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EVALUATION OF TILMICOSIN IN FEED FOR THE TREATMENT OF PASTEURELLOSIS IN COMMERCIAL RABBITS

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ABSTRACT

To evaluate the efficacy of tilmicosin for the treatment of respiratory pasteurellosis, 96 weanling rabbits showing respiratory symptoms or a risk to develop a clinical pasteurellosis were divided in two groups: a) tilmicosin at 200ppm level in feed for 7 days, b) oxytetracycline at 400ppm level in feed for 7 days. The group treated with tilmicosin showed a significant ($P < 0.0001$) reduction of clinical symptoms compared to the group treated with oxytetracycline. No significant differences have been observed in terms of body weight and feed conversion ratio at the end of the study.

INTRODUCTION

Tilmicosin is a semisynthetic macrolide antibiotic currently approved for veterinary use in cattle, swine and poultry. Tilmicosin is especially effective against *Pasteurella multocida* and *Bordetella bronchiseptica,* the most important bacteria involved in respiratory disease of rabbits (Sharon G, et al. 1996).
Pasteurellosis occurs especially in the weaning and growth period and represent in Italy the second cause of death after enteric diseases in rabbits. The breeding does provide a constant reservoir of *Pasteurella multocida*, and young rabbits are generally contaminated by contact with their own mothers (Weisbroth SH, et al. 1974 - Coudert P, et al. 1999)
In order to provide an understanding of clinical efficacy, the effect of tilmicosin was evaluated in a field trial.

MATERIAL AND METHODS

The study was carried out in a commercial rabbit farm with a recurring history of pasteurellosis situated near Bergamo. The unit contained 1800 Grimaud does. Before the study started, a preliminary bacteriological investigation was carried out to confirm *Pasteurella multocida* infection and the activity of tilmicosin/oxytetracycline in a sample of a few animals showing clinical symptoms.
A total number of 96 weanling rabbits, 35 days olds, with symptoms of respiratory disease or belonging to a nest where one or more rabbits died for respiratory disease have been randomly allocated to the two treatments.
Clinical symptoms was evaluated using the following scale:

0) No symptoms
1) Serous nasal discharge
2) Mucous nasal discharge
3) Mucopurulent nasal discharge

The rabbits were individually identified, weighed and caged two by two on cages equipped with manual feeders.

The two treatments were:

a) tilmicosin (Pulmotil® G 200 - Elanco Animal Health) at 200ppm level administered in the feed for 7 days
b) oxytetracycline at 400 ppm level administered in the feed for 7 days (positive control) as routinely used in commercial farms.

Due to welfare issue a negative control group was not included.
Before start of the treatment samples of the medicated feeds were analysed to ensure the correct dosage and treatment.
On day 7, four animals from each treatment group were necropsied to examine their lesions and to collect swabs from trachea and lungs for microbiological examination and antibiotic sensitivity.
After this period all rabbits received a non-treated feed and were kept under observation until the 14th day.
In order to evaluate the effect of the treatments the following parameters were considered:

- Daily mortality
- Individual clinical score on day 0, 3, 7, 10, 14
- Individual body weight on day 0, 7, 14
- Feed intake on day 7 and 14 (groups of four cages)

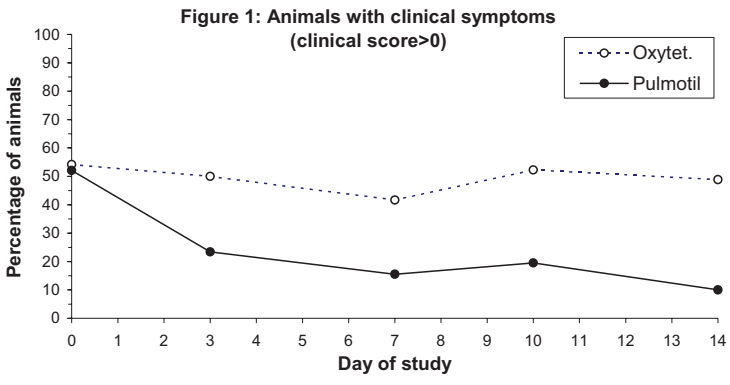
RESULTS AND DISCUSSION

At the start of the study (Day 0), the mean weight of the animals was just below 1100g in both treatment groups and just over 50% of the animals in each group had clinical symptoms, see Tables 2 and 3.
In total, five animals died during the study (four in the Pulmotil group, one in the Oxytetracycline. group). There were no significant differences between the groups in terms of mortality. In the tilmicosin group, one animal died on day 2 without having received medicated feed, the other three showed signs of enteric colibacillosis. An additional four animals in each treatment group were removed for necropsy on Day 7, see Table 1.

Table 1: Mortality and removals from the study

		Pulmotil (n=48)	Oxytet.(n=48)	P-value
Mortality Days 0-7	n (%)	3 (6%)	0 (0%)	0.24
Mortality Days 8-14	n (%)	1 (2%)	1 (2%)	1.00
Mortality Days 0-14	n (%)	4 (8%)	1 (2%)	0.36

The proportion of animals with clinical symptoms remained at around 50% in the Oxytetracycline group throughout the study, but in the Pulmotil group this proportion was below 25 % from Day 3 onwards. This difference between the treatment groups was statistically significant at each of the four time points considered (Days 3, 7, 10 and 14), see Table 2 and Figure 1. A small number of the animals with positive scores had clinical scores of 2, and the majority of these more severely affected animals were in the Oxytetracycline group, but there were not enough of these animals to show a statistically significant difference between the groups in terms of this parameter.



Probably due to the severity of clinical sintoms the average daily weight gain and the feed conversion ratio during the treatment period were particularly low.

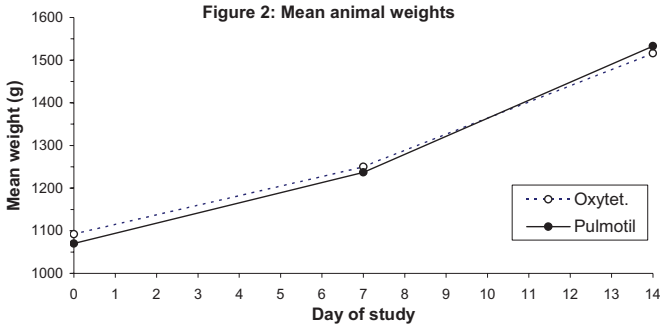
Table 2: Clinical scores

animals with clinical symptoms		Pulmotil (n=48)	Oxytet. (n=48)	P-value	N.B. Animals with clinical symptoms had scores of 1 (serous rhinitis), except for five animals on Day 7 (all Oxytet. group), five animals on Day 10 (all Oxytet. group), and six animals on Day 14 (five Oxytet. group, one Pulmotil group) which had scores of 2 (mucous rhinitis).
on Day 0	n (%)	25/48 (52%)	26/48 (54%)	1.00	
on Day 3	n (%)	11/47 (23%)	24/48 (50%)	**0.01**	
on Day 7	n (%)	7/45 (16%)	20/48 (42%)	**0.01**	
on Day 10	n (%)	8/41 (20%)	23/44 (52%)	**0.004**	
on Day 14	n (%)	4/40 (10%)	21/43 (49%)	**<0.001**	

The average weight of the animals still in the study was 1237g on Day 7 and 1533g on Day 14 in the Pulmotil group, compared with 1250g on Day 7 and 1516g on Day 14 in the Oxytetracycline group, see Table 3 and Figure 2.

Table 3: Weights and daily weight gain

		Pulmotil (n=48)	Oxytet. (n=48)	P-value
Weight on Day 0 (g)	mean	1070	1092	0.41
Weight on Day 7 (g)	mean	1237	1250	0.66
Weight on Day 14 (g)	mean	1533	1516	0.63
daily weight gain Days 0-7 (g/day)	mean	24.5	22.6	0.63
daily weight gain Days 7-14 (g/day)	mean	41.6	36.4	0.07
daily weight gain Days 0-14 (g/day)	mean	33.3	30.1	0.15



There were no significant differences between the treatment groups in terms of animal weights, average daily weight gains, average daily feed intake or feed conversion ratios, see Table 4.

Table 4: Feed intake and feed conversion

		Pulmotil (groups=6)	Oxytet. (groups=6)	P-value
daily feed intake Days 0-7 (g/animal/day)	mean	71	81	0.14
daily feed intake Days 7-14 (g/animal/day)	mean	116	111	0.26
daily feed intake Days 0-14 (g/animal/day)	mean	91	95	0.31
Feed conversion ratio Days 0-7	mean	3.18	4.42	0.31
Feed conversion ratio Days 7-14	mean	2.85	3.20	0.22
Feed conversion ratio Days 0-14	mean	2.93	3.35	0.09
Nominal tilmicosin intake (mg/kg per day)	mean	12.2	27.6	

In conclusion, the group treated with 200 ppm. of tilmicosin in the feed showed a significant reduction of clinical symptoms and zootechnical results similar to the oxytetracycline group. Clinically animals treated at this dose showed no adverse reactions.

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REFERENCES

COUDERT P. 1980. Pathologie et conduite de l'élevage des lapines reproductrices. Point Vet. 10:61-65

COUDERT P, et al. 1986. Pasteurellose non respiratoire en élevage intensif: lìotite moyenne des lapines reproductrices. Cuni-Sciences, 3:1-6

COUDERT P., et al. 1988. Establishment of a specific pathogen free rabbit breeding colony without hysterectomy and hand-rearing procedures. 4th Congress of the World Rabbit Science Association, 2:137-148

COUDERT P, et al. 1999. Le point sur la pasteurellose du lapin. 8èmes Journ. Rech. Cunicole Fr. Paris

DEEB BJ, et al. 1990 . Pasteurella multocida and Bordetella bronchiseptica infections in rabbits. J Clin Microbiol. Jan;28(1):70-5.

DEHOUX JP, et al. 1996. Epizootics of pasteurellosis in a semi-intensive breeding farm of indigenous rabbits in Senegal. Rev Elev Med Vet Pays Trop.;49(2):98-101. French.

DI GIACOMO RF, et al. 1987. Transmission of Pasteurella multocida in rabbits. Lab Anim Sci. Oct;37(5):621-3.

DI GIACOMO RF, et al. 1991. Naturally acquired Pasteurella multocida infection in rabbits: clinicopathological aspects. Can J Vet Res. Jul;55(3):234-8.

KPODÉKON et al. 1999. Pasteurellose du lapin: revue. Rev. Méd. Vét.;150(3):221-232

REDONDO E, et al. 1993. Experimental reproduction of acute pneumonic pasteurellosis in rabbits. Histol Histopathol. Jan;8(1):97-104.

RIDEAUD P, et al. 1999. Pateurellose du lapin: pathogénicité de cinc souches inoculées par voie intradermique ou intranasale. 8èmes Journ. Rech. Cunicole Fr. Paris

SHARON G, et al. 1996. Use of tilmicosin for treatment of pasteurellosis in rabbits.Am. Jour. Vet. Res. 57(8):1180-1184

SCORNEAUX B, et al. 1999. Intracellular accumulation, subcellular distribution, and efflux of tilmicosin in bovine mammary, blood, and lung cells. J Dairy Sci. Jun;82(6):1202-12.

WEISBROTH S.H, et al. 1974. The biology of the laboratory rabbit. Academic Press, New York and London, 194-198