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A Comparative Trial of Single Dose Treatment with Praziquantel and Levopraziquantel in Human Schistosomiasis Japonica

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Abstract

A comparative study on the efficacy of levopraziquantel (levo-PZQ), an optic isomer of praziquantel (PZQ), and PZQ in the treatment of *Schistosoma japonicum* infection was undertaken. All patients were positive by miracidial hatching test before treatment and were treated with a single dose of 30mg/kg. The negative conversion rates in levo-PZQ group three and six months after treatment were 85.2% and 87.7%, respectively, while those in PZQ group were 72.1% and 73.6% ($p < 0.01$). The side reactions of both groups were mild and transient. The liver and renal function tests, electrocardiography and blood and urine routine examinations showed no remarkable change before and after treatment. Evidently, levo-PZQ is superior to PZQ in therapeutic effects on schistosomiasis japonica.

Key words: *Schistosoma japonicum*, miracidial hatching, praziquantel (PZQ), levopraziquantel (levo-PZQ), dextropraziquantel (dextro-PZQ), optic isomer.

Introduction

Praziquantel (PZQ) is a racemic compound which is composed of equal halves of levo- and dextro-PZQ. In experimental therapy of rabbits infected with *Schistosoma japonicum*, levo-PZQ was found to be the active component in schistosomicidal action, while dextro-PZQ had little if any effect on the adult worms. Histopathological observations revealed that the number and size of egg granulomas in the liver were markedly reduced in levo-PZQ group as compared with those in dextro-PZQ group, while those in the PZQ group were intermediate between the two (Liu *et al.*, 1986). Based on these experimental data and after toxicological and pharmacokinetic studies, a comparative trial of levo-PZQ and PZQ was undertaken in the treatment of human schistosomiasis japonica in an endemic area of Lu-Shan county of Sichuan province, China, from Oct. 1985 to May 1986.

Materials and Methods

Selection of patients: In July 1985, a survey was conducted by a miracidial hatching technique in human population in Shenghi village, positives for miracidium was 480 out of 942 farmers examined, with an infection rate of 51%. They were reexamined by the same technique 3 months later, i.e. 1 month before treatment, 438 patients, 204 males and 234 females, remained positive and were selected as subjects of treatment trial. Their ages varied from 8 to 64, including 295 adults and 143 children. They were stratified by the number of miracidia/30g of feces and randomly allocated into 3 study groups: 245 cases in levo-PZQ group, 122 cases in PZQ group and 71 cases in placebo group, with approximate ratio of 3:2:1 (Table 1). Patients in placebo group were

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Table 1. Distribution of patients in three study groups

Study group	no. of cases	sex		age		no. of miracidia/30 g	
		male	female	adult	child	10	10
Levo-PZQ	245	112	133	158	87	104	141
PZQ	122	59	63	86	36	60	62
Placebo	71	33	38	51	20	29	42

completely treated with PZQ after completing this experiment.

Drug and dosage: Levo-PZQ in white crystalline powder was synthesized in the laboratory of chemical department of our university (batch number 84-mixed). PZQ of pure crystalline powder was supplied by the Sixth Pharmaceutical Factory of Shanghai (batch number 850931). The placebo used was glucose powder. All of them were administered in gelatin capsules. A single dose of 30mg/kg was given orally in front of the examiner.

Methods of observation: A standardized questionaire was used to record the symptoms, signs and side reactions of each patient. All of the patients were admitted to the hospital. Electrocardiographic examinations were done before treatment and 2 hours and 24 hours after treatment in 52 cases of levo-PZQ group and 43 cases of PZQ group. Liver function tests (bilirubin, thymol turbidity and SGPT), renal function test (urea nitrogen), blood and routine urine examinations were also performed before and after treatment in 43 cases of levo-PZQ group and 42 cases in PZQ group.

Follow-up examinations and assessment of therapeutic efficacy: Stool miracidial hatching tests for 3 successive times were performed for every patient in the 3 groups 3 months and 6 months after treatment. Statistical comparison of the negative conversion rates in stool miracidial hatching tests between the 3 groups were analized by the chi square test to determine the statistical difference.

Results

Therapeutic effect (Table 2): The negative conversion rates of stool miracidial hatching tests in levo-PZQ and PZQ groups after 3 months were 85.2% and 72.1%, respectively, and there was a significant difference of efficacy, ($p < 0.01$), while those after 6 months were 87.7% and 73.6%, respectively, with significant difference ($p < 0.01$). The negative conversion rates of miracidial hatching tests in placebo group at 3 month and 6 month follow-ups were 38.4% and 30.1%. The difference between placebo group and levo-PZQ and PZQ groups were highly significant. ($p < 0.01$). These results showed that with the same dosage of 30mg/kg in single-dose, the therapeutic effect of levo-PZQ was superior to

Table 2. Results of post-treatment stool miracidial hatching tests

Study group	3-month			6-month		
	no. exam.	no. of negatives	%	no. exam.	no. of negatives	%
Levo-PZQ	230	196	85.2*	228	200	87.7†
PZQ	115	83	72.2*	110	81	73.6†
Placebo	65	25	38.4	63	19	30.2

* levo-PZQ vs PZQ after 3 months. $x^2 = 8.12$, $p < 0.01$

† levo-PZQ vs PZQ after 6 months. $x^2 = 10.59$, $p < 0.01$

Table 3. Side reactions

Side reactions	Levo-PZQ (186 cases)	PZQ (45 cases)	Placebo (24 cases)
dizziness	37(19.9)*	26(22.6)*	6(25.0)
vertigo	4(2.1)	1(0.8)	0
headache	13(6.9)*	9(7.8)*	3(12.5)
malaise	7(3.8)	9(7.8)	0
nausea	4(2.1)	7(6.1)	0
vomiting	5(2.7)	2(1.7)	0
impaired appetite	5(2.7)	3(2.6)	0
abdominal pain	22(11.8)*	20(17.4)*	4(16.6)
diarrhea	8(4.3)	8(6.9)	0
palpitation	4(2.1)	2(1.7)	0
fever	4(2.1)	2(1.7)	0
skin rashes	1(1.0)	1(0.8)	0
no reaction	126(67.7)	74(64.3)	14(58.3)

( ) = % of reaction
* = not significant

that of PZQ.

Side effects (Table 3): All patients well tolerated a single dose of levo-PZQ and PZQ. The incidence of side reaction in levo-PZQ and PZQ groups was 32.3% and 35.7% respectively. ($p > 0.05$). There was no statistically significant difference even between the placebo group and levo-PZQ or PZQ groups. The occurrence of side effects like dizziness, headache and abdominal pain were more or less the same. They were mild, transient and needed no intervention.

Laboratory examinations: EKG findings before, 2-hour and 24-hour after treatment in 52 cases of levo-PZQ group and 43 cases of PZQ group showed no remarkable changes. Liver and kidney function tests, blood and urine routine examinations of both study groups also showed no significant changes.

Discussion

The current control strategies for schistosomiasis are more than ever before, emphasizing population-based mass chemotherapy. This change in control strategies has been brought about by the introduction of relatively safe and more efficacious drugs, notably PZQ which seems to be an ideal drug for schistosomiasis (Andrews *et al.*, 1983). Recent experience in its field use showed that a single oral dose of 40 mg/kg was well tolerated with therapeutic effect of 94.4% (Liu *et al.*, 1986). It has been extensively adopted in endemic area to reduce transmission of the disease at community level.

This result of our comparative trials coincides with our experimental finding in rabbits. In the same single dose of 30mg/kg the therapeutic effect of levo-PZQ is superior to PZQ. In experimental therapy of schistosomiasis japonica in rabbits, we found that dextro-PZQ at a dosage of 30, 35, or 40mg/kg had no therapeutic effect. It may be therefore concluded that levo-PZQ is the main active component for schistosomicidal action.

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