Comparative efficacy of three different doses of paromomycin administered orally to treat cryptosporidiosis in experimentally infected dairy calves

Author: Damien Achard , Naomi Isaka, Marie Cron, Adélie Goujas, Thomas Blondel, Jean-François Collin, Jiří Smola, Břetislav Koudela

Objectives

Cryptosporidiosis is a major parasitic disease of newborn calves affecting their health, growth and welfare and responsible for significant economic losses for cattle famers. Current treatments for sick calves are scarce. Paromomycin is a valuable oral treatment option (Brainard *et al.,* 2020, 2021) although data has been limited to fully support its use for treatment. In addition, the literature offers little guidance about the dose for which a clear benefit is observed in affected calves. To address this issue, the effects of three different dose of paromomycin administered as an oral solution were explored in dairy calves experimentally infected with cryptosporidia.

Material and methods

A GCP study involving 35 healthy Holstein neonatal calves was performed according to a monocentric, blinded, randomised design, with 4 parallel groups comparing three different oral doses of paromomycin (Gabbrovet Multi®, Ceva Santé Animale) to a negative control group. Calves were aged 1-2 days old at arrival, 36 to 54 kg and had fair passive immunity status (serum total IgG > 10 g/L). After 24h of acclimatization, each calf was experimentally infected orally once with a dose of $1x10^6$ sporulated oocysts of *Cryptosporidium parvum* (DC_0). Calves were included and treated according to their group if they were 3-10 days old after challenge and had faecal score ≥ 1 and positive oocyst count on the same study day (DT_0). Treatment groups were as follows:

- 9 calves were left untreated (control)
- 9 calves were treated with Gabbrovet Multi® at 75 mg/kg BW/day for 5 days (group 75)
- 8 calves were treated with Gabbrovet Multi® at 100 mg/kg BW/day for 5 days (group 100)
- 9 calves were treated with Gabbrovet Multi® at 150 mg/kg BW/day for 5 days (group 150)

The following parameters were monitored at fixed times during the 21 days of the study: fecal score (0-2), general health observation (0-3), hydration score (0-3), number of oocysts per gram of dry faeces, bodyweight and mean daily body weight gain (MDBWG). Percentages of calves cured at DT_5, diarrhoea observations (DT_0 - DT_{21}) and MDBWG (DC_0 - DT_{21}) were used to compare the efficacy between treatment groups with cure defined as calves with all clinical scores = 0, and diarrhoea regrouping calves with fecal score of ≥1. Evolution of the mean oocyst count in each group was assessed daily from DT_0 to DT_5. The statistical unit was the calf and the 5% level of significance ($p < 0.05$ for two-sided tests) was used to assess statistical differences.

Results

At DT_5, no calf was cured in the control group; a dose effect was observed in treated groups with 44.4%, 62.5% and 88.9% of calves cured in groups 75, 100 and 150 respectively. Through the study, odds ratio (OR) for diarrhoea were found 5.67 times superior in the control group compared to calves in the group 150 [CI_{95}=2.63;12.24]. A significant effect on diarrhoea observations was also observed in calves in the group 100 in comparison with the control group although with a more limited impact (OR=2.32, [CI_{95}=1.08;4.97]). Calves from group 100 were found with OR for diarrhoea 2.45 times greater than calves in the group 150 [CI_{95}=1.11;5.40]. No effect was observed on diarrhoea observations in calves in the group 75 when compared to control group (OR=1.47; [CI_{95}=0.70;3.07]). MDBWG was statistically higher only in group 150 compared to the untreated group (0.67 *vs.* 0.53 kg/day; p=0.0192). In group 150, the mean oocyst count was always lower compared to all the other groups during the treatment's phase.

Conclusions

In this study, the highest dose of paromomycin (150 mg/kg per day for 5 days) was associated with high clinical cure 24h after completion of the treatment, an important decrease in diarrhoea observations and oocyst counts, and a positive impact on the mean daily body weight gain. These findings are in line with those described in a recent multicentric European field trial (Achard *et al.,* 2022). In contrast, a lower dose of paromomycin (75 mg/kg per day for 5 days) resulted in lower clinical cure, no effect on diarrhoea observations and no impact on MDBWG. These results suggest that the high dose of paromomycin (150 mg/kg) is the most efficient when treating neonatal calves sick from cryptosporidiosis.