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Efficacy of oral, injectable and pour-on formulations of moxidectin against gastrointestinal nematodes in cattle in New Zealand

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ABSTRACT

The efficacy of moxidectin administered by different routes, against naturally acquired infections of gastrointestinal nematode parasites of cattle, was compared using faecal egg count reduction tests on 14 commercial farms throughout New Zealand. On each farm, groups of 15 calves were sampled for faecal nematode egg count and then treated with ivermectin administered orally, or with moxidectin administered either by the oral, subcutaneous injection or topical (pour-on) route. Samples were again collected 14 days after treatment and efficacy was calculated as the percentage reduction in-group mean egg count between the pre- and post-treatment samples. In addition, efficacy was calculated for individual animals, in order to compare the variability of the different treatments. On four farms untreated control groups were run and five animals from each of the control and all of the moxidectin-treated groups were bled over time to estimate plasma–moxidectin concentrations.

Averaged across all tests, the reduction in faecal egg count was significantly greater after treatment with moxidectin oral (91.1%) than following treatment with moxidectin injection (55.5%) or with moxidectin pour-on (51.3%). Low efficacies were invariably against *Cooperia oncophora*. The oral treatments were significantly less variable in efficacy than the injection and pour-on treatments. Moxidectin concentrations in plasma were highest following subcutaneous injection and lowest following pour-on administration. Plasma levels following oral administration were intermediate, being significantly lower than post-injection and significantly higher than post-pour-on. There was no evidence of transfer of moxidectin to untreated animals through licking. Based on these results, along with those of other studies, it is proposed that oral administration of macrocyclic lactone anthelmintics results in higher concentrations of active reaching the target worms in the gastrointestinal tract than following either administration by injection or by pour-on.

1. Introduction

Anthelmintic resistance in gastrointestinal nematode parasites of sheep is recognized as a significant problem in many parts of the world (Besier, 2007) and its management has been the subject of a significant amount of research over the last three decades (Leathwick et al., 2009). In contrast, resistance in those nematode species which infect cattle has received relatively little attention. The number of documented cases of anthelmintic resistance in cattle parasites is far fewer than those reported in sheep parasites, although it is not clear to what extent this reflects a lack of testing (Sutherland and Leathwick, 2011). Nevertheless, resistance has been confirmed in all the major nematode species characteristic of cattle and to each of the three currently available broad spectrum classes of anthelmintic (i.e. the macrocyclic lactone (ML), benzimidazole (BZ) and imidazothiazole (IM) classes), so there is no reason to expect

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that resistance will not eventually become widespread in cattle (Sutherland and Leathwick, 2011).

A survey of anthelmintic resistance on beef cattle farms in the North Island of New Zealand in 2004–2005 (Waghorn et al., 2006) indicated that resistance to the ML and BZ classes of anthelmintic was present on 92% and 76% of farms, respectively. Despite this very high prevalence of resistance many New Zealand farmers have not considered anthelmintic resistance to be an issue on their farm (Jackson et al., 2006), and many continue to use single-active ML anthelmintics, as opposed to combination products containing an ML and IM or an ML, IM and BZ. In addition to using single-active ML products most New Zealand farmers have shown a strong preference for the use of pour-on formulations.

However, the ability of pour-on formulations to reliably deliver accurate doses of anthelmintic has been questioned; principally due to the role of licking in drug intake (Laffont et al., 2003; Bousquet-Mélou et al., 2004, 2011; Sallovitz et al., 2005) and the effect of weather conditions on product performance (Forsyth et al., 1983; Sargent et al., 2009). Further, both pour-on and injectable formulations result in declining drug profiles which, although permitting claims of extended efficacy against ingested larvae (Williams et al., 1999; Vercruysse et al., 2000), also have the potential to allow drug-resistant but not drug-susceptible larvae to establish (Sutherland and Leathwick, 2011). All these factors have the potential to result in periods of discriminating dosage, thereby selecting for anthelmintic resistance (Bousquet-Mélou et al., 2004).

The current study was conducted to compare the efficacy of a single ML active (moxidectin) when it was administered by different routes, against naturally acquired nematode infections in cattle, in an attempt to gain insights into the possible role of route of administration on overall performance and potential to select for anthelmintic resistance.

2. Materials and methods

A standardized faecal egg count reduction test (FECRT), following the guidelines of Coles et al. (2006), was conducted on each of 14 commercial farms. The test protocol compared the efficacy of moxidectin when administered orally, by subcutaneous (sc) injection and as a pour-on. Because of the high prevalence of ML-resistance in cattle parasites in New Zealand, and the fact that the resistance status of nematodes on the different farms involved in the study was likely to be integral to the interpretation of the results, an additional experimental treatment with oral ivermectin was included. This was equivalent to the treatment used to test for ML-resistance in the survey of Waghorn et al. (2006) and was included so that the ML-resistance status of each farm could be categorized independently of the treatments under comparison.

2.1. Farms

Farms were selected for inclusion in the study primarily on the willingness of the farmer to be involved, although farms which did not have facilities for weighing and handling cattle were excluded. Candidate farms were identified through veterinarians or farm advisors, although a subset of those chosen were part of a large corporate farming business which identified willing farm managers through their internal channels. No attempt was made to select farms on the basis of the known presence or absence of anthelmintic resistance and in fact only one of the farms had previously conducted any kind of anthelmintic efficacy test in cattle. Farms were located throughout New Zealand although the majority were in the lower North Island.

Farms were of two basic types:

1. Dairy heifer replacement or dairy beef operations. Calves were sourced from dairy farms and were reared off their mothers, on milk and meal, until weaning in early summer (December–January) after which they were reared solely on pasture. Breeds were predominantly Friesian or Friesian-cross and trials on these farms occurred over summer (December 2010–February 2011).
2. Beef cow-calf operations on which calves were reared on their mothers until weaning in autumn (April–May) after which they were reared solely on pasture. These breeds were predominantly Angus or Hereford and trials on these farms occurred in autumn–winter (April–July 2011).

2.2. Test protocol

Where possible the tests were conducted on calves at the time of their first scheduled anthelmintic treatment, usually at or soon after weaning time. This was an effort to prevent pre-selection of the nematode population by a previous treatment, which if it was less than fully effective would allow an accumulation of resistant genotypes and potentially bias the test result. Where treatment of calves was deemed necessary by the farmer before the commencement of the test, every effort was made to ensure that the product used was highly effective (e.g. a combination product containing multiple actives). Prior to the commencement of each test, random sets of approximately 10 faecal samples were collected and analysed for faecal nematode egg count (FEC) to ensure that worm egg counts were sufficiently high for the test to proceed (i.e. a mean >250 epg with no zero values). If the mean FEC was <250 epg the test was delayed and the animals remained untreated until a FEC test indicated that the study could proceed.

On 8 of the farms, animals were randomly allocated to treatment group, prior to the first visit, based on liveweights supplied by the farmer. On the remaining 6 farms animals were allocated to treatment group on the day of treatment by drawing tag numbers out of a box. All animals were then weighed using a Tru-Test® load-bar scale and a faecal sample collected for FEC, before animals were treated with their allocated treatment.

The basic protocol involved four treatment groups, each of 15 calves, with no untreated control group due to the reluctance of commercial farmers to leave parasitized animals untreated. Animals with zero egg count on the day of treatment were subsequently removed from the trials. Treatments compared in all trials were, (i) ivermectin