Veterinary Parasitology 189 (2012) 308–316

Contents lists available at SciVerse ScienceDirect

Veterinary Parasitology

journal homepage: www.elsevier.com/locate/vetpar

The efficacy of a combined oral formulation of derquantel–abamectin against anthelmintic resistant gastro-intestinal nematodes of sheep in the UK

Thomas Geurden[a,*], Andrew Hodge[b], Laura Noé[a], Dana Winstanley[a], David J. Bartley[c], Mike Taylor[d,1], Colin Morgan[d], Sarah J. Fraser[e], Steven Maeder[b], David Bartram[f]

[a] *Pfizer Animal Health, Veterinary Medicine Research and Development, Hoge Wei 10, 1930 Zaventem, Belgium*
[b] *Pfizer Animal Health, Veterinary Medicine Research and Development, 45 Poplar Road, Parkville, 3052 Victoria, Australia*
[c] *Moredun Research Institute, Pentlands Science Park, Bush Loan, Penicuik, Midlothian EH26 OPZ, UK*
[d] *Food and Environment Research Agency, Sand Hutton, York YO41 1LZ, UK*
[e] *Moredun Scientific Ltd, Pentlands Science Park, Bush Loan, Penicuik, Midlothian EH26 OPZ, UK*
[f] *Pfizer Animal Health, 23/25 avenue du Docteur Lannelongue, 75668 Paris Cedex 14, France*

ARTICLE INFO

Article history:
Received 30 January 2012
Received in revised form 3 April 2012
Accepted 4 April 2012

Keywords:
Anthelmintic resistance
Derquantel
Abamectin
Moxidectin
Teladorsagia circumcincta
Nematode

ABSTRACT

The objective of the present studies was to evaluate the efficacy of a combined formulation (Startect® Dual Active Oral Solution for Sheep, Pfizer Animal Health) of derquantel (DQL) and abamectin (ABA) for the treatment of: (1) sheep experimentally infected with a moxidectin (MOX)-resistant isolate of *Teladorsagia circumcincta*, and (2) multi-drug resistant gastrointestinal nematode parasites under UK field conditions. In the first study, a total of 40 animals were allocated into 4 treatment groups, and were either left untreated or treated with DQL + ABA, MOX or ABA. Faecal samples were collected on days 1–5 and on day 7 after treatment to examine the reduction in faecal egg excretion and to evaluate the egg viability. On day 14 post treatment all animals were euthanised for abomasal worm counts. There was a 100% reduction in geometric mean worm counts for the DQL + ABA treated animals compared to the untreated control animals ($P < 0.0001$), whereas the percentage reduction in worm counts for the MOX- ($P > 0.05$) and ABA-treated ($P = 0.0004$) animals was 12.4% and 71.8%, respectively. The data from the egg hatch assay (EHA) indicated that in the MOX-treated and the ABA-treated animals, the majority of the eggs hatched after treatment. In the field study, performed on four farms, animals were allocated into 6 groups of 11–15 animals each in order to conduct a faecal egg count reduction test (FECRT), based on arithmetic mean egg counts. One group of animals remained untreated, whereas the other animals were treated with DQL + ABA, MOX, fenbendazole (FBZ), levamisole (LV) or ivermectin (IVM). On each of the farms the reduction in egg excretion after treatment with FBZ, LV or IVM was below 95.0%, indicating anthelmintic resistance. The efficacy of DQL + ABA ranged from 99.1 to 100%, yielding significantly lower egg counts compared to the untreated control group ($P \leq 0.003$). For MOX the egg counts were significantly ($P \leq 0.003$) lower compared to the untreated group at each farm, with reductions varying from 98.2 to 100%.

* Corresponding author.
E-mail address: thomas.geurden@pfizer.com (T. Geurden).
[1] Present address: VparST Limited, Maple House, Dawson Road, Market Weighton YO43 3GE, UK.

0304-4017/$ – see front matter
http://dx.doi.org/10.1016/j.vetpar.2012.04.008

The post-treatment copro-cultures for larva identification indicated that *T. circumcincta* was the most abundant worm species after treatment (52–99% of the larvae). The results of these studies confirm the high efficacy of the DQL + ABA combination formulation against anthelmintic resistant nematodes in the UK.

1. Introduction

Anthelmintic resistance (AR) in gastro-intestinal nematodes of sheep has been reported within a few years after the introduction of each new anthelmintic class (Kaplan, 2004; Waller, 2006). The early reports of AR tended to involve resistance to a single class of drugs, yet multiple drug resistance (MDR) to the three major anthelmintic classes (macrocyclic lactones—ML, levamisole—LV and benzimidazoles—BZ) has been reported for *Haemonchus contortus*, *Teladorsagia circumcincta* and *Trichostrongylus colubriformis*, mainly in New Zealand, Australia, South America and South Africa. In the UK, several surveys (Hong et al., 1996; Bartley et al., 2003, 2006) reported BZ, LV and ML resistant nematode parasites, mainly *T. circumcincta*. Furthermore, MDR has been reported in at least seven UK sheep flocks (Sargison et al., 2001, 2004, 2005; Yue et al., 2003; Bartley et al., 2004; Taylor et al., 2009). In flocks with MDR, moxidectin (MOX) is often seen as the last option for treatment, but failure of MOX to control MDR *T. circumcincta* isolates in the UK has already been described (Wilson and Sargison, 2007; Sargison et al., 2010a), and is considered as a major threat to sustainable sheep production (Sargison et al., 2005; Blake and Coles, 2007). The UK sheep industry consists of three main management types: the hill, upland and lowland farms, as such exploiting characteristics of specific breeds to maximise land use in the different grazing environments. The main disadvantage of such a stratified system is that it involves animal movement as both replacement ewes and fattening lambs are cascaded from one system into the other. Animal movement has been considered as an important factor in the spread of AR in sheep in the UK (Coles, 1997; Sargison et al., 2004).

Management measures for the sustainable use of anthelmintics have been developed (Abbott et al., 2009). Furthermore, two new classes of molecules with novel modes of action have been introduced into the UK market. The first class of new drugs is the amino-acetonitrile derivatives (Kaminsky et al., 2008), with monepantel (Zolvix®, Novartis) licensed for the treatment of gastro-intestinal parasites in sheep. The second class is the spiroindoles, which includes derquantel (DQL) which blocks cholinergic neuromuscular transmission, rapidly inducing flaccid paralysis (Robertson et al., 2002; Zinser et al., 2002). This class is approved as an oral anthelmintic in combination with abamectin (ABA) for the treatment of nematodes in sheep (Startect® Dual Active Oral Solution for Sheep, Pfizer Animal Health). The combination of these two molecules with different modes of action and similar persistent activity is expected to provide an important tool in delaying the onset of AR (Bartram et al., 2011). A high efficacy against the different stages of a wide range of sheep nematodes, including anthelmintic resistant isolates, has been previously demonstrated in New Zealand, Australia and South Africa. In the UK, an experimental infection study confirmed the efficacy of the combination formulation against a BZ/LV/ML resistant laboratory isolate of *T. circumcincta* (Little et al., 2010, 2011).

The aim of the present studies was to further investigate the efficacy of the DQL + ABA formulation against resistant nematodes in the UK. Therefore a controlled efficacy study using a MDR *T. circumcincta* isolate was conducted in conjunction with a faecal egg count reduction test (FECRT) study on 4 farms throughout the UK with a proven history of AR.

2. Materials and methods

2.1. Controlled efficacy study

This was a single site, negatively controlled and blinded study against an experimentally induced infection with a MDR (BZ/LV/IVM/MOX) resistant isolate of *T. circumcincta*. The study was performed at Moredun Scientific in Edinburgh, Scotland.

2.1.1. Animals and infection

In total, 40 sheep (*Ovis aries*) raised indoors under conditions to preclude exposure to nematodes were included in the study. A faecal sample was collected from the rectum of each animal to confirm the parasite negative status of the animals prior to infection.

On day −28, the 40 sheep were each infected with 7000 *T. circumcincta* infective 3rd stage (L3) larvae by oral gavage. The laboratory isolate used for infection was a previously characterised MOX resistant field isolate (Wilson and Sargison, 2007; Sargison et al., 2010b) that was further selected in the Moredun Research Institute as follows: after the isolation from the field, the isolate was passaged a total of 7 times in animals experimentally infected with larvae harvested from a previous passage, and further selected by treatment with a MOX formulation on 5 of those passages. Oral and injectable preparations of MOX were used at 0.1, 0.2 or 0.4 mg/kg dosages for selection. The resulting laboratory isolate was considered as highly resistant to MOX.

2.1.2. Allocation and treatment

Prior to treatment, a faecal sample was collected from the rectum for individual faecal egg counts (FEC) to confirm the success of the experimental infection. Animals were randomly allocated according to a randomised complete block design, with blocks defined by the pre-treatment *T. circumcincta* FEC. Within each block, one animal was randomly allocated to each of the four treatment groups