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Short Communication

Preventive and therapeutic efficacy of halofuginone-lactate against *Cryptosporidium parvum* in spontaneously infected calves: A centralised, randomised, double-blind, placebo-controlled study

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Abstract

The preventive and therapeutic efficacy of halofuginone-lactate (HFL) against *Cryptosporidium parvum* was evaluated in a study conducted from November 2004 to March 2005 on a dairy farm in Central Bohemia, Czech Republic, using 260 spontaneously infected calves. HFL (0.1 mg/kg/day) was administered orally for 7 days to 1-day-old and 8-day-old calves, respectively. In both treated groups the drug significantly, and in almost the same manner, decreased the intensity of diarrhoea ($P < 0.001$) and faecal oocyst count ($P < 0.001$) when compared to corresponding placebo groups. The only difference between both treated groups was the time of onset of symptoms of the infection. Over time, the clinical pattern of cryptosporidiosis in the animals treated at 8–14 days of age was similar to that seen in the groups receiving the placebo. In contrast, infection in the preventively treated group peaked about 10 days later but with the same intensity. The results of this study confirm the anticryptosporidial activity of HFL in calves, but show that the outcome of infection following preventive treatment is comparable to that observed in calves treated after the onset of symptoms.

Keywords: *Cryptosporidium parvum*; Diarrhoea; Calves; Halofuginone-lactate

Cryptosporidium parvum is recognised as one of the major causes of enteritis and diarrhoea in neonatal calves but treatment is difficult (Fayer et al., 1998; de Graaf et al., 1999). To date, halofuginone-lactate (HFL) seems to be a promising drug against bovine cryptosporidiosis (Villacorta et al., 1991; Naciri et al., 1993; Peeters et al., 1993; Lefay et al., 2001; Joachim et al., 2003; Jarvie et al., 2005), but although HFL is commonly recommended for both prevention and therapy, its efficacy has not been compared experimentally and recommendations for a rational use are not sufficiently documented. The aim of this study was to compare the effects of a recommended 7 day administration of 0.1 mg/kg HFL for the prevention and treatment of cryptosporidiosis in spontaneously infected calves.

A centralised, randomised, double-blind, placebo-controlled study with 260 newborn Holstein calves was conducted from November 2004 to March 2005 on a dairy farm located in Central Bohemia (700 dams) which had a high prevalence of cryptosporidiosis in newborn animals. Before the study began it was found that 80% of animals up to 1 month of age in the herd were positive for coronavirus. Rotavirus was found in 13% of calves, mainly between the ages of 2–4 weeks. Twenty-two percent of animals, mainly up to 3 weeks of age, were positive for *Escherichia coli* K99 and the presence of *Campylobacter jejuni* and *Clostridium perfringens* was documented in 6% and 5% of animals, respectively. The prevalence of *C. parvum* infection in calves 9–13 days of age was 100%. Neither *Salmonella* nor BVD virus was demonstrated on this farm.

During the study period, all viable newborn animals were allocated according to order of birth to four groups: (A) animals receiving HFL between 1–7 days of age; (B)

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animals receiving a placebo at the same age; (C) animals receiving HFL at 8–14 days of age, and (D) animals receiving placebo between the ages of 8–14 days. The final number of animals in each group was 64, 64, 65 and 67, respectively. HFL at a dose of 0.1 mg/kg was administered orally once a day, 1 h after morning feeding, as a 0.05% aqueous solution (Halocur, Intervet). A solution of the same composition but omitting the active ingredient was used as placebo. Throughout the study the groups were not separated and calves were randomly allocated to pens placed on a concrete floor in a farm shed, where at all times they received standard husbandry and veterinary care.

Calves were observed daily for consistency of faeces, which was scored on a four point scale. Faecal samples for parasitological examination were collected rectally every morning and examined as described by Casemore et al. (1985); oocyst counts were also expressed on a four point scale. Faecal scores were obtained daily from all calves between the ages of 1 and 31 days. In order to characterise the overall pattern of the infection, the average score during the 31-day-period (mean faecal score) was calculated for each animal. Similarly, the daily intensity of diarrhoea and the mean intensity of diarrhoea during the 31-day period were calculated. All the data were statistically compared using one-way ANOVA.

HFL significantly decreased oocyst excretion as well as the intensity of diarrhoea during the first 31 days of life when administered both preventively and therapeutically (Table 1, Figs. 1, 2). Peak oocyst shedding in the untreated groups occurred between days 12–14. The oocyst shedding pattern over time in the group treated with HFL between 8–14 days of age was the same as that of both placebo groups. In contrast, in the group receiving HFL on days 1–7 of age oocyst counts were minimal until day 9, but then the concentration of faecal oocysts increased, reaching a peak on day 20. This increased oocyst output coincided with a higher prevalence of diarrhoea (Figs. 1 and 2). In the groups receiving placebo, all but one animal in the days 1–7 placebo group were positive for cryptosporidia. A total of five negative animals was seen in each HFL treated group.

We conclude that HFL significantly inhibited *C. parvum* infection and suppressed its symptoms but, surprisingly, the final effect appeared to be independent of whether the drug was administered preventively or therapeutically. The only difference between both treated groups was a delay in oocyst output and the occurrence of diarrhoea, as infection in the preventively treated group peaked about 10 days later. The benefit of using a preventive treatment with HFL is therefore questionable. On the other hand, postnatal calves are more susceptible to acid–base balance disturbances and dehydration associated with severe diarrhoea. Since this risk decreases with age (Virtala et al.,

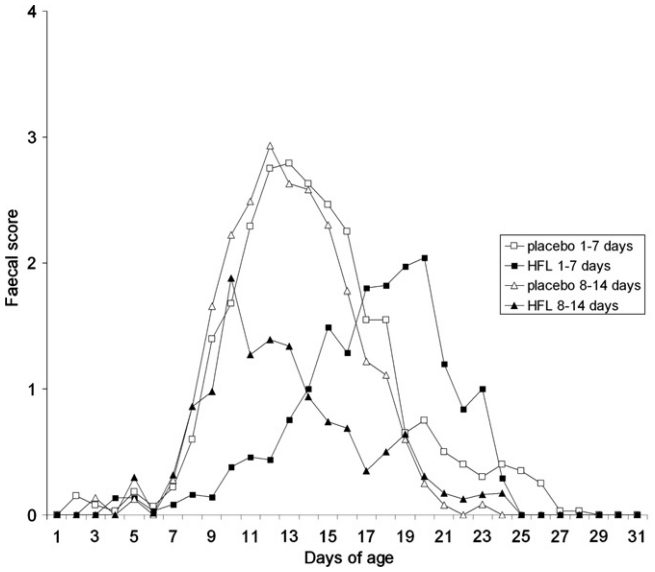

Fig. 1. Faecal oocyst score in calves receiving placebo or halofuginone-lactate (HFL) in 1st or in 2nd week of life. (Faecal score represents intensity of *C. parvum*-infection as follows: 0 = negative sample, 1 = sporadic finding of oocysts in sample, 2 = moderate infection, 3 = strong infection, 4 = very strong infection.)

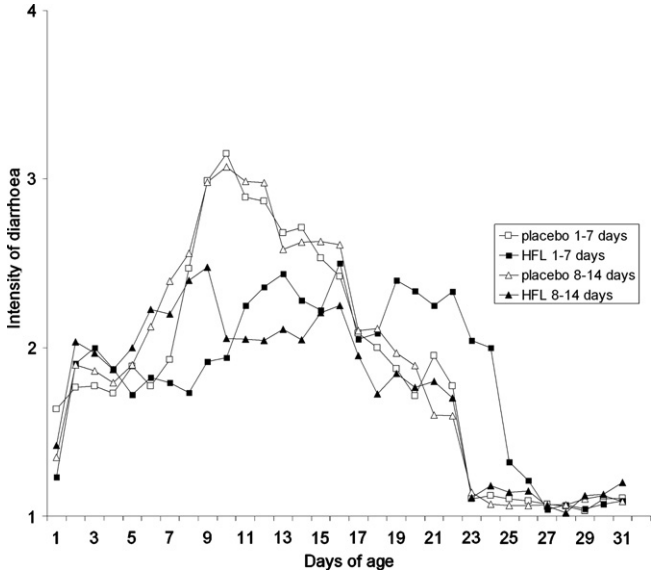

Fig. 2. Intensity of diarrhoea in calves receiving placebo or halofuginone-lactate (HFL) in 1st or in 2nd week of life. (Intensity of diarrhoea was expressed as follows: 1 = normal consistency of faeces, 2 = soft faeces, 3 = liquid faeces, 4 = profuse watery diarrhoea.)

Table 1
Mean faecal score and mean intensity of diarrhoea between 1–31 days of age in calves treated with halofuginone-lactate (HFL) at 1–7 days or 8–14 days of age

	HFL 1–7 days (64 calves)	Placebo 1–7 days (64 calves)	HFL 8–14 days (65 calves)	Placebo 8–14 days (67 calves)
Mean faecal score	$0.69^{a} \pm 0.45$	$1.37^{b} \pm 0.57$	$0.65^{a} \pm 0.49$	$1.48^{b} \pm 0.54$
Mean intensity of diarrhoea	$1.42^{a} \pm 0.31$	$1.64^{b} \pm 0.28$	$1.43^{a} \pm 0.22$	$1.64^{b} \pm 0.28$

[a,b]Values with unlike superscripts differ significantly at $P < 0.001$.

1996), it may be argued that preventive use of HFL can delay the infection to an age when the animals are more resilient. The minimal differences between the preventive and therapeutic effects of the drug allow practitioners to choose between treatment options according to circumstances.

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