EVALUATION OF THE EFFECTIVENESS OF SOLUBLE BACITRACIN (BACIVET S®) IN DRINKING WATER COMPARED TO BACITRACIN IN THE FEED (ALBAC®), DURING AN EXPERIMENTAL REPRODUCTION OF EPIZOOTIC RABBIT ENTEROPATHY SYNDROME.

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ABSTRACT

The effectiveness of soluble bacitracin in drinking water (Bacivet S®) compared to bacitracin in the feed (Albac®) was tested, during an experimental infection of ERE syndrome. Treatments were used before or after the experimental contamination. Weanlings (168) were divided at 32 days of age into 4 groups: contaminated but not medicated control group, group with bacitracin 100ppm in the feed (Albac®), 2 groups medicated with Bacivet S® (0.675g/l of drinking water) before (preventive use) or after (curative use) contamination. Results of this study confirm the efficiency of bacitracin in ERE syndrome conditions with a significant reduction in mortality and morbidity compared to the non treated group. A preventive use of Bacivet S® is as effective as bacitracin 100ppm in the feed (Albac®) during the acute period of the disease. The curative use of Bacivet S® during 14 days, after the observations of the first symptoms, also reduces rabbits mortality and morbidity compared to the control but is less effective than a preventive use.

Key words: Epizootic rabbit enteropathy bacitracin preventive curative treatment.

INTRODUCTION

Since the apparition of Epizootic Rabbit Enteropathy (ERE) syndrome in 1997 in Europe, bacitracin in the feed (under the form of Albac®, Alpharma) was an antibiotic commonly used in rabbit production to control this disease. Effectiveness of bacitracin in the feed at the dose of 100ppm in ERE syndrome conditions was demonstrated in the past by DUPERRAY *et al.* (2000). Persistency of the effectiveness of bacitracin in the feed after 4 years of utilisation was also demonstrated by DUPERRAY *et al*. (2003). In France, bacitracin in the feed had a temporary commercial authorisation that stopped in September 2003. The same month, soluble bacitracin in drinking water (Bacivet S®, Alpharma) received a temporary commercial authorisation. Results of the present study participated in the temporary commercial authorisation of Bacivet S® from the french authorities. The first objective of the present study was to check if the effectiveness of the soluble form of bacitracin (Bacivet S®) was similar to the effectiveness of Albac®

during an experimental reproduction of ERE in growing rabbits. The second objective was to compare the interest of a preventive and curative use of Bacivet S® in ERE syndrome conditions.

MATERIAL AND METHODS

This study was carried out between the 22nd of July and the 26th of August 2003 at Evialis research centre in St Nolff (56), France, under the veterinary supervision of Dr. Benoit Laureys (Landerneau, 29, France).

Animals and treatments

168 kits (Hyplus strain), coming from the Evialis experimental narrow house were divided at weaning at 32 days of age in 4 groups (A, B, C and D) of 42 individuals, homogenous in body weight and sex ratio. Rabbits from the 4 groups were placed in cages of 7 rabbits in a common room with ad libitum access to the feed. All rabbits of the study were inoculated at 42 days of age with the INRA (Institut National de la Recherche Agronomique) TEC3 inoculum (500 µl/rabbit).

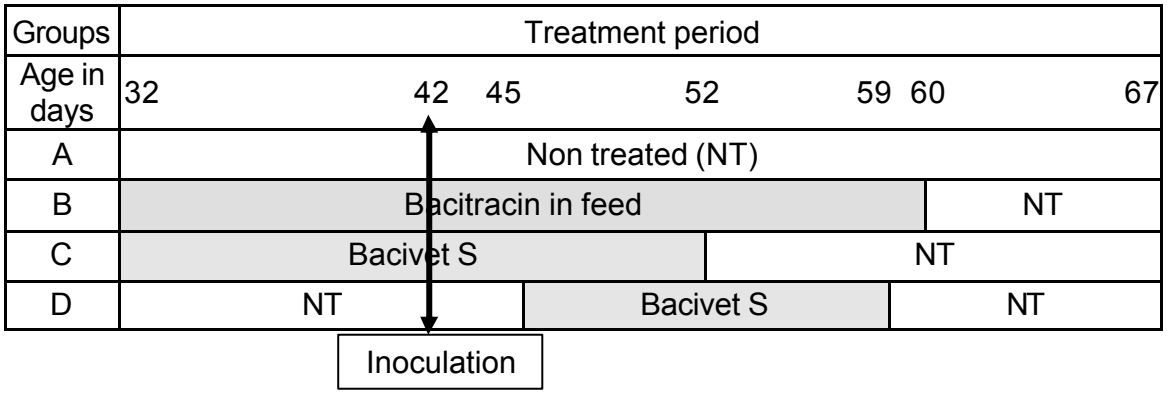

Figure 1. Type and period of treatment

All the groups (Figure 1) were fed a diet without antibiotic except group B, fed a diet with bacitracin 100ppm under the form of Albac® (Alpharma feed grade) from 32 to 60 days of age (4200 IU/kg of feed ; medical premix Santamix bacitracin 840 lapin® 0.5% in the feed). The treatment in drinking water with Bacivet S® (soluble bacitracin European Pharmacopoeia quality) was done at the dose of 0.675g/l (2835 IU/L). Group C (preventive treatment) was treated for 9 days before inoculation and 10 days after inoculation. Group D (curative treatment) was treated for 14 days, just after the first symptoms apparition at 45 days of age (3 days after inoculation). The dose of 0.675g/l of Bacivet S® was chosen to reach the target dose of 420 IU of bacitracin per kilogram of body weight and per day during the treatment period. During treatment of groups C and D, medical solution of soluble bacitracin (Bacivet S®) was renewed every 24 hours.

Zootechnical performances collected

Rabbits body weights were controlled individually the day before weaning at 31 days of age, then at 39, 46, 53, 60 and 67 days of age. Feed consumption par cage was controlled when animals were weighted. During the treatment periods, controlled poll for 24 hours of water consumption supplement with Bacivet S® were done (total of 20 controls) to estimate the average quantity of bacitracin (in IU) absorbed per kilogram of body weight. Death rate was also controlled daily.

Statistical analyses

Statistical analyses was conducted using SPSS 11.0 software. Body weights and body weight gains (including morbid rabbits) were analysed by an analysis of variance using the UNIANOVA procedure and adjusting for treatment effect. Differences among means were tested with a Duncan test. Death rates among treatments at different time point were compared by khi-square tests.

RESULTS

Dose of bacitracin absorbed

For group B, receiving bacitracin in the feed, the average daily quantity of bacitracin absorbed from 32 to 60 days was 290±4.2 IU/kg of body weight for a target value of 420 IU/kg of body weight. From the 20 controls of water consumption on treatment C and D, the average quantity of bacitracin absorbed was 439+14 IU/kg of body weight. No dilution problem of Bacivet S® was encountered during the study.

Mortality (Figure 2, Table 1).

One rabbit from group C died at 38 days of age. The death of this rabbit was not due to ERE. ERE related mortality started at 46 days, 4 days after inoculation, to end in the first place at 56 days of age.

From 42 to 56 days of age, expression period of the disease, the percentage of mortality was significantly different among groups with a death rate of 33.% on the control group and 0% on groups receiving bacitracin either under the form of Albac® (group B) or Bacivet S® in drinking water (group C). Death rate of group D, receiving a curative treatment with Bacivet S®, was intermediate with 11.9%. A resumption of mortality was observed at 66 days of age on group C, one day before departure to the slaughter house, with 2 dead rabbits over 41 rabbits.

Table 1. Mortality per group at different stages.

Groups	N°	**Mortality at 42 days (%)**	**Mortality 42 to 56 days (%)**	**Mortality at 67 days(%)**
A : control non treated	42	0	33.3	33.3
B : Bacitracin 100ppm in the feed 32-60 days	42	0	0	0
C : Bacivet S 33-52 days, preventive treatment	42	2,4	0	7.1
D : Bacivet S 45-59 days, curative treatment	42	0	11.90	11.9
Khi-square signification		NS	P<0.001	P<0.001

1 dead rabbit = 2.4%

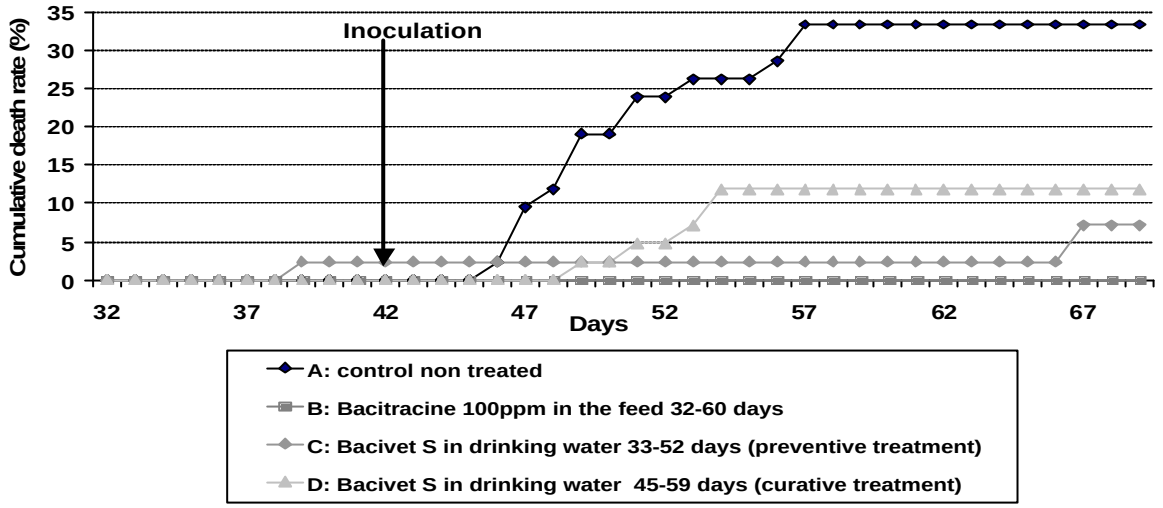

Figure 2. Cumulative death rate (%) per group.

Growth (Table 2).

Before inoculation, no growth differences among groups was observed. At 46 days of age, 4 days after inoculation, rabbits receiving bacitracin as a preventive treatment through the feed (group B) or through drinking water (group C) had a growth significantly higher than the control group receiving no treatment (group A) and than group (D), treated 3 days after inoculation. At 46 days of age, group D just had one day of treatment with Bacivet S® in drinking water and is consequently not distinguishable from the control group. At 53 days of age, at the end of disease expression, rabbits from group D had significantly higher body weight than non treated rabbits from the control group, but had a significantly lower body weight than groups B and C. Average body weight at 53 days of age of groups B, C and D were higher than group A by 17.6%, 17.6%, and 10.3%, respectively. From 53 to 67 days of age, period following disease expression, a compensatory growth was observed on groups A and D compared to groups B and C. This compensatory growth was higher for group D. At 67 days of age, no significant difference of body weight was found among groups B, C and D. Overall, total body weight of produced rabbit at the end of the trial by groups B, C and D were higher than group A by 63%, 55% and 43%, respectively.

DISCUSSION

In rabbit farms facing regular problems with ERE, all rabbits are not contaminated at the same time. It can be considered that when a treatment is applied, assuming that this one is not too late, some rabbits are treated preventively and some others curatively. The protocol of this study takes into account these two cases.

Reproduction of the disease was in accordance with what we were expecting with a death rate of 33.3% on the control group. Kinetic of mortality was similar with results previously obtained with TEC inoculum and its derivatives (LICOIS and COUDERT, 2001). Consequences of the contamination on zootechnical criteria are early and observable from the 2nd day following inoculation with significant differences on growth and a start of mortality from the 4th day following inoculation.

Table 2. Growth performances.

	Treatments				
	A : Control non treated	B : Bacitracin 100 ppm in the feed	C : Bacivet S 33-52 days, preventive treatment	D : Bacivet S 45-59 days, curative treatment	Stat
Body weight at weaning (g)	777.2	776.4	777.1	776.9	NS
Body weight 39 days (g)	1096	1085	1123	1102	NS
Body weight 46 days (g)	1223[a]	1322[b]	1336[b]	1260[a]	P<0.001
Body weight 53 days (g)	1316[a]	1547[c]	1547[c]	1451[b]	P<0.001
Body weight 60 days (g)	1599[a]	1800[b]	1796[b]	1746[b]	P<0.001
Body weight 67 days (g)	1858[a]	2021[b]	2017[b]	2010[b]	P<0.01
Total body weight of produced rabbits (kg)	52.0	84.9	78.7	74.4	

[a, b, c,] : on the same raw, means having the same letter are not significantly different at the 5% level (Duncan Test)

In difficult sanitary conditions like ERE, growth rates are very good indicators of morbidity. On this trial, growth results are in perfect agreement with results on mortality observed in the 4 groups.

This trial confirm once again, the efficiency of bacitracin in the form of Albac® to control ERE syndrome in rabbits as it has already been observed (DUPERRAY *et al.*, 2000 ; DUPERRAY *et al.*, 2003). Results of this study justify the extensive use of bacitracin in the feed in french rabbit farms in the past 4 years.

Results are equivalent between bacitracin in the form of Albac® and soluble bacitracin in drinking water (Bacivet S®) as a preventive use for a similar duration of treatment. The Bacivet S® treatment on group C was stopped at 52 days of age, 4 days before the end of mortality expression of the control group, unlike group B and D where the treatment was carried on up to 56 days of age. The restart of mortality on group C, two weeks after withdrawing the treatment (66 days of age), was possibly linked to a recontamination through the environment due, in part, to group A. The use of Bacivet S® as a curative treatment for 14 days after symptoms appear (3 days after inoculation) reduces mortality and morbidity compared to the control group but is less efficient than a preventive use. The interest of the preventive use compared to the curative use is expressed by a gain in total body weight of rabbit produced of +5.8%. In the long term, it is likely that the low morbidity ,observed with the preventive use, contribute to reduce the contamination of the rabbit farm.

Differences observed between the therapeutic objective and the real quantities of bacitracin absorbed through the feed and through the drinking water can be partially explained by the weather conditions with an extreme heat during the trial study. The

heat wave caused a reduction in feed consumption and an increase in water consumption. The dose of bacitracin absorbed for group B is in fact quite close to half of the target dose. The very good results of this group in ERE conditions confirm results obtained by MERCIER and RICHARD (2001). Theses authors had already shown the efficiency of bacitracin in the feed for a concentration of 50 ppm (2100 IU/kilos the feed).

CONCLUSION

The objective of this study was to test the efficiency of soluble bacitracin in drinking water (Bacivet S®) as a preventive or curative use compared to bacitracin in the feed (Albac®) during an experimental reproduction of ERE. Results of this study confirm the efficiency of bacitracin in ERE syndrome conditions. Bavicet S® as a preventive use is as efficient as bacitracin 100ppm in the feed (Albac®) during the acute period of the disease. The curative use of Bavicet S® for 14 days, after symptoms appear, reduces also mortality and morbidity of rabbits compared to the control group that received no treatment but is less efficient than a preventive use. This can be mainly explained by the extreme rapidity of disease apparition after contamination (less than 48 hours).

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