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DOUBLE-BLIND CLINICAL TRIAL COMPARING PRAZIQUANTEL WITH OXAMNIQUINE IN SCHISTOSOMIASIS MANSONI (*)

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SUMMARY

A double-blind comparative trial was carried out involving 120 patients with active **Schistosoma mansoni** infection, living in two endemic areas in the State of Minas Gerais, Brazil. They were randomly allocated into two parallel groups, with the same number of cases, in accordance with the administered drug: praziquantel or oxamniquine. Both were used in a single oral dose of 65 and 20 mg/kg, respectively. The patients were children, 8 to 14 years old, both sexes, body weight between 17 and 50 kg, with intestinal or hepatointestinal form of schistosomiasis, having more than 90 and less than 2,500 eggs per gram of faeces according to Kato-Katz quantitative method. Clinical examination was performed before and at least during the first three days following the drug intake. No significant difference has been found between both drugs regarding the percentage of patients complaining of side-effects, but abdominal distress was significantly more frequent in the praziquantel group and headache in the oxamniquine group. Assessment of therapeutical efficacy was based on stool examinations made at the end of the 1st, 3rd and 6th months after treatment. Parasitological cure was achieved in 76.1% of the cases treated with praziquantel and in 65.3% of those treated with oxamniquine. This difference was not statistically significant. These results indicate that praziquantel and oxamniquine bearing different chemical and pharmacological characteristics seem to have similar patterns as far as tolerance and efficacy are concerned in the treatment of schistosomiasis mansoni in Brazil.

INTRODUCTION

Oxamniquine is an antischistosomal drug which has been used, in Brazil, during the last ten years in about four million patients with **S. mansoni** infection showing good tolerance and therapeutical efficacy [19,20].

Praziquantel, a new schistosomicidal agent [8,9,16,21], is under clinical investigation since 1977 in this country also presenting favourable results [7,12,13,18].

To compare the tolerance and efficacy between these two drugs a double-blind clinical trial has been performed involving children with schistosomiasis mansoni living in endemic areas, and the obtained results are herein presented.

PATIENTS AND METHODS

This investigation was designed as a double-blind comparative trial between two parallel groups established by random allocation of patients. The experimental group with 60 cases was treated with praziquantel, 65 mg/kg body weight; the control group having the same number of cases was treated with oxamniquine, 20 mg/kg body weight. Both drugs were administered as single oral dose.

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These 120 patients with active schistosomiasis mansoni, living in two endemic areas, Baldim and Ravena, in the State of Minas Gerais, Brazil, were treated as out patients. They comprised children of both sexes, from 8 to 14 years old, with body weight between 17 and 50 kg, presenting the intestinal or hepatointestinal forms of this parasitosis and having more than 90 and less than 2,500 eggs of **S. mansoni** per gram of faeces.

In order to achieve homogenous comparative groups the patients were stratified into sub-groups according to their age and the pre-treatment number of eggs in the stool (Table I).

TABLE I

Stratification of 120 children with active schistosomiasis mansoni into two treatment groups

Patients age	Number of treated cases	
	Praziquantel	Oxamniquine
Total	60	60
8 to 10	20	20
11 to 12	20	20
13 to 14	20	20
Number of eggs per gram of faeces	**Number of treated cases**	
	Praziquantel	Oxamniquine
Total	60	60
90 to 500	42	42
501 to 1,000	12	12
1,001 to 2,500	6	6

The evaluation of tolerance relied on clinical examinations performed before and at least during the first three days following the drug administration. The assessment of therapeutical efficacy was based on three consecutive daily stool examinations, two slides from each sample of faeces, applying the Kato-Katz quantitative technique [11], prior to as well as 1, 3 and 6 months after treatment. Parasitological cure was considered when no **S. mansoni** eggs were detected in the serial stool examinations during six months follow-up period. The chi-square test was applied for the statistical analysis of the obtained data accepting 5% as the limiting level of significance.

RESULTS

Tolerance — The main side-effects reported by the patients or observed by the investigators, on both drugs, are shown in Table II. They had mild to moderate intensity and disappeared spontaneously within 24 to 48 hours following the drug intake. Significant differences were found in regard to the higher incidence of abdominal distress with praziquantel and of headache with oxamniquine. No patient required co-adjuvant medication on account of side effects. Considering the proportion of cases complaining of side-effects, 75% (45/60) in the praziquantel group and 80% (48/60) in the oxamniquine group, there was no significant difference between the two drugs.

TABLE II

Side-effects observed with praziquantel 1 x 65 mg/kg and oxamniquine 1 x 20 mg/kg, single oral dose

Side-effects	Praziquantel		Oxamniquine	
	No.	%	No.	%
Total treated cases	60	100.0	60	100.0
Cases with side-effects	45	75.0	48	80.0
Abdominal distress	30	50.0*	12	20.0
Giddiness	9	15.0	18	30.0
Headache	4	6.7	13	21.7*
Drowsiness	5	8.3	7	11.7
Diarrhoea	8	13.3	4	6.7
Vomiting	4	6.7	7	11.7
Nausea	3	5.0	3	5.0
Bitter taste	3	5.0	0	
Asthenia	2	3.3	0	
Anorexia	1	1.7	1	1.7
Urticariform reaction	1	1.7	0	

* X^2; $p < 0.05$

Efficacy — The parasitological findings obtained with both antischistosomal agents are shown in Tables III and IV.

From the two groups of 60 patients, 46 treated with praziquantel and 49 with oxamniquine have completed the required parasitological follow-up period of six months. It was attained a cure rate of 76.1% (35/46) with praziquantel and 65.3% (32/49) with oxamniquine. No statistical significant difference has been observed neither between groups or sub-groups treated with the same drug, nor between praziquantel and oxamniquine.

DISCUSSION

The results herein presented show that both drugs have similar pattern, as far as, tolerance and therapeutic activity are concerned. In fact, no significant difference was found

TABLE III

Parasitological results of children with different ages treated with praziquantel or oxamniquine

Children's Age	Number of patients					
	Praziquantel (1 x 65 mg/kg)			Oxamniquine (1 x 20 mg/kg)		
	Treated	Followed-up	Cured (%)	Treated	Followed-up	Cured (%)
Total	60	46	35(76.1)	60	49	32(65.3)
8 to 10	20	17	11(64.7)	20	16	10(62.5)
11 to 12	20	14	13(92.8)	20	16	10(62.5)
13 to 14	20	15	11(73.3)	20	17	12(70.6)

X^2 — Praziquantel x Oxamniquine: (8 to 10); (11 to 12); (13 to 14); (Total) — $p > 0.05$, N.S.

TABLE IV

Parasitological results of children treated with praziquantel or oxamniquine with different worm burdens

Number of eggs per gram of faeces	Number of patients					
	Praziquantel (1 x 65 mg/kg)			Oxamniquine (1 x 20 mg/kg)		
	Treated	Followed-up	Cured (%)	Treated	Followed-up	Cured (%)
Total	60	46	35(76.1)	60	49	32(65.3)
95 to 500	42	35	27(77.1)	42	35	24(68.6)
501 to 1,000	12	7	5(71.4)	12	9	5(55.6)
1,001 to 2,500	6	4	3(75.0)	6	5	3(60.0)

X^2 — Praziquantel x Oxamniquine: (95 to 500); (501 to 1,000); (Total) — $p > 0.05$, N.S.
Fisher — " x " : (1,001 to 2,500) — $p > 0.05$, N.S.

between them concerning the ratio of treated patients and those with side-effects. Significance was encountered only in regard to abdominal distress with praziquantel and headache with oxamniquine. The most frequent complaints comprising the two drugs involved gastrointestinal and neurological field, namely: abdominal distress, diarrhoea, giddiness, headache and drowsiness. With praziquantel it has been observed once again the occurrence of urticariform reaction [12,13].

Important central nervous system side-effects in man such as hallucination, psychic excitement and convulsion have already been published on oxamniquine administration but its estimated incidence is lower than 0.5% [4,10].

With praziquantel, hypoacusia, hyporeflexia, visual disturbance, excitement and tremor ressembling a localized convulsion of the arm, have also been described in a few cases [1,3,7,12,17].

It is worthwhile to mention that both drugs can occasionally induce neuropsychiatric side effects, and this must be taken into consideration when treatment is being administered.

The assessment of therapeutical efficacy revealed similar percentages of parasitological cure, 76.1% and 65.3% with praziquantel and oxamniquine, respectively. Such findings are in agreement with the results from a previous double blind trial, including mostly adult patients, whose cure rates were 61.0% with praziquantel (1 x 45 mg/kg) and 54.0% with oxamniquine (1 x 15 mg/kg) [5].

In a multicentric clinical trial with praziquantel, involving three Brazilian investigators and 408 patients most of them at endemic areas, to evaluate the efficacy of different doses, the following results were obtained: 41.6% with 1 x 30 mg/kg; 60.7% with 1 x 40 mg/kg; 66.9% with 2 x 25 mg/kg [1,13,17]. With oxamniquine almost the same result (about 70% of cure in children) was found in Peri-Peri, another endemic area of Minas Gerais State, where the dosage employed were the same (20 mg/kg) [14].

It is interesting to note that therapeutical response with praziquantel in patients not cured after successive oxamniquine administration has been described [2,6,15], and, that probably oxamniquine may be effective in non-cured patients treated with praziquantel.

Summing up one may conclude that these two drugs, of quite different chemical and

pharmacological characteristics, are efficient therapeutical weapon for treating schistosomiasis mansoni in Brazil. Apparently, they present similar tolerance and efficacy but it must pointed out that such conclusion is based on the clinical experience gained with the treatment of about 4 million cases with oxamniquine and only a few thousands with praziquantel.

RESUMO

Ensaio clínico duplo-cego comparando praziquantel e oxamniquine na esquistossomose mansoni

Realizou-se um ensaio comparativo, duplo-cego, abrangendo 120 pacientes portadores de infecção ativa pelo **Schistosoma mansoni** e residentes em duas áreas endêmicas de Minas Gerais, Brasil. Os pacientes foram distribuídos aleatoriamente em dois grupos paralelos, com igual número de casos, conforme a droga administrada: praziquantel ou oxamniquine. Ambos os medicamentos foram empregados em dose única, por via oral, de respectivamente 65 e 20 mg/kg de peso corporal. A casuística compreendeu crianças de 8 a 14 anos, de ambos os sexos, com peso corpóreo entre 17 e 50 kg, apresentando a forma intestinal ou hepatointestinal de esquistossomose e tendo mais de 90 e menos de 2500 ovos de **S. mansoni** por grama de fezes, segundo método quantitativo de Kato-Katz.

O exame clínico foi efetuado antes e, pelo menos, até o terceiro dia subseqüente à tomada da medicação. Nenhuma diferença significativa foi observada entre as duas drogas com referência à proporção de casos com efeitos colaterais, todavia a incidência de desconforto abdominal foi maior no grupo do praziquantel, e a de cefaléia no da oxamniquine.

A avaliação da eficácia terapêutica baseou-se em exames de fezes realizados ao se completarem um, três e seis meses após o tratamento. A cura parasitológica foi alcançada em 76,1% dos casos tratados com praziquantel e em 65,3% dos tratados com oxamniquine. Essa diferença não foi estatisticamente significativa.

Esses resultados indicam que ambas as drogas, de características químicas e farmacológicas diversas, parecem apresentar padrões semelhantes quanto à tolerância e à eficácia no tratamento da esquistossomose mansoni, no Brasil.

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