Short communication

Efficacy of doramectin against naturally acquired nematode infection in Iberian swine

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Abstract

Studies were carried out to determine the therapeutic efficacy of doramectin, administered intramuscularly at a dose of 300 μg/kg live weight, against naturally acquired helminths of extensively farmed Iberian pigs. The first study (slaughter study) evaluated, through necropsy of the study animals, the product’s efficacy against gastrointestinal and pulmonary nematodes (Ascaris suum, Oesophagostomum dentatum and Metastrongylus sp.) whilst the second, faecal egg count reduction study, (FECR study) evaluated the drug’s efficacy only against gastrointestinal helminths (A. suum, Trichuris suis and Oesophagostomum sp.).

The first study used 20 animals divided into two equal groups of 10 on the basis of body weight and faecal egg count. One group constituted saline treated controls and the other was doramectin treated. On Day 14 post treatment half of the animals in each group were necropsied and the number of parasites present counted. On Day 15 the remaining half of each group underwent the same procedure. The second study was carried out with 40 animals divided equally into two groups of 20. This study determined the effect of doramectin treatment on faecal egg counts as an indicator of parasite burden.

The first study demonstrated an efficacy of 100% against adult Metastrongylus sp. and A. suum, whilst the efficacy against O. dentatum was 96.3%. The second study indicated that at Day 21 post treatment there was a 100% reduction in egg counts in faeces in comparison to untreated controls.

Keywords: Pig-Nematoda; Doramectin; Control methods-Nematoda

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1. Introduction

The antiparasitic activity of doramectin (Dectomax®, Pfizer) against gastrointestinal helminths and/or pulmonary nematodes in cattle, has been described by several authors including Goudie et al. (1993), Verdrussse et al. (1993), Eddi et al. (1993), Jones et al. (1993) and Weatherley et al. (1993), who observed a very high efficacy of the endectocide following a single injection at a 200 μg/kg dose rate. Similar activity has been recorded in swine treated at a dose of 300 μg/kg (Logan et al., 1996; Stewart et al., 1996a, b).

The present work describes two studies carried out to evaluate the efficacy of doramectin against a range of swine nematodes (Ascaris, Oesophagostomum and Metastrongylus) in Iberian swine. The studies were carried out in Extremadura, a western region of Spain close to the Portuguese border, where 40% of Iberian swine (approximately 100,000 animals) are reared, mainly in extensive husbandry systems characterized by acorn pastures of which the region possesses 936,500 ha.

2. Materials and methods

2.1. Study sites

Both studies were carried out in the Caceres province (Extremadura, Spain). The first one (slaughter study) was carried out in the Caceres Faculty of Veterinary Medicine, following the identification and transfer of naturally infested animals from three nearby farms. The animals were stocked in an approximate surface area of 0.4 m² per animal with natural ventilation. The second study (FECR study) was carried out in an extensive Iberian swine farm, in the western region of Extremadura (Spain). These animals were allocated a surface area of 1 m² per animal whilst confined at night.

2.2. Animals

The studies were conducted in either Iberian or Iberian×Duroc pigs with a history of natural helminth infestations acquired under extensive management conditions. 20 males and females, ranging from 12 to 14 weeks of age, were used in the first study. A total number of 40 male and female Iberian×Duroc animals with ages ranging from 10 to 14 weeks, was used in the second study. On both occasions, all animals were naturally infested with gastrointestinal and/or pulmonary nematodes, and received a daily concentrate supplement of 800 g animal together with water ad libitum.

2.3. Experimental design

In the first study 20 animals from surrounding farms, shown to harbour gastrointestinal nematode infections by analysis of faecal samples collected on Day −13, were transferred to the Faculty of Veterinary Medicine of Caceres.
On Day 0 (the day of treatment), the animals were weighed and a faecal sample was collected to determine the parasite burden prior to treatment. Animals were allocated equally to either a control (T1) or a treated group (T2) on the basis of body weight and faecal egg count. The 10 animals used as controls (T1) received a 1 ml per 33 kg intramuscular (IM) injection of saline administered on the lateral side of the neck. The other group (T2), containing the same number of animals were administered an IM injection of doramectin at a 300 µg/kg dose rate (1 ml of doramectin solution per 33 kg body weight) on the lateral side of the neck.

Fourteenth day post-treatment, five animals from each group (treated and controls) were selected at random, and faecal samples collected prior to slaughter. Following slaughter, samples from lungs, stomach, small and large intestines including the caecum, were obtained for subsequent identification and helminth counts according to standard procedures (see Section 2.4). On the following day (15th day post-treatment) the remaining animals were slaughtered and samples collected by the same procedure.

In the second study, 40 animals with naturally acquired parasitic infestations were used. On Days −7 and 0, all animals were weighed and faecal samples collected, for both faecal egg count determination and coproculture. On Day 0, based on Day −7 faecal egg counts and body weights, the animals were allocated to either a control (T1) or a treatment group (T2) with 20 animals in each group. Subsequently, the animals received either a dose of saline (T1) or doramectin (T2) as described previously. In addition, faecal samples were collected from all animals on Days 7, 14 and 21 after treatment, for egg count determination. Finally, all animals were weighed at the end of the study (Day 21).

During both studies, all animals were observed for a 24 h period in order to detect possible side effects following treatment. In addition, clinical examinations were carried out on a weekly basis to evaluate the clinical symptoms caused by the parasitic infestations.

2.4. Parasitological techniques

Following post-mortem examination of the animals involved in the Caceres Faculty of Veterinary Medicine study, parasitological examinations were carried out as follows:

(a) Collection and count of adult and immature nematodes from stomach: For this the stomach contents were washed out with 31 of water and a 10% sample (4 × 75 ml) of this passed through a filter of 38 µm pore size. The contents of the filter contents made up to 300 ml in water and this made up to 10% formalin solution. This 10% sample was inspected and worm numbers counted.

(b) Collection and count of adult and immature nematodes from small intestine: This procedure was similar to that for the obtention of parasites from the stomach with the exception that 41 of water were used to wash through and a 63 µm pore size filter was used. Additionally 100% of the adult A. suum were recovered and counted.

(c) Collection and count of adult and immature nematodes from large intestine and caecum: This was similar to method (b) with the exception of the use of 81 of wash water.

(d) Collection and count of adult and immature nematodes from lungs: The lungs were perfused with 101 of water and this volume was filtered through a filter of 63 µm pore size. The contents of this were suspended in 300 ml of water with the addition of 30 ml
formalin solution and 5 g salt. 100% of the sample thus obtained was inspected and counted. Afterwards each lung was sectioned and checked along the bronchi and bronchioles for the presence of adult worms adhering to the mucosa.

In addition, faecal sample analysis for the evaluation of parasite burdens in the experimental animals were carried out on Days −13, 0, 14 and 15 by means of a modified McMaster technique (Ministry of Agriculture Fisheries and Food, 1986).

In the second study, faecal egg counts and coprocultures for the identification of third stage larvae (L3) were carried out (Henriksen and Korsholm, 1983; Ministry of Agriculture Fisheries and Food, 1986).

2.5. Statistical analysis

In the first study, the percentage efficacy of doramectin against each nematode species or larval stage was calculated according to the following formulae:

\[
\text{Efficacy} = \left( \frac{\text{Geometric mean of non-treated animals} - \text{geometric mean of treated animals}}{\text{Geometric mean of non-treated animals}} \right) \times 100
\]

The efficacy of doramectin against each parasite species, was calculated including only those control animals positive for that particular species, together with an equal number of animals from the treated group in order to carry out the statistical analysis. Statistical analyses were carried out using a linear model to partition the total variation in log worm burdens into sources that were functions of the design and treatment structure of the study. The error term (i.e., the between animal within treatment group variation) was then used to test the statistical significance of the difference between treatments in their mean log worm burdens.

In addition, faecal egg counts were carried out on Days −7, 0, 7, 14 and 21 in the farm’s study. Animals with negative egg counts on Days −7 or 0 were excluded from the study. Total counts were transformed using natural log (total count + 1). Treatment differences at each sampling day were analysed using a split-plot, repeated measures model. Total variation in the log egg count was partitioned into the attributable treatment, animal within treatment, sampling day, treatment×sampling day interaction and residual. The percentage reduction in the geometric mean faecal egg count from the first to the last day of the study was calculated for each treatment group. The percentage reduction in egg count was also calculated for each animal. A mean percentage reduction for the doramectin treated group was calculated from the arithmetic average of the individual percentage reductions. Finally, an analysis of variance was calculated to evaluate liveweight gain differences between the two groups at the end of the study.

3. Results

3.1. Clinical observations

None of the animals involved in either study showed any clinical symptoms of parasitic infestation, nor any adverse reactions following the administration of doramectin.
3.2. Parasitological results

The following species of gastrointestinal nematodes were recovered during the two studies: Firstly in the Caceres Veterinary School study, *Metastrongylus* spp., *A. suum*, *O. dentatum* and *T. suis* were isolated after slaughter. In the second study, eggs from *A. suum*, *T. suis*, *Strongyloides ransoni* and strongyles were microscopically detected prior to treatment and, in addition, *Oesophagostomum* spp. larvae were identified following coproculture.

The results showing the efficacy of doramectin during the study carried out in the Faculty of Veterinary Medicine (slaughter study) are shown in Table 1. Geometric means of the number of adult worms present in the gastrointestinal and respiratory tracts recovered from both the control and treated animals are shown in Table 1 together with the respective ranges, the percentage efficacy for each species and the statistical significance. A total number of 12 animals (six from each group) were used to evaluate the efficacy of doramectin against *Metastrongylus* spp infestations. The values ranged from 19 to 77 adults per animal (geometric mean = 39) in the control group at the end of the study compared to 0 adults at the end of the study in the doramectin treated group, thereby representing a 100% efficacy of the product against this species. Similarly, a total number of 12 animals (six per group) was used for the calculation of doramectin’s efficacy against *A. suum* infestations. Adult parasite numbers ranged from 3 to 34 (geometric mean = 10) in the control group at the end of the study. The efficacy of doramectin against this species was 100% as no worms were recovered from any animal in the treated group at the end of the study. The differences between control and doramectin treated groups in parasitemia with both these parasites was highly statistically significant (*p* < 0.0001). Although not 100%, the percentage efficacy obtained against adult *O. dentatum* was high; specifically 96.3%. Eight animals were included in this comparison (four in each group). At the end of the study the four untreated animals were all

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic efficacy of doramectin at 300 μg/kg against swine nematodes — adult worm counts and percentage efficacies*</td>
</tr>
<tr>
<td>Species</td>
</tr>
<tr>
<td>---</td>
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<tr>
<td></td>
</tr>
<tr>
<td><em>Metastrongylus</em> sp.</td>
</tr>
<tr>
<td><em>Ascaris suum</em></td>
</tr>
<tr>
<td><em>Oesophagostomum dentatum</em></td>
</tr>
<tr>
<td><em>Trichuris suis</em></td>
</tr>
</tbody>
</table>

* Non-medicated animals with parasite burdens of zero for a particular species/stage and an equal proportion of zero burden animals from the doramectin treated group were excluded from the analysis of that species/stage.

* Significant level of testing the null hypothesis (H₀) on mean log worm burdens (H₀ control group=treated group).

** Not estimable due to insufficient data.

*** Efficacy not calculated due to insufficient data.
Table 2
Therapeutic efficacy of doramectin at 300 μg/kg against swine nematodes — faecal egg counts in eggs per gram (e.p.g) and percentage reduction in faecal egg counts

<table>
<thead>
<tr>
<th>Day of trial</th>
<th>Non-medicated swine worm counts</th>
<th>Doramectin treated swine worm counts</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group size</td>
<td>Geometric mean e.p.g</td>
<td>Range</td>
</tr>
<tr>
<td>−7</td>
<td>14</td>
<td>607</td>
<td>100–5400</td>
</tr>
<tr>
<td>0</td>
<td>14</td>
<td>387</td>
<td>100–2900</td>
</tr>
<tr>
<td>7</td>
<td>14</td>
<td>1209</td>
<td>200–8300</td>
</tr>
<tr>
<td>14</td>
<td>13</td>
<td>827</td>
<td>200–2900</td>
</tr>
<tr>
<td>21</td>
<td>12</td>
<td>314</td>
<td>0–2600</td>
</tr>
</tbody>
</table>

% reduction in geometric mean e.p.g Day 0 to Day 21: 19 for control group and 100 for treated group.

* Significant level of testing the null hypothesis (H₀) on mean log worm burdens (H₀ control group=D treated group).

infected (range 10–290 adult worms, geometric mean 37) whereas only one animal from the treated group was infected (with 30 worms). Finally it was only possible to include two animals infected with *T. suis* in each group. At the end of the study a geometric mean of 250 adult worms were recovered from the untreated group and a geometric mean of only two worms was obtained from the treated group. On this basis it was not possible to estimate the efficacy of doramectin against *T. suis* due to the low prevalence of this parasite in the experimental population.

The results of the second study, designed to determine the effects of doramectin on nematode egg output per gram of faeces (Faecal Egg Reduction Study) are given in Table 2. The geometric mean of egg output per gram of faeces was similar in the two groups (T1 and T2) at Day −7. Animals with no eggs in their faeces at Day −7 were excluded from the data analysis. This category comprised six animals in the control group (T1) and seven in the treated group (T2). With this proviso the analysis was carried out on 14 animals in the control group and 13 in the treated group. The first analysis carried out post treatment (Day 7) demonstrated an appreciable reduction in the number of eggs per gram of faeces. Some animals in group T2 showed a total absence of eggs from their faeces. This represented a statistically significant difference between the two groups with a confidence level of 99.9%. Later, at Day 14 post treatment there was a complete absence of eggs from the faeces of group T2. From this point until the end of the study no treated animal showed the presence of nematode eggs in their faeces. The reduction in egg counts per gram of faeces was 100% in relation to Day 1 in group T2. A statistically significant difference between the groups T1 and T2 with a confidence level of 99.99% was demonstrated. In addition, the egg per gram values were also slightly reduced in the control group (T1; 19% reduction) by Day 21. This was probably the result of husbandry changes including improved housing conditions, increased food consumption and water ad libitum, being reflected in a moderate reduction in faecal egg count values (geometric mean).
Table 3
Liveweight gains — average daily weight gains from Day 0 to Day 21.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Group size</th>
<th>Mean average daily weight gain (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-medicated</td>
<td>20</td>
<td>0.21</td>
</tr>
<tr>
<td>Doramectin</td>
<td>20</td>
<td>0.24</td>
</tr>
</tbody>
</table>

*p value* 0.0871

*Significant level of testing the null hypothesis (H₀) on mean log worm burdens (H₀ control group=D treatment group).

3.3. Liveweight gains

Results from liveweight gains obtained during the FECR study are shown in Table 3. They indicate a greater average daily weight gain from Day 0 to Day 21 in the animals treated with doramectin compared to the control group (0.24 kg per day in the doramectin treated group versus 0.21 kg per day in the control group). However, these results were not statistically significant.

4. Discussion

The appearance of the avermectins has transformed the treatment of parasites in livestock. Thus, in theory, with the exception of the coccidia all the important parasites of pigs (helminths and arthropods) can now be controlled. With respect to this doramectin represents a suitable endectocide, intrinsically effective and with a long period of activity against both ecto and endo parasites (Goudie et al., 1993; Mackinnon, 1996).

At the moment there are few reported studies of the efficacy of doramectin in pigs (Logan et al., 1996). The present studies were carried out in Iberian pigs, a pig with a high commercial value. The two studies described here, were carried out according to the ‘WAAVP guidelines for evaluating the efficacy of anthelmintics in swine’ (Düwell et al., 1986). Their objective was to evaluate the efficacy of doramectin against helminth infestations in Iberian or Iberian×Duroc reared pigs under extensive management systems. The results showed that a single subcutaneous administration of doramectin at a 300 µg/kg dose rate was highly effective against pulmonary and gastrointestinal helminths including *Metastrongylus* spp., *A. suum* and *O. dentatum*.

On the basis of the recovery of adult parasites following the administration of doramectin during the slaughter study, the results indicated an efficacy of 100% for doramectin against *Metastrongylus* spp. and *A. suum*, and of 96.3 % against *O. dentatum*. On both occasions the effect on worm burden of doramectin was calculated to be highly significant with respect to untreated control animals (*p*<0.0001).

These results, showing a very high efficacy of doramectin, are in agreement with previous studies on the efficacy of doramectin in cattle and pigs (Ritzhaupt et al., 1996).

In cattle, the administration of injectable doramectin at 200 µg/kg maintains an adequate plasma level to maintain activity for a prolonged period (Weatherley et al., 1993; Wicks et al., 1993).
With relation to the duration of activity of doramectin and ivermectin in swine, studies with experimental A. suum infections by DiPietro et al. (1996) demonstrated that both drugs gave good protection out to at least 63–64 days post treatment. When this period was extended, however, doramectin demonstrated better duration of activity efficacy. These results concurred with the pharmacokinetic studies of Friis and Bjoern (1995) using both products.

It therefore appears that the antiparasitic activity of doramectin against endoparasites should be used for the treatment and control of parasitic infestations which have economic consequences on swine production reared under extensive management systems.

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