Rev. Inst. Med. trop. São Paulo
25(4):173-177, *julho-agosto*, 1983

UDC 616.995.122

CLINICAL TRIAL WITH OXAMNIQUINE AND PRAZIQUANTEL IN THE ACUTE AND CHRONIC PHASES OF SCHISTOSOMIASIS MANSONI (*)

Naftale KATZ, R. S. ROCHA, J. R. LAMBERTUCCI, D. B. GRECO, E. R. P. PEDROSO, M. O. C. ROCHA and S. FLAN

SUMMARY

One hundred thirty individuals (18-19 years of age) in practicing manouvres near a pond in Belo Horizonte, Brazil, got in contact with water and 2 months later, 78 of them were found eliminating **Schistosoma mansoni** eggs. Clinical and laboratory examination disclosed 39 patients in the acute phase of schistosomiasis, 17 in the chronic and in the remaining 22 the phase was undefined. A clinical trial was carried out in these 78 individuals, administering either oxamniquine (15 mg/kg body weight in a single oral dose) or praziquantel (50 mg/kg body weight, divided in two equal doses). The only statistically significant difference in side effects was a higher incidence of abdominal distress and bitter taste in the praziquantel cases, and dizziness in the chronic phase patients post oxamniquine administration. Therapeutic efficacy was assessed by three consecutive stool examinations (Kato-Katz method) performed pre-treatment, and at one, three and six months post-treatment. Parasitological cure was achieved in 93.3% of acute phase patients with either drug, and in 100% and 87.5%, respectively with oxamniquine or praziquantel in the chronic cases. No statistical difference exists between those two drugs or between the different clinical phases as far as efficacy is concerned. The Authors conclude that oxamniquine and praziquantel present good tolerance and therapeutic efficacy in both the acute and chronic phases of adult schistosomiasis mansoni.

INTRODUCTION

Oxamniquine and praziquantel are two drugs that present good tolerance and therapeutic efficacy in human schistosomiasis mansoni [3,8,9,14,15,17].

Recently, a double-blind clinical trial with these drugs has been carried over in children with schistosomiasis mansoni living in endemic areas in Brazil [7]. No significant difference in side effects has been found between oral oxamniquine (20 mg/kg body weight) and oral praziquantel (65 mg/kg body weight), except that abdominal distress was more frequent with the latter and headache with the former. Assessment of therapeutical efficacy disclosed an index of parasitological cure in 76.1% post praziquantel and in 65.3% post oxamniquine. This difference was not statistically significant [7].

In the present paper is compared the tolerance and efficacy of these drugs in the acute and chronic phases of adult schistosomiasis mansoni.

(*) Work carried out at the Centro de Pesquisas René Rachou, FIOCRUZ and Núcleo de Estudos sobre Esquistossomose — Faculdade de Medicina — UFMG, and supported in part by grant from the Conselho Nacional de Desenvolvimento Científico e Tecnológico — CNPq, Brazil. Address for reprints: NAFTALE KATZ, C.P. 1743 — Belo Horizonte — 30.000 — Brazil

KATZ, N.; ROCHA, R. S.; LAMBERTUCCI, J. R.; GRECO, D. B.; PEDROSO, E. R. P.; ROCHA, M. O. C. & FLAN, S. — Clinical trial with oxamniquine and praziquantel in the acute and chronic phases of schistosomiasis mansoni. **Rev. Inst. Med. trop. São Paulo 25:173-177, 1983.**

PATIENTS AND METHODS

One hundred thirty individuals (18-19 years of age) in practicing manouvres near a pond in Belo Horizonte, Brazil got in contact with water, and 2 months later, 78 of them were found eliminating **S. mansoni** eggs in their feces.

Clinical and laboratory examinations disclosed 39 cases in the acute phase of schistosomiasis (eosinophilia above 1000 cells/mm^3, fever, diarrhea) 17 in the chronic, and in the remaining 22 the phase was not defined.

The following tests were performed: leucocyte count (pre and five days post-treatment), electrocardiogram (pre and 1 and 5 days post) and thorax X-ray (pre, five and 30 days post-treatment). Pre examinations were performed 30 days before treatment. A similar number of patients in each phase received either oxamniquine (15 mg/kg body weight in a single oral dose) or praziquantel (50 mg/kg body weight, divided in two equal oral doses taken 6 hours apart). They were treated 3 months post contact.

The evaluation of drug activity was based on 3 consecutive daily stool examination by Kato-Katz quantitative method[5] (two slides from each stool sample) performed pre, and one, three and six months post treatment. Patients were considered cured when no **S. mansoni** eggs were detected in their feces in the 3 and 6 month period of follow-up.

Statistical analysis was done using the chi-square test with a 5% significance level.

RESULTS

The symptomatology reported pre-treatment is shown in Table I. Thirty four out of 39 patients in the acute phase had signs and/or symptoms, in the following frequence: fever, diarrhea, cough, abdominal distress, loss of body weight, hepatomegalia, asthenia and facial edema. In chronic phase patients, diarrhea and abdominal distress were the commonest symptomatology.

Post treatment the main side effects with both drugs are shown in Table II. Significant difference was found in regard to the higher incidence of abdominal distress and bitter taste post praziquantel, and of dizziness in chronic patients post oxamniquine. No patients required coadjuvant medication on account of side-effects, but it must be mentioned that one individual had convulsion post-oxamniquine and another had a severe urticariform reaction post praziquantel. Considering the total number of patients with side effects no significant difference has been found between the two drugs, or between the patients with different phases of the disease.

TABLE I

Signs and symptoms observed or reported by patients in different phases of schistosomiasis mansoni

Signs an symptoms	Number of cases		
	Acute phase	Chronic phase	Undefined
Fever	26	0	0
Diarrhea	26	5	8
Cough	18	0	0
Loss of body weight	15	0	0
Abdominal distress	15	4	1
Asthenia	14	1	1
Dizziness	10	3	1
Facial oedema	10	0	0
Headache	9	3	0
Arthralgia	8	0	0
Urticaria	5	0	0
Expectoration	6	0	0
Anorexia	6	0	0
Myalgia	5	0	0
Skin pruritus	1	0	0
Ronchi and wheezing	1	0	0
Obstipation	0	1	0
Hepatomegaly	12	1	0
Splenomegaly	3	0	0
Others	3	0	0
Numbers of cases with signs or symptoms/ total cases	34/39 (87.2)	11/17 (64.7)	9/22 (40.9)

( ): percentage

Leucocyte counts, pre and post-treatment with either drug is shown in Table III. The mean number of total leucocytes as well as of the eosinophils is much higher in the acute phase patients. In these a decrease in the number of white blood cells was observed when the results of the 30 days pre treatment were compared with those post-treatment.

There was no difference in the ECG tracings pre and one and five days post-treatment in all

T A B L E II

Side-effects observed in patients treated with praziquantel or oxamniquine in different phases of schistosomiasis mansoni

Side-effects	Acute phase		Chronic phase		Undefined	
	Praziquantel	Oxamniquine	Praziquantel	Oxamniquine	Praziquantel	Oxamniquine
Dizziness	7 (36.8)	7 (38.9)	3 (37.5)	8 (88.9)*	5 (45.5)	7 (63.6)
Abdominal distress	12 (63.1)*	4 (22.2)	5 (62.5)*	1 (11.1)	7 (63.6)*	2 (18.2)
Somnolence	6 (31.6)	4 (22.2)	2 (25.0)	3 (33.3)	1 (9.0)	3 (27.2)
Bitter taste	6 (31.6)*	0	5 (62.5)*	0	4 (36.3)*	0
Headache	5 (26.3)	2 (11.1)	0	0	3 (27.2)	0
Malaise	3 (15.8)	0	1 (12.5)	3 (33.3)	0	0
Nausea	2 (10.5)	2 (11.1)	1 (12.5)	4 (44.4)	2 (18.2)	2 (18.2)
Vomiting	2 (10.5)	0	0	1 (11.1)	0	0
Dyspepsia	1 (5.2)	1 (5.5)	2 (25.0)	0	0	0
Diarrhea	0	1 (5.5)	0	0	0	0
Asthenia	5 (26.3)	5 (27.8)	4 (50.0)	2 (22.2)	1 (9.0)	2 (18.2)
Urticariform reaction	1 (5.2)	0	0	0	0	0
Convulsion	0	0	0	0	0	1 (9.1)
Number of treated patients/ with side-effects	19/17 (89.5)	18/16 (88.9)	8/8 (100.0)	9/8 (88.9)	11/9 (81.8)	11/9 (81.8)

( ): percentage * — $p < 0.05$

T A B L E III

Leucogram of patients in different phases of schistosomiasis mansoni treated with praziquantel or oxamniquine

Cells	Clinical phase	Praziquantel		Oxamniquine	
		Pre treatment	Post treatment	Pre treatment	Post treatment
Leucocyte	Acute	10497 (4450-21950)	8065 (4750-14500)	10832 (5550-20600)	8584 (4950-14450)
	Chronic	7156 (4000-99000)	5816 (4500-9400)	6855 (4000-10250)	5883 (4250-10100)
	Undefined	7177 (4350-10500)	7633 (5450-8850)	6572 (4750-9000)	7036 (4900-10100)
Neutrophil	Acute	32 (13-53)	39 (16-62)	35 (14-59)	46 (24-70)
	Chronic	52 (40-69)	56 (40-67)	52 (42-64)	54 (49-67)
	Undefined	47 (37-72)	45 (30-57)	51 (30-72)	50 (36-67)
Eosinophil	Acute	39 (14-62)	25 (10-55)	37 (8-78)	22 (4-16)
	Chronic	7 (1-14)	10 (6-19)	9 (6-23)	11 (2-20)
	Undefined	14 (2-23)	17 (5-29)	12 (2-36)	11 (3-28)

The data for leucocyte are absolute numbers, for individual peripheric blood cells are percentage.
( ): range.

but one patient. This was an acute phase individual which presented sinusal bradycardia one day post praziquantel with a normal tracing in the fifth day. Thorax X-ray was performed in 36 acute phase patients. Post-treatment 8 cases revealed some alteration, being four cases with each drug. Post oxamniquine, the changes observed were area of infiltration in the base of the right hemithorax, dilated pulmonary trunck, and also micro and macro nodules in both pulmonary bases. Post-praziquantel, micronodules in both bases, thickening of the bronchial wall, retification of the pulmonary trunck and a prominent pulmonary artery were seen. The X-ray alterations had no correlation with the pulmonary symptomatology (cough, wheezing etc.). In 7 cases (87.5%) the changes have disappeared completely on the 30th day radiologic control.

The number of **S. mansoni** eggs per gram of feces pre-treatment varied from four to 462 in the acute phase patients (median: 54), and from 24 to 1662 (median: 222) in the chronic patients. In the undefined cases the range was 6 to 882 (median: 90).

Therapeutic efficacy is summarized in Table IV. Cure has been achieved in approximately 90% of individuals treated either with oxamniquine or praziquantel. No statistically significant difference in efficacy has been ob-

served in the various phases of the disease nor between the two drugs.

TABLE IV

Rate of cure post praziquantel or oxamniquine, in patients with different phases of schistosomiasis mansoni

Phase	Drug	Number of patients		
		Treated	Followed-up	Cured (%)
Acute	Praziquantel	19	15	14 (93.3)
	Oxamniquine	20	15	14 (93.3)
Chronic	Praziquantel	8	8	7 (87.5)
	Oxamniquine	9	8	8 (100.0)
Undefined	Praziquantel	11	8	7 (87.5)
	Oxamniquine	11	11	10 (90.9)

DISCUSSION

The treatment of patients in the acute phase of schistosomiasis mansoni with antimonial salts, niridazole or hycanthone shows only a partial activity of these drugs. In fact, a temporary interruption of egg-laying or a diminution of the number of **S. mansoni** eggs in the feces has been observed, but the complete and definitive disappearance of the eggs (cure) was accomplished only in less than 50 percent of patients treated with these drugs [2,4,11,12,16].

In the present work, the efficacy of oxamniquine and praziquantel was very high both in the chronic phase (100% and 87.5% respectively) and in the acute phase patients treated three months post infection (93.3% for both drugs).

It is worthwhile to mention that LAMBERTUCCI et al. [10] treated 11 children 55 to 77 days post infection with oral oxamniquine (20 mg/kg body weight) and the percentage of cure was only 45%. Nevertheless previous experience by KATZ et al. [6] with oxamniquine by intramuscular injection showed a complete cure in all 15 (adult and children) with four to nine months infection, and also in 3 cases by PRATA et al. [13].

As far as we know this is the first report on praziquantel in the acute phase of schistosomiasis mansoni.

No statistical difference in relation to tolerance or efficacy has been found between these two drugs in the acute and chronic groups. Similar results were obtained by KATZ et al. [7] in children living in an endemic area treated with oxamniquine (20 mg/kg body weight) or praziquantel (65 mg/kg body weight), and also by BRANCHINI et al. [1] treating mostly adult patients. Nevertheless, it is important to remark that in the present study more than 90% of the patients were cured, where as in the other two trials the percentage of cure varied from 54 to 76%. One possible explanation for our high rate of cure is the very low worm burden of these acute phase patients as shown by the median of number of **S. mansoni** eggs in the feces of 54.

Side effects with these drugs were more frequently reported than in previous studies. However, no special care was necessary with the exception of one patient that had convulsion post oxamniquine. It must be also emphasized that all individuals were collectively treated and stayed together for the whole day for clinical evaluation.

Twenty percent of the patients had some kind of thorax X-ray alteration post-treatment such as thickening of the bronchial wall, macro and micronodules, etc, with spontaneous remission when the 30th day control examination was performed.

Summing up, our results show that oxamniquine and praziquantel present a high therapeutic efficacy in both the chronic and acute phases of adult schistosomiasis mansoni and no complications observed would preclude the administration of these drugs in the early phase of the disease.

RESUMO

Ensaio clínico com oxamniquine e praziquantel nas fases aguda e crônica da esquistossomose mansoni

Cento e trinta recrutas (18-19 anos) em manobras militares, tiveram contacto com água em uma lagoa de Belo Horizonte, Brasil e 2 meses após, 78 deles estavam eliminando ovos de **S. mansoni** nas fezes.

Exames clínicos e laboratoriais diagnosticaram 39 pacientes na fase aguda, 17 na crônica e em 22, não foi possível definir em que fase se encontravam. Os 78 pacientes foram tratados com oxamniquine (15 mg/kg em dose única

oral) ou com praziquantel (50 mg/kg dividido em duas doses).

Em relação aos efeitos colaterais, houve uma incidência significativamente maior de dor abdominal e boca amarga no grupo tratado com praziquantel, e de tontura nos pacientes da fase crônica, tratados com oxamniquine.

A eficácia terapêutica foi avaliada por 3 exames de fezes (método de Kato-Katz) realizados antes e 1, 3 e 6 meses após o tratamento. A cura parasitológica foi de 93,3% na fase aguda com ambas as drogas e de 100% e 87,5% com oxamniquine e praziquantel respectivamente, na fase crônica. Não houve diferença estatística entre as duas drogas ou entre as diferentes fases clínicas da doença em relação a eficácia.

Os Autores concluem ter o praziquantel e a oxamniquine boa tolerância e eficácia, nos pacientes com fase aguda ou crônica da esquistossomose mansoni.

ACKNOWLEDGEMENTS

We thank Dr. Marcos Vinicius S. Amorim and Sgt. Matheus J. Reis Filho for the helpfull collaboration.

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Recebido para publicação em 29/6/1982.