Small Ruminant Research 127 (2015) 74–79

Contents lists available at ScienceDirect

Small Ruminant Research

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

Anthelmintic efficacy and pharmacokinetics of pour-on eprinomectin (1 mg/kg bodyweight) against gastrointestinal and pulmonary nematode infections in goats

Dietmar Hamel[a,*], Martin Visser[a], Michael Kellermann[a], Valerie Kvaternick[b], Steffen Rehbein[a]

[a] Merial GmbH, Kathrinenhof Research Center, Walchenseestr. 8-12, 83101 Rohrdorf, Germany
[b] Merial Inc., PKDM, 631 Route 1 South, North Brunswick, NJ 08902, USA

ARTICLE INFO

Article history:
Received 7 November 2014
Received in revised form 31 March 2015
Accepted 7 April 2015
Available online 16 April 2015

Keywords:
Eprinomectin
Topical
Efficacy
Nematodes
Pharmacokinetics
Goats

ABSTRACT

Two controlled studies were performed to assess the efficacy and pharmacokinetics of topical 0.5% w/v eprinomectin (EPRINEX® Pour-on, Merial) against nematode infections of goats. Each study included 16 male castrated goats, less than one year old, harboring induced infections of adult gastrointestinal and pulmonary nematodes. Following blocking on pre-treatment bodyweight and random allocation to one of two groups, half the goats in each study were treated once with eprinomectin (1 mg/kg bodyweight, administered topically), and half remained untreated and served as controls. Plasma concentrations of eprinomectin were determined in blood samples collected prior to and at multiple time points up to necropsy. Efficacy was determined based on the nematode counts of the animals following necropsy 14 days after treatment.

Efficacy of treatment was 100% against adult *Haemonchus contortus*, *Nematodirus battus*, *Nematodirus spathiger*, *Oesophagostomum venulosum*, *Teladorsagia circumcincta* and *Dictyocaulus filaria* was >94% against adult *Cooperia curticei*, *Trichostrongylus axei* and *Trichostrongylus colubriformis*, and was 89.4% against adult *Strongyloides papillosus* ($p < 0.01$). Basic pharmacokinetic parameters of eprinomectin (B1a component) for the goats in the two studies were: AUC_{last}, $23.5 \pm 5.19/36.0 \pm 8.74$ day*ng/mL; and C_{max}, $3.65 \pm 1.12/5.25 \pm 1.39$ ng/mL, respectively; individual maximum plasma concentrations were observed 1 or 2 days after treatment. Results of the studies consistently demonstrated a high therapeutic efficacy of topical eprinomectin at 1 mg/kg bodyweight against a broad range of gastrointestinal and pulmonary nematode parasites of goats.

1. Introduction

The macrocyclic lactone eprinomectin is a broad range endectocide registered as a 0.5% w/v topical formulation (EPRINEX® Pour-on, Merial) for use in cattle (Shoop et al., 1996; Shoop and Soll, 2002). An exceptional feature of eprinomectin within the avermectin/milbemycin class of anthelmintics is the low milk partitioning coefficient and therewith the nil milk withholding in milking cows (Alvinerie et al., 1999b; Shoop et al., 1996).

The unique properties of eprinomectin have generated numerous publications on topical treatment in goats including pharmacokinetics and antiparasitic potency (e.g., Alvinerie et al., 1999a; Chartier et al., 1999; Gawor et al.,

* Corresponding author. Tel.: +49 8032 70750; fax: +49 8032 707525.
E-mail address: dietmar.hamel@merial.com (D. Hamel).

http://dx.doi.org/10.1016/j.smallrumres.2015.04.003
0921-4488/

2000; Dupuy et al., 2001; Chartier and Pors, 2004; Cringoli et al., 2004; Anastasio et al., 2005; Geurden and Vercuysse, 2007; Lifschitz et al., 2008; Molina et al., 2008; Rehbein et al., 2014; Yadav et al., 2014). The eprinomectin plasma profile in goats differs from that in cattle and this is thought to be linked to the lower amount of body fat in goats (Alvinerie et al., 1999a; Dupuy et al., 2001; Lespine et al., 2012; Lespine, 2013). Thus, in contrast to the topical dose of 0.5 mg eprinomectin/kg bodyweight approved for use in cattle, a higher dose of 1 mg eprinomectin/kg bodyweight was suggested to reach adequate anthelmintic efficacy in goats (Alvinerie et al., 1999a; Dupuy et al., 2001).

To add to the current knowledge on topical eprinomectin treatment in goats, anthelmintic efficacy and pharmacokinetics of a single topical eprinomectin treatment at 1 mg/kg bodyweight was evaluated in two studies with experimentally infected goats.

2. Material and methods

The study protocols, which were essentially identical, were approved by the Merial's Institutional Animal Care and Use Committee (IACUC). All animals were handled with due regard to their welfare, and studies were conducted in compliance with any applicable local regulations after approval by the local authorities.

2.1. Animals

Each study included 16 healthy, ruminating, male castrated Weiße Deutsche Edelziege goats (German white noble goats), approximately 8 (Study 1) or 10 (Study 2) months of age and weighing 28.0–35.2 kg (Study 1) and 33.6–52.2 kg (Study 2) prior to treatment. The animals were raised indoors from birth and were worm-free as determined by fecal examination prior to inoculation. Throughout the studies, the goats were kept indoors. Until allocation to treatment groups, animals were housed in groups; after allocation, animals were housed in individual pens. Animals had continuous access to water and were offered a roughage based diet for ad libitum consumption.

2.2. Study design

The studies were conducted as randomized block design studies with replicates of two animals formed based on pretreatment bodyweight. Goats were either left untreated (control) or were treated with 0.5% w/v eprinomectin (1 mg/kg; EPRINEX® Pour-on, Merial; 0.2 mL/kg bodyweight) topically along the back line, from the withers to the tail head using 0.2 mL graduated disposable syringes once on Day 0. The goats were closely observed for 4 h following treatment and once daily for health problems and/or adverse drug events until the end of the studies.

2.3. Inoculation and parasite counts

From Day −35 (Study 1) or Day −28 (Study 2) on, animals were inoculated with a combination of infective third-stage larvae (L3) of gastrointestinal and/or pulmonary nematode species by oral gavage (Table 1). The inoculation schedule was designed so that nematodes were expected to be adults on Day 0 (=day of treatment). The parasites used were recent field isolates from Germany as defined per VICH GL 7 (Vercruysse et al., 2001). The number of larvae given was generally in accord with the W.A.A.V.P. guidelines for testing of anthelmintics in ruminants (Wood et al., 1995).

Table 1
Schedule of inoculation and number of larvae administered to induce adult nematode infections in the goats.

Nematode species	Days[a] of inoculation		Number of infective larvae given per animal	
	Study 1	Study 2	Study 1	Study 2
Dictyocaulus filaria	−35	ND[b]	~350	–
Cooperia curticei	−21	−21	~3000	~3000
Haemonchus contortus	−25	−25	~1000	~1500
Nematodirus battus	−23	ND	~3000	–
Nematodirus spathiger	ND	−23	–	~3000
Oesophagostomum venulosum	−28	−28	~500	~800
Strongyloides papillosus	−16	ND	~10,000	–
Teladorsagia circumcincta	−28	−28	~3000	~4000
Trichostrongylus axei	−23	−23	~3000	~3000
Trichostrongylus colubriformis	−21	−21	~3000	~3000

[a] Relative to topical eprinomectin treatment.
[b] Not done.

2.4. Parasite counting and analysis of parasite counts

For nematode recovery and count, animals were humanely euthanized 14 days after treatment. For parasite recovery and count, the contents (including parasites attached to the mucosal wall) of the abomasum, small intestine, large intestine (including caecum) and the lungs (Study 1 only) were collected. Before counting of gastrointestinal nematodes, the individual organ contents were washed through appropriate sized sieves. The abomasum was incubated in saline (abomasum soak) for recovery of mucosal stage larvae for 24 h. Gastrointestinal nematode counts were made on appropriate aliquots (abomasum soak and abomasum and small intestine contents – 10%; large intestine – 20% [Study 1] or 25% [Study 2]); lungworms were isolated and totally counted.

Nematode counts were transformed to the natural logarithm (count + 1) for calculation of geometric means. Efficacy was calculated as $100[(C-T)/C]$, where C is the geometric mean for the control group and T the geometric mean for the eprinomectin 0.5% w/v treated group. For each study, the untreated control group nematode counts were compared to the eprinomectin-treated group counts using the Wilcoxon rank sum test. A two-sided test was used at the significance level of 0.05.

2.5. Blood sample collection

Blood samples for the determination of eprinomectin (B1a component) plasma concentrations were collected from the jugular vein into lithium heparinized tubes prior to treatment (Day −1), approximately 2, 4, 8, and 12 h after