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ARTIGOS

RATE OF REVERSION OF HEPATOSPLENIC SCHISTOSOMIASIS AFTER SPECIFIC THERAPY

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Seventy patients with hepatosplenic schistosomiasis were treated with oxamniquine. The patients lived in an endemic area and were evaluated 6, 18 and 24 months after treatment, during which time transmission in the area was interrupted. After treatment, clinical improvement occurred in 49 (70%) of the patients, as seen by reduction in visceromegaly and reversion of liver nodules. Reversion of hepatosplenic disease occurred in 28 (40%) patients and in liver nodularity in 26 (47.3%) patients after 24 months. Reversion of hepatosplenic disease was seen in 12 (21%) patients and liver nodules disappeared in 4 (8.5%) as early as 6 months after treatment. In general, hepatosplenomegaly reverses earlier than liver nodularity. It is notable that reversion of hepatosplenic disease occurred in many individuals with a history of previous treatment and also in some with advanced age. In four cases this clinical form of the disease had existed for 20 years.

Therefore, there must exist factors other than age and duration of the condition which determine the reversibility of this clinical form. Our results reinforce the concept that, in patients with hepatosplenic disease without esophageal hemorrhages, specific treatment should preceed surgical intervention even in those with a history of previous treatment. At least 18 months should be allowed for the effects of treatment to be manifest.

Key words: Schistosomiasis. Treatment. Oxamniquine. Reversion of hepatosplenic disease.

After 1922 mass treatment of schistosomiasis in Egypt gave the first indications that the prevalence of serious forms of the disease could be reduced as a consequence of specific therapy [1 9]. The same observation was made by Sette [10], after treating patients in Catende, Pernambuco (Brazil). Caio Benjamin Dias[4], in addition to mentioning the benefits of treatment in the prevention of hepatosplenic forms of the disease, suggested the possibility of reversion of these forms "when not yet formed of irreversible lesions." Rodrigues da Silva [11] emphasized the benefits that could result from treatment in the prevention of severe forms of schistosomiasis. Kloetzel [7] demonstrated that the number of eggs in feces diminished after treatment, in spite of reinfections and that treatment would prevent the occurrence of clinically severe forms. Bina [2] confirmed that treatment could prevent hepatosplenic disease. Bina and Prata [3] demonstrated the disappearance of hepatosplenic disease in some patients when this had lasted for less than six years.

The object of this study was to ascertain the effect of specific therapy on the reversion of hepatosplenic schistosomiasis and to determine the rate at which reversion proceeds.

MATERIALS AND METHODS

This study was conducted in Caatinga do Moura, Bahia, Brazil, an area hyperendemic for schistosomiasis, where a project for control of the disease was initiated in 1982. Seventy patients were classified as having hepatosplenic schistosomiasis according to the criteria of having the left lobe of the liver enlarged, usually prominent, hardened and/or nodular, and a spleen palpable in the absence of inspiration [13]. Those patients which, after treatment, did not meet at least one of these criteria were considered to have had a reversal of

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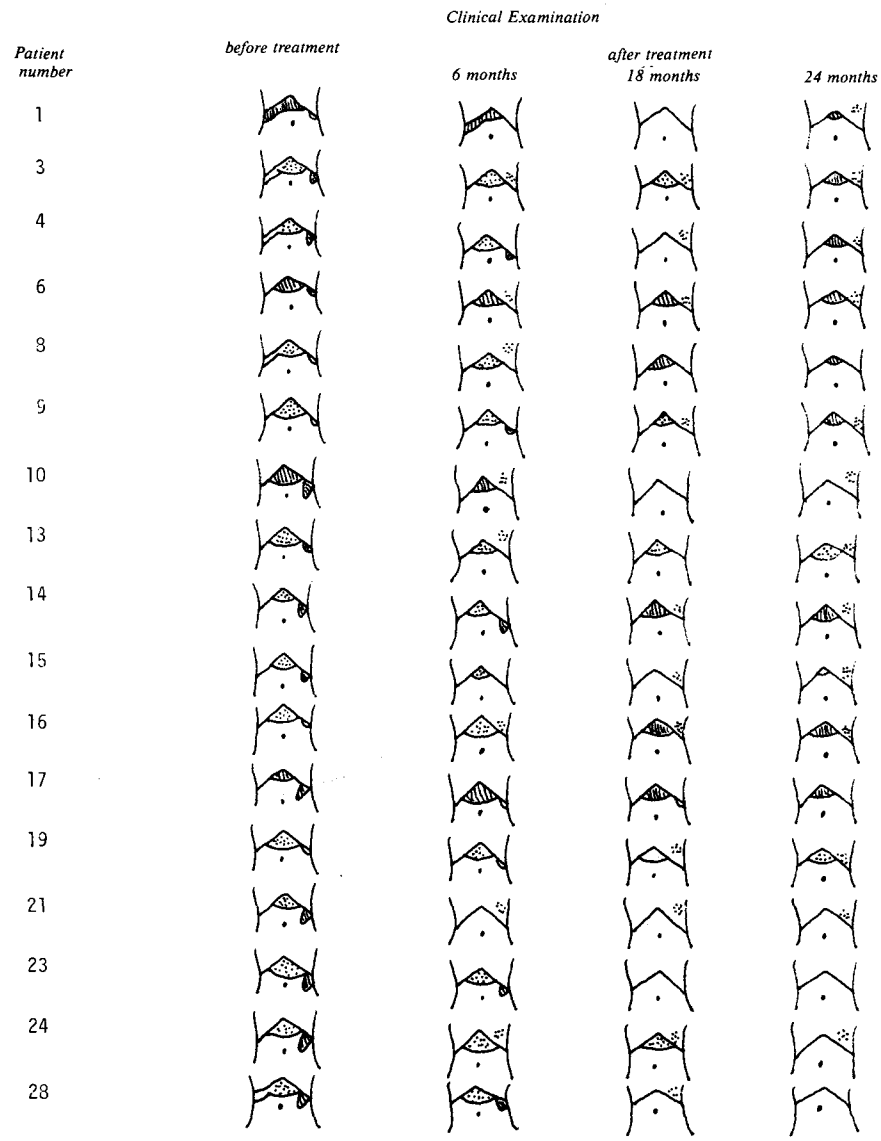
Table 1 – *Rate of reversion of nodules of the liver and the hepatosplenic form of schistosomiasis mansoni after treatment in patients on whom all the clinical examinations were performed.*

After Treatment Months	*Clinical Examination Reversion*	
	Nodular liver	*Hepatosplenic Disease*
6	2(5%)	10(22.2%)
18	6(15%)	6(13.3%)
24	15(37.5%)	1(4.2%)
Total of Patients	40	45

Figure 1 – *Rate of reversion of hepatosplenic disease after treatment in seventeen patients on whom were performed all clinical examination.*



the hepatosplenic disease. Nodular liver was present in 55(78,6%) patients. Only one patient admitted to having had hematemesis.

Ages varied from 9 to 74 years, with a mean of 36.6 and a median of 37 years. Fifty (71.4%) were females and 20(28.6%) were males. Forty (57.1%) had never had specific treatment for schistosomiasis and 30(42.9%) admitted to at least one previous treatment. All were passing eggs of *Schistosoma mansoni* as detected by the Kato-Katz method [6].

Patients were given a single oral dose of oxamniquine in capsule form using 15mg/kg for adults and 20mg/kg for children of up to 30 kilograms body weight. The medicine was taken in our presence.

The patients were treated in January, 1983, and evaluated clinically, always by the same observer, before and 6, 18 and 24 months after treatment. Because they could not be found at the time of follow-up, 13 of the patients did not receive the second examination, 11 the third and 11 the fourth. All, however, received at least one clinical examination after treatment. Our index of clinical improvement relative to condition at initial examination was a reduction greater than 2 cm of splenomegaly or of the left hepatic lobe and a reversion of the nodular liver. Progression in the opposite sense was considered as worsening of the condition.

After treatment two fecal examinations were made, at 6 and 18 months, to determine cure. The patients remained in the endemic area.

RESULTS

After treatment with oxamniquine, negative stool examinations were encountered at six months and at 18 months in 61 patients (87.2%).

The possibility of reinfection was small as a result of the use of molluscicide in the area (Bayluscide). This measure, in addition to drastically reducing the snail population, also reduced to zero the presence of infections in snails and in sentinel mice used to evaluate disease transmission during the time of the study [5].

Six months after treatment, clinical examination of 57 patients revealed that the size of the left lobe of the liver had diminished in 24(42.1%) patients, remained unchanged in 28(49.1%) and increased in 5(8.8%). The mean reduction in liver size was 3.0 cm. Of the patients evaluated at that time, 47(82.5%) had nodular livers before treatment. Of these, 4(8.5%) became smooth after six months. The size of the spleen remained unchanged in 24(42.1%) patients, increased in 5(8.8%) and reduced in 28(49.1%), with a mean reduction of 4.0 cm. Reversion of hepatosplenic schistosomiasis occurred in 12(21%) patients during this period.

In the clinical evaluation of 59 patients 18 months after treatment, the left hepatic lobe was reduced in 32(54.2%) patients, remained unchanged in 20(34%) and grew in 7(11.8%). The mean reduction was 4.3 cm. Of the patients examined at this time, 48(81.4%) had nodular livers before treatment. Of these, 11(22.9%) became smooth to palpation. The size of the spleen remained unchanged in 18(30.5%) of the patients, increased in 3(5%) and was reduced in 38(64.4%), with a mean reduction of 4.4 cm. Reversion of hepatosplenic disease occurred in 23(39%) patients.

The final clinical examination of 59 patients 24 months after treatment demonstrated that the left hepatic lobe diminished in 28(47.5%) of patients, remained unchanged in 25(42.4%) and increased in size in 6(10.2%) patients. The mean reduction in size was 5.7 cm. Of the 59 patients examined, 48(81.3%) had nodular livers at initial palpation. Of these, 25(52.1%) became smooth. The size of the spleen remained unchanged in 25(42.4%) of patients increased in 4(6.8%) and was reduced in size in 30(50.8%), with a mean reduction of 4.9 cm. Reversion of hepatosplenic disease occurred in 22(37.3%) patients.

Cumulatively, we had reversion of hepatosplenic disease in 28(40%) patients and of nodular livers in 26(47.3%). Two patients were sent to government hospitals for splenectomy after examination at 18 months. One of these, (aged 61 years) was done because of hematemesis and the other, (15 years of age) because of anemia related to hypersplenism. Considering both hepatosplenomegaly and the liver surface in the 70 patients, it can be concluded that specific treatment of schistosomiasis improved the condition of 49(70%) patients. The condition of 6(8.6%) patients worsened, and the condition of 15(21.4%) was not changed.

In 45 patients that completed all of the examinations, it was possible to study the rate of reversion. Reversion of hepatosplenic disease was found in 10 (22.2%) patients after 6 months, in 6 (13.3%) after 18 months and in 1 (4.2%) after 24 months (Table 1). In the same periods, reversion of nodular liver occurred respectively in 2(5%), 6(15%) and 15(37.5%) patients (Table 1). The regression of spleen occurs earlier than that of the liver nodules (Fig. 1).

Of the 28 patients with reversion of hepatosplenic disease 13 were over 30 years old (Table 2). Their ages varied from 9 to 74 years with a mean of 32.5. Among them were 8(28.6%) who gave a history of previous treatment 19(67.8%) who had never been treated and 1(3.6%) who could not remember. Of the 26 patients with a liver which was no longer nodular, 12(46.2%)

gave a history of specific treatment and 14(53.8%) had no such history.

DISCUSSION

The reversion of the hepatosplenic form of schistosomiasis can occur soon after specific treatment. In the present study we found that this had occurred in 21% of those treated within six months. Favourable results can occur later as indicated by our examinations after 18 and 24 months. The percentage of improved patients and of reversion in hepatosplenic disease after specific treatment is similar to that observed by Bina and Prata.[3] The same occurred in relation to nodular livers. The nodules tended to disappear later than splenomegaly. We believe that the interruption of transmission by snail control did not influence our results since Bina and Prata[3] obtained a similar percent of reversion of hepatosplenic disease than we did in a study in which transmission was not interrupted.

It is interesting to note that reversion of hepatosplenic disease also occurred in older individuals. In endemic areas the infection is initiated early in life, and hepatosplenic disease is often established before the age of 20.[12] Four of our patients already had hepatosplenic disease in 1964.

Table 2 – *Data on 28 patients with oxamniquine induced reversion of hepatosplenic disease due to schistosomiasis mansoni*

Patient Nº	*Age (Yrs.)*	*Extension of Left Hepatic Lobe (ACM)*				*Extension of Spleen (ACM)*			
		Before	*After*			*Before*	*After*		
			6 mo	*18 mo*	*24 mo*		*6 mo*	*18 mo*	*24 mo*
01	09	7	5	EDB	ACM	ACM	IMP	IMP	DDB
02	10	9		4		2		IMP	
03	11	8	8	8	7	4	EDB	EDB	EDB
04	12	6	6	EDB	5	4	3	EDB	EDB
05	12	8	7	4		6	6	EDB	EDB
06	12	7	8	6	6	ACM	EDB	EDB	EDB
07	13	9		6	IMP	5		DDB	IMP
08	13	8	8	7	ACM	ACM	DDB	IMP	IMP
09	14	9	8	6	6	ACM	ACM	EDB	EDB
10	19	11	8	IMP	EDB	6	DDB	IMP	DDB
11	22	9	7			ACM	EDB		
12	24	10	9		8	5	EDB		EDB
13	29	11	7	8	11	ACM	DDB	IMP	EDB
14	29	6	7	8	9	6	5	EDB	DDB
15	36	6	3	EDB	ACM	3	IMP	EDB	EDB
16	37	10	12	11	11	ACM	EDB	EDB	EDB
17	42	4	10	8	6	4	REB	ACM	IMP
18	42	ACM		EDB		9		EDB	
19	43	9	8	6	6	ACM	ACM	DDB	EDB
20	45	11	8		ACM	ACM	DDB		IMP
21	46	6	DDB	DDB	EDB	5	DDB	DDB	EDB
22	53	9	8			4	EDB		
23	54	17	10	IMP	IMP	6	5	IMP	IMP
24	54	6	9	6	IMP	10	DDB	DDB	DDB
25	60	11		6		ACM		DDB	
26	62	13		8	7	ACM		EDB	EDB
27	64	9		6	8	6		EDB	EDB
28	74	12	9	IMP	IMP	9	4	EDB	IMP

ACM = At costal margin
IMP = Impalpable
EDB = Easily palpable on deep breathing
DDB = Palpation difficult on deep breathing.

Thus, treatment is not only beneficial to patients with recently established hepatosplenic disease, as was previously thought.[3] Therefore, factors independent of the duration of the condition exist which regulate the reversibility of this clinical form of schistosomiasis. It would be important to determine if there exists differences in the type of hepatic fibrosis in those cases which do and do not regress following specific therapy.

The fact that many patients improved, including 8(28.6%) patients with hepatosplenic disease who had previous treatment, shows that another treatment may be beneficial. We do not know if they had hepatosplenic disease at the time of their previous treatment and if such treatment failed to prevent or cure this clinical form.

These observations indicate that it is inappropriate to attribute only to surgery the improvements seen in hepatosplenic patients presenting without hemorrhages in the digestive system who received both surgical treatment and specific therapy for schistosomiasis. It is evident that, at least among those schistosomiasis patients without a history of bleeding, specific therapy should be prescribed even in those with history of previous treatment. Patients should be followed for at least 18 months before surgical intervention is contemplated.

RESUMO

Foram tratados com oxamniquine 70 esquistossomóticos, com a forma hepatosplênica. Os pacientes permaneceram na área endêmica e foram avaliados clinicamente antes, 6, 18, e 24 meses após o tratamento. Durante este período a transmissão foi interrompida na área. Após o tratamento específico ocorreu melhora clínica em 49(70%) pacientes, traduzida por diminuição nas visceromegalias e reversão do fígado nodular. Houve reversão da forma hepatosplênica em 28(40%) e do fígado nodular em 26(47.3%) após 24 meses. A reversão da forma hepatosplênica já havia ocorrido após seis meses em 12(21%) pacientes e a do fígado nodular em 4(8.5%). Em geral a regressão da hepatosplenomegalia ocorre mais precocemente do que a do fígado nodular. Ela foi observada em alguns pacientes com história de tratamento específico anterior. Interessante assinalar que a reversão da forma hepatosplênica ocorreu também em indivíduos com idade avançada e que em quatro deles esta forma clínica já estava instalada há pelo menos 20 anos. Portanto devem existir outros fatores regulando a reversibilidade desta forma clínica, independentemente do seu tempo de evolução. Nossos resultados reforçam o conceito de que nos pacientes com hipertensão porta esquistossomótica que não tiveram hemorragias digestivas, o tratamento específico deve preceder qualquer indicação cirúrgica em pelo menos 18 meses, mesmo em doentes que referem já tê-lo feito antes.

Palavras Chaves: Esquistossomose. Tratamento. Oxamniquine. Reversão da forma hepatosplênica.

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