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Decreased strongyle egg re-appearance period after treatment with ivermectin and moxidectin in horses in Belgium, Italy and The Netherlands

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ABSTRACT

The objective of the present study was to evaluate the efficacy of an oral treatment with ivermectin (IVM) or moxidectin (MOX) against gastro-intestinal strongyles in naturally infected horses by performing a faecal egg count reduction test (FECRT) and by monitoring the egg reappearance period (ERP) after treatment. Therefore, a field efficacy study with a randomised complete block design for each study site was conducted, with the individual animal as the experimental unit. At least 10 study sites in Italy, Belgium and The Netherlands were selected and animals were allocated to one of the two treatment groups based on the pre-treatment faecal egg counts (FEC). Animals were treated on Day 0 with an oral paste containing either IVM (at 0.2 mg/kg bodyweight) or MOX (at 0.4 mg/kg bodyweight). After treatment, faecal samples were collected at least every fortnight during 56 days after treatment with IVM and during 84 days after MOX treatment. In total, 320 horses on 32 farms were examined. The FECRT on Day 14 indicated a 100% efficacy in 59 of the 64 treatment groups and >92% efficacy in the remaining 5 groups. The ERP was decreased for at least one of the anthelmintics on 17 out of 32 study sites (15 sites or 47% for MOX and 17sites or 53% for IVM) and on 9 sites (28%) the ERP was decreased for both anthelmintics. On some of these study sites the efficacy declined at the end of the expected ERP, often with good efficacy 2 weeks earlier. Nevertheless, on 1, 3 and 5 study sites in Italy, Belgium and The Netherlands respectively, an efficacy below 90% for IVM and MOX was identified as soon as Day 42 or Day 56. In The Netherlands, the efficacy of IVM was below 90% from Day 28 or Day 35 after treatment on 1 site each. The present study reports a high efficacy of MOX and IVM in a FECRT 14 days after treatment, yet does indicate a shortened ERP for these treatments in more than half of the selected study sites.

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1. Introduction

Small strongyles or Cyathostominae are ubiquitous parasites of grazing horses. Treating these parasitic nematodes is often required to avoid health or animal welfare issues. Several anthelmintics are commercially available to control these infections. The ease of use and the over-the-counter availability of cheap formulations have led to a worm management practice in which whole herd treatments are preferred over targeted treatments (van Doorn et al., 2012a; Relf et al., 2012). Whole herd or blanket treatments and treating more frequently than required are considered to contribute to the development of anthelmintic resistance (AR), as these treatment regimes reduce the refugia with susceptible isolates. Furthermore, other management practices contribute to the spread of resistance genes: for instance, more than half of the horse establishments in the UK receive visiting horses and, of these horses, 3 out of 4 are actually dewormed prior to integration (Relf et al., 2012). As a result, AR in horse Cyathostominae has been reported worldwide for benzimidazoles and to a lesser extent for pyrantel. Recent studies on the efficacy of ivermectin (IVM) and moxidectin (MOX) seem to indicate that both anthelmintics are still effective against small strongyles, although treatment failures are reported in a limited number of yards and a limited number of animals (Canever et al., 2013; Lester et al., 2013; Slocombe et al., 2008; Stratford et al., 2013; Traversa et al., 2007, 2009, 2012). The treatment efficacy in most studies is evaluated shortly after treatment (10–21 days), and might underestimate a potential reduction in anthelmintic efficacy. As demonstrated by Lyons et al. (2011) and Lyons and Tolliver (2013), reduced activity of IVM and MOX is initially apparent from a shortened egg reappearance period (ERP) after treatment, and not necessarily from a reduced efficacy within 2–3 weeks after treatment. In several studies with IVM in Kentucky (US), the shortened ERP has been related to the low efficacy of treatment against immature small strongyles. This leads to incomplete elimination of cyathostomins in the intestinal lumen or to a reduced time for maturation of the parasite, and hence to a shorter ERP (Lyons et al., 2011; Lyons and Tolliver, 2013). These data suggest that the efficacy of treatment with IVM and MOX is preferably evaluated on a regular basis and over a prolonged period after treatment. Therefore, the objective of the present study was to evaluate the efficacy of oral treatment by faecal examinations up to 56 days for IVM and 84 days for MOX in Italy, Belgium and The Netherlands.

2. Materials and methods

2.1. Study design

This study was designed as a field efficacy study in horses naturally infected with strongyles. Study sites were selected based on the history of deworming management in the previous years: all study sites had followed a strategy with either regular (at least twice a year) to frequent deworming (more than twice a year). In the three countries, study sites of different sizes were included as well as horses of all ages, with no difference in management or population between countries. The assessment of efficacy was based on individual faecal egg counts (FEC) before and at defined time points after treatment. The study used a randomised complete block design for each study site, with the individual animal as the experimental unit. The available animals were allocated to blocks of 2 animals defined by the pre-treatment strongyle FEC. The mean pre-treatment FEC was targeted to be above 150 eggs per gram of faeces (epg), with a minimum of 100 epg. Within each block, animals were randomly allocated to one of the treatment groups. The horses were either treated with ivermectin (IVM: Eqvalan®oral paste, Merial at 0.2 mg/kg bodyweight) or moxidectin (MOX: Equest® oral gel, Zoetis; at 0.4 mg/kg bodyweight).

Treatment was administered on Day 0. Animals were identified using an electronic chip, and the weight was estimated using a girth tape. Any misdosing was recorded. All test animals were observed for the duration of the treatments until at least 30 min after the last animal was treated. Any abnormal health was recorded.

The diagnostic technique used to monitor the faecal egg excretion was a modified McMaster technique (MAFF, 1986), with a sensitivity of 25 epg. Laboratory personnel involved in FECs were masked to the allocation of animals to treatment groups. From the animals allocated to the IVM group and the MOX group, faecal samples were collected on Days 14 (except BE03), 28, 42 and 56. For the MOX treated animals, additional samples were collected on Days 70 and 84. In The Netherlands, FEC were also performed on Days 21 and 35.

2.2. Statistical analysis

The primary outcome measure in this study was the evaluation of the length of the ERP. The ERP was evaluated as suggested in Larsen et al., 2011 and was defined as the time between treatment and the first breaching of a 90% efficacy threshold, based on the group arithmetic mean FEC. As there is no clear consensus on a ERP definition, we chose this method as we agree with the rationale as outlined in Larsen et al. (2011). We did not aim to evaluate the pro and cons of the different definitions of ERP within the framework of this study. The expected ERP was 56 days for IVM and 84 days for MOX, as indicated on the product label.

The secondary outcome measure was the percentage reduction in the arithmetic mean strongyle FEC on Day 14 (after) relative to Day 0 (before): $(FEC_{D0} - FEC_{D14})/FEC_{D0}$. A 95% confidence interval (CI) around the efficacy was calculated using bootstrap analysis. Anthelmintic efficacy was defined as in Coles et al. (1992) and advocated by von Samson-Himmelstjerna (2012): a reduction in FEC ≥ 95% with the lower 95% CI >90% was considered as efficacious. AR was present if (1) the percentage reduction in FEC was ≤95% and (2) the lower 95% confidence interval (CI) was ≤90%. Suspected anthelmintic resistance (SAR) was present if (1) the percentage reduction in FEC was ≤95% or (2) the lower 95% CI was ≤90%.