THERAPEUTIC TRIAL OF IVERMECTIN AGAINST *NOTOEDRES CATI* VAR. *CUNICULI* INFECTION IN RABBITS

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Summary:

Effect of 400 µg/kg of ivermectin against natural infection of *Notoedres cati* var. *cuniculi* mange in rabbits was evaluated in twenty rabbits which showed typical symptoms of notoedric mange and were randomly divided into two groups. Group I consisted of 15 rabbits treated with single s/c injection of ivermectin (Ivomec®, Dynamic Pharmacals, Bombay). In group II, five infected untreated rabbits were kept as control. Daily observations of clinical improvement and on the basis of examination of skin scrapings on days 0, 3, 6, 9, 16, 23 and 30 post treatment were done. Complete visual shedding of lesions was seen on day 6 after treatment and skin scrapping were found negative for mites after 7th day of treatment till the end of experiment. Histopathologically mites were present in stratum corneum and many were noticed in the burrows in epidermis. Marked hyperkeratosis, hyperplasia and acantholysis along with ballooning degeneration of epithelial cells of epidermis were seen.

KEY WORDS : *Notoedres cati*, ivermectin, rabbit.

Résumé : ÉTUDE THÉRAPEUTIQUE DE L'IVERMECTINE CONTRE L'INFECTION À *NOTOEDRES CATI* VAR. *CUNICULI* CHEZ LE LAPIN

L'effet de 400 µg/kg d'ivermectine contre l'infection naturelle du lapin par Notoedres cati *var.* cuniculi *a été évalué chez 20 lapins montrant des signes typiques de gale notoédrique et divisés en deux groupes randomisés. Le groupe I comportait 15 lapins traités par une injection sous-cutanée unique d'ivermectine. Le groupe II a été formé de cinq lapins témoins infectés et non traités. L'observation quotidienne de l'amélioration clinique, basée sur l'examen des lésions de grattage, a été effectuée aux jours 0, 3, 6, 9, 16, 23 et 30 après traitement. Une disparition complète des lésions cliniques a été observée au 6e jour après traitement, et l'examen cutané s'est négativé à partir du 7e jour. Sur le plan histopathologique, les agents infectieux était présents dans la couche cornée et nombreux dans les galeries creusées dans l'épiderme. Une hyperkératose, une hyperplasie et une acantholyse marquées ainsi qu'une dégénérescence ballonniforme des cellules épithéliales de l'épiderme ont été observées.*

MOTS CLÉS : Notoedres cati, *ivermectine, lapin.*

INTRODUCTION

Ivermectin has been extensively used in domestic animals against ecto and endoparasitic infestations (Campbell & Benz, 1984). In rabbits it has been tried against ectoparasites but for this, as per the literature it does not have a product licence (Mc Kellar *et al.*, 1992). However, ivermectin was shown to have activity against ectoparasites of rabbits for the first time by Wilkins *et al.* (1980). Subsequently, it was effectively used 400 µg/kg by subcutaneous (s/c) injections against ear mite *Psoroptes cuniculi* (Wright & Riner, 1985; Singh & Gill, 1989; and Pandey, 1989) and also against *Notoedres cati* (Singh & Gill, 1989). Ivermectin is easy to administer and as the drug reaches to the skin it can affect the mites which otherwise would not be affected by the topical application of any other drug (McKeller *et al.*, 1992). Therefore, in the present study it was decided to use ivermectin (Ivomec® Injection, Dynamic Pharmacals, Bombay) for the treatment of clinical cases of mange in rabbits.

MATERIAL AND METHODS

Twenty New Zealand white rabbits of either sexes weighing 2.0 to 3.5 kg (average 2.7 kg) were kept in the department for the experimental studies. All rabbits were kept in iron cages (two rabbits per cage) and maintained on nutritionally balanced diet. Almost all were found infected with mange at different degree of infestation. The symptoms and lesions of the clinical cases were recorded. Skin scrapings of the affected rabbits were collected for examination and identification of the mange mites after routine treatment with 10 % KOH (Soulsby, 1982). Microscopic examination of skin revealed abundant mites at various developmental stages. The mites were identified as *Notoedres cati* var. *cuniculi* on the basis of description given in Muller *et al.* (1983). All the rabbits showing clinical symptoms and lesions of the disease were randomly divided into two groups. The

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group I consisted of 15 rabbits and group II of five rabbits. The rabbits of group I were treated subcutaneously (behind the shoulder) with undiluted Ivomec® Injection (ivermectin 1 % w/v) 40 µl/kg body weight with 24 gauge needle. Group II rabbits served as untreated control. This form of ivermectin was selected on the basis of prior successful use in rabbits, availability and ease of administration. The treated rabbits were physically examined daily for clinical improvement and their skin scrapings were examined on day 0, 3, 6, 9, 16, 23 and 30 post treatment for the presence of mange mites.

For histopathology skin biopsies were taken randomly from infected untreated rabbits to detect mites and their pathological effects. These were preserved in 10 % neutral buffered formalin and 5 µ thick paraffin sections were cut and stained with haematoxylin and eosin (H & E).

RESULTS

In the infected rabbits lesions were noticed in the form of whitish crusts and scabs which were found chiefly in the areas where hairs were spars and short i.e. on the nose, head, eyelids and ears. In some cases lesions were found on the feet specially in toe region. There was formation of remarkable wart-like or horn-like excrescences of considerable size on the nose. Heavy crusts around the eyes interfered with vision, in some rabbits there was conjunctivitis and greyish white exudate was coming out from both the eyes.

The group I of rabbits were infected with an average of 120 mites/cm^2 before treatment which included various stages of life cycle viz. eggs, larvae, nymph and adults. Two days after treatment with ivermectin, rabbits stopped scratching and biting. Marked progressive improvement in the appearance of lesions was observed. The sheding of lesions i.e. crusts and scars started on 3rd day and complete visual sheding of lesions was recorded on 6th day of treatment respectively. There was no visible change in the lesions and symptoms of infected, untreated control rabbits except that two of the rabbits developed generalised infection (group II). Twelve rabbits of treated group had no mites by the 7th day of treatment and all the rabbits were negative by 9th day. The rabbits remained free of mites until the end of trial. The corresponding figures for untreated controls were 115 mites/cm^2. By the 25th day all the treated animals were recovered completely with the new growth of hairs (Table I).

The sections of skin of infected rabbits showed cut sections of the mites in the stratum corneum and most of them had dug burrows deep into the epidermis (Fig. 1). Pathological changes apparent in the skin were marked hyperkeratosis, hyperplasia and acantholysis of the epidermis and at places ballooning degeneration of epithelial cells in the epidermis. There was infiltration of eosinophils, lymphocytes, fibroblasts and few neutrophils.

Days after treatment	Infected and treated		Infected and untreated	
	Mites/cm^2 (means ± SEM)	Clinical observations	Mites/cm^2 (means ± SEM)	Clinical observations
0	120 ± 4.34	—	115 ± 5.93	No visible change in lesions and symptoms except two rabbits in which there was progressive development of generalized infection. Pruritis and crust formation was there and rabbits kept on scratching.
2	—	Stopped scratching and biting	—	
3	70.53 ± 5.17	Shedding of crusts and scars started	118.2 ± 5.27	
6	14.06 ± 2.55 (four rabbits negative)	Crusts and scars disappeared	114.8 ± 4.17	
7	2.6 ± 1.43 (three rabbits positive)	Wrinkling and keratinization decreased	—	
9	All were negative	Healing of lesions started	126.8 ± 2.15	
16	Negative	Normal texture visible with new growth of hairs	124.8 ± 2.87	
23	Negative	—	120.8 ± 2.35	
25	Negative	Complete cure with new growth of hair	—	
30	Negative	Complete cure with new growth of hair	127.4 ± 2.82	

Table I. — Clinical observations and parasitic burden (mites/cm^2) in Notoedric rabbit mange.

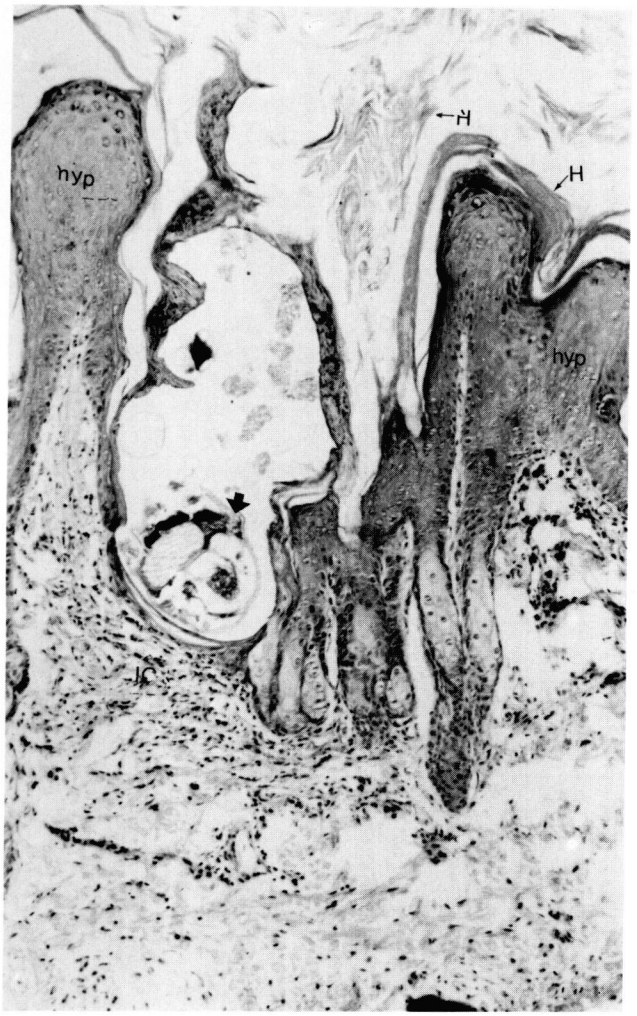

Fig. 1. — Section of skin showing *Notoedres cati* var. *cuniculi* mite (arrow) in a burrow in the epidermis along with marked hyperkeratosis (H), hyperplasia (hyp) in the epidermis and infiltration of inflammatory cells (IC) in the dermis below the parasite. H & E × 70.

DISCUSSION

The present study demonstrates that 400 µg/kg body weight single injection of ivermectin is successful in clinical and parasitological cure of *Notoedres cati* var. *cuniculi* associated mange infection in rabbits. These findings are in accordance with Renukaprasad *et al.* (1989). However, Wright & Riner (1985) reported that a single injection of ivermectin of 400 µg/kg b.w. could not eliminate *Psoroptic* mange infestation in rabbits. Ivermectin has no ovicidal effect (Pandey, 1989). Normally the eggs of *Notoedres* species hatch in four to five days (Gordon *et al.*, 1943). The absence of mites from 7th day to the end of experiment after ivermectin treatment indicates that sufficient concentration of drug is available to kill any larvae hatching from the eggs. It has been suggested that drug persists in rabbit tissues sufficiently long to remove new generation of mites as the egg hatch (Pandey, 1989 and McKellar *et al.*, 1992). These results suggest that the prolonged availability of ivermectin in the rabbits has a residual effect against mites (Pandey, 1989). The efficacy of ivermectin against the mange mite *Notoedres cati* var. *cuniculi* which were present in the keratin layer may be because of high concentration which is achieved in the skin (McKellar *et al.*, 1992). It is concluded that a single subcutaneous injection of ivermectin of 400 µg/kg body weight could be used for successful elimination of mange in rabbits.

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REFERENCES

CAMPBELL W.C. & BENZ G.W. Ivermectin: a review of efficacy and safety. *Journal of Veterinary Pharmacology and Therapeutics,* 1984, *7,* 1-16.

GORDON R.M., UNSWORTH K. & SEATON D.R. The development and transmission of scabies as studies in rodent infections. *Annals of Tropical Medicine and Parasitology,* 1943, *37,* 174-184.

MCKELLAR Q.A., MIDGLEY D.M., GALBRAITH E.A., SCOTT E.W. & BRADLEY A. Clinical and Pharmacological properties of ivermectin in rabbits and guinea pigs. *Veterinary Record,* 1992, *130,* 71-73.

MULLER G.H., KIRK R.W. & SCOTT D.W. *Small animal Dermatology.* 3rd ed. W.B. Saunders Company, Philadelphia, 1983, 351-363.

PANDEY V.S. Effect of ivermectin on the ear mange mite, *Psoroptes cuniculi,* of rabbits. *British Veterinary Journal,* 1989, *145,* 54-56.

RENUKAPRASAD C., RAMASWAMY M., KUMAR M.M., GOPAL T. & KESHAVAMURTHY B.S. Therapeutic effect of ivermectin on rabbit mange. *Indian Veterinary Journal,* 1989, *66,* 1055-1057.

SINGH J. & GILL B.S. Treatment of mange of rabbits with ivermectin. *Indian Journal of Parasitology,* 1989, *13,* 115-118.

SOULSBY E.J.L. *Helminths, Arthropods and Protozoa of Domesticated Animals.* 7th Edn. ELBS and Bailliere Tindall, London, 1982, 764.

WILKINS C.A., CONROY J.A., HO P., O'SHANNY W.J., MALATESTA P.F. & EGERTON J.R. Treatment of Psoroptic mange with avermectins. *American Journal of Veterinary Research,* 1980, *41,* 2112-2113.

WRIGHT F.C. & RINER J.C. Comparative efficacy of injection routes and doses of ivermectin against *Psoroptes* in rabbits. *American Journal of Veterinary Research,* 1985, *46,* 752-754.

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