

ULTRASONOGRAPHIC STUDY OF THE BILIARY SYSTEM IN OPISTHORCHIASIS PATIENTS AFTER TREATMENT WITH PRAZIQUANTEL

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INTRODUCTION

In Thailand, *Opisthorchis* infection is common. It was estimated that about seven million people had this liver fluke infection (Preuksaraj *et al.*, 1982).

Praziquantel is very effective in treating opisthorchiasis (Bunnag and Harinasuta, 1980; 1981). It has been used in a large scale control programme in the Northeastern part of Thailand since 1981.

The association between liver fluke infection and biliary stone formation has been observed. Dead *Clonorchis* has been shown to be the nucleus of stone formation (Cook *et al.*, 1954, and Teoh, 1963). There is an evidence of *Opisthorchis* associated with gallstone formation (Riganti *et al.*, 1988). Praziquantel kills the flukes (Mehlhorn *et al.*, 1983). The dead fluke may be the nidus of biliary stone. It has been observed that, ever since praziquantel has been introduced for the treatment of opisthorchiasis, the incidence of biliary stones in the northeastern Thailand seem to increase.

Opisthorchis viverrini live in the bile ducts. The pathology confines to the biliary system,

including hyperplasia of the epithelial cells lining the bile ducts, obstruction of the biliary tract, bile retention, dilatation and cystic formation of the bile ducts, gallbladder enlargement and in late cases, cholangiocarcinoma. (Harinasuta *et al.*, 1984).

The purpose of this study is to find out the residual pathological changes of the biliary system and the incidence of biliary stone in opisthorchiasis patients after treatment with praziquantel by using ultrasonography which is noninvasive and accurate procedure. (Detwiler *et al.*, 1980, Hessler *et al.*, 1981).

MATERIALS AND METHODS

The study was carried out in 1981 to 1987 in three villages (Bung Swang, Non Hua Chang and Nong Sang village) in Khon Kaen Province, 450 km northeast of Bangkok. They were within the Water Resources Development Project of Khon Kaen Province. The main occupations of the villagers were rice cultivation and cash crop farming.

Stool examinations

Stool from each adult villager was collected and preserved in Merthiolate

(thiomersal) – iodine-formaldehyde solution. All specimens were transferred to the laboratory in the Faculty of Tropical Medicine, Bangkok where they were examined for *O. viverrini* egg by the merthiolate iodine formalin concentration method. If eggs were found, they were quantified by Stoll's method. (Stoll, 1923).

Follow-up examinations were conducted once annually from 1981 to 1986.

Treatment

All infected individuals were treated with a single dose of praziquantel (40 mg per kg. body weight) in 1981. Individuals who became reinfected were retreated with the same dose of the drug.

Ultrasonographic examinations

Using a portable ultrasound machine (Model 8AL 32B, Toshiba), ultrasonography of the biliary system and liver was performed at the villages during 22nd – 29th December 1987. The findings were recorded on videotape and evaluated at the Faculty of Tropical Medicine, Bangkok.

RESULTS

In 1981, the three villages had a total population of 1,384 with an *Opisthorchis* infection rate of 57%. Six hundred and forty seven opisthorchiasis patients were recruited for the ultrasonographic examination. Their ages ranged from 15–87 years (mean 42.6). The male to female ratio was 1:1. The intensity of infection ranged from detectable *O. viverrini* eggs by concentration method only to 23,600 EPG. (egg per gramme of faeces) with a geometrical mean of 333 EPG. 53.9 per cent were reinfected in the first year after treatment. The rate of

reinfection gradually decreased in subsequent years (Table 1). Half of the infected individuals received one treatment only and the average number of treatment was 1.7 per person.

The ultrasonographic examination findings in 1987 are summarized in Table 2. 80.6 percents were normal. The most common abnormal finding was liver enlargement (14.8%); the size of the liver measured downward from the costal margin at the right midclavicular line, ranged from 0.5 to 3.5 cm. A simple cyst was found in one case; its diameter was 4.4 cm. and located at the lower part of the right lobe.

Dilatation of the gallbladder was found in 23 cases (3.5%); 14 cases had sludge which was thick, viscid bile collected at the bottom of gallbladder. Dilatation of intrahepatic bile ducts, honeycomb pattern was observed in one patient.

Gallstones were present in 7 cases (1.0%); a single stone (Fig. 1) was found in 3 and two stones in 4 cases. Three cases with gallstones also had liver enlargement. The parasitological data of the calculous and non-calculous groups are compared in Table 3. The in-

Table 1

Number and percentages of 647 opisthorchiasis patients receiving various numbers of treatment with praziquantel.

No. treatment	No. patient	Per cents
1	349	53.9
2	189	29.2
3	73	11.2
4	28	4.3
5	7	1.0
6	1	0.1

Table 2

Ultrasonographic findings of the biliary system in 647 opisthorchiasis patients after treatment with praziquantel.

Sonographic findings	No. patient	Per cent
Normal	522	80.6
Liver enlargement	96	14.8
Cyst	1	0.1
Gallbladder		
Dilatation	23	3.5
Sludge	14	2.1
Thickened wall	7	1.0
Stones	7	1.0
Dilation of intrahepatic bile ducts	1	0.1

Table 3

Age, sex, parasitological data and number of treatment in calculous and acalculous patients.

	Calculous	Acalculous
Number of patient	7	640
Age. . .year Mean	48.2	42.6
(range)	(28-66)	(15-87)
Sex M:F	1:2.5	1:1
Faecal egg output (EPG) Geometric mean (range)		
year 1981 (before treatment)	50	104
	(0-3,800)	(0-23,600)
1982	18	10
	(0-1,400)	(0-7,600)
1983	2	2
	(0-50)	(0-3,600)
1984	0	3
		(0-5,900)
1985	0	2
		(0-2,600)
1986	0	2
		(0-1,000)
Mean number of treatment per person	1.1	1.7

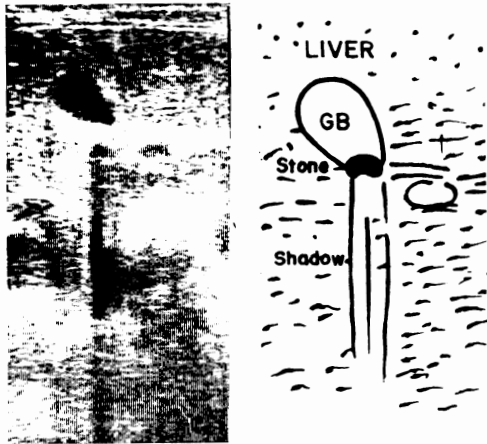


Fig. 1—Ultrasonography showing single gallstone with acoustic shadow.

tensity of opisthorchis infection in calculous group was light, with a maximum faecal egg output of 3,800 EPG. Six individuals received praziquantel treatment once in 1981 and one was treated twice in 1981 and 1983. There were no statistic difference in the two groups. Ultrasonographic examination was repeated in five patients at the Hospital for Tropical Diseases, Bangkok and the diagnosis was confirmed. One patient agreed to elective cholecystectomy. A stone, 0.9 cm. in diameter, was obtained from the resected gallbladder. A cluster of *O. viverrini* eggs was found at the center of the stone.

In the patient with dilatation of intrahepatic bile duct, the site of biliary tract obstruction was not located at surgery. The gallbladder was contracted and its histology revealed chronic inflammation.

DISCUSSION

This study reports on the ultrasonographic findings in 647 patients who had been treated with praziquantel for opisthorchiasis

in the preceding six years. Twenty percent of the study population had abnormal findings, of which liver enlargement was the commonest. Other abnormalities included dilatation and thickening of the wall of the gallbladder, sludge formation, and gallstones. The characteristic honeycomb pattern of intrahepatic bile duct dilatation, as described by Pausawasdi (1986), was found in one case. A direct causal relationship between opisthorchiasis and any of these findings could not be established, as other causes of liver enlargement and changes in the biliary system were not excluded.

Eversince the use of praziquantel in the treatment of opisthorchiasis, there have been anecdotal reports that the incidence of gallstones is higher in the treated population. Dead adult flukes have been demonstrated in stones removed from patients with treated opisthorchiasis (Riganti *et al.*, 1988), in whom they presumably act as nidi for stone formation. The finding suggests that not all dead worms are expelled after treatment, and they may lead to an increased incidence of gallstones in patients treated with praziquantel.

In the present study, gallstones were found in seven individuals (1.0%). Analysis of the parasitological data suggests that gallstone formation may be associated with lighter infection with *Opisthorchis*. These findings can at best be preliminary, as no baseline ultrasonographic studies were performed in the study population and no untreated cohort was followed for comparison. However, it can be said that even if all 7 cases of gallstones resulted from praziquantel treatment, the incidence of gallstones in treated patients (1.0%) was similar to that previously reported in 8,006 necropsies of a general hospital population (1.2%) (Satitnimankarn,

1960). Thus the results do not substantiate the claim that the incidence of gallstones increases after praziquantel treatment of opisthorchiasis. Prospective studies are urgently needed to establish the association between opisthorchiasis, praziquantel treatment and gallstone formation.

SUMMARY

Ultrasonographic examination of the liver and biliary system using a portable ultrasound unit was performed in 1987 in 647 opisthorchiasis patients who had been treated with praziquantel during 1981 to 1986. Treatments were repeated annually in those reinfected. The reinfection rate was 53.9% in the first year and gradually declined. Ultrasonographic findings were normal in 80.6% of subjects. The most common abnormal finding was liver enlargement (14.8%), followed by dilatation of the gallbladder (3.5%), sludge formation (2.1%) and thickening of the wall of the gallbladder (1.0%). Gallstones were found in 7 cases (1.0%). Dilatation of intrahepatic bile ducts was detected in one subject (0.1%). The incidence of gallstones in treated patients was similar to that reported in a large necropsy series of the general population. Prospective studies will be needed to further investigate the association between opisthorchiasis, treatment and gallstone formation.

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