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Short Communication

Effectiveness of several anthelmintics to control a *Strongyloides* sp. outbreak in Creole-de-Guadeloupe male kids aged 7 months

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ABSTRACT

Routine faecal examination of a herd of weaned male goats revealed heavy infections with gastrointestinal strongyles (GIS) and *Strongyloides* sp. Moxidectin (routinely dosed at 0.3 mg·kg^{-1}, i.e., 1.5 times the sheep dose), although fully effective against GIS, failed to control *Strongyloides* sp., with an estimated faecal egg count reduction (FECR) of only 55.5%. In addition, levamisole (11.25 mg·kg^{-1}) and ivermectin (0.3 mg·kg^{-1}) also failed to control *Strongyloides* sp., with FECRs of 1.4% and 53.5%, respectively. On the other hand, albendazole (7.5 mg·kg^{-1}) and netobimin (11.25 mg·kg^{-1} and 22.5 mg·kg^{-1}) reduced by 96.3–99.9% the *Strongyloides* sp. faecal egg counts according to dose and remained effective, although, in the past, this drug family has been used extensively on the same farm and was no longer effective against GIS. Albendazole or netobimin at 3 times the dose for sheep may be effective for *Strongyloides* sp. control in case of severe infection.

1. Introduction

Strongyloides papillosus is usually a minor parasite and routine faecal egg counts (FEC) commonly show only light infections in goats although reported prevalence is often high, ranging from < 5% up to > 80% (Akhter et al., 2011; Barua et al., 2009; Sissay et al., 2007; Belem et al., 2005; Achi et al., 2003; Barry et al., 2002; Arosemena et al., 1999; Nwosu et al., 1996; Anderson and Roberson, 1996; Ndao et al., 1995; Bonfoh et al., 1995; Waruiru et al., 1994; Cardoso and Oliveira, 1993; Quesada et al., 1990; Jansen and Pandey, 1989; Charles, 1989; Guimaraes and Lima, 1987; Islam, 1984; Specht, 1982; Joshi, 1978). However, massive infection of this species or its sister species *S. viteli* (Eberhardt et al., 2008) may result in lung damage and sudden death in calves (Taira et al., 1992; Kvac and Vitovec, 2007). Severe infection with *S. papillosus* causes anorexia, poor growth or even loss of weight, slight to moderate anaemia, lassitude, difficult respiration, abnormal stools, abnormal thirst and polyuria (Turner, 1959), oxidative/nitrosative stress (Dimitrijevic et al., 2012) and even cardiac arrest (Nakamura et al., 1998) or hepatic rupture (Pienaar et al., 1999). Moreover, infective larvae penetrating the skin above the hoof may cause or at least promote lameness in sheep (Beveridge, 1934).

Weaned male kids of the INRA experimental unit in Guadeloupe showed clinical signs of parasitism (e. g., anaemia and poor body condition) along with lameness (over 50% of the herd) and coughing in an undetermined percentage of animals. This clinical picture allowed the suspicion of resistance to moxidectin (used continuously every 2 months for the last 8 years) among the strongyle population having been already found resistant to benzimidazoles, levamisole and ivermectin (Mahieu et al., 2014). Therefore, we seized the opportunity to check the effectiveness of moxidectin against the gastrointestinal parasites. The control coproscopy of this test having revealed a severe infection by *Strongyloides* sp. we tested also the effectiveness of the other locally available anthelmintics against this parasite.

2. Material and methods

2.1. Animal management and study design

The data were collected in Guadeloupe (French West Indies) at the Tropical Platform for Experimentation on Animals (PTEA, 16°18′ N, 61°19′ W, 35 m above sea level). The base herd of Creole of Guadeloupe goats (breeding goats and their offspring not involved in experiments) was routinely raised on pastures and thus naturally infected with gastrointestinal parasites. Two strongyle species, *Haemonchus contortus* and to a lesser extent *Trichostrongylus colubriformis*, are usually the dominant components of the gastrointestinal nematode population in this farm. The weaned male kid herd, about 7 months old (4 months after weaning), showed signs of severe parasite infection. Therefore, we

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Table 1
test of moxidectin (Mox), albendazole (Alb), netobimin at usual goat dose (Net) or double dose (Netx2), ivermectin (Ivm) and levamisole (Lev). Efficacy (FECR) with the lower and upper 95% confidence limits (LCL and UCL) and the estimated probability that the true FECR was greater than or equal to 95%. FEC estimates took into account the Poisson errors and data distribution (Wang et al., 2017).

Treatment	n	FEC mean before treatment (epg)	FEC mean 14 days after treatment (epg)	FECR (%)	LCL (%)	UCL (%)	Probability (FECR ≥ 95%) (%)
Mox[a]	15	7990	3550	55.5	52.1	59.0	0
Alb	10	1910	74	96.3	94.3	97.7	89.1
Net[b]	8	1380	150	99.2	23.0	100.0	68.1
Netx2	10	922	5	99.9	98.5	100.0	99.6
Ivm[b]	9	233	115	53.5	27.8	69.8	0
Lev	10	321	294	1.4	0	21.0	0

[a] Moxidectin was tested first; the other five treatments were tested later on another kid batch.
[b] Two animals (Net) and one animal (Ivm) were not sampled at least one time and were discarded.

decided to monitor the effectiveness of the routine moxidectin treatment in late September 2015.

Animals were traited orally at the routine dose, 0.3 mg·kg^{-1} moxidectin (Cydectine® 0.1%, Pfizer Olot S.L.U. Ctra. Camprodon s/n "La Riba" 17,813 Vall de Bianya, Girona, Spain), i.e. 1.5 times the sheep dose in order to take into account the specificity of goat pharmacokinetics (Sanyal, 1996; Sangster et al., 1991; Hennessy et al., 1993b; Hennessy et al., 1993a; Hennessy et al., 1993c). The same day (d0) to minimise the handling time, individual faecal samples were collected from the rectum and kept at 4 °C until numeration. Gastrointestinal strongyle (GIS) eggs and *Strongyloides* sp. embryonic eggs were counted within two days using a modified McMaster method (Mahieu et al., 2014). A second faecal egg count was carried out 14 days later on the same individuals, each animal being its own control. GIS eggs were counted on each of both dates for 46 individuals and the unexpected *Strongyloides* sp. eggs for 15 individuals.

Given that moxidectin failed to control *Strongyloides* sp. (see Results and discussion section), a second series of FECR tests was carried out in March 2016 on another batch of 50 male kids aged about seven months and grazing on the same pastures, with the objective of selecting an effective drug among those available locally. Five treatments were tested on five groups of ten randomly assigned individuals: albendazole (Valbazen®, 19 mg·ml^{-1}, Zoetis-France, 23/25 avenue du Docteur Lannelongue, 75014 Paris, France) dosed at 7.5 mg·kg^{-1} (Alb); netobimin (Hapadex® 50 mg·ml^{-1}, Schering-Plough Santé Animale 49500 Sergé, France) was used at 11.25 mg·kg^{-1} (Net) and at twice this dose, i.e. 22.5 mg·kg^{-1} (Netx2). Levamisole (Polystrongle® 200 mg·g^{-1}, Merial 29 Avenue Tony Garnier 69007 Lyon, France) was dosed at 11.25 mg·kg^{-1} (Lev) and ivermectin (Oramec® 0.8 mg·ml^{-1}, Merial 29 Avenue Tony Garnier 69007 Lyon, France) at 0.3 mg·kg^{-1} (Ivm).

All animals involved were raised in farm conditions and treated according to the French and European bioethic and animal welfare guidelines.

2.2. Calculations and statistical methods

The faecal egg count reduction (FECR) thresholds were set according to the World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines (Coles et al., 2006): parasites are declared drug-susceptible if the FECR is greater than or equal to 95%, with a lower confidence interval limit greater than or equal to 90%, and resistant if none of these conditions are met. FECR was calculated using the R package "eggCounts", which uses zero-inflated Bayesian hierarchical models to estimate the reduction in faecal egg counts (Torgerson et al., 2014; Wang et al., 2017). This method takes into account the precision of individual measurements (Poisson errors) and the over-dispersed distribution of parasites between hosts. The Poisson errors were computed for each individual, from the raw egg count and the dilution ratio calculated from the sample weight, volume of flotation solution and actual volume of numeration (if the egg count reached 100 or more in *n* subdivisions of the two McMaster cell grids, the count was stopped and this volume was *n* times 0.3 ml/12). The MCMC Bayesian inference results allowed calculating the 95% highest posterior density interval (HPDLow95 and HPDHigh95, noted LCL and UCL in Table 1), the posterior mode of the FECR estimates (noted FECR in Table 1) and the probability that the true FECR would be greater than or equal to 95%. For comparison, we also calculated the FECR and its confidence interval from individual estimates, using a 2000-bootstrap procedure (Cabaret and Berrag, 2004).

3. Results and discussion

Results taking into account Poisson errors and the distribution of data for the FEC estimations are reported in Table 1, while the bootstrap estimates are displayed in Table 2 for comparison.

The first test (2015) revealed heavy infections with an estimated average of 10,100 GIS eggs and 7990 *Strongyloides* sp. eggs per gram of faeces. Moxidectin was still fully efficient against GIS (FECR = 99.9%). Although some authors (Lespine et al., 2012) recommend doubling the doses of drugs for goats, in practice PTEA managers have always drugged goats at 1.5 times the dose for sheep, as prescribed by the referring veterinarian, moxidectin being used outside the Marketing Authorisation. This was done without degrading the effectiveness of moxidectin on GIS, and achieving substantial savings on veterinary

Table 2
test of moxidectin (Mox), albendazole (Alb), netobimin at usual goat dose (Net) or double dose (Netx2), ivermectin (Ivm) and levamisole (Lev). FECR calculation according to Cabaret and Berrag (2004), with a 2000-bootstrap estimation of the confidence limits.

Treatment	n	FEC mean before treatment (epg)	FEC range before treatment (epg)	FEC mean 14 days after treatment (epg)	FECR (%)	LCL (%)	UCL (%)
Mox[a]	15	12,800	702; 29,500	6090	52.3	18.5	72.6
Alb	10	2300	306; 15,500	71	96.9	86.2	98.7
Net[b]	8	1840	54; 10,400	4	99.8	97.4	100.0
Netx2	10	921	48; 3890	0	100.0	100.0	100.0
Ivm[b]	9	210	35; 550	100	52.3	16.6	78.5
Lev	10	307	92; 775	278	9.4	−69.9	61.5

[a] Moxidectin was tested first; the other five treatments were tested later on another kid batch.
[b] Two animals (Net) and one animal (Ivm) were not sampled at least one time and were discarded.