

COMPARISON OF IVERMECTIN AND ALBENDAZOLE TREATMENT FOR GNATHOSTOMIASIS

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Abstract. Comparative treatment of ivermectin in 21 patients (Group 1) and albendazole in 49 patients (Group 2) of gnathostomiasis gave the cure at 95.2% and 93.8% respectively. The ELISA OD and eosinophil counts were reduction after treatment. Side effects in ivermectin were hypotention, dizziness, weakness and diuresis; and side effects of albendazole were nausea, dizziness and increased alkaline phosphatase in two cases. Ivermectin should be an effective drug against gnathostomiasis and more convenient in treatment single dose.

INTRODUCTION

Gnathostomiasis is a public health problem in Thailand; between 1989-1999 there were about 600 laboratory reported, outpatient cases of gnathostomiasis per year at the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University. The infection rate has increased every year because of the popularity of eating raw fish and raw meat and because gnathostomiasis treatments do not bring about easy cures. There are five species of gnathostome that cause disease in man: *Gnathostoma spinigerum* is the most common infection in Thailand. The others are *G. hispidum*, *G. doloresi*, *G. vietnamicum* and *G. malasiae*. Man is an accidental host, infected by eating raw freshwater fish, freshwater crab, frog, snake or chicken. When a human ingests the third stage larvae from the flesh of freshwater fish, for example, without further development the larvae move to the various organs such as the stomach, muscles, liver, eye, brain and the subcutaneous tissues where they produce symptoms of migratory swelling. The patient may die from brain damage when the larvae move into the brain (Daengsvang, 1980). Albendazole 400 mg twice daily or once daily for 21 days has been used to treat human gnathostomiasis, giving a cure rate of 93.9% and 94.1%, respectively (Kraivichian *et al*, 1992). The side-effects are mild, with only nausea and dizziness, and no abnormality of liver function. Ivermectin has been shown to be effective in onchocerciasis (Duke *et al*, 1990), filariasis (Contiho *et al*, 1994) and strongyloidiasis (Marti *et al*, 1996). The effect of ivermectin on larvae of *G. spinigerum* in rabbits, at a dose of 0.2 and 2 mg/kg subcutaneously, yielded a worm-load

reduction of 74.2% and 84.2%, respectively (Anantaphruti *et al*, 1992). Ivermectin (0.2 mg/kg x 5 days) was used to treat gnathostomiasis in rats and gave a worm reduction rate of 87.9% and a cure rate of 25% (Waikagul *et al*, 1994).

Ivermectin stimulates the release of gamma aminobutyric acid (GABA) from the nerve endings and enhances binding of GABA to its receptor on the postsynaptic membrane of the motor neurones by combining with some other part of the GABA-receptor-ionophore complex. This results in hyperpolarization, blocking of neuromuscular transmission and paralysis of the worm (Campbell, 1985). This current study was designed to investigate the comparative effectiveness of ivermectin and albendazole in the treatment of human gnathostomiasis.

MATERIALS AND METHODS

The study was conducted between October 1998 and November 1999 with 70 patients; 21 cases were treated with ivermectin 0.2 mg/kg single dose (Group 1) and another 49 cases (Group 2) were treated with albendazole 400 mg twice daily. The age of the patients did not exceed 60 years, and only those with symptoms of *Gnathostoma* infection were recruited. To be included in the study, subjects had to have: a history of exposure to infection by eating raw or partially cooked freshwater fish, freshwater crab, frog, snake or chicken; signs and symptoms of migratory swelling, and; signs of inflammation on the affected skin. In addition, a positive immunoblot test using antigen from third stage larvae, eosinophilia >5%, and the

detection of antibody IgG in the patients' sera by enzyme-linked immunosorbent assay (ELISA) at an interval of every 2 months post-treatment until the expiry of 6 months was required. Patients were excluded if they were under 7 years of age or over 60, if pregnant or lactating, or if sensitive to benzimidazoles. Patients with chronic renal, hepatic or cardiac disease, or with a history of epilepsy, proteinuria or blood dyscrasia were also excluded. All patients who were enrolled into the study were required to be free of other parasitic infections and should not have taken any anthelmintic drug in the previous 14 days. They were informed of the study methods and their consents to participate were signed. Patients were also informed of their right to stop at any time without prejudice. All patients who fulfilled the criteria were clinically examined and blood was obtained for hematological, biochemical and immunological testing. Female patients of child-bearing age were required to have a pregnancy test performed with a negative test result, before entry into the study.

RESULTS

There were 36 cases in Group 1 and 100 cases in Group 2 at the outset, but after follow-up for six months there remained a combined total of 70 patients; Group 1 comprised 21 patients and Group 2 comprised 49 patients. The skin lesions in both groups disappeared within 7 days. In some patients, after receiving the drugs, the larvae came close to the skin surface, so that they could be removed by biopsy or with the use of a needle. There was one larva from a patient in Group 1 and 3 larvae from 3 patients in Group 2 (Figs 1, 2). The eosinophil counts of both groups dropped to a normal level within 180 days, as shown in Table 2. The highest eosinophil levels in Group 1 and Group 2 were 15.6% and 17.4%, respectively. Arithmetic means of ELISA OD of both groups are shown in Table 1. The mean OD dropped steadily in both groups and dropped below positive level

after 6 months. By Student's *t*-test, there was no significant difference in eosinophil counts and ELISA OD ($p>0.05$) in both groups. The cure, that means no migratory swelling being visible, a drop in ELISA OD and eosinophil, was 95.2% in treatment with ivermectin 0.2 mg/kg single dose, and 93.8% in treatment with albendazole 400 mg for 21 days. These results were similar to those reported by Kraivichian (1992) who found a cure rate of 94.1% (Table 3). There was no significant difference ($p>0.05$) by Student's *t*-test.

Side-effects of ivermectin were recorded in 8 patients with hypotension, dizziness, weakness and



Fig 1-The head-bulb of the larva *G. spinigerum* removed from the patient after treatment with albendazole.



Fig 2-The larva removed from a skin vesicle at left hand after treatment with ivermectin.

Table 1
The ELISA test before and after treatment in gnathostomiasis with ivermectin (Group 1) and albendazole (Group 2).

	Before treatment	Day 30	Day 60	Day 180
Group 1	0.591	0.465	0.306	0.254
Group 2	0.704	0.579	0.397	0.258

Table 2

The percent eosinophil in patients before and after treatment in gnathostomiasis with ivermectin (Group 1) and albendazole (Group 2).

	Before treatment	Day 30	Day 60	Day 180
Group 1	15.6	11	6	3
Group 2	17.4	9	5	2

Table 3

The efficacy of ivermectin and albendazole in comparative treatment for gnathostomiasis.

	Number of patients	Cured	Not cured	Percentage cured
Albendazole 400 mg once daily for 21 days (Kraivichian <i>et al</i> , 1992)	51	48	3	94.1
Albendazole 400 mg once daily for 21 days	49	46	3	93.8
Ivermectin 0.2 mg/kg single dose	21	20	1	95.2

one case with diuresis. The side effects of albendazole were nausea, dizziness and 2 cases were increased alkaline phosphatase.

DISCUSSION

Treatment of gnathostomiasis with albendazole 400 mg for 21 days in this study and also that of Kraivichian *et al* (1992), gave a similar cure rate of 94.1% and 93.8% respectively, which indicates highly effective treatment. The side effects were mild, only nausea, dizziness, and slightly elevated alkaline phosphatase in 3 cases. The side-effects may be the result of the prolonged treatment, for 21 days. By comparison, a single dose 0.2 mg/kg of ivermectin gave a cure rate of 95.2% with no significant difference, $p > 0.05$ by Student's *t*-test. The side-effects of ivermectin were mild, with only slight hypotension for 24 hours and diuresis in only one case, which are effects on the nervous system.

The tendency for larvae to migrate superficially, so that they could then be removed, was found in one case in Group 1 (5%) and 3 cases in Group 2 (6%), which was very similar to the report by Suntharasamai *et al* (1992) at 7%. There

was no significant difference, $p > 0.05$ Student's *t*-test.

The eosinophilia and ELISA tests are useful in long-term follow-up cases. In this study, eosinophils were reduced to normal within 6 months and ELISA OD returned to a normal level within one year.

In conclusion, this study showed that ivermectin was an effective drug against gnathostomiasis, had mild side-effects and was more convenient for treatment than was albendazole.

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