

‡ENILCONAZOLE AS A TREATMENT OF NATURALLY OCCURRING DERMATOPHYTOSIS IN RABBIT FARMS : A REVIEW.

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ABSTRACT : This article summarises six clinical trials with the antimycotic enilconazole carried out in four countries. It is concluded that disinfection with enilconazole spray of the total environment (walls, ceiling, cages, etc.) in rabbit stables is an effective way of controlling dermatophytosis. The number of ringworm lesions regressed substantially after the application of the ready-to-use

spray. A high dosage of 50 mg/m² enilconazole was applied because caging and nest materials and other litter were present. No side-effects were observed. This treatment should be carried out twice weekly in batteries filled with rabbits and should be continued for at least 3 weeks.

RESUME : Emploi de l'enilconazole pour traiter la dermatophytose spontanée survenant dans les élevages de lapins : une revue.

Cet article résume six essais cliniques de l'antimycosique enilconazole menés dans quatre pays. On peut en conclure que la désinfection par vaporisation de l'enilconazole dans la totalité de l'environnement (murs, plafond, cages...) des élevages de lapins est un moyen efficace de contrôler la dermatophytose. Le nombre de

lésions cutanées diminue substantiellement après l'application du spray prêt-à-l'emploi. Il a été utilisé un dosage élevé de enilconazole (50 mg/m²) à cause de la présence des cages, de la garniture des nids et des litières. Nous n'avons pas observé d'effets secondaires. Ce traitement peut être appliqué deux fois par semaine dans les cellules d'élevage contenant des lapins et doit être poursuivi pendant au moins 3 semaines.

INTRODUCTION

There has been an increase in the incidence of dermatophytosis in rabbit farms since large-scale breeding began. Generally *Trichophyton mentagrophytes* is detected. However, another ringworm fungus, *Microsporum canis*, is increasingly isolated in Western Europe in rabbit-breeding units. Carriers such as rats, mice, cats, dogs and even man can introduce the infection. It spreads very rapidly in these units, with their high population density, and persists as a chronic condition.

Generalised infection can lead to poor condition and ultimately the death of young rabbits. The condition of the young rabbits is poor and morbidity and economic losses are considerable.

The zoophilic dermatophytes affecting rabbits are also pathogenic to man. The zoonotic infection of persons handling these rabbits, as well as of the members of their family, is a real danger.

enilconazole*, an antimycotic of the miconazole series, has proven its antiseptic value in dermatophytosis in cattle, horses and dogs, as well as against aspergillosis in poultry.

This article summarises the results of the most recent clinical trials with the antimycotic enilconazole in rabbit farms in four countries.

BELGIUM

Disinfection of the environment with the enilconazole ready-to-use spray can be practised as an indirect treatment of the animals. As shown below in the next two trials, spraying the rabbit farms, without directly treating the rabbits, is an alternative in the control of dermatophytosis.

In a study by VAN CUTSEM *et al* (1985) the optimum dosage was determined for a spray of enilconazole emulsifiable

concentrate (15%) as a disinfectant in rabbit farms. During the antifungal disinfection of the environment the rabbits remained in their cages.

In rabbit farm A :

with 826 cross-bred rabbits (Californian x New Zealand White) all the animals were older than 4 weeks. The rabbits were housed in galvanised wire mesh cages in batteries on flat-deck: the breeding animals were confined to the inner rows, the fattening rabbits to the outer rows.

Before treatment and at regular intervals during and after treatment, samples were taken from infected areas of the rabbits for laboratory investigations using Wood's light, microscopy and culture media. At each sampling, 20 petri-dishes were distributed equidistant from one another on the wire mesh cages. Just before treatment, the open plates with Sabouraud agar (Sab) were exposed for 30 minutes so that the agar would collect fluff and spores from the environment. The plates were incubated at 25°C for 30 days, and were examined every 2 days. The colonies growing on each plate were identified and the number of colonies of *M.canis* was counted.

Once weekly the fluff accumulated on the wire meshes and the floor was burned superficially with a propane burner. The emulsifiable concentrate of 15% enilconazole was diluted in 99 parts of water at 60°C and sprayed twice weekly in the environment, especially on the walls and ceiling.

Initially a low dosage of 15 mg enilconazole per square metre of floor area was applied twice weekly for 27 weeks. After this treatment the dosage was doubled to 30 mg/m² and applied twice weekly for 22 weeks. In the following 23 weeks a final dosage of 50 mg/m² twice weekly was administered.

In rabbit farm B :

harbouring 440 rabbits all animals were cross-bred rabbits (Californian x New Zealand White) with 20 young breeding

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Table 1: Treatment of ringworm lesions with enilconazole spray at 15, 30 and 50 mg/m² (Rabbit farm A)

Week	No of rabbits	% Ringworm lesions	Mean no. of colonies per plate (n=20)
15 mg/m²			
0	826	23.4	55.0
2	782	29.6	66.8
4	832	17.6	71.4
7	905	19.1	61.0
9	762	16.5	37.4
12	839	13.9	32.7
15	855	12.8	20.6
18	803	8.5	20.9
21	804	13.4	34.0
23	797	24.7	40.0
25	828	19.3	37.7
27	706	21.3	34.4
30 mg/m²			
0	706	21.3	34.4
3	561	14.6	8.0
6	463	12.9	6.8
9	614	8.5	16.4
13	766	9.7	3.5
16	873	9.6	5.8
19	714	17.2	6.7
22	653	9.1	4.8
50 mg/m²			
0	653	9.1	4.8
3	670	8.1	2.8
6	718	4.0	3.0
9	751	1.3	2.8
13	709	1.8	3.1
16	744	4.3	2.5
23	896	0.7	0.7
After treatment			
0	896	0.7	0.7
2	789	1.0	1.3
9	857	2.2	3.2
15	1,028	5.7	25.3

Chi-square test on ringworm lesions:

15 mg/m ²	0-27 weeks	P>.05
30 mg/m ²	0-22 weeks	P<.0001
50 mg/m ²	0-23 weeks	P<.0001
after treatment	0-15 weeks	P<.0001

females and 5 males, 40 adults and 5 males, and between 309 to 648 young and fattening rabbits of 4 and 14 week old. The rabbits were housed in galvanised wire mesh cages in batteries on flat-deck.

On mycological investigation, these rabbits were found to be positive under Wood's light as well as by microscopic examination of hair. In cultures, *M. canis* was isolated from all specimens. In this rabbit farm a dosage of only 50 mg enilconazole per square metre was applied on the walls, floor and ceiling twice weekly for 18 weeks to evaluate the validity of this dosage in the first investigation.

Results:

In rabbit farm A :

193 or 23.4% of the animals had ringworm lesions on the head and/or ears due to *M. canis*. Wood's light gave strong

green fluorescence in all infected animals. The microscopically examined samples, hairs and squames were largely invaded by dermatophyte spores and hyphae. In cultures *M. canis* was isolated from all specimens. Seventeen cultures of hairs collected from 30 lesion-free rabbits were positive for *M. canis*.

As shown in table 1 (farm A) an enilconazole concentration of 15 mg per square metre failed to reduce the infection. At 30 mg/m², the number of infected animals and the number of isolated fungal colonies decreased significantly. At 50 mg/m², the number of clinically infected rabbits and the number of isolated *M. canis* colonies fell below 1%. Hairs collected from 50 lesion-free rabbits at the end of the treatment gave one positive culture or an estimated carrier incidence of 2% of the total population. Two weeks subsequent to the end of the treatment, the infection pressure remained very low, as shown by the small number of dermatophyte colonies per Petri dish and the low number of positive animals. Two months after the end of the treatment the percentage of infected rabbits had risen to 2.2%. A check carried out 6 weeks later revealed that 5.7% of the rabbits presented ringworm lesions and the concentration of fungal elements in the environment had increased to 25.3 *M. canis* colonies per plate.

In rabbit farm B :

157 rabbits or 35.7% presented clinical ringworm lesions on the head and/ or ears (table 2). On mycological investigation, these were found to be positive under Wood's light as well as by microscopic examination. In cultures, *M. canis* was isolated from all specimens. The number of rabbits presenting clinical ringworm lesions regressed from 35.7% to 1.7% after 14 weeks. The number of infected hairs and spores collected from the environment declined rapidly during 11 weeks. These effects persisted for at least 17 weeks after the end of the last application. No clinical side-effects were observed.

THE NETHERLANDS

BRAEM and VAN CUTSEM (1985) investigated the efficacy of the final dosage of 50 mg per square metre in a rabbit farm with 856 rabbits (New Zealand x White Californian cross-bred) in the Netherlands. The trial site was a commercial breeding and fattening unit housing approximately 120

Table 2: Treatment of ringworm lesions with enilconazole spray at 50 mg/m². (Rabbit farm B)

Week	No of rabbits	% ringworm lesions	Mean no. of colonies per plate (n=30)
0	440	35.7	50.8
3	402	46.0	45.8
7	395	13.1	32.9
11	357	12.9	6.2
14	347	1.7	2.3
After treatment			
2	309	0.97	0.07
11	524	0.38	0.7
17	648	0.46	0.9

Chi-square test on ringworm lesions: 50 mg/m²: 0-14 weeks P<.0001
after treatment: 2-17 weeks P> 0.5

Table 3 : Number of rabbits showing lesions after a disinfection programme with enilconazole 50 mg/m² in a Rabbit Farm with poor hygiene and management practices (The Netherlands).

Week	Breeders		Unweaned		Fatteners		Total	
	No	% with lesions	No	% with lesions	No	% with lesions	No	% with lesions
-3	106	18.8	205	ND	545	28.1	856	26.6*
0	124	17.7	409	5.9	365	35.6	898	19.6
4	120	22.5	342	7.0	374	29.1	836	19.1
9	123	5.7	398	1.8	391	21.2	912	10.6
14**	118	1.7	427	1.2	395	12.7	940	6.1
17**	121	1.6	408	3.2	385	18.7	914	9.5
21	126	0	371	0.5	497	7.0	994	3.7
27	115	0.9	421	2.6	413	12.6	949	6.7
31	124	3.2	374	5.1	438	20.3	936	11.9

* unweaned, not taken into account. ** inadequate disinfection.

Chi-square test on total ringworm lesions: week 0-4: $P < .86$; week 0-27: $P < 0.0001$; week 0-31: $P < 0.0001$

rabbits for breeding, a number of young unweaned rabbits (between 205 and 427) and a number of fattening rabbits (between 365 and 545). The breeding and fattening rabbits were kept in 4 rows of galvanised wire mesh cages on flat-deck.

Dermatomycosis was diagnosed by the Animal Health station in Boxtel - The Netherlands. This commercial farm was severely infested with *M. canis* and had very poor hygienic conditions and management practices. Of the 856 rabbits present 26.6 % of the breeding and fattening rabbits had ringworm lesions caused by *M. canis*. Cleaning of the rabbit farm was not performed regularly; large amounts of fluff and dust were present, which was a constant source of infection.

To obtain a dosage of 50 mg enilconazole/m² floor surface, 50 ml of the emulsifiable concentrate was diluted in 5 litre water at 60°C. This emulsion was nebulized in the environment, on the walls and ceiling of the stable twice a week. Before introducing newly weaned rabbits for fattening in the cages, the cages were burned with a propane burner to destroy the accumulated fluff and pathogenic agents. The rabbit farm was treated twice weekly for 27 weeks. From weeks 14 to 17 cold water was used to prepare the end

emulsion instead of water at 60°C. If cold water is used for the emulsion, saponification often occurs, resulting in inadequate disinfection.

The farm was visited 3 weeks before the start of the treatment, at the start, every four weeks during the treatment period and one month after the last treatment. On each observation day the incidence of dermatophyte lesions was determined. From 10% of the affected rabbits a sample of hair and crusts was taken for laboratory investigations at Janssen Pharmaceutica: microscopy and culture on Sabouraud agar containing penicillin, streptomycin and actidione. At each visit 40 Petri-dishes with Sabouraud PSA were exposed to the air for 30 minutes by open plate technique. The exposed Petri-dishes were incubated at 25°C and the number of colonies of *M. canis*, grown on each plate, was counted after 10 days. Before the start and one month after the last treatment hair samples were taken from rabbits without skin lesions for mycological examination in order to assess carrier incidence.

Results:

Three weeks before the start of the disinfection program 26.6 % of the rabbits showed ringworm lesions see table 3).

Rabbit farms in The Netherlands

