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INTEREST OF ZINC BACITRACIN IN THE TREATMENT AND THE PREVENTION OF THE EPIZOOTIC RABBIT ENTEROCOLITIS SYNDROME IN GROWING RABBIT.

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ABSTRACT

Since the end of 1996, a new digestive syndrome appeared in France and then in Europe generating a very high mortality in rabbit farms : the Epizootic Rabbit Enterocolitis (ERE). The presence of Clostridia was very often showed in rabbits which were struck down by this syndrome.

In this context, the zinc bacitracin incorporated in feeds was tested on experimentally infected rabbits by the ERE. Three trials were realised : in the trial n°1, the treatment with 70 and 100ppm bacitracin allowed a high decrease of the mortality. It diminished from respectively 40.5 and 42.0% for groups with no treatment in their feeds, to 6.2 and 3.1% for rabbits which received a zinc bacitracin treatment. The trial n°2 follow immediately, without cleaning and disinfecting the fattening room, the use of bacitracin at the same rates was again significantly efficient to control the losses induced by the syndrome. A 3rd trial was run with the same feeds as in the trial n°2 (except the contaminated feed) but on a different site which was not contaminated by the ERE. The mortality rate was globally very low (0.2%) and no significant differences were found between the tested diets. All trials emphasised the importance of the contamination level of the buildings in the expression of the ERE.

INTRODUCTION

Since the ERE has appeared in 1997 (Coudert and *al.*, 1997), numerous works have been run to understand, describe and identify its origin. Today, according these works, we know with assurance that it concerns an infectious pathology with epidemic characters.

The most common admitted hypothesis is the presence of an unidentified infectious agent (virus?) which weaken the rabbit by inducing huge lesions of the digestive tract and lung mucous membrane (Licois, 1998). We also know that there is a development of secondary digestive troubles of bacterial origin. In accordance with this, clostridia (perfringens and/or spiroform type) play an active role in the expression of the ERE (stomach distending, gas in the caecum, mucus hypersecretion, light yellowish diarrhoea). The consequence of these troubles is the outbreak of a brutal mortality in fattening rabbits, most of the time between 35 and 60 days of age. This mortality can vary from 1 to 3% per day or even more (Lebas and *al.*, 1999 ; Licois and Coudert, 1999).

In this context, it is not surprising that antiobiotherapy reveal itself as an efficient treatment against the ERE. It is particularly true for active antibiotics Gram+ germs which include clostridia (Carman and Wilkins, 1991). On the other hand, it is well known that the zinc bacitracin has a positive effect on rabbit zootechnical performances and mortality (King, 1976; King, 1980 ; Berta and *al.*, 1983 ; Abdel-Samee, 1995). It is also not astonishing that hygiene prevention is efficient : strong disinfection with a part-time sanitary stop or even better a total stop. It is feasible by doing an one group breeding management or a complete annual renewal of the breeder flock.

For one year at the Guyomarc'h research station (Saint-Nolff, France), huge resources have been involved to run trials on the ERE in order to find solutions permitting to "manage"

the problem. Therefore, an experimental model was built in such a way that it is possible to systematically reproduce the enterocolitic syndrome by giving to the rabbits in trials a feed which is got back from a contaminated farm.

MATERIAL AND METHODS

To realise this type of trial, a room for fattening rabbits has been isolated from the others in the experimental farm. It is in a such context that the efficiency of several antibiotics of which the zinc bacitracin were tested. The zinc bacitracin is a bactericide antibiotic from the polypeptides family with a main GRAM+ activity. Therefore it is very active on *Clostridium perfringens* and *spiroforme.* In other respects, we know that in the pig and the broiler, the bacitracin does not pass through the intestine fence. These results might be confirmed in the rabbit by actual trials. Consequently on this subject, we can reasonably think that zinc bacitracin offers an important security.

Two successive trials were run at the Guyomarc'h experimental farm to test the efficiency of the zinc bacitracin in prevention and treatment of the ERE of fattening rabbits. The first trial was named n°1 (from 19/01/98 to 24/02/98): zinc bacitracin was tested at two doses. The second was named n°2 (from 02/03/98 to 06/04/98) : zinc bacitracin was tested again at two doses and also compared with an association of two other antibiotics (tiamulin and apramycin) used in the field A 3rd trial (n°3) was run at the AFSSA[1] (Agence Française de Sécurité Sanitaire Alimentaire, Ploufragan, France) in an healthy environment in March/April 1998.

Trial n°1. Experimental conditions

After cleaning, disinfection and a 7 days sanitary stop (use of formol), 256 rabbits were weaned at 31 days of age and distributed, according to their weight and the origin litter, in 4 homogeneous groups in an isolated room. In order to enhance the expression of the disease, the density was increased to 25,7 rabbit/m² and important deviation of the day-night temperature (> 8°C) was generated during the all trial period. The drugs were taken out 7 days before the slaughtering. The feed distribution is presented in table 1. The basic feed is the same for each group.

Table 1. Distribution of feeds for the trial n°1

Group 1	Feed which is taken back from a rabbit farm contaminated by the ERE
Group 2	not contaminated Feed
Group 3	not contaminated Feed + zinc bacitracin 70 ppm
Group 4	not contaminated Feed + zinc bacitracin 100 ppm

Trial n°2. Experimental conditions

Table 2. Distribution of feeds for the trial n°2

Group 1	contaminated Feed (same as in the n°1)
Group 2	not contaminated Feed
Group 3	not contaminated Feed + Tiamulin 100 ppm + Apramycin 100 ppm
Group 4	not contaminated Feed + zinc bacitracin 70 ppm
Group 5	not contaminated Feed + zinc bacitracin 100 ppm
Group 6	not contaminated Feed + zinc bacitracin 100 ppm + Apramycin 100 ppm

The same room as in the trial n°1 was used but it was not cleaned and disinfected between the two trial. 360 rabbits were weaned at 31 days of age and distributed in 6 homogeneous groups

according to their weight and the origin litter. The high density is over 25 rabbits/m². The same temperature conditions were applied. The drugs were also taken out 7 days before the slaughtering.. The feed distribution is presented in table 2. The basic feed is the same as in the LP4 experiment.

Trial n°3. Experimental conditions (March/April 1998)

This trial was run at the experimental farm of the ASSFA. Density and temperature were standard and no group with contaminated feed was included in this experiment. The 5 non-contaminated feeds from the trial n°2 were also distributed here, as showed by table 3.

Table 3. Distribution of feeds for the trial n°3 in non contaminated environment

Group 1	**Feed which is not contaminated**
Group 2	**Feed + Tiamulin 100 ppm + Apramycin 100 ppm**
Group 3	**Feed + zinc bacitracin 70 ppm**
Group 4	**Feed + zinc bacitracin 100 ppm**
Group 5	**Feed + zinc bacitracin 100 ppm + Apramycin 100 ppm**

Measurements and statistical analysis

Weights (W) measurements were performed at the age of 31 days (weaning), 53 days and 67 days (slaughtering) for the n°1 and n°2 trials. For the trial n°3, rabbits were weighted at 32 days, 53 days and at the slaughtering (74 days). From this, weight gain (WG) were calculated. Mortality was also recorded as the temperature. Differences between groups were analysed at P=0.05 using the SPSS statistical software.

RESULTS AND DISCUSSION

The n°1 and n°2 trials showed a very strong capability to be contagiousness of the ERE with a chain contamination from the groups which received a contaminated feed. In the trial n°1, the group1 (contaminated feed) mortality began at 16 days of feed distribution (see Figure 1). It is only 5 days after that the group 2 (standard feed) started to die. For these 2 groups animal losses were over 2% a day and exceeded 40% at the end of the experiment. It has to be noticed that at the same time the observed mortality on rabbits reared in healthy conditions on another part of the experimental farm (3 non contaminated rooms) was very low with the standard feed : 1,9% of 778 rabbits.

Figure 1. Evolution of mortality in trial n°1

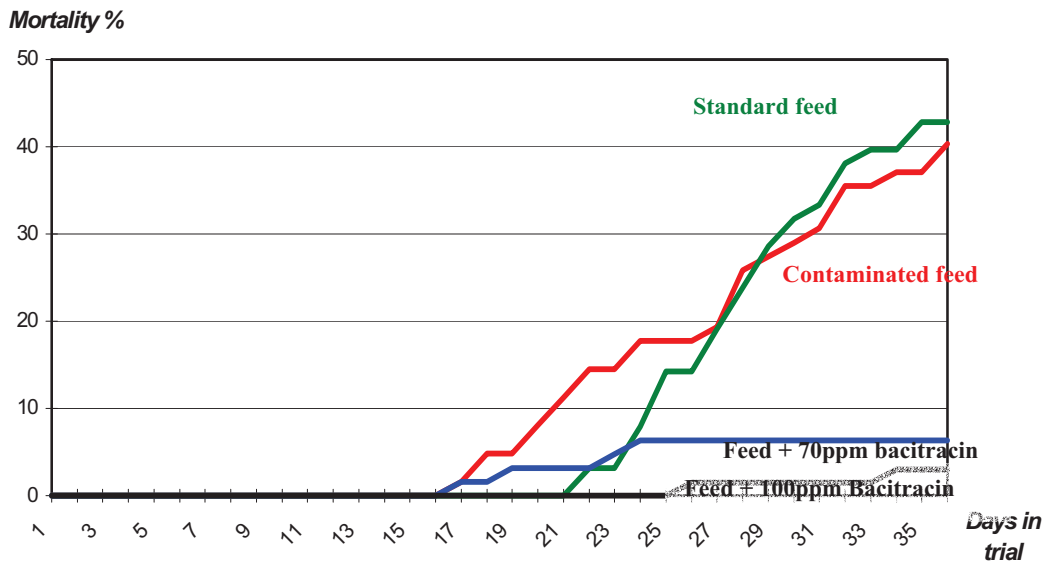
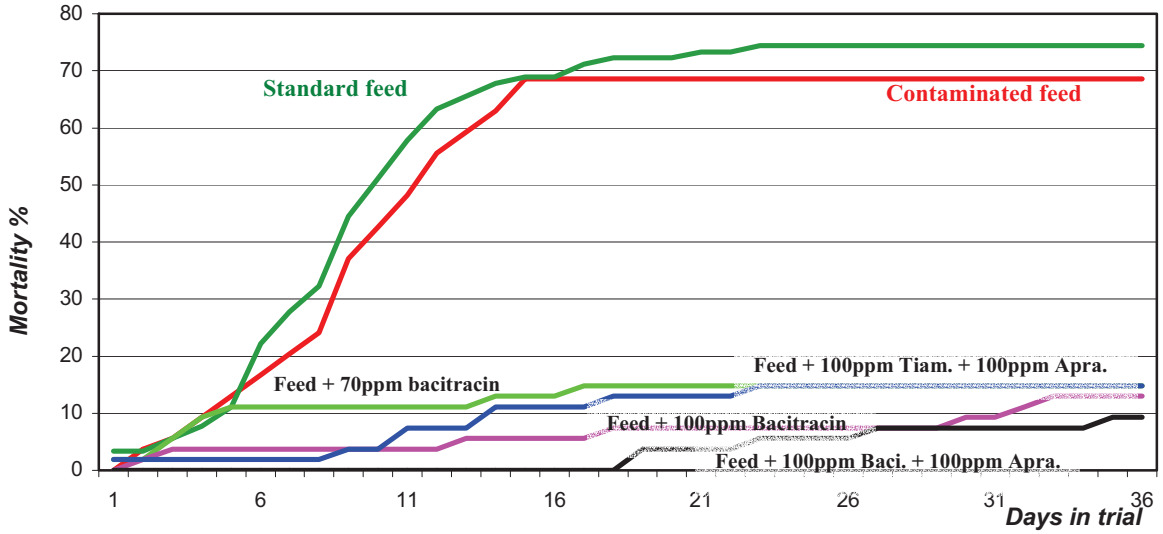


Figure 2. Evolution of mortality in trial n°2



The trial n°2 showed that the ambient environment is strongly contaminating because the lack of cleaning and disinfecting reinforced the ERE virulence : losses of groups 1 and 2 appeared from the weaning and reach 68.5% in 15 days (more than 4.5% per day) (see figure 2). As show tables 4 and 5, figures 1 and 2, bacitracin allowed a strong decrease of mortality of contaminated rabbits with a high statistical significance : the mortality differences between groups with bacitracin supplemented feeds and uncontaminated groups were very important, respectively -33,8 and -61,4 % for both n°1 and n°2 trials. In trial n°1, there is slight dose response with a lower mortality (but not significant)with 100 ppm bacitracin compared with 70 ppm. .In trial n°2, the 100 ppm bacitracin diet give comparable results to the 100 ppm Tiamulin / 100 ppm Apramycin diet. The add of 100 ppm Apramycin to the 100 ppm bacitracin did not improve results.

The trial run at the ASSFA with the same feeds (but without contaminated feed) at the same time shows a very low mortality (0.2%) without any disease. In a healthy environment y, the antibiotic contribution logically gave no effect.

In a contaminated environment (Trials n°1 and 2), the ERE syndrom shows a strong reduction in BWG and final live weight compared with rabbits maintained in a healthy environment (Trial n°3).The use of antibiotics improved significantly the growth rate and the slaughtering weight in Trials n°1 and 2.

Table 4. Results of the trial n°1.

Trial n°1	Contaminated feed	Standard feed	Feed + 70ppm bacitracin	Feed + 100ppm bacitracin
Rabbits in trial	63	62	62	66
Weaning weight at 31 d (g)	808	810	808	815
Slaughtering weight At 67 d (g)	2106 (100) B	2116 (100,5) B	2420 (114,9) A	2429 (115,3) A
DWG* 31-67 d (g)	36,1 B	36,3 B	44,8 A	44,8 A
Mortality (%)	40,3 A	42,9 A	6,5 B	3,0 B

*DWG : Daily Weight Gain

Table 5. Results of the trial n°2 and n° 3.

Trial n°2	Contaminated feed	Standard feed	100ppm Tiamulin + 100ppm Apramycin	70ppm bacitracin	100ppm bacitracin	100ppm bacitracin + 100ppm Apramycin
Rabbits in trial	90	54	54	54	54	54
Weaning weight at 31 d (g)	741	742	737	743	742	742
Slaughtering weight at 67 d (g)	2158 c	2183 c	2224 b	2296 a	2234 ab	2269 a
DWG* 31-67 d (g)	39.2 c	39.1 c	41.3 b	42.8 a	41.2 ab	42.4 a
Mortality (%)	74,4 a	68,5 a	9,3 b	14,8 b	13,0 b	14,8 b
Trial n° 3						
Rabbits in trial		98	98	96	98	98
Weaning weight at 31 d (g)		822	822	820	822	822
Slaughtering weight at 67 d (g)		2554 a	2555 a	2588 a	2582 a	2567 a
DWG* 31-74 d (g)		41.3 a	41.3 a	42 a	41.9 a	41.5 a
Mortality (%)		0	0	1	0	0

*DWG : Daily Weight Gain

CONCLUSION

The synthesis of the 3 trials put in evidence the infectious character of the ERE.

1. The trial n°1 showed that rabbit which have eaten the contaminated feed are the first to get sick. In comparison to those rabbits, the contamination of rabbits eating non contaminated and medicinal feeds was observed with a delay of 5 days.
2. The level of mortality in the trial n°2 was almost twice higher than in the trial n°1 and this in relation with the lack of cleaning and disinfecting of the room.
3. In a non contaminated environment (Trial n°3), the mortality rate stay very low in presence or not of medicine treatments.

The trial n°1 clearly showed the efficiency of the zinc bacitracin on the ERE in fattening rabbits. In Trial n°2 , zinc bacitracin is as efficient as other antibiotics commonly used in the field (tiamulin and apramycin). According to the literature not much scientific works showed a such positive effect for the bacitracin. Indeed , the positive effects known of bacitracin (growth promoter and decrease of mortality) were observed in healthy environment (King, 1976 ; Berta and al.,1983 ; Abdel Samee ,1995).

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