

## Efficacy of Ivermectin in Combination Treatment with Amitraz in Dogs with Generalized Demodicosis

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### 개의 전신성 모낭충증에 대한 ivermectin과 amitraz의 병용치료효과

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**ABSTRACT** : 난치성 전신성 모낭충증에 감염되어 약 4개월간 모낭충 치료제인 amitraz(0.0125%) 처치에도 불구하고 치유되지 않은 한국산 풍산개 2두에 대한 ivermectin 및 amitraz의 병용치료효과를 알아보았다. 전신성 모낭충증은 신체의 50% 또는 4개의 발에 모두 모낭충이 검출된 것으로 정의하였다. 내원시 신체검사, 심장사상충검사 및 최소 5부위에 대한 피부 박리검사를 실시하여 모낭충을 진단하였고 치료는 돼지용 ivermectin을 체중 kg당 0.5 mg을 피하로 매일 주사하였으며 1주일에 2회 amitraz 약욕을 실시하였다. 피부농피증은 cephalixin 20 mg/kg을 경구로 일일 2회 투여하여 치료하였다. 치료후 4주에 피부병변이 치유되기 시작하였으며 6주에는 탈모 및 소수의 발진을 제외하고는 피부병변이 정상으로 회복하였다. 피부박리검사는 6주에 모낭충이 검출되지 않았다. 이들 제제에 의한 부작용은 관찰되지 않았으며 매일 ivermectin 투여와 amitraz 약욕치료의 병용치료는 amitraz로 치료가 되지 않는 난치성의 전신성 모낭충증에 대한 치료기간을 단축시키는 효과적인 치료방법으로 생각된다.

**Key word** : generalized canine demodicosis, ivermectin, amitraz

### Introduction

Canine demodicosis is an inflammatory, parasitic skin disease in which a larger than normal number of the follicular mite *Demodex canis* inhabit in the hair follicles and sebaceous glands of various mammals and is one of the most frustrating canine skin diseases to treat. This mite is a normal inhabitant of the skin of most dogs<sup>1</sup>. This parasitic dermatose can be localized or generalized and is most often encountered in dogs younger than 1 year of age. Generalized demodicosis can occur in a squamous or pustular form due to the secondary pyoderma, and a spectrum of dermatologic lesions can be seen<sup>2</sup>. Generalized demodicosis often requires prolonged treatment that can be expensive, and sometimes unre-

warding.

Amitraz is currently the approved treatment for canine demodicosis and reported cure rate for amitraz vary from 0 to 92% of the cases<sup>3,4,5</sup>. In the treatment of chronic generalized demodicosis, with 6-month follow-ups, cure rates are reported to be no better than 50%<sup>4</sup>. This miticide is used in aqueous solution, freshly prepared, in concentrations varying from 250-600 ppm as topical applications weekly or every two weeks. In one study, 75% of cure rate achieved by treatment with 0.025% amitraz at 7-day intervals and 80% of cure rate in dogs treated with 0.050% amitraz at 7-day intervals<sup>4</sup>.

Ivermectin was a commonly used for the prevention of heartworm infection at monthly doses of 6 µg/kg in dogs<sup>6</sup>. In case of generalized canine demodicosis ivermectin was effective at 600 µg/kg weekly<sup>7</sup>. Also there is a report that a dog with am-

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itraz-resistant generalized demodicosis treated with 600 µg/kg of ivermectin orally once a day for 7 months<sup>1</sup>.

In present no studies have been conducted to evaluate the effectiveness of ivermectin in combination with amitraz. The purpose of the present clinical report was to evaluate the efficacy of ivermectin in combination with amitraz in recurrent generalized demodicosis in Korean native poongsan dogs.

## Case presentation

### Dogs

Privately owned Korean Native Poongsan dogs with generalized demodicosis that had failed to respond to biweekly or weekly applications of 0.025% amitraz solution were referred to Veterinary Teaching Hospital, College of Veterinary Medicine, Seoul National University. One adult dog was 1-year-old, female and has 21 kg of body weight. The other dog was 1-year-old, male and has 22 kg of body weight. Generalized demodicosis was defined as demodicosis involving at least 50% of the body or as demodicosis involving all 4 paws. The dogs were considered to have adult-onset demodicosis.

### Treatment protocol

The study was conducted as a clinical trial. All dogs were hospitalized for study with owner's agreement. At the time of initial examination, a complete physical examination, Heartworm test, and multiple skin scrapings were performed on each dog. For multiple skin scrapings minimum 5 sites were selected and the same skin scraping were performed every 2 weeks. Blood samples for a CBC and serum biochemical analyses were obtained. Swab samples were collected from dogs with pyoderma and submitted for aerobic bacteriologic culture and susceptibility testing. Cephalexin was administered at a dosage of 20 mg/kg, PO, every 12 hours concurrently with ivermectin in dogs with pyoderma. Two adult dogs were treated with undiluted ivermectin formulated for use in pig at a dosage of 500 µg/kg, SC, every 24 hours and bathed with 0.025% amitraz solution 2 times weekly.

### Monitoring during treatment

A physical examination and multiple (at least 5) skin scrapings were performed every 2 weeks while dogs were receiving ivermectin. Skin scrapings were performed at approximately the same sites at every examination, and results of microscopic examination of skin scrapings were compared with those obtained at the previous examination. If any mites, dead or alive, were seen, treatment was continued as before. If no mites were seen, treatment was continued for at least 2 more weeks and then stopped. Blood chemistry was performed at the beginning of treatment and 4 weeks.

## Results

The dogs have a good appetent, and were bright and alert. Physical examination revealed male dog with a generalized deep pyoderma, multifocal areas of alopecia, erythema, crusting and pododermatitis. They were a good appetent, bright, alert and responsive except skin problems. The dermatological lesions were face, skull, cervical area, dorsal part of body, four feet, four paws and tail (Fig 1, 2).

Dermatologic examinations showed moderate to severe focally extensive thick crusted dermatitis and the bloody purulent discharge in dorsal part of neck (Fig 3). Moderate patchy alopecia presented around eyes and face with moderate scale throughout the head area. Severe pododermatitis with pustules, erythema, and moist dermatitis were observed in paws (Fig 4). Severe swelling, crusting, purulent exudate, alopecia, erythema was observed in the ventral neck (Fig 5). Mild to moderate hyperpigmentation was observed in both lateral hind limb thigh.

Skin scrapings from various sites, including head, dorsal part of neck and feet contained numerous *Demodex canis* mites at various stages of development. Skin cytologies showed very large numbers of cocci, degenerative neutrophils and many RBC. Superficial skin scraping was negative. A bacterial culture from a furuncle yielded coagulase-positive *Staphylococcus intermedius*.

Complete blood count shown normal findings and blood chemistry panels were normal except for hy-



**Fig 1.** Demodicosis on the face, skull, cervical area, dorsal part of body, four feet, four paws and tail showing more severe large patches of intense erythema and alopecia in male dog.



**Fig 2.** Demodicosis on the face, skull, cervical area, dorsal part of body, four feet, four paws and tail showing large patches of intense erythema and alopecia in female dog.

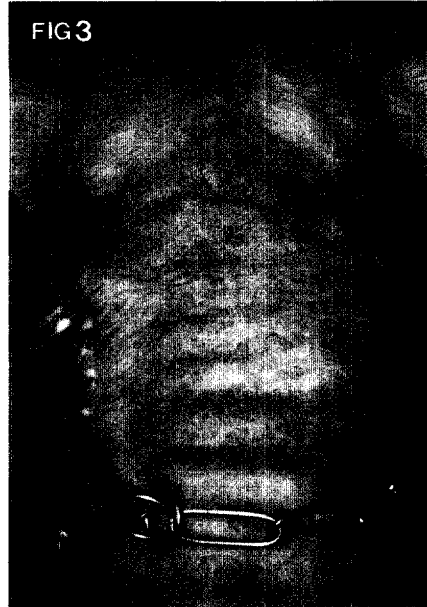
pcholesterolemia. Heartworm test was negative in both dogs. Thyroid function was normal in both dogs.

### Outcome

Treatment was classified as a success in two dogs. All dogs begin to resolve the clinical lesions from 4 weeks after treatment. At 6 weeks the dogs have received combination therapy of ivermectin and amitraz bath appeared clinically normal (Fig 6, 7, 8). Skin scraping results were negative at 6 weeks in adult dogs.

### Discussion

Ivermectin is a potent broad-spectrum antiparasitic



**Fig 3.** Moderate to severe focally extensive thick crusted dermatitis and the bloody purulent discharge in dorsal part of neck in male dog.



**Fig 4.** Pododermatitis with pustules, erythema, and moist dermatitis in paws.

agent produced by an actinomycete, *Streptomyces avermitilis*. It is believed to act on susceptible nema-



**Fig 5.** Swelling, crusting, purulent exudate, alopecia, erythema in the ventral neck.



**Fig 6.** Clinically normal skin of male dog after the treatment for 6 weeks.



**Fig 7.** Clinically normal skin of female dog after the treatment for 6 weeks.



**Fig 8.** Healed ventral neck after the treatment for 6 weeks in male dog.

todes and arthropods by stimulating the presynaptic release of gamma-aminobutyric acid (GABA) and by potentiating its binding to its receptors. The result is a blockade of the postsynaptic transmission of nerve impulses, and thus parasites become paralysed and die<sup>8</sup>.

Ivermectin is used for heartworm prevention in dogs at the recommended dosage of 5 to 7  $\mu\text{g}/\text{kg}$  given orally once a month. However, the preparation most commonly used in dogs for the treatment

of other endo- and ectoparasites is the bovine injectable product, 1% solution (10,000 mcg/ml) that can be given subcutaneously or orally. Some observations showed that the *Demodex canis* is able to develop the resistance to amitraz. This capability of *D. canis* apparently to become refractory to miticide such as ronnel and rotenone has been reconized previously<sup>9</sup>. Ivermectin had been shown to be without benefit in dogs with chronic generalized demodicosis<sup>3,10</sup>, but it was given at 400  $\mu\text{g}/\text{kg}$  weekly for 8 treat-

ments. At a dosage of 600 µg/kg, PO, daily ivermectin had been shown to be effective on dogs with amitraz resistant generalized demodicosis. Other study showed that daily use of ivermectin at a dosage 0.6 mg/kg, PO was found to be effective in treatment of generalized demodicosis in dogs and the median duration of treatment was 10 weeks (6 weeks-5 months)<sup>11</sup>. In this study ivermectin was administered at a dosage of 500 µg/kg, SC, every day, and it was very effective with amitraz baths (0.025%) simultaneously. We observed clinical improvement in this study at 5 weeks and skin scraping results were negative at 6 weeks. However the more cases treated with daily ivermectin and amitraz bath are needed to know the rate of cure and duration of cure.

Ivermectin appears to be a safe drug in dogs but the use of ivermectin may result in adverse reactions such as tremors, ataxia, mydriasis, stupor, coma, and death in dogs<sup>12</sup>. These reactions are idiosyncratic and occur rarely in most breeds. However, purebred and mixed-bred Collies, Shetland Sheepdogs, Old English Sheepdogs, and Australian Shepherds may be more likely to develop adverse reactions<sup>13</sup>. Signs of acute toxicosis may develop from as early as 4 to 6 hours after oral administration of ivermectin to as long as 10 to 12 hours later<sup>14</sup>. The earlier onset of toxicosis may be associated with more severe symptoms<sup>14</sup>. In this study, any adverse reactions were not seen in Korean Native Poongsan dogs.

### Conclusion

Canine demodicosis is a commonly encountered dermatological disease in small animal practice. The clinical presentation of demodicosis varies, and deep skin scraping should be performed all suspicious skin lesions and *Demodex canis* is more easily found than other skin parasites. In case of amitraz-resistant canine generalized demodicosis ivermectin and more frequent amitraz bathing was effective therapy.

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