

TREATMENT OF *OPISTHORCHIS VIVERRINI* AND INTESTINAL FLUKE INFECTIONS WITH PRAZIQUANTEL

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Abstract. The study was carried out from September to November 1997 in Phrae Province of northern Thailand. A total of 95 adult patients with *Opisthorchis*-like ova in their stools were randomly treated with two different manufactured Praziquantels. Group 1, consisting of 49 patients, received a single dose of 40 mg per kg Praziquantel manufactured by the Thai Government Pharmaceutical Organization. Group 2 (46 patients) received Biltricide® at the same dosage. *Haplorchis taichui*, *H. yokogawai*, *Echinostome* spp., *O. viverrini*, *Taenia saginata* and *Enterobius vermicularis* were expelled in the stools after treatment. Minute intestinal flukes were detected in 64% of patients. *O. viverrini* was found in lower proportion of 17%. By formalin-ether concentration examination one stool specimen from each patient, the cure rate in both groups on the 30th day of treatment was 100%. The side effects of the two different Praziquantel treatments were mild with no significant difference. Praziquantel, regardless of its manufacture, proved effective against *O. viverrini* and other minute intestinal flukes (*H. taichui*, *H. yokogawai* and *Echinostome* spp.).

INTRODUCTION

Opisthorchiasis was considered a major public health problem in Thailand for many years. A survey conducted in 1990 by the Ministry of Public Health in Thailand showed a prevalence rate of 15% nationwide and 24% in the upper northeastern provinces of the country (Jongsuksantigul *et al*, 1992). A special extensive control program was launched in 1988 and later extended to the whole country. An important control procedure was to treat infected individuals with Praziquantel. Opisthorchiasis prevalence in the northeast of Thailand has dropped in the past decade, but *Opisthorchis* infection in the north has gradually increased from 5.6% in 1980 (Preuksaraj *et al*, 1982) to 22.9% in 1990 (Jongsuksantigul *et al*, 1992).

The opisthorchiasis situation in northern Thailand needs to be clarified. The Praziquantel treatment provided there should also be re-valuated. The objective of this study was to test the efficacy of Praziquantel manufactured by the Thai Government Pharmaceutical Organization (GPO) as compared with Biltricide® for the treatment of opisthorchiasis in northern Thailand. Praziquantel manufactured by GPO was used in the control

program. Biltricide® manufactured by Bayer was the first Praziquantel introduced to Thailand.

MATERIALS AND METHODS

Patients

The study was carried out from September to November 1997 in the Phrae Province, northern Thailand, 613 km north of Bangkok. A preliminary survey was conducted in 4 subdistricts (Mae Yom, Wang Hong, Tung Kaew and Wang Laung) of 2 districts (Maung and Nong Muang Kai). Out of 1,119 people, 250 had *O. viverrini*-like ova in their stools. Ninety-five infected individuals volunteered to participate in this study. These were adults aged between 13 and 74 years who were not suffering from other serious diseases. Forty-five males and 40 non-pregnant females participated in the study. Clinical symptoms were recorded before, during and on the 30th day after treatment.

Treatment

The patients were divided by random into two groups. Group I received Praziquantel manufactured by GPO (Group I) at a single dose of 40mg

per kg. Group II received Biltricide® at the same dosage. The drugs were taken in the presence of an observer. 30-45 ml of saturated magnesium sulfate solution was given to each individual 6-8 hours later.

Retrieved worms

After treatment, 24 hour-stool samples were collected. The expelled worms were retrieved by the sedimentation method (Radomyos, 1984). The different species of worms found were identified.

Follow-up

The patients were requested to return on the 30th day after treatment. One stool sample was collected from each patient and examined by the formalin-ether concentration method (Ritchie, 1948). The treatment was considered successful if *O. viverrini*-like ova was not found.

Data analysis

The efficacy of the two different Praziquantels was compared through parasitic cure rate and adverse effects. Statistical analysis was done by Student's *t*-test and the chi-square test.

RESULTS

Group I consisted of 49 patients and Group II 46 patients. All patients in both groups completed the 30-day follow-up period. The age, weight, and concomitant helminthic infections of the two groups were compared (Table 1).

Table 1

Background data and parasitism in the 2 groups of patients.

Patient characteristics	Group I	Group II
No. of patients	49	46
Male : female	1.13 : 1	1.58 : 1
Mean age yrs	45.4	42.7
(range)	(13-67)	(13-74)
Mean weight kg	54.3	56.8
(range)	(30-72)	(40-82)
No. of patients with other parasitic infections	6	5

Fifty-five percent had no symptoms or they had symptoms not related to opisthorchiasis. Common complaints were low back pain and myalgia or arthralgia. Eighteen percent of the patients had epigastric pain with flatulence (16.8%). Six percent complained of dizziness and nausea (5%) and a few of them had chronic diarrhea (3%) or dysentery (2%). Hot sensation over the abdomen was reported only by 2% of the patients.

Twenty-four hour post-treatment stool samples were collected from 44 and 43 patients in Group I and II respectively. Most of the helminths expelled in the stools were the intestinal flukes. *Haplorchis taichui* was retrieved in the stools of 56 patients (64%). *H. taichui* was recovered together with *H. yokogawai* and *Echinostome* spp in 2 and 3 patients respectively. *O. viverrini* was found with and without intestinal flukes in 15 cases (17.2%). The result of retrieved worms after Praziquantel treatment is shown in Table 2.

On the 30th day of follow-up, no *O. viverrini*-like ova was detected in the stools of all the patients. Therefore, the cure rate in both groups was 100%.

Side effects were observed in 53% and 58% in Group I and II respectively (Table 3). Common symptoms were dizziness, nausea, vomiting, lassitude, abdominal pain and palpitation. There was one patient complaint of each symptom of dryness in the mouth, light-headedness, flatulence and cutaneous itch all over the body with no rash. These symptoms were mild and subsided within one or two days. No significant differences of severity or frequency of side effects were observed in both groups.

DISCUSSION

Studies demonstrating the high efficacy of Praziquantel as treatment for opisthorchiasis have been conducted. With a single dose of 40 mg per kg, the cure rate was found to be between 91-96% (Bunnag *et al*, 1980, 1981). This study shows that treatment with the two different Praziquantel at the same dosage has proved to be still effective against *O. viverrini*. Furthermore, Praziquantel at this dosage was also effective against other intestinal flukes (*H. taichui*, *H. yokogawai* and *Echinostome* spp).

Table 2

Various retrieved parasites in group I (44 patients) and group II (43 patients).

Retrieved parasites	Group I No. of patients (%)	Group II No. of patients (%)
No. of patients with parasites	35 (79.5)	32 (74.4)
Intestinal flukes :		
<i>Haplorchis taichui</i>	29 (65.9)	27 (62.7)
<i>H. yokogawai</i>	1 (2.3)	1 (2.3)
<i>Echinostome</i> spp	1 (2.3)	2 (4.7)
Mixed intestinal flukes	2 (4.5)	3 (6.9)
Mixed intestinal flukes with <i>Opisthorchis viverrini</i>	4 (9.1)	7 (16.3)
<i>Opisthorchis viverrini</i>	1 (2.3)	3 (6.9)
<i>Taenia saginata</i>	5 (11.4)	3 (6.9)
<i>Enterobius vermicularis</i>	11 (25)	5 (11.6)

Table 3

Side effects of treatment with two different Praziquantel preparations.

Side effects	Group I No. of patient (%)	Group II No. of patient (%)
Dizziness	14 (28.6)	22 (47.8)
Nausea	9 (18.4)	11 (23.9)
Vomiting	5 (10.2)	7 (15.2)
Lassitude	2 (4.1)	3 (6.5)
Abdominal pain	1 (2)	2 (4.3)
Palpitation	1 (2)	2 (4.3)
Others	2 (4.1)*	2 (4.3)**

* Dryness in the mouth 1, cutaneous itch 1

** Light-headedness 1, flatulence 1

In epidemiological surveys, stool examinations were traditionally conducted. Diagnosis of opisthorchiasis was usually based on detecting characteristic minute operculated, ovoid eggs in stools. *Opisthorchis* eggs are similar in appearance to many tiny intestinal flukes of the genus *Heterophyes* and *Metagonimus*, such as *Prosthodendrium molenkempi*, *Phaneropsolus bonnei*, *Haplorchis pumilio*, *Heterophyes heterophyes*, *Stellantchasmus falcatus* and *Metagonimus yokogawai*. (Harinasuta *et al*, 1987). It is practically impossible to distinguish *O. viverrini* eggs from intestinal flukes. A definite diagnosis could be reached only by identifying adult flukes after anthelmintic therapy. These

intestinal fluke infections have been reported also in the same opisthorchiasis endemic areas in north-east Thailand (Bhaibulaya *et al*, 1964; Manning and Lertprasert, 1973; Pungpak *et al*, 1984; Radomyos *et al*, 1984).

In this study, minute intestinal fluke infections were predominant. Opisthorchiasis occurred in lower proportions. This evidence is new in this area. The high prevalence of opisthorchiasis in the north, as reported in previous surveys, might be the result of inaccurate reporting due to the similarity in appearance of the eggs of intestinal flukes and *Opisthorchis* eggs.

In conclusion, minute intestinal flukes (*H. taichui*, *H. yokogawai* and *Echinostome* spp) were commonly found in the same opisthorchiasis endemic areas in northern Thailand. Praziquantel was effective as treatment against liver and intestinal flukes.

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