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Patterns of faecal nematode egg shedding after treatment of sheep with a long-acting formulation of moxidectin

James Patrick Crilly, Amy Jennings, Neil Sargison*

Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush, Roslin, Midlothian EH25 9RG, UK

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ABSTRACT

Much of the current information on the effects of long-acting anthelmintics on nematode populations derives either from research farms or mathematical models. A survey was performed with the aim of establishing how moxidectin is currently being used on sheep farms in the south-east of Scotland. A study was undertaken on a subsection of the surveyed farms to examine the effects of long-acting moxidectin treatments in both spring and autumn on faecal nematode egg output. The survey showed that whole flock treatments of injectable 2% moxidectin were used to control sheep scab on 21% of farms. Injectable 2% moxidectin and oral moxidectin were used to control the periparturient rise in faecal nematode egg shedding by ewes on 13% and 55% of farms respectively. The effects of injectable 2% moxidectin treatment on faecal nematode egg shedding post-treatment in both the autumn and spring were investigated by faecal nematode egg counts at the time of treatment and at 2-weekly interval thereafter on eight and six farms in the autumn and spring, respectively. Faecal egg shedding recommenced at 8 weeks (autumn) and 4 weeks (spring) post-treatment. Counts increased to a peak and then declined. The mean (95% confidence interval) peak counts post-treatment were 2.8 (0.6, 5.1), 3.6 (1.7, 5.5) and 53.5 (25.1, 82.0) eggs per gram (EPG) for autumn-treated ewes, autumn-treated lambs and spring-treated ewes respectively. The spring treated sheep showed a statistically significantly earlier return to faecal egg shedding ($p = 0.0125$, $p = 0.0342$) compared to both other groups, statistically significantly higher peak in egg counts than the autumn treated sheep ($p < 0.001$) and a statistically significantly longer period of positive egg counts ($p = 0.0148$). There was no statistically significant difference in the timing of the peak FECs between autumn and spring ($p = 0.211$). The FECs of all groups of sheep treated with an injectable long-acting formulation of moxidectin became positive earlier than would be expected from the period of persistence given on the datasheet, but post-treatment FECs were very low compared to pre-treatment counts.

1. Introduction

Moxidectin is a highly lipophilic macrocyclic lactone endectocide. It is many times more efficacious than ivermectin against ovine gastrointestinal nematodes, being effective against ivermectin resistant strains of *Haemonchus contortus* and *Trichostrongylus colubriformis* (Pankavich et al., 1992; Gopal et al., 2001) and also has a prolonged residence time (Alvinerie et al., 1998). Moxidectin is licensed for use in sheep in the UK as an oral drench formulation, a 1% subcutaneous injection and a 2% long-acting injectable formulation given subcutaneously at the base of the ear.

Injectable formulations of moxidectin have found favour with farmers for control of sheep scab due to their efficacy against *Psoroptes ovis* and convenience of use. Their persistent activity prevents re-infection and negates the need for repeat treatments (O'Brien et al., 1996; Williams and Parker, 1996). Treatments are administered to all the sheep on the farm, usually in the autumn (Lewis, 2013). The persistent action of oral moxidectin is widely exploited to suppress the periparturient rise (PPR) in faecal nematode egg output in ewes. Injectable formulations of moxidectin are used less frequently in this manner but have been shown to both delay the return to egg shedding relative to oral moxidectin and to reduce the total number of eggs shed by treated ewes, thus reducing the challenge to lambs (Kerboeuf et al., 1995; Sargison et al., 2012).

There have been relatively few studies which have examined the effect of moxidectin on the faecal nematode egg output of treated sheep under UK conditions (Taylor et al., 1993; Sargison et al., 2002, 2012). The effects of long-acting anthelmintics on faecal

* Corresponding author at: Farm Animal Practice, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush, Roslin, Midlothian EH25 9RG, UK.
E-mail addresses: jcrilly@ed.ac.uk (J.P. Crilly), amy.jennings@ed.ac.uk (A. Jennings), neil.sargison@ed.ac.uk (N. Sargison).

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nematode egg output are of interest, both because increased pasture contamination can increase the nematode challenge to growing lambs with significant impacts on growth rates (Coop et al., 1982), and because of the potential prolonged advantage afforded to less susceptible nematodes. The latter has led to concerns that use of long-acting moxidectin may change the species balance within the gastrointestinal nematode population and might afford a selective advantage to certain nematodes, including those with alleles conferring anthelmintic resistance (Le Jambre et al., 1999; Smith et al., 1999; Barnes et al., 2001; Sutherland et al., 2002; Sargison et al., 2005; Lawrence et al., 2006; Waghorn et al., 2008; Falzon et al., 2014).

As much of the current information on the effects of long-acting anthelmintics on nematode populations derives from studies on research farms (Taylor et al., 1997; Le Jambre et al., 1999; Barnes et al., 2001; Sutherland et al., 2002; Leathwick et al., 2006; Papadopoulos et al., 2009; Sargison et al., 2012) and mathematical models (Dobson et al., 1996; Le Jambre et al., 1999; Smith et al., 1999), a study was therefore performed to examine the effects of long-acting moxidectin treatments, used for the control of sheep scab in ewes and lambs and for the control of the peri-parturient rise in ewes, on faecal nematode egg output during the period of drug persistence.

2. Materials and methods

2.1. Telephone survey of moxidectin use

A telephone survey was performed over a period of six weeks of all known sheep-farming clients (57) of the Royal (Dick) School of Veterinary Studies Farm Animal Practice who had been clients longer than six months. This was first performed to inform the choice of study farms and to aid in the interpretation of the findings. Those who responded ($n = 38$) were asked if they currently (within the past production cycle) performed whole flock treatments for the control of sheep scab and which method was used. They were also asked if they currently used moxidectin in periparturient ewes and if so which formulation. Any other routine use of moxidectin was also recorded. Where moxidectin was used ($n = 32$) clients were asked how long they had been using the product in this manner.

2.2. Study of the effects of treatment with injectable 2% moxidectin on the faecal nematode egg output of sheep

2.2.1. Selection of study farms

Clients using injectable long acting moxidectin flock treatments in the autumn as a sheep scab control measure (autumn treatment farms) and using moxidectin in the spring for treatment of periparturient ewes (spring treatment farms) were asked to participate in the study. Nine and five farmer clients agreed to participate in the autumn and spring studies respectively. One farm utilised whole flock long-acting injectable moxidectin for the control of sheep scab but due to management reasons treatment was delayed until late January, as such the results were included in the spring study rather than the autumn study.

2.2.2. Selection of study animals

The participating farmers and shepherds were asked to present 10 ewes (4 autumn treatment farms), 10 lambs (2 autumn treatment farms), 10 ewes and 10 lambs (2 autumn treatment farms), as determined by whether these groups of animals were present on farm and routinely included in the whole flock sheep scab control treatment, or 10 twin-bearing ewes as determined by routine ultrasound pregnancy diagnosis (all spring treatment farms). True randomisation was not feasible but instructions were given not to specifically select animals for treatment. No control animals were included in this study. Other animals in the flock were treated by the farmer according to the normal protocols on the farm. No farm was included in both the spring and autumn study periods.

2.2.3. Sample collection and parasitological methods

All selected animals were treated by the investigators with a 2% long-acting injectable formulation of moxidectin (Cydectin 2%, w/v LA injection for sheep; Zoetis) at a dose rate of 1 mg/kg in accordance with the datasheet recommendations. All of the lambs and two groups of ewes (those from farms where both ewes and lambs were included in the study) were dosed for measured bodyweight. All remaining sheep were dosed for the estimated weight of the heaviest animal in the group. The study animals were spray-marked, ear tag numbers recorded and faecal sampled directly from the rectum into individually labelled containers. The study animals were then re-sampled in a similar fashion 10–14 days later and then at approximately fortnightly intervals throughout a period of 18–20 weeks. The samples were refrigerated at 4 °C and individual faecal trichostrongyle egg counts (FECs) were performed within 48 h. FECs were performed using a saturated saline flotation method using a cuvette, with a potential sensitivity of 1 egg per gram (epg) (Christie and Jackson, 1982). Throughout the period of the study all sheep remained on pasture which had been grazed by sheep within the previous year, with the exception of two groups of autumn lambs, one of which moved onto turnips and the other was housed between the penultimate and last sampling session. Movement of sheep between individual fields occurred as dictated by the management considerations of the individual farms.

2.3. Data analysis

Results were recorded in Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA). Calculation of percentage reduction in FEC and 95% confidence intervals in accordance with World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines (Coles et al., 1992) were also performed in this programme.

Data were placed into three groups for statistical analysis. All study ewes treated in the autumn were classified as "autumn ewes (AE)", all study lambs treated in the autumn as "autumn lambs (AL)" and all ewes treated in the spring as "spring ewes (SE)". The individual FEC values for each group (AE, AL & SE) at a given post-treatment interval were tested for normality using an Anderson–Darling test. In order to control for the effect of "farm", the farm was treated as the experimental unit, the values for each farm being the arithmetic mean egg count at each time period (further information on data management is given in Appendix 1). As all data sets were non-normally distributed, data were compared using a Kruskal–Wallis test. Where statistically significant differences were found pairwise post hoc comparisons were performed using a Mann–Whitney U test. Chi-squared tests were used to compare the categorical data sets generated by the telephone survey, 2-sample t-tests were used to compare the parametric data from this survey. Minitab 17 Statistical Software (Minitab Inc. State College, PA, USA) was used to perform each of these tests. In all cases $p < 0.05$ was taken to indicate statistical significance. Commencement of faecal shedding on a group level was determined by the first occurrence of a positive egg count in any ewe within a group which had had previously negative egg counts.

3. Results

3.1. Survey results

Thirty-eight sheep clients, representing over 26,000 ewes, responded to the survey (66% response rate). Flock size varied from