TREATMENT OF EOSINOPHILIA WITH ALBENDAZOLE

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Abstract. Twenty-five patients with eosinophil counts > 1,000/mm^3 of unknown etiology were treated with albendazole 400 mg twice daily for 7 days were compared with 25 eosinophilic control patients who were not treated. The average eosinophil count in the treated group was 2,079/mm^3 (range 1,002-7,629/mm^3) and in the control group was 2,047/mm^3 (range 1,002-6,468/mm^3). One month later the eosinophil counts of both groups were re-evaluated. Effective treatment was defined as an eosinophil count < 1,000/mm^3. In the treatment group, 80% had a reduction in the eosinophil count to < 1,000/mm^3 while only 12% of the control had a reduction to this level. No side effects were observed in either group. In conclusion, albendazole was found to be highly-effective in the management of patients with eosinophilia without obvious causes.

INTRODUCTION

Eosinophilia is defined as a blood eosinophil count > 500 (Holland and Gallin, 2005) -1,000 (Cho, 2001) eosinophils/mm^3. Eosinophilia is commonly found as an incidental finding. The incidence of eosinophilia in Thais is around 14% (Triteeraprapab ***et al***, 2000). The etiology of eosinophilia can be identified in only 50% of patients even at sophisticated institutes (Libman ***et al***, 1993). Parasitic infection is the most common cause (Teo ***et al***, 1985; Nutman ***et al,*** 1987; Weller, 1992), especially extra-luminal parasites (Tefferi, 2005). Such parasite infections may not be easily diagnosed due to a lack of specific symptoms or signs. The diagnosis of many tissue parasites may be made using immunologic methods which are specific but not easily available. Therefore, in eosinophilia without obvious causes, some experts recommended treatment with a broad spectrum anthelminthic drug, such as albendazole, which is more costeffective (Muennig ***et al***, 1999) than to perform a full investigation to identify the cause. Albendazole has been approved for use by the United States Food and Drug Administration. It has been found to be a safe broad spectrum anthelminthic, effective against various parasites, including nematodes and flukes.

The purpose of this study was to evaluate the effectiveness of albendazole as a treatment for eosinophilia without obvious causes. We carried out a prospective nonrandomized controlled trial.

PATIENTS AND METHOD

Inclusion criteria: Patients, from both the in- and out-patient departments of medcine who had an absolute eosinophil count >1,000/mm^3, were included in the study. Nearly half of the patients had Non-Hodgkin's lymphoma. The physical examination and other basic laboratory tests were otherwise normal in all cases. In most cases, the stool was not examined. The patients were alternately allocated into

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experimental and control groups. The experimental group was treated with albendazole 400 mg twice daily for 7 days and the control group was not. Members of both groups were examined physically and basic laboratory tests were repeated 4 weeks later. If the eosinophil count was <1,000/mm^3, the treatment was considered effective. And the response rates for both groups were compared and analyzed.

As a second step in the control group, eosinophilia persistently >1,000/mm^3 were treated with albendazole 400 mg twice daily for 7 days. One month later, a physical examination and basic laboratory tests were repeated. Using the same criterion, the treatment efficacy rate was calculated.

Percentages and the chi-square method were used for non-related ratios. A $p<0.01$ was considered statistically significant.

Patients with the following conditions were excluded from the study : cardiopulmonary compromise, pregnancy, a history of albendazole allergy, liver or kidney diseases, heart failure or refusal of treatment.

RESULTS

Fifty patients were allocated into 2 equal groups: 25 cases in the experimental group and 25 in the control group. All the patients had a normal physical examination and normal laboratory results other than eosinophilia, even though the majority of them had some underlying disease, such as lymphoma, ITP, etc. Stools were not examined in any of the cases. Nobody had a history of any allergic diseases. The ranges, mean eosinophil counts, age ranges, mean ages and sex ratios for both groups were similar. Some ITP patients were being treated with low dose prednisolone, but the dose was not changed during study. The general characteristics of both groups are shown in Table 1.

By 4 weeks, one member from each group was lost to follow-up,these were included in failure component of the respective group during analysis. All members of each group had normal physical examinations and other than eosinophilia, had normal basic laboratory tests, including liver function tests. Comparison of the results of treatment group with albendazole with the control group are shown in Table 2.

Table 1
General characteristics of patients in control and experimental groups.

	Experimental group (*n*=25)	Control group (*n*=25)
Age range (years)	16-82	16-87
Mean age (years)	46.9	55.4
Sex ratio (male:female)	12:13	11:14
Underlying diseases		
Lymphoma	9	11
Routine check-up	5	3
ITP	4	2
Anemia	3	5
Miscellaneous	4	4
Eosinophil count		
Range (/mm^3)	1,002-7,629	1,002-6,468
Mean (/mm^3)	2,079.0	2,047.2

Table 2
Results of treatment of eosinophilia with albendazole compared with non-treatment group.

	Experimental group(%)	Control (%)
Success	20 (80)	3 (12)
Failure	4	21
Loss	1	1
Total	25	25
χ^2 Yates correction	20.16	
p-value	<0.0001	

Of 25 cases in the experimental group, albendazole was effective in 20 cases and had failure in 4 cases. The effective rate was 80%. Three of 25 (12%) had improvement in the

control group. This difference was statistically significant ($p < 0.0001$).

In the second step, all 21 cases in the control group who did not have improvement, *ie,* eosinophil count >1,000/mm^3 were treated with albendazole 400 mg twice daily for 7 days. One month later, 16 were found to have effective treatment, 3 failed to respond and 2 were lost to follow-up. The effective rate was 76.1%, while physical examination and laboratory tests were normal.

DISCUSSION

The effective rate for albendazole in treating eosinophilia was 80%, compared to 12% in the control group. This difference was significant ($p < 0.0001$) and was presumed to be due to the effect of albendazole. However, one study (Cho, 2001) found spontaneous reduction in eosinophilia in 76.2% by 2 years for those with an eosinophil count <1,000/mm^3 . In our study, most of the subjects in the control group had no spontaneous improvement until treated with albendazole, the 76.1 % improved.

Albendazole (Weller, 2005) is broad spectrum anthelminthic effective against various parasites, including neurocysticercosis, *Echinococcus* infection, *Ascaris*, hook worm, *Trichuris*, some tissue parasites, such as cutaneous larva migrans (Davies *et al*, 1993), visceral and ocular larva migrans (Sturchler *et al*, 1989), gnathostomiasis (Kraivichian *et al*, 1992, 2004), intestinal capillariasis (Cross and Basaca-Sevilla, 1987) and clonorchiasis (Liu *et al*, 1991). Albendazole has also been shown to reduce elevated eosinophil counts due to visceral or ocular larva migrans and gnathostomiasis (Kraivichian *et al*, 2005).

Parasitoses are common in any humid tropical areas. In Thailand parasites may be found in 8.9-35% of the population (Jongsuksantigul, 1997; Nuchprayoon *et al*, 2002). Common parasites are hook worm (Triteeraprapab *et al*, 1998), *Opisthorchis viverrini* and *Gnathostoma spinigerum*.

Mechanism by which albendazole decreases the eosinophil counts is conjectured to be due to its anthelminthic activity. Since most cases of eosinophilia in tropical areas are caused by parasites (Bain, 1999), after their elimination by albendazole, eosinophilia dramatically decreased.

Other causes of eosinophilia, such as allergic diseases, myeloproliferative disorders and hypereosinophilic syndrome (Brigden and Horak, 1993), are not improved with albendazole. This may explain why eosinophilia was persistent in some cases after taking albendazole. However, before parasitosis is excluded, a longer duration of albendazole should be tried to cover for capillariasis, which is found in Thailand (Pradatsundarasar *et al*, 1973; Tesana *et al*, 1983;) and needs treatment for at least 10-21 days (Chichino *et al*, 1992) before elimination.

Because of its effectiveness and minimal side effects, cases of eosinophilia in tropical areas, without abnormalities on physical examination, should be considered for treatment with albendazole as an early step in the management of eosinophilia, before meticulous investigation is started. This would be a practical and economical approach.

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