin (Cydectin 2% LA, Pfizer) was administered to the animals at the dosages for sheep (1 mg kg^{-1} body weight). Due to the extralabel use of moxidectin,

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adverse reactions in animals were monitored after the drug was administered. Individual faecal samples were taken rectally from all surveyed animals prior to the experiment (D0) and then weekly for 15 weeks (D105) after treatment. The Baermann technique according to McKenna (1999) was used to assess the number of larvae per gram (LPG) in faeces. First stage lungworm larvae were identified morphologically according to van Wyk and Mayhew (2013). Two of the examined goats, selected according to their pre- and post-treatment LPG levels, were slaughtered on day 105 post-treatment. The lungs were macroscopically examined for pathological abnormalities associated with small lungworm infections. Visible lung lesions were excised and processed for histopathological examination. The samples were processed using standard histological methods—they were embedded in paraffin blocks, cut into three to five μm-thick slices, mounted on glass slides and stained with haematoxylin-eosin.

Treatment efficacy was calculated as the individual faecal larval count reduction (FLCR), according to Chartier et al. (1995). Using the formula ((LPG D0 – LPG D7)/LPG D0) × 100, the reduction in larval shedding was expressed as the difference between larval counts before drug application (D0) and 7 days after treatment (D7). The FLCR for all other surveyed days was calculated in a similar way. There are no clearly defined guidelines regarding appropriate limits for determining particular drug efficacy against lungworms, based on FLCR. For this reason, we applied the reduction threshold (≥95%), recommended by the WAAVP (Coles et al., 1992), for anthelmintic drug efficacy against gastrointestinal nematodes based on faecal egg count reduction test. Data sets concerning LPG counts during particular sampling intervals (D0–D105) were tested for normal distribution using the Shapiro–Wilk test. Since normal distribution was not met, the non-parametric Wilcoxon signed rank test for related samples was applied to assess differences in larval excretion between D0 and each individual sampling day post-treatment (D7–D105). Differences were considered significant when the P value was <0.05. To eliminate individual animal effect, typical FLCR values were expressed as a mean in each sampling interval.

3. Results

M. capillaris was the only small lungworm species recovered from goat faeces. Pre-treatment larval count levels differed considerably between individual goats; LPG values ranged from 2.5 to 1143.5 (see Table 1). Adverse reaction to moxidectin were observed in 70% of goats; light neurological signs, such an apathy and a drowsiness, were evident. These signs disappeared within 24 h. *Muellerius* larval counts significantly ($P < 0.001$) decreased 14 days after treatment in all surveyed animals, regardless of the initial infection intensity (see Table 1). Faecal larval shedding was eliminated 21 and 28 days post-treatment in all goats. In general, high moxidectin efficacy (>98%) against muelleriosis was observed in all examined animals even two months after drug application. Larval count in goat no. 5 increased gradually from day 70, and drug efficacy failed 84 days post-treatment. In all other animals, moxidectin effectively reduced *M. capillaris* faecal larval shedding for the entire surveyed period.

Parasitic lesions were seen on the lungs of both slaughtered goats. Fully differentiated, clearly visible parasitic elements (eggs and larvae) were present (see Fig. 1) in all tissue samples obtained from the first slaughtered goat (no. 5). Slightly dilated alveoles (a certain number of which were almost completely collapsed), smooth muscle hypertrophy and thickened membranous pouches were also observed. All of the above described abnormalities were accompanied by sparse inflammatory cell reaction. Areas almost totally permeated with diffuse inflammatory cell infiltrate were observed in processed material from the second slaughtered goat (no. 7); several granulomatous deposits with central necrosis were also reported (see Fig. 2). The residual part of the lung tissue was infiltrated with blood and permeated with shapeless cells of a macrophagous character.

4. Discussion

Muelleriosis treatment efficacy can be affected for several reasons. *M. capillaris* in goat lung tissue has nodular localisation. These nodules are firm and resist structures which can eventually calcify. For this reason, anthelmintic drugs might not reach the full therapeutic effect for small lungworm elimination (Papadopoulos et al., 2004). The reappearance of small lungworm larvae in faeces may be caused by the development of arrested larvae that survived treatment. These larvae resumed development after the destruction of the original lungworm population (McCraw and Menzies, 1986).

Moxidectin is one of the most potent anthelmintic drugs that is also known for its persistent efficacy. A long-acting moxidectin formulation was especially shown to prevent the reinfection of sheep with gastrointestinal nematodes for several months (Balmer et al., 2015). This persistency is an important feature that contributed to the high moxidectin efficacy against muelleriosis observed in our study. *Muellerius* larvae (or adults) that were not targeted during the initial exposure to the drug were eventually eliminated thanks to moxidectin persistence.

Parasitic lung lesions and muelleriosis-related histological abnormalities associated with *M. capillaris* infection observed in our survey have also been generally described by other authors (Valero et al., 1992; Panayotova-Pencheva and Alexandrov, 2010). However, our study provides one interesting finding. Even though there were no parasititic elements evident in sections of the lungs belonging to the one goat with almost zero post-treatment larval

Table 1
The individual faecal larval counts (LPG) before treatment and the individual faecal larval count reduction (FLCR) at weekly intervals after moxidectin treatment. SD – standard deviation.

Animal No.	Pre-treatment LPG D0	Faecal larval count reduction														
		D7	D14	D21	D28	D35	D42	D49	D56	D63	D70	D77	D84	D91	D98	D105
1	230	92.7	99.9	100	100	99.9	99.9	100	100	99.9	100	100	100	99.9	100	100
2	32.2	60.6	100	100	100	100	99.7	99.1	100	100	99.8	100	100	100	100	100
3	6.2	100	100	100	100	91.1	100	92.4	100	98.5	100	100	100	100	100	100
4	91	27	100	100	100	99.8	100	100	99.8	100	100	100	100	100	100	100
5	1143.5	−81, 1	99.9	100	100	100	100	100	99.9	100	99.8	95.3	83.4	59.9	4.7	−55.7
6	73.8	98	100	100	100	100	100	99.7	100	99.9	99.9	100	99.2	95.3	93.1	96.3
7	966.3	83.8	99.9	100	100	99.9	100	100	100	100	100	100	100	100	99.9	99.9
8	2.5	−20	98.4	100	100	100	100	100	100	100	100	96.4	100	100	96.4	96.3
9	89.3	80.5	100	100	100	100	100	100	100	100	100	99.7	100	100	99.8	99.9
10	11.2	−75.9	100	100	100	99.1	100	100	100	100	97.4	100	100	100	100	100
Mean	264.6	36.5	99.8	100	100	98.9	99.9	99.1	99.9	99.9	99.7	99.1	98.3	95.5	89.4	83.7
SD	423.9	71.1	0.5	0	0	2.8	0.1	2.4	0.1	0.5	0.8	1.8	5.2	12.6	29.9	49.0