

DOUBLE-BLIND THERAPEUTICAL EVALUATION BASED ON THE QUANTITATIVE OOGRAM TECHNIQUE, COMPARING PRAZIQUANTEL AND OXAMNIQUINE IN HUMAN SCHISTOSOMIASIS MANSONI

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S U M M A R Y

A total of 54 adult patients with chronic intestinal or hepato-intestinal schistosomiasis mansoni were included into a double-blind clinical trial to compare praziquantel and oxamniquine. Following a randomized allocation, 27 patients received praziquantel — 65 mg/kg bwt — and 27 oxamniquine — 18 mg/kg bwt — in a single oral dose divided into two intakes. The incidence, severity and duration of side-effects were similar for the two drugs.

The assessment of therapeutical efficacy was based on the quantitative oogram technique via biopsy of the rectal mucosa, performed at the end of 1, 2, 4 and 6 months after treatment. At these same occasions, stool examinations according to Hoffman, Pons & Janer (HPJ) and Kato-Katz (K-K) methods were undertaken to confront their results with the oogram findings. In order to evaluate the immediate effect of the therapy upon the egg laying activity of the parasite, a limited number of patients was submitted to rectal biopsies on the 6th. and 18th. days subsequent to the drug administration.

Both drugs proved to be active anti-schistosomal agents as their coefficients of variation, determined from the oograms made immediately following the treatment, were above 60%. Furthermore, out of 27 patients in each group, 24 treated with praziquantel and 22 with oxamniquine have completed the required six months parasitological follow up period. The respective cure rates in accordance with the oogram, HPJ and K-K findings were: 29.2%, 50% and 91.7% for praziquantel; 22.7%, 50% and 86.3% for oxamniquine. Despite a quite low cure rate, a sharp fall (-83%) in the mean number of living eggs per gram of tissue was observed in the post-treatment oograms.

These results indicated that both anti-schistosomal agents were similarly efficacious

On the other hand, a striking difference in the cure rates amongst the three parasitological control methods became evident. The oogram was the most accurate one, followed by HPJ and lastly by K-K. Since there was a direct correlation between the number of living eggs in the oogram and the positivity of the stool examinations, the percentage of false-negative results has augmented remarkably after treatment reaching 47.3% with HPJ and 92.9% with K-K. Prior to therapy they were 0% and 64.8%, respectively.

The authors infer that the different accuracy of the applied methodology to assess therapeutical efficacy may explain the discrepancy between the cure rate achieved in this clinical trial and those reported by other investigations with either praziquantel or oxamniquine.

KEY WORDS: Human schistosomiasis mansoni — Therapeutical evaluation — Quantitative oogram technique — Praziquantel — Oxamniquine.

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INTRODUCTION

Oxamniquine, a 2-aminomethyl tetrahydroquinoline derivative, was selected by BAXTER and RICHARDS in 1971 as one of the most promising schistosomicidal agents¹.

Several authors, mainly in Brazil, have reported excellent therapeutical results with this drug in mansoni schistosomiasis despite variable cure rates administering similar doses, either to adults or to children, and using the same parasitological evaluation method (stool examination according to Kato-Katz) 4,11,21,27,28,

On the other hand, when we investigated through the quantitative oogram technique the efficacy of oxamniquine in a single dose of 15 to 18 mg/kg bwt in adult patients living away from any focus of this infection, contrariwise to the papers published so far, we found out a quite low (38%) cure rate¹². We concluded that although oxamniquine acts against *Schistosoma mansoni* its activity is only transient. In most of the cases the drug reduced the worm burden but without being able to suppress the persistence of the parasitosis.

Praziquantel, a novel schistosomicidal agent, is a low toxicity isoquinoline-pyrazine compound active against all schistosome species pathogenic to man, namely *S. mansoni*, *S. haematobium* and *S. japonicum* 1,16,17,36. Moreover, in the treatment of experimental as well as human schistosomiasis this drug proved to be highly efficacious 7,8,14,19,22,23,30,31,33.

Double-blind clinical trials comparing praziquantel with oxamniquine in single doses have been carried out as well, revealing no significant difference between their efficacy in accordance with the evaluation by stool examinations following the Kato-Katz method 5,15, 24,25.

On the other hand, in consequence of divergent findings attained by us with oxamniquine in previous therapeutical evaluation based on the quantitative oogram, we decided to undertake a double blind clinical trial using this same technique to compare these two anti-schistosome agents. In addition stool examination according to both, Hoffmann, Pons & Janer and Kato-Katz methods, were performed

to confront the accuracy of these different parasitological methods in the diagnosis and in the assessment of therapeutical efficacy.

PATIENTS AND METHODS

A total of 54 patients, 52% males and 48% females, in between 15 and 55 years of age, weighting from 38 to 86 kg, were forwarded to our outpatient clinical having a previously positive stool examination for *S. mansoni* eggs. They presented the intestinal (54%) or hepato-intestinal (46%) form of chronic schistosomiasis and have not been treated yet with any specific medication. All of them lived in the city of Belo Horizonte, away from contact with any focus of this infection and they were instructed not to return to endemic areas during the six months subsequent to the treatment. Pregnant or nursing women, patients with associated liver, kidney, lung or heart disease, acute or severe chronic illnesses, as well as marked anemia or nutritional deficiencies, were excluded from the trial.

Following the parallel group design, the patients upon entering the trial were allocated into one of two groups which distribution according to age, sex body weight, clinical form of the disease and worm burden (as determined by the quantitative oogram findings) is disclosed in Table I. Both groups had an equal number of cases (27 patients) and were homogeneous regarding these features. One was treated with praziquantel and the other with oxamniquine, in accordance with a double blind administration. The two drugs were dispensed in individually coded bottles and presented in capsules of identical appearance but containing different dosages — praziquantel 325 mg and oxamniquine 90 mg. Therefore, the number of capsules to be taken in relation to each patient's bodyweight was the same for either drug to reach an average dose of 65 mg/kg and 18 mg/kg, respectively. The total medication was administered in a single dose divided into two intakes, four hours apart, always at morning, under the direct supervision of the nurses. The double-blind code was provided prior to the beginning of the study within sealed enve-

T A B L E I

Distribution of 54 schistosomic patients into two treatment groups according to age, sex, body weight, clinical form and worm burden (quantitative oogram)

Treatment group		Praziquantel 27 cases		Oxamniquine 27 cases	
Age	Mean	31.3	ys	25.4	ys
	Median	30	"	25	"
	Range	15 — 55	"	15 — 53	"
Sex	Male	13 cases	(48.1%)	15 cases	(55.6%)
	Female	14 "	(51.9%)	12 "	(44.4%)
Weight	Mean	59.7	kg	57.2	kg
	Median	61	"	57	"
	Range	42 — 79	"	38 — 86	"
Clinical form	Intestinal	17 cases	(63.0%)	12 cases	(44.4%)
	Hepato intestinal	10 "	(37.0%)	15 "	(55.6%)
Number of living eggs	Mean	3156	eggs	3539	eggs
	Median	3001	"	2842	"
	Range	1085 — 6879	"	1525 — 9442	"
> 5000		3 cases	(11.1%)	5 cases	(18.5%)
	3000 — 5000	11 "	(40.7%)	7 "	(25.9%)
	2000 — 3000	8 "	(29.6%)	12 "	(44.4%)
	1000 — 2000	5 "	(18.5%)	3 "	(11.1%)

lopes, for each case, to be opened only at the end of the trial.

Prior to treatment all patients were submitted to rectal mucosa biopsy for performing a quantitative oogram⁶. Except for eight cases in whom the number of living *S. mansoni* eggs per gram of tissue ranged from 1,085 to 1,926, all others had more than 2,000 eggs. The stool examination was repeated according to the spontaneous sedimentation HOFFMAN, PONS & JANER¹⁸ method (HPJ) and the quantitative Kato method modified by KATZ²⁰ (K-K). The former was performed along the established classical procedures and the latter using the Vermifec® kit from Boehringer Mannheim. Three slides were taken of each stool sample and the arithmetical mean of the countings indicated the result of the examination. As demonstrated in Table II, whereas the HPJ was positive in all cases in relation to the oogram results, the K-K was positive only in 35.2% of them.

The control of parasitological cure at the end of 1, 2, 4 and 6 months after the drug administration included quantitative oogram evaluation, as well as stool examinations in conformity to both aforementioned methods. In

T A B L E II

Positive results for *S. mansoni* eggs prior to treatment according to different parasitological methods in each treatment group

Group	Method	Quantitative oogram		Stool examination	
		No.	%	HPJ	K-K
Praziquantel		27	100.0	27	100.0
Oxamniquine		27	100.0	27	100.0
Total		54	100.0	54	100.0

HPJ = Hoffmann, Pons & Janer; K-K = Kato-Katz.

addition, rectal mucosa biopsies were taken on the 6th. and 18th. days following the treatment, in a limited number of patients, that is, 9 patients with the praziquantel and 5 patients with the oxamniquine, to verify the immediate effect of the therapy and its coefficient of variation⁹.

On the day of treatment the patients underwent a thorough physical examination and remained under observation during six to eight hours after the drug intake to look for any adverse drug reaction. Two days afterwards they returned to the outpatient clinic to be investigated concerning the occurrence of late side-effects.

RESULTS

Tolerability — The occurrence of side-effects is displayed in Table III. Their incidence, severity and duration were similar for both drugs. They occurred in 43% of the patients, were mostly (88%) of slight to moderate in-

tensity and did not last longer than four hours in 28% of the cases, than eight hours in 47% and than 24 hours in 98%. Usually (91%), they appeared within the first four hours subsequent to the drug intake and all of them disappeared spontaneously without any medication.

T A B L E III
Occurrence of side effects

Treatment group		Praziquantel *	Oxamniquine		
Single oral dose		65 mg/kg	18 mg/kg		
Number of treated cases		27	27		
Total incidence		37.0%	48.1%		
Intensity	light	33.3%	29.6%		
	moderate	54.2%	59.3%		
	severe	12.5%	11.1%		
Time of appearance	1/2 to 2 hours	45.8%	53.8%		
	2 to 4 hours	45.8%	38.5%		
	4 to 6 hours	8.3%	7.7%		
	up to 4 hours	36.4%	20.8%		
	up to 8 hours	18.2%	20.8%		
Duration	up to 24 hours	40.9%	58.3%		
	longer than 1 day	4.5%	—		
Complaints		No.	%	No.	%
Dizziness		5	18.5	8	29.6
Drowsiness		2	7.4	6	22.2
Heart-burn		5	18.5	3	11.1
General malaise		6	22.2	2	7.4
Nausea		4	14.8	2	7.4
Abdominal pain		—	—	2	7.4
Headache		1	3.7	—	—
Generalized urticaria		—	—	1	3.7
Sialorrhea		1	3.7	—	—

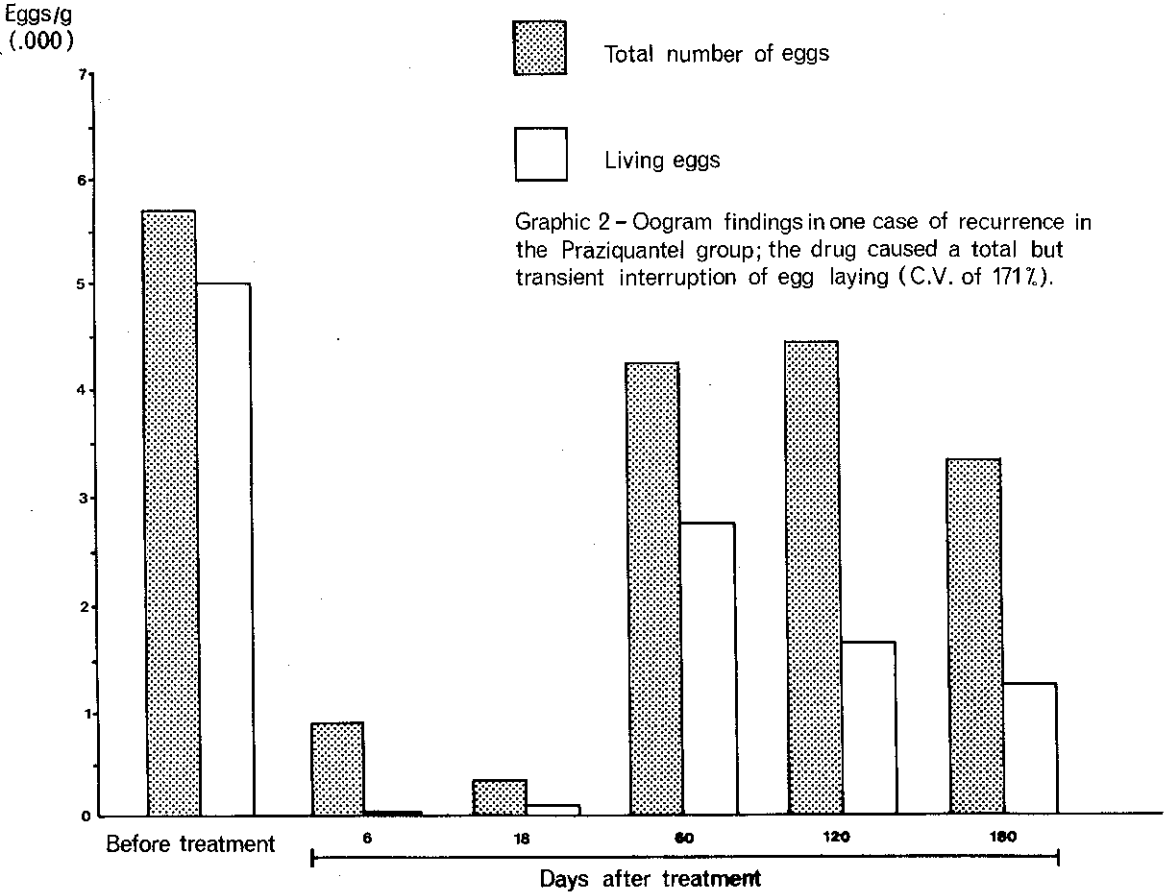
* One case of Loeffler Syndrome was seen on the 5th. day after treatment.

The main complaints were dizziness (24%), drowsiness (15%), heartburn (15%), general malaise (15%) and nausea (11%). The first two had a tendency to be more frequently observed under oxamniquine and the last two under praziquantel. On the fifth day after taking this drug one patient developed eosinophilic pneumonitis, Loeffler Syndrome, diagnosed by X-Ray and laboratorial examinations.

Efficacy — In order to investigate the immediate effect of the two drugs on the egg laying capacity of *S. mansoni*, quantitative oograms were performed on the 6th. and 18th. days after therapy in nine patients treated with

praziquantel and in five with oxamniquine. The method's coefficient of variation (CV) was then calculated. It ranged from 103 to 171% with the former drug and from 99 to 164% with the latter one, as shown in Table IV. The Graphics 1 2 and 3 illustrate three examples from the praziquantel group and Graphics 4, 5 and 6, three from the oxamniquine group. They also indicate the outcome of the treatment, recurrence or cure, at the end of the six month follow up.

In the assessment of the therapeutical efficacy it is noteworthy that the results in regard to the three parasitological control methods



were not concordant. As observed in Table V, in 24 patients who have completed the six month follow up out 27 treated with praziquantel the cure rates were: 29.2% (7/24) according to the oogram; 50.0% (12/24) to the HPJ and 91.7% (22/24) to the K-K. In the 22 controlled

patients out of 27 treated with oxamniquine these rates were 22.7% (5/22), 50.0% (11/22) and 86.3% (19/22), respectively.

On the other hand, the mean number of living eggs per gram of tissue taken by biopsy

T A B L E V
Assessment of therapeutical efficacy according to different parasitological control method

Treatment group	Praziquantel			Oxamniquine		
	Quantitative oogram	Stool examination		Quantitative oogram	Stool examination	
Single oral dose		65 mg/kg			18 mg/kg	
Treated cases		27			27	
Controlled cases		24			22	
Control methods		HPJ	K-K		HPJ	K-K
Cured cases	7	12	22	5	11	19
Cure rate (%)	29.2	50.0	91.7	22.7	50.0	86.3
Recurrences	17	12	2	17	11	3
Recurrence rate (%)	70.8	50.0	8.3	77.3	50.0	13.7

HPJ = Hoffman, Pons & Janer; K-K = Kato-Katz

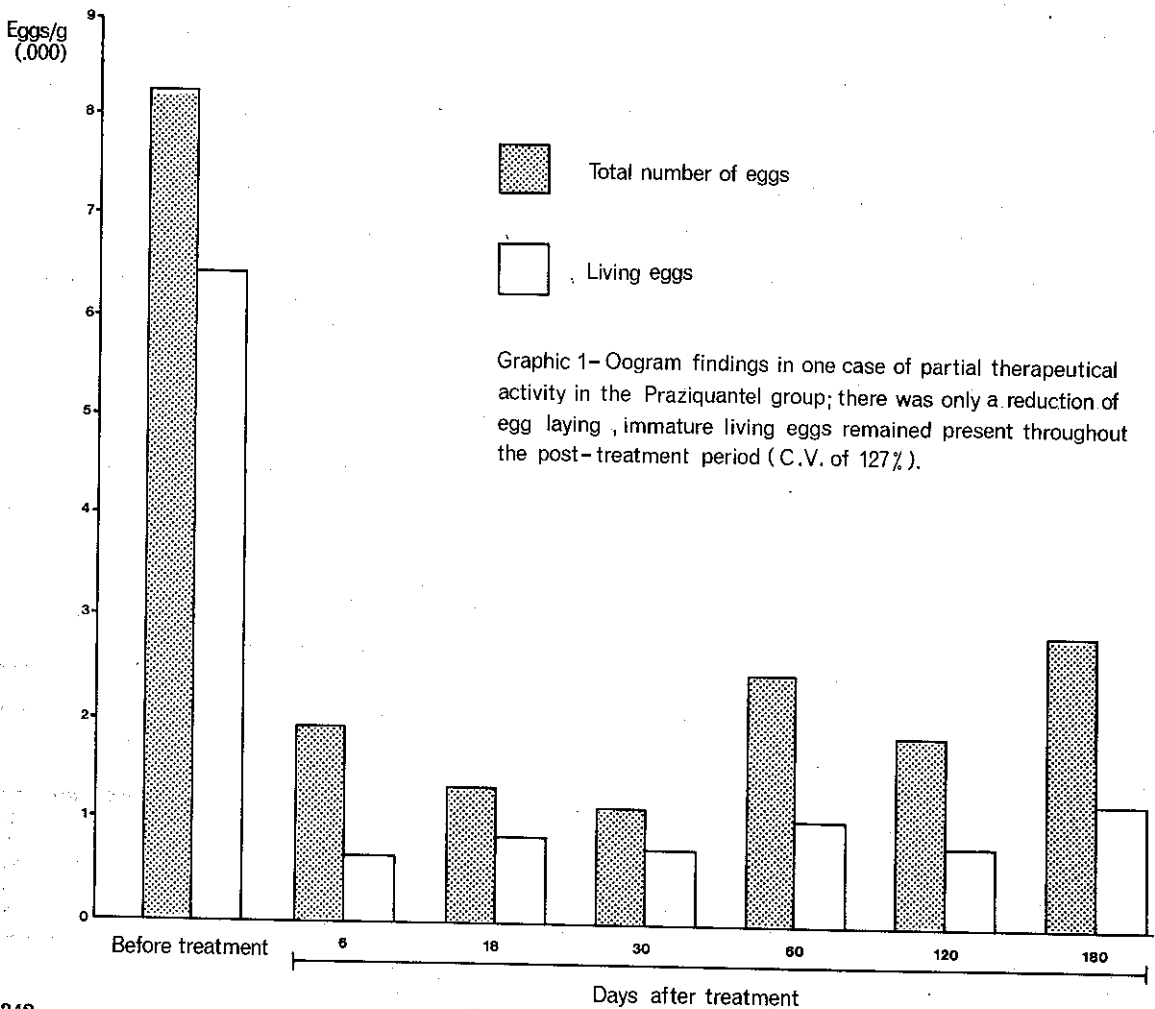
T A B L E I V
Number of living *S. mansoni* eggs found in the quantitative oogram before and soon after treatment

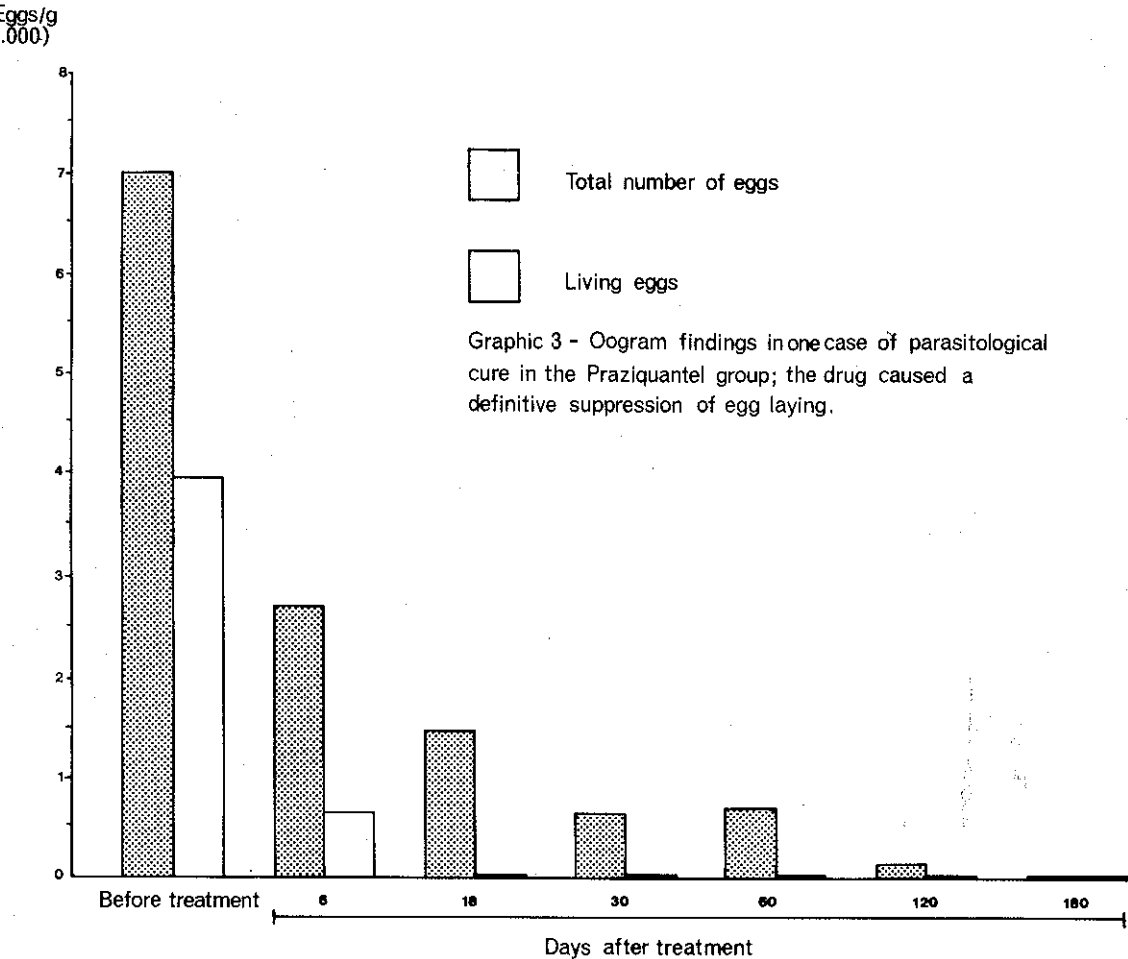
Treatment group	Before treatment	Number of living eggs After treatment		S	Statistical analysis	
		6th. day	18th. day			C.V. (%)
Praziquantel (9 patients)	6,450	578 *	800 *	3,327		127
	4,999	0	29	2,877		171
	3,906	604	0	2,102		140
	3,902	714 **	417 **	1,932		115
	3,600	1,239 **	208 **	1,730		103
	2,977	364	0	1,623		146
	2,589	617	0	1,352		126
	2,028	463	0	1,062		128
	1,823	229	0	990		145
Oxamniquine (5 patients)	9,442	54	272 *	5,358		164
	6,350	200	0	2,945		134
	5,526	572	0	3,040		156
	3,027	208	0	1,690		156
	1,525	426	0	642		99

S = Standard deviaton; C. V. = Coefficient of variation

* Immature eggs also present

** Mature eggs only





of the rectal mucosa prior to treatment in the two groups, 3,348, has decreased to 571 following the drug administration, meaning a reduction of 83% in the worm burden, as indicated in Table VI (54 cases before the treatment and 112 cases with living eggs in the oograms after the treatment).

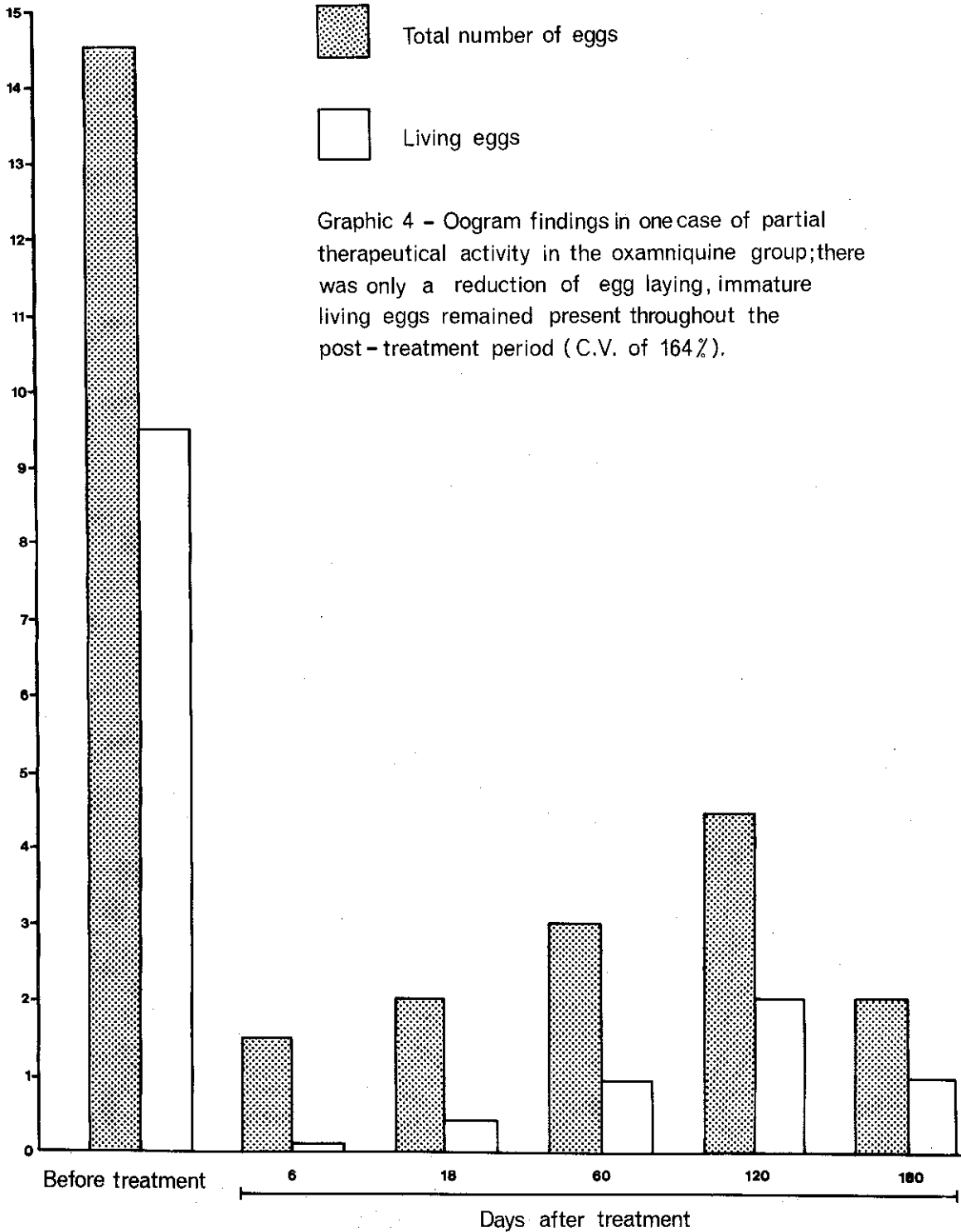
Furthermore, the relationship between the number of living *S. mansoni* eggs found in the quantitative oograms and the positivity of the correspondent stool examinations, before as well as after treatment with either praziquantel or oxamniquine, was established. It became evident, as displayed in Table VII, that there is a direct correlation between both techniques; the greater the number of living eggs per gram of tissue taken by biopsy of the rectal mucosa, the higher the percentage of positive findings in the stool examination. However,

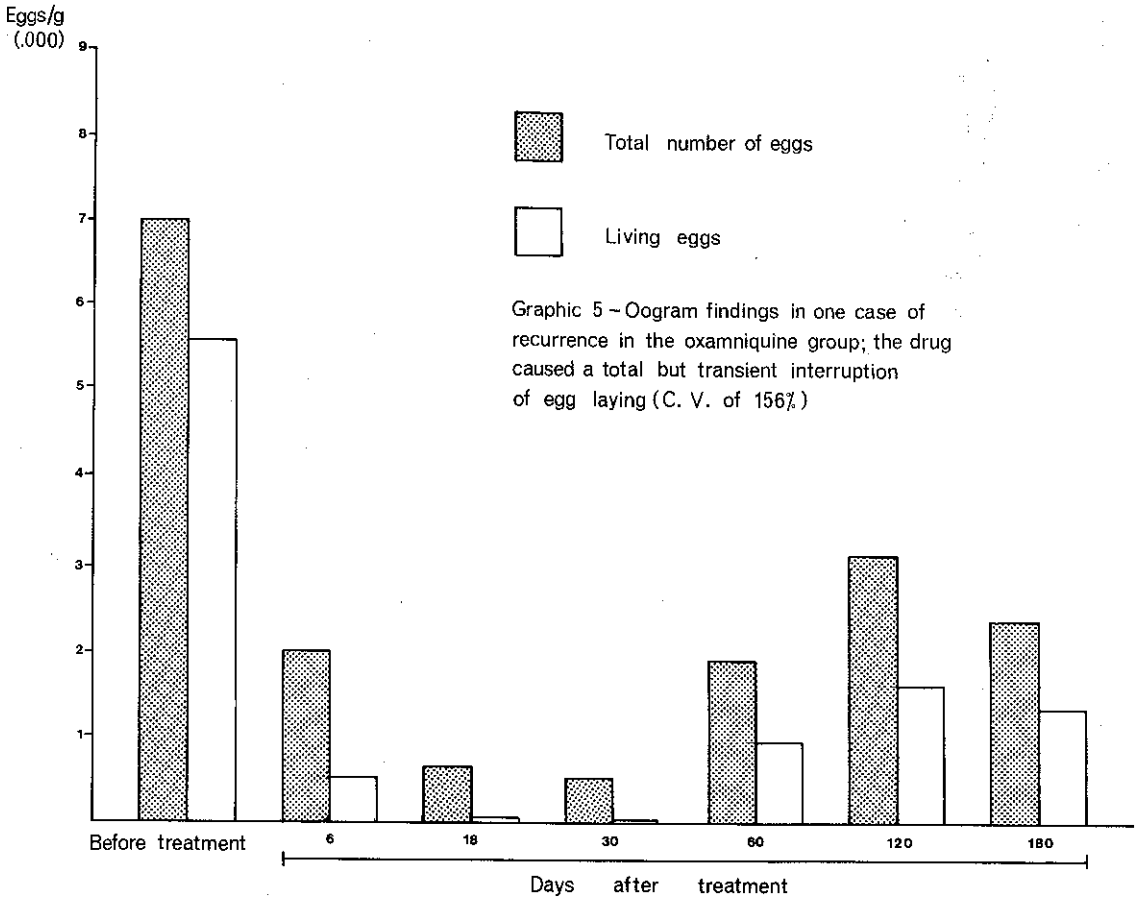
TABLE VI
Comparison between the number of living EGGS in the oogram, before and after treatment with both praziquantel and oxamniquine

Number of living eggs	Before treatment	After treatment
Mean	3348 eggs	571 (-83%) eggs
Median	2972 "	1033 "
Range	1085 — 9442 "	29 — 2736 "
> 4000	11 cases	—
2000 — 4000	35 "	4 cases
1000 — 2000	8 "	58 "
< 1000	—	50 "
Total	54 cases	112 "

the K-K method showed a lower sensitivity than the HPJ method. When the number of eggs in the oogram was above 2,000 the HPJ was positive in 100% of the cases but the K-K

Eggs/g
(.000)





in 25.6%, between 1,000 and 2,000 the HPJ was positive in 66.7% and the K-K in 9.1% below 1,000 the HPJ was positive in 38% and the K-K only in 6%.

T A B L E V I I
Correlation between the number of living EGGS in the oogram and the positivity of two stool examination methods, before and after treatment with either praziquantel or oxamniquine

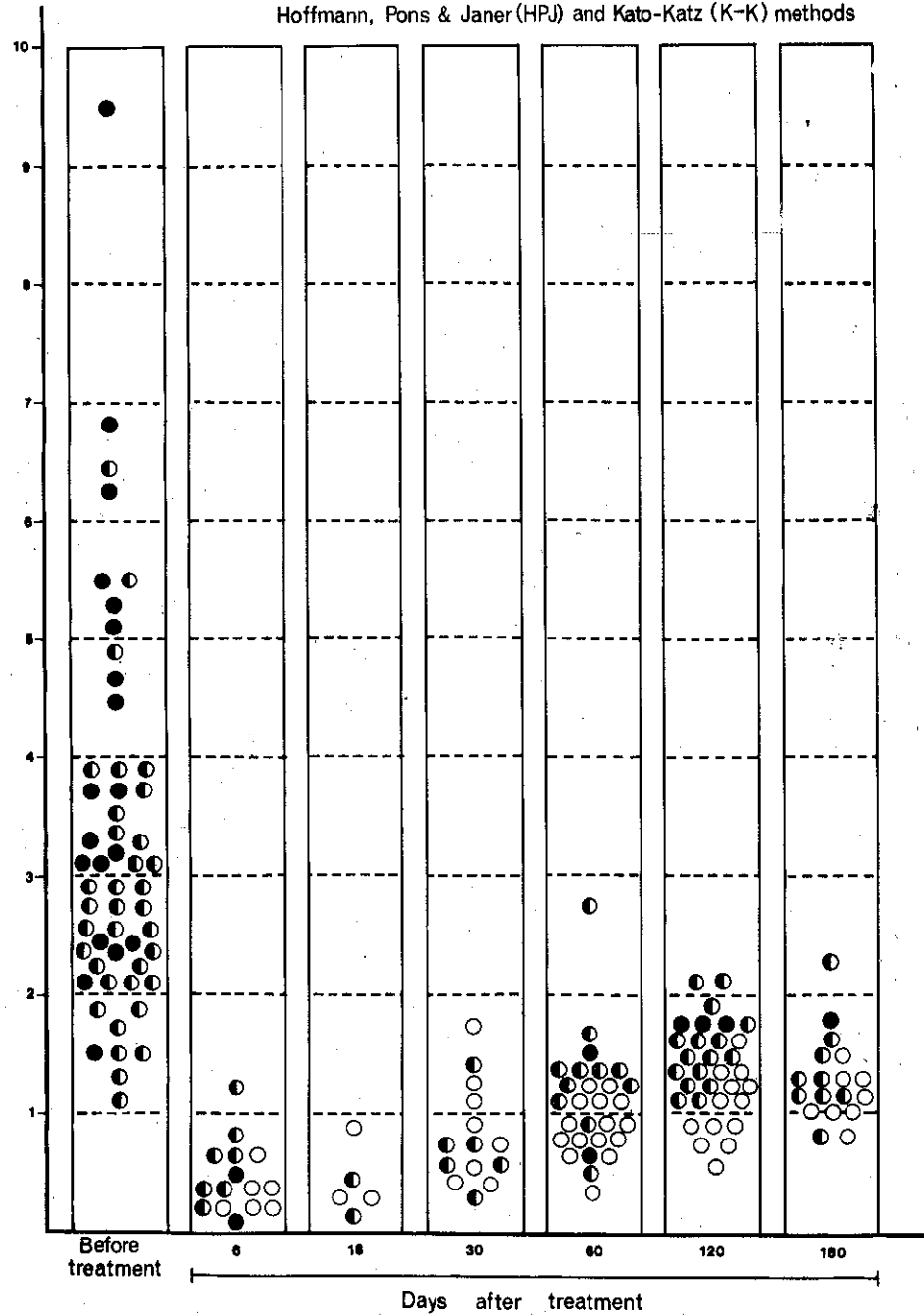
Number of living eggs	Quantitative oogram		Positive stool examinations					
	Examinations		HPJ		K-K			
	No.	%	No.	%	No.	%	No.	%
> 4000	11	100.0	11	100.0	8	72.7		
2000 - 4000	39	100.0	39	100.0	10	25.6		
1000 - 2000	66	100.0	44	66.7	6	9.1		
< 1000	50	100.0	19	38.0	3	6.0		
Before treatment	54	100.0	54	100.0	19	35.2		
After treatment	112	100.0	59	52.7	8	7.1		
Total	166	100.0	113	68.1	27	16.3		

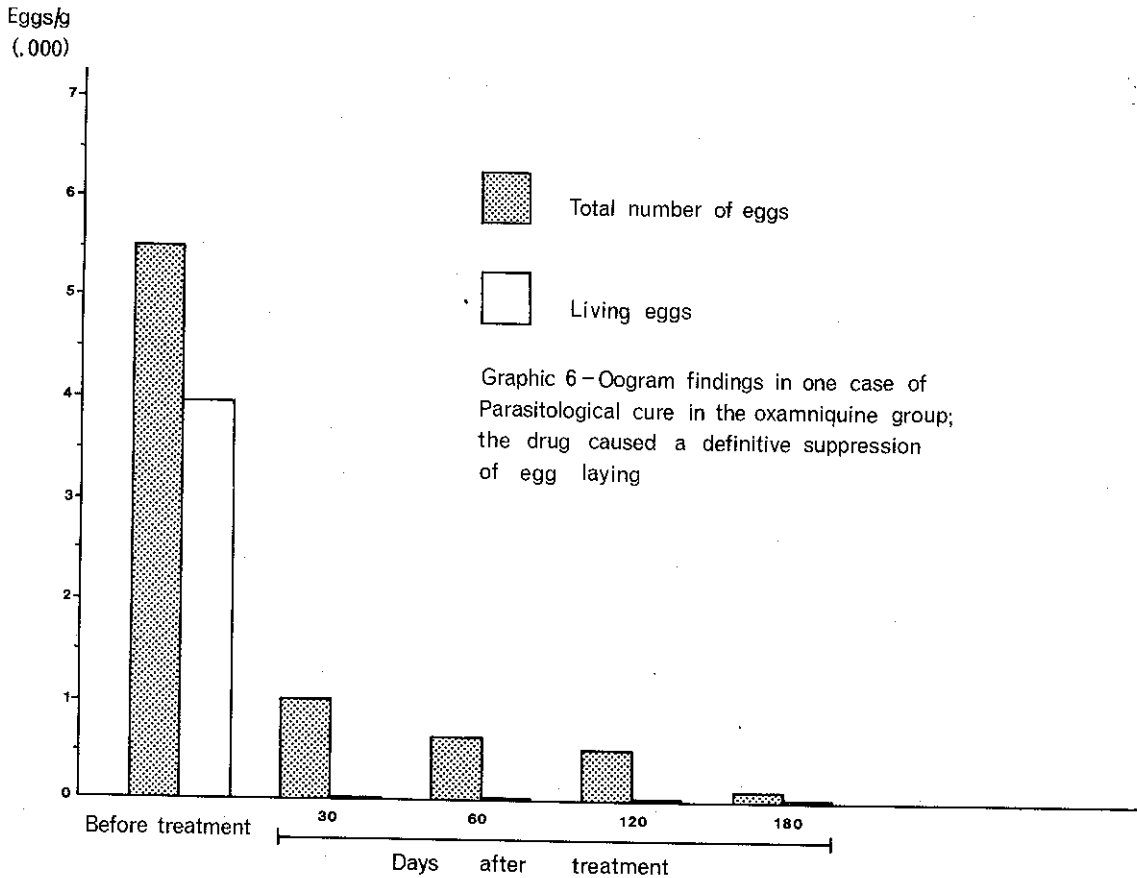
HPJ = Hoffman, Pons & Janer; K-K = Kato-Katz

Such correlation is also illustrated by Figure A for both treatment groups. It demonstrates that the reduction in the number of living eggs in the oogram consequent to the

treatment leads to a diminished positivity of the stool examinations. Again, the K-K is associated with a higher degree of false negative results 92.9% than the HPJ method 47.3%.

Figure A - Correlation between the number of living eggs in the oogram and the positivity of stool examinations by the Hoffmann, Pons & Janer (HPJ) and Kato-Katz (K-K) methods





DISCUSSION

From our point-of-view the therapeutical evaluation of new drugs for treating human schistosomiasis mansoni should be accomplished through the quantitative oogram via rectal mucosa biopsies due to the trustworthiness of this method^{6,9,10}.

The therapeutic effects of schistosomicides have an initial phase (shift of worms from mesenteric veins to the liver) and a second phase (ensheathment, degeneration and phagocytosis in the liver) which depends upon the time the worms are in the liver. If the worms are not killed, remigration to the mesenteric veins will occur. Since there is normally a continuity in the process of egg-laying by females, the first result of an active drug is to cause interruption of oviposition with consequent alterations in the oogram. Because no drug acts on the eggs themselves they continue their development in

the tissue up to maturation and elimination in the stools. After some time no immature egg is observed. If the effect of the drug is of short duration or temporary—just sufficient to produce a major shift of the worms from mesenteric veins to the liver—but does not kill the worms, remigration to the mesenteric veins occurs and the oogram will show reestablishment of oviposition some time later, with reappearance of viable eggs, giving a picture of clinical relapse. If this does not occur and the effect is definitive, there is cure. Indeed, if the suppression lasts longer than six months a parasitological cure is achieved.

When the drug does not act on the worms — i.e., when it is inactive — no alteration of the distribution of the worms in the portal system is produced and the oogram will not change; this is treatment failure.

Finally, some drugs are partially active. During treatment some worms which did not

shift to the liver may remain in the intestinal venules and maintain oviposition, which of course, will be reduced. There is a significant reduction, both immature and mature living eggs but not their disappearance in the oograms subsequent to the treatment.

In case of either a partially or a transient active drug, modifications within the chemical structure of the substance could be made in order to obtain a definitive active anti-schistosome agent.

Under this standpoint and taking into account the results of our clinical trial, both drugs have proved to be partial or transient active substances against *S. mansoni* infection, although in the few cured cases their action has been a definitive one. Actually, we already had demonstrated this fact in regard to oxamniquine^{11,12,27}. The current findings showing a C.V. greater than 60% (from 99 to 164%) have confirmed it once again. Praziquantel was a potent agent being able to interrupt egg laying in practically all patients with a C.V. ranging from 103 to 171%. Solely in one case there was an incomplete egg laying suppression, immature living eggs being found until the 18th. day after the drug intake, in spite of a C.V. of 127% (Table IV). Considering the results of previous experimental studies involving praziquantel^{3,26}, we believe that it would be feasible to render it a definitive acting schistosomicidal agent in almost all cases if its administration is prolonged beyond a single day treatment using this same daily dose. To confirm such assumption would mean an important objective, particularly in view of this drug being active against *S. mansoni* strains resistant to oxamniquine¹³.

At the end of the six month follow up the cure rates according to the oogram findings were 29% with praziquantel and 23% with oxamniquine, that is, a recurrence rate of 71% and 77%, respectively. It should be emphasized that although these cure rates were quite low, there was a marked decrease (83%) in the mean number of living eggs in the non-cured cases, leaving no doubt about an obvious reduction of the parasitic load induced by the treatment with either drug. Hence, the efficacy of the two agents was similar, in agreement

with reports from other investigators^{5,15,24,25}. However, the recurrences observed after oxamniquine occurred invariably between the first and second months whilst it took a little longer, between the second and third months, after praziquantel. Since all patients did not come into contact with any focus of this infection during the parasitological control period, one can dismiss the possibility of reinfections.

The oograms in the cured patients showed absence of living eggs and reduction or sometimes disappearance of dead ones. Firstly the recently dead, then the calcified eggs and later the granulomas disappeared. In the non-cured case, dead eggs — recently and calcified ones as well as granulomas — were always present besides the living eggs.

On the other hand, in accordance with stool examinations the cure rates were: 50% for both drugs using the HPJ method; 92% with praziquantel and 86% with oxamniquine using the K-K method. Therefore, a clear difference in the percentage of cure was observed amongst the three methods. The oogram proved to be the most accurate one, followed by HPJ and lastly by K-K.

Prior to therapy, the oogram and the HPJ were positive in 100% of the cases but the K-K only in 35%. Since the positivity of the stool examinations correlates directly with the number of living eggs in the oogram, the accuracy of both HPJ and K-K has diminished markedly following the sharp fall of these eggs caused by treatment. For 112 (110%) positive oograms subsequent to therapy, the HPJ was positive in only 53% of the cases and the K-K in no more than 7%. Due to this rather high frequency of false-negative results (93,0%) observed with K K, a question is raised on the validity of using this method in clinical trials to establish the efficacy of new drugs.

Confronting our results, according to the oogram findings, with those from other investigations based on stool examinations, a remarkable difference in the therapeutical efficacy becomes evident. Such discrepancy in cure rates already has been pointed out in our previous study involving oxamniquine¹². Concerning praziquantel, several authors have re-

ported relatively high cure rates: 84.4% with 2 x 25 mg/kg in hepatosplenic cases⁸; 92.0% with 1 x 50 mg/kg and 97.0% with 3 x 20 mg/kg²²; 93.3% in acute cases and 87.5% in chronic ones with 2 x 25 mg/kg²⁵; 94.4% with 1 x 40 mg/kg in hepatosplenic cases³³. If we also would rely solely on the figures from the K-K method the cure rate achieved in our study, 91.7%, is similar to these. Consequently, we may infer that the divergence between our therapeutical results, either with praziquantel or oxamniquine, and those referred by other investigators, stem from the different accuracy of the applied methodology for assessing parasitological cure.

In our opinion, the quantitative oogram is the most reliable technique for the evaluation of new schistosomicidal agents in man and a methodological uniformity regarding the parasitological control of cure should be reached to avoid divergent interpretations about therapeutical efficacy of drugs.

RESUMO

Avaliação terapêutica duplo-cega baseada na técnica do oograma quantitativo, comparando praziquantel com oxamniquine na Esquistossomose mansônica humana.

Um total de 54 pacientes adultos, com esquistossomose mansônica crônica, nas formas intestinal ou hepatointestinal, participou de um ensaio clínico duplo-cego, para comparar o praziquantel com a oxamniquine. De acordo com uma distribuição aleatória, 27 casos receberam o praziquantel (65 mg/kg de peso corporal) e 27 a oxamniquine (18 mg/kg), administrados em dose oral única.

A incidência, intensidade e duração dos efeitos colaterais foram similares para os dois medicamentos. A avaliação da eficácia terapêutica baseou-se na técnica do oograma quantitativo por biópsia da mucosa retal, realizada ao final de um, dois, quatro e seis meses depois do tratamento. Nessas mesmas ocasiões foram feitos exames de fezes pelos métodos de HOFFMAN, PONS e JANER e de KATO-KATZ, com a finalidade de confrontar seus resultados com os achados do oograma. Para

averiguar o efeito imediato do tratamento sobre a atividade ovipositora do parasito, um número restrito de pacientes foi submetido a biópsias retais no 6.º e 18.º dias subsequentes à administração da medicação.

Ambas as drogas provaram ser ativas contra o esquistossoma, vez que os respectivos coeficientes de variação, determinados a partir de oogramas efetuados imediatamente após o tratamento, foram superiores a 60%. Ademais, dentre os 27 pacientes de cada grupo, 24 tratados com praziquantel e 22 com oxamniquine completaram o período de seis meses, requerido para controle parasitológico.

Os índices de cura, segundo os achados do oograma e dos exames de fezes pelos métodos de HPJ e K-K, foram, respectivamente, 29%, 50% e 92% com o praziquantel; 23%, 50% e 86% com a oxamniquine. Apesar do baixo percentual de cura, observou-se nos oogramas pós tratamento, uma pronunciada queda no número de ovos vivos por grama de tecido.

Esses resultados revelam que ambas as drogas foram semelhantemente eficazes, embora já se tenha comprovado que a susceptibilidade do *S. mansoni* não seja sempre igual para cada um desses medicamentos, pois linhagens resistentes à oxamniquine evidenciaram ser 100% sensíveis ao praziquantel.

Por outro lado, constatou-se uma nítida diferença nos percentuais de cura em função do método utilizado para controle parasitológico. O oograma foi o mais preciso, seguido pelo HPJ e, finalmente, pelo K-K. Tendo ocorrido uma correlação direta entre o número de ovos vivos no oograma e a positividade dos exames de fezes, a percentagem de resultados falso-negativos aumentou acentuadamente após o tratamento, alcançando 47,3% com o HPJ e 92,9% com o K-K. Antes da medicação esses índices eram, respectivamente, 0% e 64,8%.

Os autores depreendem que a diferença de precisão da metodologia aplicada para avaliar a eficácia terapêutica pode explicar a divergência encontrada entre o índice de cura obtido neste ensaio clínico e os relatados por outros investigadores, tanto com o praziquantel quanto com a oxamniquine.

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