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Short Communication

Long-term effect of toltrazuril on growth performances of dairy heifers and beef calves exposed to natural *Eimeria zuernii* and *Eimeria bovis* infections

Fabrizia Veronesi, Manuela Diaferia, Orfeo Viola, Daniela Piergili Fioretti *

Department of Biopathological Science and Hygiene of Animal and Food Productions, University of Perugia, 4 San Costanzo Street, Postal Box 06126, Perugia, Italy

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ABSTRACT

The long-term effects of a toltrazuril treatment against natural *Eimeria bovis* and/or *Eimeria zuernii* infections were investigated in comparison with diclazuril and untreated controls on two dairy (Italian Friesian breed) and two beef (Chianina breed) farms. At each trial site, 30 calves were allocated into three groups of 10 calves each: T (treated with toltrazuril), D (treated with diclazuril) and C (left untreated). For 40 weeks post-treatment, the calves were weighed and examined clinically and parasitologically.

The oocyst counts as well as the number of scour days were significantly lower in the T group than in the D and C groups. Final bodyweights and body condition scores of the T group exceeded those of groups C and D. The results confirmed that toltrazuril was highly efficacious, safe and provided productive benefits in dairy and beef calves.

Bovine coccidiosis is a parasitic disease affecting calves all over the world and results in considerable economic losses each year for the beef and dairy industries (Daugschies and Najdrowski, 2005). The disease can be caused by several *Eimeria* species of which *E. bovis* and *E. zuernii* are the most pathogenic.

The goal of the present study was to compare the long-term effect (40 weeks) of two anti-coccidial drugs (toltrazuril and diclazuril) commonly used for the treatment and control of natural infection by *E. bovis* and *E. zuernii* in dairy and beef calves. The comparative assessment was based on the clinical signs, oocyst counts and growth performances.

The study was conducted as a blind, randomised, controlled, multi-centric field trial on selected commercial cattle farms (two Italian Friesian dairy farms and two Chianina beef farms). Preliminary epidemiological studies were performed to ascertain the presence of *E. bovis* and *E. zuernii* as well as the timing and frequency of clinical coccidiosis in each trial site.

A total of 120 calves (30 from each farm) were selected; the calves had not received anti-coccidial treatment during the 3 weeks prior to the start of the trial nor showed clinical coccidiosis before or at the beginning of the study period. At each trial site groups of 10 calves were assigned to the three different treatments using an on-line randomizer program[1]: T (treated with toltrazuril, Baycox bovis, Bayer Animal Health); D (treated with diclazuril, Vecoxan, Janssen Animal Health); C: left untreated, as shown in Table 1.

The study was conducted in accordance with national animal welfare requirements and current laws.

The study lasted a total of 40 weeks. The calves were maintained in the original contaminated areas and were weighed and examined clinically and coproscopically on the treatment day (Day_0), weekly for the first 10 weeks (Day_1–Day_{10}) and subsequently every 2 weeks (Day_{11}–Day_{25}) until the end of the study period.

Individual faecal samples were used for faecal examinations and the number of oocysts per gram (opg) was assessed using McMaster chambers (sensitivity 10 opg) (MAFF, 1986). *Eimeria* oocysts were differentiated based on morphological criteria (Eckert et al., 1995) and the faecal oocyst counts (FOC) were documented separately for the major pathogen species (*E. bovis*, *E. zuernii*), as well as for the sum of all the *Eimeria* spp. oocysts recovered.

Faecal consistency scores were also recorded as follows: 1 = normal; 2 = soft, does not hold form; 3 = runny, spreads easily; 4 = devoid of solid matter.

Animal growth was monitored by individual bodyweight (BW; kg) and daily weight gain (DWG; kg/day). The mean BW (±standard deviation, SD) and the mean DWG (±SD) were calculated from Day_0 to Day_{25}. The body condition score (BCS) of the calves was determined at D_{25} using a five-point scale for Friesian calves (Edmonson et al., 1989) and a nine-point scale for beef calves (Vizcarra and Wettemann, 1996). For each group and for each sampling time, the opg count geometric mean (GM) and the faecal oocyst count reductions (FOCR), compared to the control group, were calculated.

A generalised linear model (GLM) was used to evaluate the *Eimeria* opg output considering groups, farms and sampling times as independent variables. The effect of treatments on BW, DWG,

* Corresponding author. Tel.: +39 075 5857744; fax: +39 075 5857743.
E-mail address: daniela.piergilifioretti@unipg.it (D.P. Fioretti).

[1] http://www.randomizer.org.

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Table 1
Overview of trial sites according with the treatment groups (T: toltrazuril-treated group 15 mg/kg orally once; D: diclazuril-treated group 1 mg/kg orally once; C: untreated group).

Trial site	Group	Number of calves	Age range (days) of treatment	Breed	Gender	Initial bodyweight (kg) (mean ± SD)
Farm 1	T	10	51–60	Friesian	Both	72.7 ± 17.78
	D	10	50–56			71.3 ± 15.78
	C	10	52–62			71.1 ± 9.43
Farm 2	T	10	52–58	Friesian	Both	71.9 ± 10.54
	D	10	54–60			70.4 ± 18.26
	C	10	50–61			65.1 ± 11.43
Farm 3	T	10	20–25	Chianina	Both	62.6 ± 21.45
	D	10	23–31			63.6 ± 12.03
	C	10	20–31			68 ± 32.63
Farm 4	T	10	25–29	Chianina	Both	63.3 ± 25.21
	D	10	20–30			65.1 ± 17.09
	C	10	24–29			66.5 ± 20.05

BCS and on the number of scour (faecal score of 3 or 4) days combined with oocyst shedding were analysed by ANOVA. The faecal consistency in the treated and control groups were compared statistically in terms of percentage of animals with diarrhoea while opg-positive for *Eimeria* spp. across the study period. All statistical analyses were performed using R software (GNU version 2.7) and the cut off for statistical significance was fixed at $P < 0.05$.

The BWs (mean ± SD) for the calves are shown in Figs. 1 and 2 and in Table 2. There was no farm effect on either the average initial or final BW of the animals ($P > 0.05$). The final BW and BCS of the T group animals significantly ($P < 0.05$) exceeded that of the animals in both groups C and D, although there were no significant differences in growth performance between groups over the complete 40-week study period. There were also no significant differences in BW, DWG and BCS between groups C and D.

The data for faecal oocyst counts of all *Eimeria* spp. are summarised in Table 3, although only two species were considered for the differential counts: *E. bovis* (the most frequent species identified on each evaluation date) and *E. zuernii*. The mean opg counts observed across the whole study period differed significantly between groups ($P < 0.01$): T group calves excreted a lower number of oocysts, compared to group D and C animals (Table 3).

A strong 'short-term effect' (within 48 h post-treatment, corresponding to the peak plasma concentration) (FOCR > 90%) was observed in calves treated with toltrazuril and diclazuril. In the diclazuril-treated animals, a marked increase in oocyst counts (FOCR < 50%) was observed starting from Day_{12} (98 days post-treatment) in Friesian calves and from Day_{14} (124 days post-treatment) in Chianina calves. However, the oocyst counts remained persistently low (FOCR ranging from around 99% to 85%) in the group receiving toltrazuril.

The highest percentage of animals with diarrhoea (Friesian: 15.6%; Chianina: 12.25%) was in the untreated group, compared

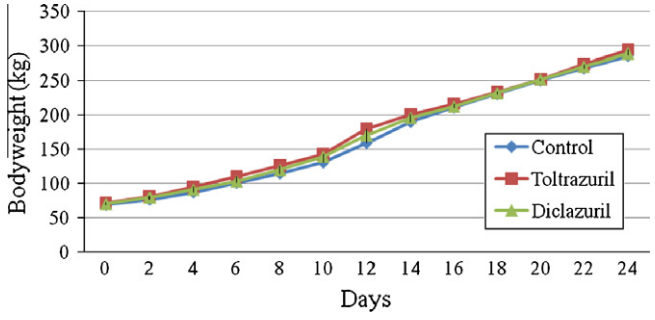

Fig. 1. Friesian calves: mean bodyweight (BW; kg) of D group (treated with diclazuril) and C (untreated) group, in comparison to T group (treated with toltrazuril) over the study period.

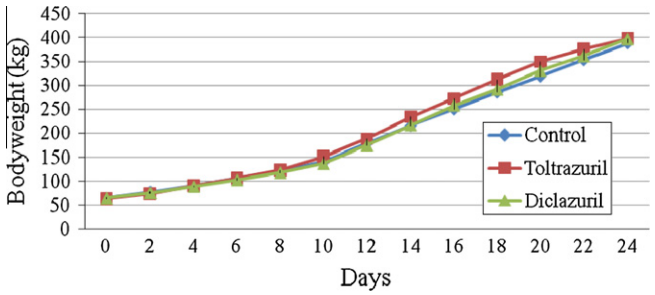

Fig. 2. Chianina calves: mean bodyweight (BW; kg) of D group (treated with diclazuril) and C (untreated) group, in comparison to T group (treated with toltrazuril) over the study period.

to the toltrazuril (Friesian: 0.2%; Chianina: 0%) and diclazuril (Friesian: 3.4%; Chianina: 1.2%) treated animals. Furthermore, group T showed significantly fewer days of diarrhoea combined with oocyst shedding, compared to groups D and C ($P < 0.05$). A significant difference was also observed between groups D and C ($P < 0.05$).

Several studies have previously demonstrated the positive impact of toltrazuril and diclazuril treatments on *Eimeria* infections under various field conditions (Mundt et al., 2003; Epe et al., 2005; Daugschies et al., 2007). In the present survey, the observations were extended to 40 weeks post-treatment and the long-term positive effects of such treatments on productive parameters were also evaluated.

Treatment with toltrazuril, applied according to the epidemiological aspects of each farm, was able to reduce oocyst excretion and the number of scour days significantly and for a long period (40 weeks), also improving the BW of the beef and dairy calves. Similar findings have been reported previously (Epe et al., 2005; Mundt et al., 2005, 2007) and showed that despite the fact that treatment with diclazuril was beneficial for calves in terms of overall health and excretion of oocysts (Mundt et al., 2005; Daugschies et al., 2007), a single treatment with toltrazuril had a considerably longer lasting effect and therefore provided more productive benefits (Mundt et al., 2007).

The clinical and productive benefits of toltrazuril cannot be attributed exclusively to a longer elimination half-life (toltrazuril: 64.2 h vs. diclazuril: 30 h) or higher dose rate used (toltrazuril: 15 mg/kg vs. diclazuril: 1 mg/kg). Furthermore, toltrazuril is more slowly eliminated than diclazuril, due to a slower absorption rate, and its major metabolite, 'ponazuril' (toltrazuril sulfone), has pharmacological activity against coccidia. However, the pharmacokinetic properties of either compounds cannot account for the long-term benefits during this study period (40 weeks).