Efficacy of an oral solution of paromomycin for the treatment of suckling beef calves with cryptosporidiosis in a multicentric field study

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Objectives

Cryptosporidiosis is a frequent parasitological infection of mammals including but not limiting to humans and neonatal ruminants. In newborn calves, cryptosporidiosis has been repeatedly identified as a major contributor of neonatal diarrhoea, a dominant calfhood disease with detrimental health and economic consequences.

Current treatment options for clinically affected newborn calves are limited. A recent meta-analysis work reported halofuginone and paromomycin as valuable oral treatment options while recognizing that halofuginone can present important safety issues and that data is insufficient to fully support the use of paromomycin (*Brainard et al.,* 2020, 2021). To address this lack of evidence, a study under field conditions was performed in beef calves clinically affected by cryptosporidiosis comparing a new dose regimen of an oral paromomycin solution (Gabbrovet Multi®, Ceva Santé Animale) to a reference product based on halofuginone (Halocur®, MSD).

Material and methods

A GCP compliant study was performed according to a multicentric, blinded, positively controlled and randomised design in 40 commercial suckling beef farms located in France and Belgium. The farms were enrolled based on the presence of cryptosporidiosis through positive laboratory or strip testing, absence of recent or current BVD infections, and no recent history of diarrhoea due to coronavirus, *E. coli* and rotavirus, or a dedicated vaccination.

Each newborn calves in this study were required to meet the following criteria for enrollment: age between 3-14 days on first treatment, faecal score ≥ 2, negative rapid test for *E. coli*, coronavirus, rotavirus, and positive rapid test for *C. parvum*. Any calf that presented with diarrhoea for > 24 hours or that has been previously exposed to antibiotics, parasiticides or probiotics was excluded. Animals were randomly allocated to two treatment groups. Calves in group A received 150 mg paromomycin sulfate/kg b.w. (Gabbrovet Multi®), once daily, for 5 days by oral route while calves in group B were orally administered 100 µg halofuginone/kg b.w. (Halocur®), once daily, for 7 days. The following clinical and parasitological parameters were monitored at fixed times during the 21 days of the study: faecal score (0-3), general health observation (0-3), hydration score (0-3), and oocyst counts (number of oocysts per gram of dry faeces). Percentages of calves cured at day 8 was the main criteria to evaluate the efficacy in both treatment groups. Other criteria such as time to clinical cure, number of days when calves were asymptomatic from Day 0 to Day 8 and the parasitological cure at day 7 (oocyst count = 0) were also assessed. The statistical unit was the calf.

Results

One hundred nighty-one suckling calves of beef or crossbred origin from 40 different commercial farms, with a median age of 7 days and an initial mean body weight of 47.7 kg were enrolled. 95 calves were allocated to treatment group A, 96 in the treatment group B. At inclusion, the treatment groups were found clinically comparable.

91.5% (86/94) of newborn calves in group A and 68.1% (64/94) in group B were considered clinically cured at day 8. Clinical cure rate in group A was found superior to those observed in group B ($p<0.001$). In addition, the time to first cure was significantly shorter in group A (log rank test, $p=0.0028$) than in group B. Considering the clinical score on D0, probability of being cured at any time was 48% higher in group A than in group B. The parasitological cure on Day 7 was 16% higher in group A *vs.* group B, with a rate of 79.3% (73/92) and 63.7% (58/91) respectively ($p=0.0466$). In group A, a median of 7 days with normal clinical scores was recorded, whereas in group B, a median of 5 days was reported. In each group, serious adverse events have been reported for 6 calves. Adverse events were considered as possibly/probably related to the product for 2 calves in group B and none in group A.

Conclusions

In this multicentric field study, daily oral treatment with 150 mg/kg of paromomycin (Gabbrovet Multi®) for 5 days was found safe and highly effective to cure sick beef suckling calves with cryptosporidiosis and to control their oocyst burden. In addition, this new treatment regimen was found superior to the current reference treatment based on halofuginone.