

DOUBLE-DOSE IVERMECTIN VS ALBENDAZOLE FOR THE TREATMENT OF GNATHOSTOMIASIS

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Abstract. A comparative study was performed for the treatment of gnathostomiasis patients with ivermectin 0.2 mg/kg for 2 days in 15 patients vs albendazole 400 mg twice daily for 21 days in 14 patients. The ivermectin and albendazole gave cure rates of 100% and 78.5%, respectively, however the difference was not statistically significant between the two drugs (Fisher's exact, $p=0.0996$). One year after treatment, the patients who had no migratory swellings and a drop in ELISA titers or a negative immunoblot test were considered to be cured. The side effect of ivermectin for two days was dizziness. The side effects of albendazole were nausea, dizziness, and an increased alkaline phosphatase.

INTRODUCTION

Gnathostomiasis is a public health problem, especially in Southeast Asia and in Central and South America. In Thailand at the Hospital for Tropical Diseases, Bangkok, there were 800 cases in 2004 which were immunoblot test positive for gnathostomiasis. The infection rate has increased about 10% each year due to the popularity of raw or under-cooked freshwater fish dishes. The most common *Gnathostoma* species found in humans in Thailand is *G. spinigerum*; other species include *G. hispidum*, *G. doloresi*, *G. vietnamicum* and *G. malaysiae*. Humans are infected by eating raw or under-cooked freshwater fish, freshwater crab, frog, snake or chicken. When a human ingests the 3rd stage infective larvae from the flesh of freshwater fish, the larvae migrate to the stomach, liver, eye, and brain. The most common site is the subcutaneous tissue. Patients may die from brain damage when larvae migrate to the brain (Daengsvang, 1980). Treatment with ivermectin as a single dose (0.2 mg/kg) has been shown to be effective

in curing up to 95.2% of gnathostomiasis cases in one study (Nontasut *et al*, 2000), and 76% in another study (Kraivichian *et al*, 2004). Ivermectin stimulates the release of gamma aminobutyric acid (GABA) from the nerve endings in the larvae and enhances the binding of GABA to its receptor on the postsynaptic membrane of the motor neurons by combining with some other part of the GABA-receptor-ionophore complex. This results in hyperpolarization and blocking the neuromuscular transmission causing paralysis in the worm (Campbell, 1985). Albendazole 400 mg once or twice daily for 21 days has been used for the treatment of gnathostomiasis and gave cure rates of 93.9% and 94.1%, respectively (Kraivichian *et al*, 1992). Our study compared repeated single doses of ivermectin 0.2mg/kg for two consecutive days with albendazole 400 mg twice daily for 21 days for the treatment of gnathostomiasis.

MATERIALS AND METHODS

The study was conducted between January 2003 and December 2004 at the Out-patient clinic, Hospital for Tropical Diseases, Bangkok, Thailand. The patients who were positive for gnathostomiasis by the immunoblot test (Dekumyoy *et al*, 2000), were treated with 2 single doses of ivermectin 0.2 mg/kg/day for 2

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consecutive days or albendazole 400 mg twice daily for 21 days. To be included in the study, the subjects had to have a history of eating raw or under-cooked freshwater fish or chicken, and signs of migratory swelling and inflammation in the affected skin. A blood examination for eosinophil count and liver function was performed on the day before taking the drugs and after 30 days. ELISA titers (Dekumyoy *et al*, 1998) were examined every two months for one year. If the patient had a disappearance of migratory swelling and decreased ELISA titers after one year, it was assumed that the patient was cured. Patients were excluded if they were pregnant or lactating. All the patients who were enrolled in the study were required to be free of other parasitic infections and should not have taken any anti-helminthic drugs in the previous 14 days. Written informed consent was signed by all participants in the study allowing them to withdraw at any time. The study was approved by the Ethics Committee at the Faculty of Tropical Medicine in Bangkok.

RESULTS

There were 15 patients who were treated with ivermectin 0.2 mg/kg for two consecutive days (group 1) and 14 patients who were treated with albendazole 400 mg twice daily for 21 days (group 2). The skin lesions disappeared and the eosinophil counts were normal in both groups after 4 weeks. The ELISA titers decreased in both groups one year after treatment. In only one patient, the immunoblot test was negative one year

after treatment with ivermectin. The disappearance of migratory swelling and a decrease in ELISA titers or a negative immunoblot test one year after treatment was defined as cure of the infection. All the patients in group 1 were cured (100%), and most of the patients in group 2 were cured (78.5%). The three patients who had recurrent symptoms after albendazole treatment were cured by the double-dose ivermectin treatment. The side effects of ivermectin during treatment were dizziness in one patient and no symptoms in 14 patients. The side effects of albendazole were nausea (one patient), dizziness (two patients), and increased alkaline phosphatase (one patient).

DISCUSSION

The treatment of gnathostomiasis with albendazole 400 mg daily or 400 mg twice daily for 21 days has been reported to be highly effective with cure rates of 94.1% and 93.8%, respectively (Kraivichian *et al*, 1992). Side effects included nausea, dizziness, and elevated alkaline phosphatase. The side effects disappeared by one month in our study. Ivermectin 0.2 mg/kg given as a single dose has also been reported to give high cure rates with minimal side effects (Nontasut *et al*, 2000). In our study, double-dose ivermectin 0.2 mg/kg gave a cure rate of 100%, with mild side effects. The recurrence of gnathostomiasis in the three patients after treatment with albendazole, were all cured by double-dose ivermectin. After treatment with ivermectin, the symptoms disappeared within one month in

Table 1
Outcomes after treatment of gnathostomiasis with double-dose of ivermectin compared to albendazole for 21 days.

	No. of patients	Cured	Not cured	Proportion cured
Group 1				
Ivermectin 0.2mg/kg, double-dose	15	15	0	100%
Group 2				
Albendazole 400 mg bid 21 days	14	11	3	78.5%

Statistical analysis was done by the Fisher's exact test and the p-value between the 2 groups was 0.0996, not significant.

most patients and in all patients within two months. Both drugs seem to be effective in the treatment of gnathostomiasis with few side effects. If there is recurrence of infection after treatment with one drug, it may be useful to use the other drug for treatment.

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