

## Successful Treatment of *Brugia pahangi* in Naturally Infected Cats with Ivermectin

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**Abstract:** Lymphatic filariasis is a common parasitic disease of cats in tropical regions including Thailand. The objective of this study was to determine the efficacy of ivermectin against microfilariae of *Brugia pahangi* in naturally infected cats. Eight cats naturally infected with *B. pahangi* were divided into control (untreated) and treated groups. Cats in the latter group were given ivermectin injection at 400 µg/kg weekly for 2 months. Microfilariae were counted every week until 48 weeks. Microfilaremia was significantly decreased in the treated group 4 weeks after starting the treatment and become zero at week 9 and afterwards. On the other hand, cats in the control group had high microfilaremia throughout the study. It was successful to treat and control *B. pahangi* infection in naturally infected cats using ivermectin.

**Key words:** *Brugia pahangi*, treatment, cat

Lymphatic filariasis is a major problem in tropical and sub-tropical countries including Thailand. Lymphatic filariasis in cats is caused by *Brugia* spp., such as *B. malayi* and *B. pahangi*. The former species is a significant cause of human lymphatic filariasis which is also endemic in southern parts of Thailand [1]. However, *B. pahangi* is commonly found in cats and dogs in Bangkok area [2]. Both *Brugia* species are transmitted by mosquitoes especially *Armigeres* spp. and *Mansonia* spp. [3]. Pathology is progressed when lymphatic vessels are obstructed. The severity of disease depends on the number of worms present [2].

Macrocyclic lactones are broad-spectrum anthelmintics that are used to treat a variety of nematode infections. Ivermectin is the only macrocyclic lactone that is approved for use in human [4]. In control program for filariasis, ivermectin is the drug of choice, especially in areas with onchocercosis [5]. There are several studies about the efficacy of ivermectin against filarial worms [1,6-8]. For *Onchocerca volvulus*, treatment with ivermectin reduces microfilarial motility in vitro [9], and embryogenesis is impaired in adult female worms [6]. Moreover, a single dose of ivermectin was effective to cure cats naturally infected

with *B. malayi*, although microfilariae could not be completely cleared in cats [10]. However, treatment of *B. pahangi* infection with ivermectin in cats has never been reported. Thus, the objective of this study was to determine the efficacy of multiple doses of ivermectin against microfilariae of *B. pahangi* in naturally infected cats.

This study was conducted as a blinded, randomized study following the standard protocol accepted by the Laboratory Animal Ethics Committee of the Faculty of Veterinary Science, Chulalongkorn University (Approval No. 0831006), Bangkok, Thailand.

Eight cats were naturally infected with *B. pahangi*. The species of worms was confirmed by staining microfilariae using the acid phosphatase technique [11]. All cats were kept individually in the Parasitology Unit, Faculty of Veterinary Science, Chulalongkorn University, Bangkok, Thailand.

Eight cats were divided into 2 groups (n=4 each), an untreated control group and a group given subcutaneous ivermectin injections at 400 µg/kg every week for 2 months. After treatment (day 0; Fig. 1), 60 µl blood smears from ear pricks were examined for microfilariae every week until 48 weeks. Smears were stained with 2.5% Giemsa to estimate the numbers of microfilariae (mf) per ml blood.

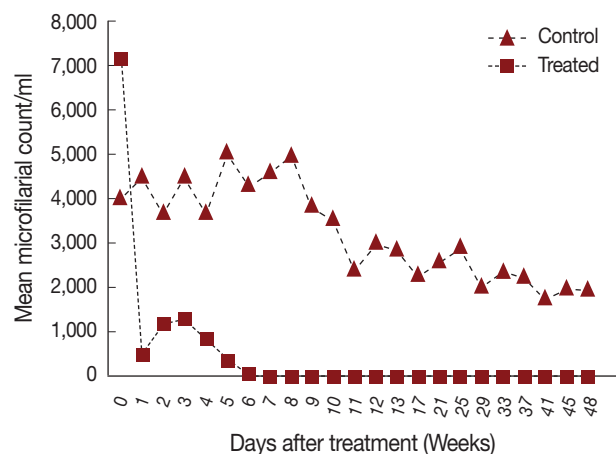
The efficacy of ivermectin treatment was calculated based on the arithmetic mean of microfilarial counts from the untreated control group and treated group. Microfilarial counts were summarized and compared at multiple time points using the

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**Fig. 1.** Mean values of microfilaremia at pre- (day 0) and post-treatment days (weeks) with ivermectin compared with untreated control group.

powerful multivariate Wilcoxon-Mann-Whitney test with the simultaneous application of a 1-sided Wei-Lachin procedure [12,13], accepting a significance level of  $\alpha=0.025$ .

At day 0, the mean microfilarial count was 4,070 mf/ml in the control group ( $n=4$ ) and 7,130 mf/ml in the treated group ( $n=4$ ). The mean microfilarial count decreased significantly in the treated group after 4 weeks from the start of the treatment. From week 9 and onwards, no microfilariae were found in any of the treated cats. The difference between the groups was statistically significant ( $P<0.0001$ ) from week 5 after treatment until the end of the experiment at week 48. By contrast, the microfilarial counts remained high ( $1,990 \pm 1,059.53$  mf/ml) in the untreated control group for the rest of the study period (Fig. 1).

Ivermectin is known to reduce the motility of microfilariae of filarial nematodes and inhibit molting of the third-stage larvae (L3) [14]. Its efficacy against various stages of filarial parasites such as *Dirofilaria immitis* in dogs, *Setaria equina* in horses, and *Onchocerca* spp. in cattle was observed [15]. In *B. malayi*, ivermectin induces muscular passivity in microfilariae and impairs exsheathing [4]. In this study, we demonstrated a significant decrease in microfilaremia after 4 weekly treatments with ivermectin injection via the subcutaneous route at the dose of 400  $\mu\text{g}/\text{kg}$ . The cat received 400  $\mu\text{g}/\text{kg}$  ivermectin injections weekly for 2 months. The reason for this long-term treatment was because 1 of the cats in the treated group which had high parasitemia from the beginning (at day 0; 26,550 mf/ml) remained microfilaremia until week 7 post-treatment. However, microfilaremia did not appear in the blood circulation after

week 8.

In our study, cats naturally infected with *B. pahangi* were successfully treated using multiple ivermectin injections. Clinical side effects such as salivation and ataxia after treatment were not observed in these cats. The results of the present study indicated that adult worms were possibly affected by ivermectin by sterilization of female worms resulting in a decrease of microfilaremia. A similar effect was reported for *Wuchereria bancrofti* [8]. Therefore, it seems that the main target of ivermectin is reproduction of filarial worms, as the drug impairs embryogenesis and decrease microfilaremia [4,7,16].

In conclusion, ivermectin can be used for treating *B. pahangi* in cats. This host-parasite system can therefore be used as a model to develop control and treatment protocols for *B. malayi* in cats which is a reservoir host for human lymphatic filariasis.

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