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Strategic control of gastrointestinal nematodes in grazing sheep with a long-acting moxidectin formulation

Nicole Balmer[a], Paul Torgerson[b], Hubertus Hertzberg[a,*]

[a] Institute of Parasitology, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 266a, 8057 Zurich, Switzerland
[b] Section of Epidemiology, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 270, 8057 Zurich, Switzerland

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ABSTRACT

A field study was undertaken on three Swiss sheep farms (A, B, C) to evaluate the efficacy of a long-acting moxidectin formulation (Cydectin® 2% LA) against gastrointestinal nematodes (GIN). Naturally infected ewes (all three farms) and their winter-borne lambs (farms A and B) were allocated to two groups (MOX, CON). At day 0 ewes of the MOX-groups were treated with 1 mg moxidectin s.c. CON- and MOX-groups were grazed on separate pastures and were sampled for faeces and blood at 28-day intervals. Larval cultures demonstrated that *Haemonchus contortus* was the dominant GIN-species in ewes throughout the season. Over the entire observation period faecal egg count (FEC) of the MOX-ewes in farms A, B, C was 56%, 84% and 87% less than the CON-ewes ($p < 0.05$). FEC of lambs grazing with MOX-ewes was reduced in farms A and B by 56% and 61%, respectively ($p < 0.05$), compared with the respective CON-groups. None of these lambs received anthelmintic treatment during the experiment. Therefore, the differences were due to an indirect effect mediated by the lower pasture contamination with GIN-larvae. These were reduced by 73%, 81% and 74% in farms A-C respectively compared to the CON-groups ($p < 0.05$). In farm B, where lambs remained with their mothers during the entire grazing season, these differences were also reflected by a higher daily weight gain ($p < 0.05$) and reduced pepsinogen levels in lambs of treated ewes. This strategy offers an interesting potential for expanding refugia by propagation of GIN in untreated lambs.

1. Introduction

In Switzerland, as elsewhere, infections with gastrointestinal nematodes (GIN) are regarded as high priority by sheep farmers. Virtually all farms are affected and the dominance of *Haemonchus contortus* prevailing in altitudes up to 1500 m may result in life-threatening disease in all age groups in the absence of adequate control measures. From May to September mean temperatures between 12 and 18 °C and average monthly rainfall of 99 mm provide favorable conditions for development and migration of infective larvae (O'Connor et al., 2006). Currently, helminth control is almost entirely dependent on the use of anthelmintics. Usually, ewes and their spring-born lambs graze together until late summer. Anthelmintic treatment is usually done either at fixed intervals, or when indicated by monitoring of bulk faecal samples. For sheep kept on community pastures on which regular access to the animals is often hampered there is an increasing demand by owners to perform parasite control by long acting anthelmintics. In contrast to cattle, formulations providing a season-wide protection were not available for sheep in Europe until recently. Worldwide, only few long-acting products are registered for sheep. These include a controlled-release albendazole capsule (Proftil-Captec, Merial) (Bell and Thomas, 1992; Munyua

* Corresponding author. Tel.: +41 44 635 85 16; fax: +41 44 635 89 07.
E-mail address: hubertus.hertzberg@access.uzh.ch (H. Hertzberg).

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et al., 1997) or an ivermectin capsule (IVOMEC maximize, Merial) (Gogolewski et al., 1997; Rehbein et al., 1998). Product indications suggests a protection of sheep for 100 days from reinfection with gastrointestinal helminths (Bell and Thomas, 1992; Rehbein et al., 1998) and are supposed to be a highly effective method of seasonal parasite control. However, the use of these products is limited to Australia and New Zealand and many farmers are reluctant to use intraruminal capsules because of the risk of injury by poor administration techniques (Macrae et al., 2003; Harwood and Hepple, 2011). The easy to handle pour-on formulations are not suitable for sheep as wool and skin surfaces are coated with a lipophilic emulsion of sweat and sebum. This layer can act as a solvent for chemicals and therefore diffusion of a drug within the emulsion competes with the absorption into the skin and thus limits the systemic availability (Pitman and Rostas, 1981; Rehbein, 1993; Magnusson et al., 2001; Baynes, 2004; Monteiro-Riviere et al., 2008). For these reasons an injectable long-acting anthelmintic is desirable. Injectable ivermectin has a persistent activity for up to 10 days against reinfection with *H. contortus* at a dosage of 0.2 mg/kg (Borgsteede, 1993). Likewise, moxidectin at a dosage of 0.2 mg/kg protects for up to 35 days from a reinfection with *H. contortus* and *Teladorsagia circumcincta* and 21 days from *Trichostrongylus colubriformis* (Kerboeuf et al., 1995). Recently, a new injectable long-acting formulation of moxidectin (Cydectin 2% LA, Zoetis, Switzerland) was introduced to the market for meat sheep. For Switzerland, the manufacturer is claiming a persistent activity against reinfection with *H. contortus*, *T. circumcincta* and *T. colubriformis* for 111, 97 and 44 days, respectively. The aim of the present study was to evaluate the efficacy of a single administration of moxidectin at a dose rate of 1 mg/kg during one grazing season in three sheep farms in the Swiss midland region. In two of these farms, it was investigated if treatment of the ewes may also provide indirect protection of the untreated lambs. Furthermore, lambs could serve to maintain refugia (van Wyk, 2001) and mitigate the expansion of resistant populations given that the resistance level is still low.

2. Materials and methods

2.1. Experimental design

The study was conducted on three privately owned farms in the Swiss midland region during the 2011 grazing season. Key data of the different sites are summarized in Table 1. All ewes had been naturally infected with helminths during the previous year and all farms were free from *F. hepatica*. On day 0, the adult sheep were randomly divided into two similar groups, in farm A and B based on the number of their winter-born lambs. Sheep in Farm C are neither lactating nor pregnant on day 0. Moxidectin (Cydectin 2% LA, Zoetis Switzerland) was administered subcutaneously at the base of the left ear according to the manufacturer's recommendations to the adult sheep of one group on each farm (MOX-A, MOX-B, MOX-C) at a dose rate of 1.0 mg/kg BW. Ewes of the control groups (CON-A, CON-B, CON-C) and all lambs remained untreated. On the following days, the injection site was investigated by the owner for observation of side effects. On each farm several smaller pastures were included in the trial. Each pasture was divided into two equal paddocks, on which the groups grazed separately at equal stocking rates. Sheep were rotated between the pastures according to the same schedule for both groups and did not receive any supplement. All pastures had been grazed by sheep the previous year. Because of dry weather conditions in the early season, all groups were offered a similar portion of additional grazing area in June, which previously had been used for hay. According to the owners' management, lambs on farms A and B were excluded from the trial at 2–3 months of age for final indoor fattening with the exception of six lambs per group at farm A which remained in the trial to assess the indirect effect of moxidectin application to the adults on their offspring. In farms A and C, rams were kept together with the ewes to maintain breeding activities in the flocks from day 0 onwards, whereas the ram in farm B was integrated at the beginning of August. The rams in farms A and B were moved several times between the groups and were therefore kept under repeated dosing with moxidectin LA. Additionally, the absence of helminth egg shedding was controlled at monthly intervals. Parasitological data of the rams in farms A and B were not included in any analysis. To simplify description of the results, adult sheep in farm C are also referred to as ewes despite the included rams. One adult MOX-sheep of Farm A died in September, due to unknown reason, not related to parasitic infection. One CON-lamb of farm B disappeared at the end of June and was possibly killed by foxes. At the end of September, one clinical healthy ewe of the treated group on site C had to be removed due to misbehaviour (constant bleating) which was not accepted by the community living close to the pastures.

2.2. Samplings and measurements

All animals were examined and sampled on day 0 and then at 4-weekly intervals. The sheep were clinically examined including an assessment of the color of the eye mucosa using the FAMACHA system (van Wyk and Bath, 2002) to determine the level of anaemia. The live weight of lambs at every other sampling date was recorded. Blood samples were taken from the jugular vein for determining the packed cell volume (PCV) in all animals and pepsinogen was additionally recorded in lambs according to the method of Berghen et al. (1987). Faecal samples, directly collected from the rectum, were scored for consistency (1: watery diarrhoea; 5: well-formed dry faeces) and numbers of helminth eggs were determined quantitatively using a modified McMaster-technique (Schmidt, 1971) with a sensitivity of 50 eggs per gram (epg). Eggs other than strongyles were counted separately. Blood and faecal samples were chilled during transport and stored at 4 °C prior to processing. Third-stage larvae were cultured for each group separately according to Eckert (1960) and differentiated according to the MAFF guidelines (Ministry of Agriculture, 1986).

Table 1
Basic data on location, animals and treatments in the three experimental flocks.

	Farm A	Farm B	Farm C
Geographic latitude and longitude	47°53′N/8°22′E	47°46′N/8°25′E	47°39′N/8°85′E
Height above sea level (m)	370	470	593
Sheep breed	Mixed meat breeds	Shropshire	Swiss White Alpine
Trial period	12 April–22 November	14 April–24 November	26 April–1 November
Date of administration of moxidectin LA	12 April	14 April	26 April
Number of ewes	10[a]/10[b]	7[a]/8[b]	11[a]/11[b]
Number of lambs	10[a]/8[b] (6[a]/6[b])[c]	(9[a]/6[b])[d]	–
Number of paddocks per group	8	4	4

[a] MOX group.
[b] CON group.
[c] Number of lambs remaining in the trial until the end (in brackets, only farm A).
[d] Lambs remained in the trial for only 3 months.