Efficacy of oxamniquine and praziquantel in the treatment of *Schistosoma mansoni* infection: a controlled trial

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Objective To evaluate the therapeutic efficacy of oxamniquine and praziquantel, the two most clinically important schistosomicide drugs, and to compare the accuracy of faecal examination with the accuracy of oogram in testing for *Schistosoma mansoni* infection.
Methods In a triple-masked and randomized controlled trial, 106 patients infected with *S. mansoni* were randomly allocated to one of three statistically homogeneous groups. One group was given 60 mg/kg praziquantel per day for three consecutive days, another was given two daily doses of 10 mg/kg oxamniquine, and the placebo group received starch. Faecal examinations (days 15, 30, 60, 90, 120, 150, and 180 after treatment) and biopsy of rectal mucosa by quantitative oogram (days 30, 60, 120, and 180) were used for the initial diagnosis and for evaluating the degree of cure. The χ^2 test and the Kruskal–Wallis test were used to compare variables in the three groups. Survival analysis (Kaplan–Meier) and the log-rank test were used to evaluate the efficacy of the treatments.
Findings The sensitivity of stool examinations ranged from 88.9% to 94.4% when patients presented with >5000 *S. mansoni* eggs per gram of tissue (oogram); when the number of eggs dropped to <1000 eggs per gram, sensitivity was reduced (range, 22.7–34.0%). When cure was evaluated by stool examination, oxamniquine and praziquantel had cure rates of 90.3% and 100%, respectively. However, when the oogram was used as an indicator of sensitivity, the oxamniquine cure rate dropped dramatically (to 42.4%), whereas the rate for praziquantel remained high, at 96.1%.
Conclusion Praziquantel was significantly more effective than oxamniquine in treating *S. mansoni* infection. The oogram was markedly more sensitive than stool examinations in detecting *S. mansoni* eggs and should be recommended for use in clinical trials with schistosomicides.

Keywords Schistosomiasis mansoni/drug therapy; Oxamniquine/therapeutic use; Praziquantel/therapeutic use; Placebos; Schistosomiasis mansoni/growth and development; Feces/parasitology; Parasite egg count; Sensitivity and specificity; Comparative study; Randomized controlled trials; Brazil (*source: MeSH, NLM*).

Mots clés Schistosomiase intestinale/chimiothérapie; Oxamniquine/usage thérapeutique; Praziquantel/usage thérapeutique; Placebo; Schistosomiase intestinale/croissance et développement; Fèces/parasitologie; Numération œuf parasite; Sensibilité et spécificité (Epidémiologie); Etude comparative; Essai clinique randomisé; Brésil (*source: MeSH, INSERM*).

Palabras clave Esquistosomiasis mansoni/quimioterapia; Oxamniquina/uso terapéutico; Praziquantel/uso terapéutico; Placebos; Esquistosomiasis mansoni/crecimiento y desarrollo; Heces/parasitología; Recuento de huevos de parásitos; Sensibilidad y especificidad; Estudio comparativo; Ensayos controlados aleatorios; Brasil (*fuente: DeCS, BIREME*).

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Voir page 195 le résumé en français. En la página 195 figura un resumen en español.

Introduction

Schistosomiasis mansoni infection, an endemic disease of worldwide importance in terms of public health, affects large geographical areas in several countries. In Brazil, its prevalence is estimated to be 8–10 million infected people, and about 30 million people living in areas of *S. mansoni* transmission are currently at risk of the disease (*1*).

Approximately 4% of untreated parasitized people develop severe forms of *S. mansoni* — hepatosplenic schistosomiasis. In areas in which the disease is endemic, a marked correlation between worm burden and disease severity has been reported. Chemotherapy plays a very important role in reducing morbidity in those areas; it is also valuable for resolving the disease in individual cases (*1*).

Oxamniquine and praziquantel are the only drugs used to treat schistosomiasis in Africa and the Americas. Oxamniquine, a 2-aminomethyltetrahydroquinoline derivative, is produced by biological synthesis and is one of the most promising schistosomicides. It has an anticholinergic effect, which increases the parasite's motility (*2*) and inhibits nucleic acid synthesis (*3*). It is more effective against male than female parasites and has no notable effect on other *Schistosoma* spp. that parasitize humans. In Brazil, oxamniquine was shown to be well tolerated — a single oral dose of 15 mg/kg for adults and

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two daily doses of 10 mg/kg for children showed cure rates of over 83%, when its efficacy was evaluated by means of stool examinations (6–10 examinations) (*4–6*). However, when rectal biopsy (quantitative oogram) was used to evaluate cure after treatment with oxamniquine (15–18 mg/kg), the cure rate was only 38.3% (*7*).

Praziquantel, a pyrazinoisoquinoline derivative with low toxicity, has proved to be effective against *S. mansoni* and other species of the genus *Schistosoma* that parasitize humans. It affects mainly the female parasite, and causes tegument changes (*8*) and a reduction in the glutathione concentration (*9*) in the worm. A single dose of 40–60 mg/kg was shown to give a cure rate of 80% (*10*), when the cure was evaluated by the Kato & Katz (KK) method of stool examination (*11*). Cunha et al. (*12*), who reported that a single oral dose of 60 mg/kg praziquantel cured only 29% of patients when cure was evaluated by rectal biopsy (*13*), showed that a new therapeutic schedule of 60 mg/kg per day for three consecutive days produced a cure rate of 91% evaluated over a six-month period (*13*).

In the light of conflicting published data on therapeutic evaluation, the present study was undertaken with two main aims. The first was to evaluate the clinical treatment of *S. mansoni* by oxamniquine and praziquantel, comparing these drugs with a placebo, in a prospective triple-masked and randomized clinical trial. The second aim was to compare the sensitivity of parasitological stool examinations by both qualitative and quantitative methods; the results obtained by quantitative stool examinations were also compared with those from quantitative oograms (rectal mucosa biopsy).

Methods

In total, 106 outpatients at the University Hospital, Universidade Federal de Minas Gerais (UFMG), Brazil, were selected for the trial on the basis of stool examinations that tested positive for *S. mansoni*. Children of pre-school age, aged patients, pregnant women, suckling infants, patients with acute or severe chronic concomitant diseases, patients with the hepatosplenic form of the disease and individuals whose behaviour (e.g. contact with natural waters suspected to contain cercariae) put them at risk for acquiring new infections, were excluded. In all, 101 (95.3%) of the selected patients had not taken any drugs for the treatment of *S. mansoni* infection, and five patients, previously treated more than five years ago, had had new contacts with natural waters after the first treatment.

The research was evaluated by the Ethical Committee for Human Research of the Santa Casa de Misericórdia Hospital, Belo Horizonte, Brazil, which approved all the procedures of the present clinical trial. All but three participants lived in Belo Horizonte, State of Minas Gerais, Brazil and all of them denied contact with natural waters in which the parasite was known to be endemic.

All the 106 patients were clinically examined before and during treatment, and throughout the follow-up period. They were randomly allocated to one of three groups and treated for three consecutive days, using a similar three-day schedule. The first group was given praziquantel (60 mg/kg per day) for three consecutive days. The second one was given two daily doses of 10 mg/kg oxamniquine on the first day, and a placebo containing starch on days 2 and 3. The third group were given a placebo (starch) on all three days.

The drugs and placebo were taken orally in capsules. The capsules were identical in appearance, and designated A (praziquantel), B (oxamniquine), and C (placebo). Patients in all three groups were given their daily dose in two morning sessions, separated by a four-hour interval, under the supervision of one of the investigators. To facilitate the calculation for the dose per body weight, all capsules for the group treated with praziquantel contained 360 mg of the drug, whereas capsules prepared with oxamniquine contained 90 mg. The investigators were blind to which patients were given which treatment; the identity of each group was kept in a sealed envelope.

The patients were kept under observation for assessment of side-effects throughout the experimental period. All patients were advised to stay away from the transmission foci of the disease, and they reported doing so. Ninety (85%) patients were followed up for a minimum of six months, whereas for 16 (15%) patients the follow up was incomplete and the duration of follow-up varied.

Stool examinations to test for the presence of the parasite took place at the Department of Parasitology, Institute of Biological Sciences/Federal University of Minas Gerais; the quantitative oograms, by biopsy of rectal mucosa, and the clinical examinations were carried out at the University Hospital. Three methods were used for stool examination: the quantitative KK method (*11*), the quantitative Kato thick-smear technique, described by Martin & Beaver (MB) (*14*), and the semi-quantitative sedimentation method by Hoffman, Pons & Janer (HPJ) (*15*). Two microscope slides were used in each examination by the KK and MB methods, and the total sediment of each faecal sample was examined in the HPJ method. Thus, for the cure evaluation of each patient carried out at 15, 30, 60, 90, 120, 150, and 180 days after treatment (seven samples), 28 slides were examined by the KK and MB methods, and seven examinations were made by the HPJ method. Quantitative oograms by biopsy of rectal mucosa (*16*) were also undertaken for all patients before treatment and were repeated 30, 60, 120, and 180 days after treatment, resulting in a total of four examinations for cure evaluation.

The end-point used for evaluating drug efficacy was negative parasitological stool examinations and the absence of viable *S. mansoni* eggs in the oograms, in a sixth-month follow-up period. At the end of the six months, all patients from the placebo group, as well as all patients who were not cured, were treated with 60 mg/kg per day praziquantel for three consecutive days.

Data analysis

The variables tested in the three treatment groups were compared using the χ^2 test and analysis of variance (whenever necessary, the Kruskal–Wallis test). The results of stool examinations and oograms were compared throughout the follow-up period. Survival analysis (Kaplan–Meier) and log-rank test were used to evaluate the efficacy of the treatments (*17*).

At the end of the investigation (and data analysis) the sealing wax on the envelopes that held the identity of the three groups was broken in the presence of all the investigators.

Results

Baseline measurements

Of 106 infected patients, 78 (74%) were males and 28 (26%) were females (Table 1). The ages ranged from 12 years (one

Table 1. **Baseline characteristics of study patients with *Schistosoma mansoni* infection randomly allocated to one of three treatment groups**

Baseline characteristics	Treatment groups		
	Oxamniquine (*n* = 34)	Praziquantel (*n* = 36)	Placebo (*n* = 36)
No. of males	22 (64.7)[a]	30 (83.3)	26 (72.2)
No. of females	12 (35.3)	6 (16.7)	10 (27.8)
Age (years)			
Mean	28; *12.20*[b]	24; *9.6*	25; *8.2*
Range	12–59	13–51	12–41
Weight (kg)			
Mean	56.5; *12.5*	60.3; *14.3*	60.4; *10.3*
Range	28.5–90	30–105	41.5–80
Clinical form			
Intestinal	23 (67.6)	26 (72.2)	22 (61.1)
Hepatointestinal	11 (32.3)	10 (27.8)	14 (38.9)
No. of viable eggs per gram of tissue			
Mean	3486; *2746.4*	3920; *3063.7*	2865; *2298.3*
Median	2514	3000	2249
Range	1667–5375	1594–5230	1176.5–3799
>5000	9 (26.5)	9 (25.0)	5 (13.9)
3001–5000	7 (20.6)	9 (25.0)	9 (25.0)
2001–3000	5 (14.7)	4 (11.1)	6 (16.7)
1000–2000	10 (29.4)	10 (27.8)	9 (25.0)
<1000	3 (8.8)	4 (11.1)	7 (19.4)
No. of eggs per gram of faeces			
Mean	92.8; *209.5*	114.6; *159.6*	78.4; *138.6*
Median	23	29	33

[a] Figures in parentheses are percentages.
[b] Figures in italics are standard errors.

patient) to 59 years, with an average age of 26 years. The weight varied from 28.5 kg to 105.3 kg (average 50.6 kg). In all, 71 (67%) patients had the chronic intestinal form of the disease and 35 (33%) patients had the hepatointestinal form. No significant differences between the groups were found. Analysis of the number of live eggs per gram of tissue and the number of eggs per gram of faeces indicated homogeneity between the three groups.

Comparison of methods

No significant difference between the two quantitative stool examination methods (KK and MB) was found when the numbers of eggs per gram of faeces were compared. So, for the final statistical analysis, the results obtained by both methods were grouped, and the mean of four slides (two from each examination) was used. Therefore, the two examinations together will be referred to hereafter as KK+MB.

Therapeutic efficacy

The therapeutic efficacy of both drugs, plus the placebo, is shown in Table 2, and in Fig. 1 and Fig. 2. No significant difference between the two drugs was found when stool examinations were used to evaluate cure, taking into account the association of the parasitological methods (either the KK+MB or the HPJ). The cure rates were 90.3% (oxamniquine) and 100% (praziquantel); the placebo group presented 16% "false cures" as detected by faecal examination (KK+MB and HPJ). Nevertheless, when the therapeutic evaluation was based on the quantitative oogram by biopsy of rectal mucosa, the cure rate for oxamniquine dropped to 42.4%, whereas it remained high for praziquantel, at 96.l%. In the placebo group, 100% of patients presented with viable eggs as detected by oogram, compared with 84% detected by stool examinations (Table 2).

The number of live eggs found in the oograms from patients who were treated but not cured was markedly reduced (Table 3). The average number of eggs before treatment with oxamniquine was 3486 and dropped to 543 eggs per gram of tissue after treatment. With praziquantel treatment, an average of 3920 eggs per gram of tissue decreased to 683 eggs. This indicates a decrease in the worm burden due resulting from the activity of the drugs studied.

A direct relationship between the percentage of patients testing positive in stool examinations (KK+MB or HPJ) and the number of viable eggs in the rectal mucosa was found when the quantitative oogram was used as a reference of 100% (Table 4).

All patients in the placebo group presented viable *S. mansoni* eggs in tissue fragments after day 90 of follow-up (Fig. 1), but 16% remained negative after 180 days of follow-up when stool examinations were used for cure evaluation (KK+MB and HPJ) (Fig. 2). There was no significant difference in the failure rate of oxamniquine and praziquantel when viable *S. mansoni* eggs in stool were used as an end-point (either KK+MB or HPJ), (P = 0.21) but praziquantel was significantly more effective in treating the infection when *S. mansoni* eggs in rectal tissue fragments were used to evaluate treatment efficacy (P = 0.03).

The side-effects of both drugs were similar and mild, with most common being headache, dizziness, drowsiness, and abdominal pain. Patients from the placebo group had drowsiness and abdominal pain also.

Discussion

More than 90% of patients taking praziquantel (60 mg/kg for three days) were cured of *S. mansoni* infection, whereas oxamniquine (20 mg/kg per day) cured only 42% of patients. The oogram was more sensitive compared with stool examinations, when used to evaluate cure in clinical trials of the two schistosomicides.

Criterion for cure

The presence of the parasite's living eggs indicates *S. mansoni* oviposition. The living and mature eggs are able to migrate from submucosa to the intestinal lumen by means of histolytic enzymes and inflammatory reactions. The absence of eggs over a long period of time, e.g. six months after treatment, indicates that the worms have died. This constitutes the criterion for parasitological cure (*18*). Sometimes dead eggs are found with stool examinations, but this is rare and, the eggs may be morphologically different.

Cure rates

Previous studies using an oral formulation of oxamniquine showed cure rates of 78–93% in adults, at doses of 12.5–15 mg/kg. In children, the most effective schedule was a single dose of 20 mg/kg or two daily doses of 10 mg/kg each, which

Table 2. **Therapeutic efficacy of oxamniquine, praziquantel, and placebo evaluated by quantitative oogram and stool examination**

Treatment group	Oxamniquine (*n* = 34)		Praziquantel (*n* = 36)		Placebo (*n* = 36)	
Method of evaluation	Oogram	HPJ[a]+KK[b]	Oogram	HPJ+KK	Oogram	HPJ+KK
No. of cases cured	14	28	25	26	0	2
Cure rate (%)	42.4	90.3	96.1	100	0	16
No. of evaluated cases	33	31	26	26	31	29

[a] HPJ = Method of Hoffman, Pons & Janer (*15*).
[b] KK = Method of Kato & Katz (*11*).

Fig. 1. **Kaplan–Meier survival curves: *Schistosoma mansoni* eggs in tissue (rectal biopsy)**

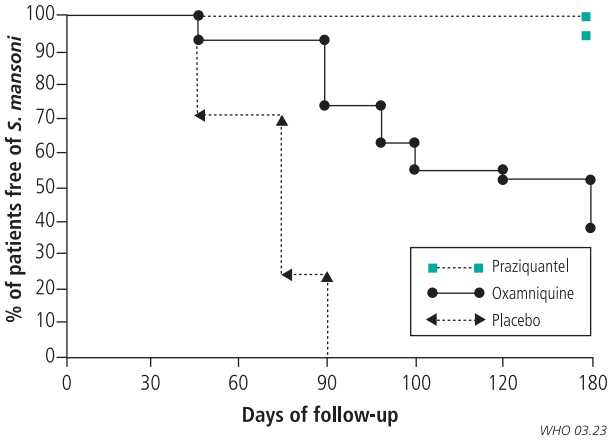
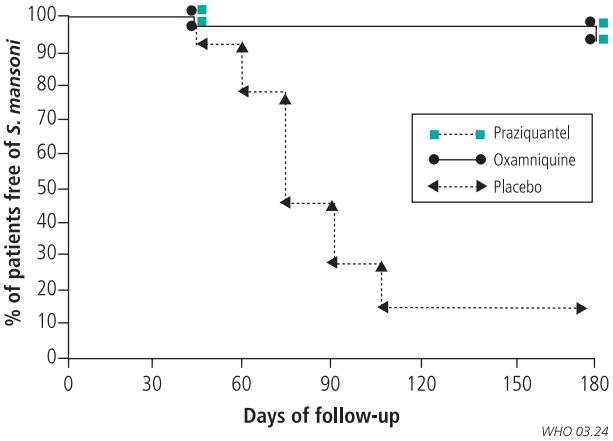


Fig. 2. **Kaplan–Meier survival curves: *Schistosoma mansoni* eggs in stools (KK + MB and HPJ).** See text for explanation



gave cure rates of 66% and 89%, respectively. Kato's method was used to evaluate cure (*4–6*). When rectal biopsy (quantitative oogram) was used to evaluate adult patients treated with oxamniquine, the cure rate was 38.3% (*7*).

In previous studies, praziquantel, when given orally at a single dose of 40–60 mg/kg per body weight, was shown to have a cure rate of 80% when evaluated by the KK and HPJ methods (*19–21*). Another group found that the cure rate was much lower when the quantitative oogram method was used for cure evaluation, compared with stool examination. A single oral dose of 65 mg/kg gave a cure rate of 29.2% with the oogram method, compared with 91.7% and 50% for the KK and HBJ methods, respectively (*13*).

The results of the present study corroborate previously published data obtained when stool examination was used to evaluate the efficacy of oxamniquine (*4–6*). When rectal biopsy was used, the cure rate fell to 42.4%, confirming previous results obtained by Cunha (*7*). The oogram detected a cure rate of 96.1% for praziquantel (Table 2).

By contrast, our results do not agree with those by Rabelo et al. (*22*), who showed that oxamniquine gave a high cure rate in adults treated at a single oral dose of 15 mg/kg. Evaluation was by quantitative oogram (rectal biopsy; a single examination after treatment) and by stool examination (18 slides for KK, plus 18 slides for HPJ) after treatment. Perhaps the differences in results were due to the criteria used for selecting patients and to the number of rectal biopsies used for cure evaluation. Their patients were selected by cutaneous skin test and serology, whereas the patients in our study were selected by stool examination.

Worm burden

The mean initial worm burden should be taken into account when attempting to explain any discrepancies between the results of different clinical trials on schistosomicides. A schistosome pair produces an average of 400 eggs per day, 50% of which are eliminated in the faeces (*23, 24*). The human faecal mass excreted is about 200 per gram per day, and about 200 eggs per worm pair are discharged in the faeces, thereby giving 1 egg per gram of faeces per worm pair. This estimation is thought to be very accurate (*25*). Moreover, given that only about 40 mg of faeces can be examined at a time by a slide according to Kato's technique, 25 slides would need to be examined for a single egg to be found for in infections with only one worm pair (*26*).

The present experiment shows an average of 93 eggs per gram of faeces (estimated by KK+MB methods), which is typical of infection with a light worm burden (*27*). However, when chemotherapy was used to treat *S. mansoni*, DeVlas & Gryseels (*28*) showed that eggs could not be detected in the faeces of several patients with a light worm burden using Kato's technique, which led to the parasitological cure rates being overestimated. Mott & Cline (*29*) showed that the results of individual stool examinations can vary greatly, whereas the quantitative oogram shows a mean variability coefficient of 32% in relation to viable eggs, which illustrates the stability of *S. mansoni* egg laying (*18*). These considerations strengthen the argument that it is difficult to detect eggs by means of stool examinations when there is a light worm burden.

Table 3. **No. of viable eggs detected by oogram, before and after treatment**

No. of viable eggs per gram of tissue	No. before treatment			No. after treatment		
	Oxamniquine	Praziquantel	Placebo	Oxamniquine	Praziquantel	Placebo
Mean	3486;*2746.4*[a]	3920;*3063.7*	2865;*2298.3*	543; *343.0*	683	3056; *2094.5*
Median	2514	3000	2249	475	683	2127
Range	1667–5375	1594–5230	1176.3–3799	0–567	(1 case)	926–3939
<1000	3 (8.8)[b]	4 (11.1)	7 (19.4)	17 (89.5)	0	8 (25.8)
2001–3000	5 (14.7)	4 (11.1)	6 (16.7)	0	0	4 (12.9)
3001–5000	7 (20.6)	9 (25)	9 (25)	0	0	7 (22.6)
>5000	9 (26.5)	9 (25)	5 (13.9)	0	0	6 (19.3)

[a] Figures in italics are standard error.
[b] Figures in parentheses are percentages.

Table 4. **No. of viable eggs in tissues (quantitative oogram) and percentage of patients testing positive for eggs in stools before treatment**

No. of viable eggs per gram of tissue	% Patients testing positive for eggs in stools	
	KK[a]+MB[b]	HPJ[c]
>5000 (18)[d]	88.9 (16)	94.4 (17)
3001–5000 (16)	87.5 (14)	81.2 (13)
2001–3000 (11)	63.6 (7)	63.6 (7)
1001–2000 (22)	50.0 (11)	59.0 (13)
<1000 (44)	22.7 (10)	34.0 (15)

[a] KK = Method of Kato & Katz (*11*).
[b] MB = Thick-smear technique of Kato, described by Martin & Beaver (*14*).
[c] HPJ = Method of Hoffman, Pons & Janer (*15*).
[d] Figures in parentheses are numbers of patients.

In the present study, 72.2% (by KK+MB methods) and 86.1% (by HPJ) of patients in the placebo group tested positive for eggs in faeces, and all patients presented viable eggs in tissues detected by oogram. At the end of the experiment, all patients from the placebo group presented viable eggs in tissues (Fig. 1), whereas by stool examination 16% were negative for eggs (Table 2). Thus, 16% of the placebo group would be considered to have been "cured" if evaluated by stool examination.

Although oxamniquine was unsuccessful in curing most patients, it greatly reduced the number of viable eggs in rectal mucosa (Table 3). These findings corroborate the above indications that non-cured patients have a light worm burden, and highlight the difficulties in detecting infection by means of stool examinations.

Methods of cure evaluation

There is an evident correlation between viable eggs per gram of tissue and positivity rate detected by stool examinations. For example, when the number of eggs per gram of tissue was higher than 5000, most patients tested positive for eggs in faeces by stool examinations (88.9% for KK+MB and 94.4% for HPJ). When the number of eggs per gram of tissue fell to <1000, the number of patients testing positive for eggs in faeces was markedly reduced (22.7% for KK+MB and 34.0% for HPJ) (Table 4). Similarly, uncured patients who presented with a marked reduction in the number of patients testing positive for eggs also had a small number of eggs in tissues.

Therefore, the discrepancies in the literature on the efficacy of drugs, especially oxamniquine, are based mainly on the number and type of examinations used. Furthermore, the quantitative oogram by rectal biopsy was more accurate than the methods used in stool examinations (KK+MB and HPJ), and this was more evident when the uncured patients with light worm burdens were assessed. So, the quantitative oogram by rectal biopsy is the most sensitive and accurate method for diagnosing parasitological cure in clinical trials of drugs in patients with *S. mansoni*. In terms of therapeutic schedule, praziquantel (daily oral dose of 60 mg/kg for three consecutive days) showed a cure rate markedly superior to that of oxamniquine (20 mg/kg, divided into two daily doses of 10 mg/kg each, by mouth).

Even though not all patients who take oxamniquine (15 mg/kg for adults and 20 mg/kg for children) would be cured in areas endemic for *S. mansoni*, with cure evaluated by the KK method, in Brazil use of oxamniquine has caused a marked reduction in disease morbidity, with a significant reduction in the hepatosplenic forms (*1*). Several authors have already shown the presence of resistant strains to oxamniquine in Brazil (*30–33*), and resistance to oxamniquine has been statistically shown in all isolates from five treated patients who were not cured (*32*). Resistance to drugs is therefore a more serious and complex problem than previously thought.

Future studies

New clinical trials using oxamniquine could be undertaken at higher doses than the ones currently used in Brazil. In Egypt, the total dose of 60 mg/kg (two daily doses of l5 mg/kg for two consecutive days) was well tolerated by the population. From a logistical point of view, it would be desirable to obtain a treatment schedule with a single oral dose administered to populations.

Clinical trials should be undertaken to determine a new treatment schedule with praziquantel in a single oral dose, to be used in prophylactic campaigns, given that the dose of 65 mg/kg used in an established schedule cured only 29.2% of the patients when evaluation was performed by rectal biopsy (*13*).

Further study on the resistance of *S. mansoni* to oxamniquine in endemic areas is also needed. ■

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Conflicts of interest: none declared.

Résumé

Efficacité de l'oxamniquine et du praziquantel dans le traitement des infections à *Schistosoma mansoni*: essai contrôlé

Objectif Evaluer l'efficacité thérapeutique de l'oxamniquine et du praziquantel, les deux antibilharziens les plus importants au plan clinique, et comparer le degré d'exactitude de l'examen coprologique à celui de l'oogramme pour la recherche des infections à *Schistosoma mansoni*.

Méthodes Dans un essai contrôlé randomisé à l'aveugle, 106 patients infectés par *S. mansoni* ont été répartis aléatoirement dans trois groupes statistiquement homogènes. L'un des groupes a reçu 60 mg/kg de praziquantel par jour pendant trois jours consécutifs, le suivant deux doses quotidiennes de 10 mg/kg d'oxamniquine, tandis que le groupe placebo recevait de l'amidon. Le diagnostic initial et le degré de guérison ont été déterminés d'après l'examen coprologique (aux jours 15, 30, 60, 90, 120, 150 et 180 après traitement) et la biopsie de muqueuse rectale pratiquée pour obtenir un oogramme quantitatif (aux jours 30, 60, 120 et 180). Le test du χ^2 et l'analyse de variance (test de Kruskal-Wallis si nécessaire) ont été utilisés pour comparer les variables dans les trois groupes. L'évaluation de l'efficacité des traitements a été faite par l'analyse de survie (méthode de Kaplan-Meier) et la méthode du log-rank.

Résultats L'examen coprologique avait une sensibilité de 88,9 % à 94,4 % quand le nombre d'œufs de *S. mansoni* par gramme de tissu (oogramme) était >5000 ; la sensibilité était diminuée quand le nombre d'œufs tombait en-dessous de 1000 par gramme (22,7-34,0 %). Quand la guérison était appréciée par examen coprologique, l'oxamniquine et le praziquantel avaient des taux de guérison de respectivement 90,3 % et 100 %. En utilisant l'oogramme comme indicateur de la sensibilité, le taux de guérison avec l'oxamniquine s'effondrait à 42,4 %, tandis que le taux de guérison par le praziquantel se maintenait à 96,1 %.

Conclusion Le praziquantel s'est montré significativement plus efficace que l'oxamniquine dans le traitement de l'infection à *S. mansoni*. L'oogramme s'avère bien plus sensible que l'examen coprologique pour la recherche des œufs de *S. mansoni* et il convient de le recommander dans les essais cliniques des antibilharziens.

Resumen

Eficacia de la oxamniquina y el prazicuantel en la infección por *Schistosoma mansoni*: un ensayo controlado

Objetivo Evaluar la eficacia terapéutica de la oxamniquina y el prazicuantel, los dos esquistosomicidas más importantes a nivel clínico, y comparar la precisión del examen coprológico y la precisión del oograma como medios diagnósticos de la infección por *Schistosoma mansoni*.

Métodos En un ensayo controlado y aleatorizado a triple ciego, se procedió a asignar aleatoriamente a 106 pacientes infectados por *S. mansoni* a alguno de los tres grupos estadísticamente homogéneos establecidos: a un grupo se le administraron 60 mg/kg diarios de prazicuantel durante tres días consecutivos, a otro se le dieron dos dosis diarias de 10 mg/kg de oxamniquina, y al tercero, el grupo placebo, se le administró almidón. El diagnóstico inicial y la evaluación del grado de curación se basaron en los exámenes coprológicos (días 15, 30, 60, 90, 120, 150 y 180 después del tratamiento) y la biopsia de la mucosa rectal mediante oograma cuantitativo (días 30, 60, 120 y 180). Para comparar las variables en los tres grupos se utilizaron la prueba del chi-cuadrado y la prueba de Kruskal-Wallis, y la evaluación de la eficacia de los tratamientos se basó en el análisis de la supervivencia (Kaplan–Meier) y la prueba del rango logarítmico.

Resultados La sensibilidad de los exámenes coprológicos fue del 88,9%-94,4% cuando los pacientes acudieron al médico con más de 5000 huevos de *S. mansoni* por gramo de tejido (oograma); en los casos en que el número de huevos caía por debajo de 1000 por gramo, la sensibilidad disminuía (intervalo: 22,7%-34,0%). Cuando la curación se evaluó mediante examen coprológico, la oxamniquina y el prazicuantel lograron tasas de curación de 90,3% y 100%, respectivamente; sin embargo, cuando se utilizó el oograma como indicador de la sensibilidad, la tasa de curación con oxamniquina descendió pronunciadamente (a 42,4%), mientras que la tasa correspondiente al prazicuantel siguió siendo alta, 96,1%.

Conclusión La eficacia del prazicuantel fue significativamente mayor que la de la oxamniquina como tratamiento de la infección por *S. mansoni*. En lo que respecta a la detección de los huevos, el oograma fue mucho más sensible que los exámenes coprológicos, por lo que se recomienda el uso del primero en los ensayos clínicos de esquistosomicidas.

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