

ULTRASONOGRAPHIC ASSESSMENT OF THE REGRESSION
OF BLADDER AND RENAL LESIONS DUE TO *SCHISTOSOMA*
HAEMATOBIMUM AFTER TREATMENT WITH PRAZIQUANTEL

by

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Summary — The effect of praziquantel on urinary tract lesions due to *Schistosoma haematobium* was assessed by ultrasound in an endemic village in Niger. Ten months after treatment with praziquantel, bladder and renal lesions among the 149 patients were assessed. The parasitological cure rate was 87%.

Ultrasonography proved to be an excellent tool to assess pathological changes. It is reliable, quickly performed, well accepted by the community and permits the definition of a «regression-rate» of the pathological lesions. Ten months after treatment, the «regression-rate» of bladder lesions was 68% and of renal lesions was 73%.

The presence of bladder lesions had a negative influence on the regression of renal lesions. Nearly all renal lesions, without bladder lesions, regressed within the ten months period of observation.

This study permitted the identification of a group of persons whose bladder lesions did not regress and who were possibly more vulnerable to the development of bladder cancer, thus requiring long-term follow-up.

KEYWORDS: *Schistosoma haematobium*; Ultrasonography; Praziquantel; Pathology; Niger.

Introduction

The efficiency of antischistosomal drugs in urinary schistosomiasis has often been demonstrated by the egg count regression, and the study of urologic lesions regression confirmed by heavy and invasive complementary examinations (intravenous pyelography (2, 14, 18, 21), cystoscopy⁽²⁵⁾, or radio-isotope renography (1, 24)).

Ultrasonography, a simple, reliable technique, easily replicated, appropriate for use in the field, has been recently introduced in community-based surveys (3, 4, 7, 8, 9, 10, 16).

The objective of this study was to assess the changes in bladder and renal lesions due to *Schistosoma haematobium* through the use of ultrasonography in two endemic villages 10 months after treatment with praziquantel.

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1. Study population and methods

1.1. Study population

The study was performed in two villages, Seberi and Saga near Niamey in a rice irrigation area. The preliminary parasitological and ultrasound data were previously reported (16). The present study included 149 subjects (91 from Seberi, 58 from Saga) with positive egg output who were treated in August 1985 with a single dose (40 mg/kg) of praziquantel.

In addition to the parasitological and ultrasound examination prior to treatment, follow-up parasitological examinations were repeated at seven and ten months and ultrasound examination was repeated ten months after treatment.

Forty-two persons with positive egg output at the first control, seven months after the initial treatment, were retreated with praziquantel (40 mg/kg).

1.2. Methods

A quantitative parasitological urine filtration technique was used (26). Urine was collected between 9 AM and 1 PM.

Ultrasound examinations were performed with a 3.5 MHz realtime sectorial scanner (ADR 4000) in a health center near the villages of the study. All examinations were conducted by the same radiologist (F. L) who was unaware of the parasitological status of the patients. The types and classification of bladder lesions encountered during the initial ultrasound examination and the images found in the follow-up examination are consistent and are defined as follows:

Three types of bladder lesions were observed (16): thickened wall, regular with thickness > 6 mm; irregular wall showing a pattern of thick and thin areas; and localized hypertrophy (single or multiple) showing a «large based» polypoid image in the bladder.

The lesions were classified into 3 stages according to their severity:

- stage 0, absence of bladder lesion,
- stage 1, minor lesions with a wall thickness between 6-10 mm and/or moderate irregularity and/or a single localized hypertrophy,
- stage 2, major lesions with a thickness > 11 mm and/or marked irregularity and/or two or more localized hypertrophies.

Bladder calcifications and their evolutions were not considered as they appear to remain elements of radiological examination.

For the renal lesions three stages of hydronephrosis were used according to the Weill *et al.* classification (29):

- absence of hydronephrosis (stage 0),
- mild hydronephrosis, characterized by a slight pyelocalyceal dilatation (stage I),
- moderate hydronephrosis, with marked pyelocalyceal dilatation corresponding to conventional urographic pictures (stage II),

— major hydronephrosis, with lack of functional parenchyma (stage III) (not observed in this study).

Significance of difference was tested with χ^2 test and Wilcoxon ω test.

2. Results

2.1. Parasitology

Results of the first control done seven months after treatment show parasitologic cure in 100 patients (67%). The reduction of ova output was 97%. Parasitologic cure rate was 87% for patients with ova output < 100 per 10 ml of urine and 41% for those with ova output > 100 per 10 ml. The difference between both groups is significant ($\chi^2 = 34$, $p < 10^{-8}$).

Three months after the second treatment, just before ultrasonography control, parasitologic cure was obtained in 130 patients (87%). The reduction of ova output increased to 98.5%.

2.2. Ultrasonography

2.2.1. Bladder lesions

Regression observed

Of the 149 cases treated, 119 had bladder lesions prior to treatment, of which 58 were stage 2 and 61 stage 1 (table 1).

TABLE 1
Evolution of bladder lesions after treatment according to their initial stage

Before	After	Stage 0	Stage 1	Stage 2
Stage 0	(n) (%)	20 67%	9 30%	1 3%
Stage 1	(n) (%)	41 67%	17 28%	3 5%
Stage 2	(n) (%)	40 69%	15 26%	3 5%

n : number of patients

The difference in lesions before and after treatment is highly significant, whether considering the lesions as a whole ($\chi^2 = 67.2$, $p < 10^{-12}$) or the stage 2 lesions alone ($\chi^2 = 51.2$, $p < 10^{-10}$).

Regression of bladder lesions is defined as stage 2 and stage 1 lesions reverting to stage 0 after treatment. Under these conditions a regression rate of 68% was found in our study.

The cure rates are: 65.2% for irregularities of the bladder wall (45/69), 63% for the thickness of the bladder wall (29/46), 50% for localized

hypertrophies (34/68). The cure rate for each of these three types of lesions is not statistically different (irregularity vs localized hypertrophy, $\chi^2 = 3.6$ $p < 0.1$; thickening vs localized hypertrophy, $\chi^2 = 1.91$, $p < 0.2$; irregularity vs thickening, $\chi^2 = 0.056$, $p < 0.9$).

Regression in relation to age, sex, urinary egg count, bladder lesion stage and type of initial lesion.

The rate of regression was similar in all age groups (table 3) as well as among women (34/44, 77.3%) and men (47/75, 62.7%), $\chi^2 = 2.6$ $p < 0.2$.

The importance of initial urinary egg count has no influence on regression of bladder lesions, whether considered as a whole (Wilcoxon test: $p = 0.53$) or separately by stage 1 and 2 (Wilcoxon test: $p = 0.26$ and $p = 0.16$).

The regression rates of each stage of bladder lesion were similar (Table 1). The distribution of the different initial lesion types (thickening, irregularity, localized hypertrophy) in the patients with no regression was almost identical to that of the patients with regression and to that of the entire population undergoing ultrasound examination, regardless of the extent and the size of lesions encountered.

TABLE 2
Evolution of renal lesions after treatment in relation to their stage

Before	After	Stage 0	Stage 1	Stage 2
Stage 0	(n)	70	6	0
	(%)	92%	8%	—
Stage 1	(n)	43	11	7
	(%)	77%	19,5%	3,5%
Stage 2	(n)	10	5	2
	(%)	59%	29,5%	11,5%

n : number of patients

Bladder wall measuring between 6 and 10 mm (defined as «thickness 1») which persists after treatment may be considered as a sequela.

Evolution of stage 0 cases

Thirty cases of stage 0 were treated and examined by ultrasound: nine evolved into stage 1 and one into stage 2.

This evolution is independant of age, sex, and egg count (Wilcoxon test: $p < 0.80$). Seven times out of nine, the lesion 1 type reveals a thickness between 6 and 10 mm.

2.2.2. Renal lesions

Regression observed

Among the 149 patients treated, 73 had renal lesions prior to treatment: 17 stage II and 56 stage I. Ten months after treatment only 4 cases of stage II and 22 cases of stage I persisted. There is a significant difference when both stages are considered together ($\chi^2 = 34.5$, $p < 10^{-8}$) or in stage II lesions alone ($\chi^2 = 8.6$, $p < 0.01$).

As for bladder lesions, «renal regression» is defined as stages II and I reverting to stage 0 after treatment. Thus, in this study, the regression rate obtained is 73% (53 regressions out of 73 initial cases of hydronephrosis).

Regression in relation to age, sex, initial urinary egg count, stage of hydronephrosis and initial bladder lesions

Regression of renal lesions after treatment is most important among children between 5 and 9 (Table 3).

TABLE 3
Regression of bladder lesions and hydronephrosis after treatment with praziquantel according to age

	5/9 years	10/14 years	> 15 years	Total
Bladder lesions	n = 39	n = 58	n = 22	n = 119
Regression	27 (69%)	40 (69%)	14 (64%)	81 (68%)
No regression	12 (31%)	18 (31%)	8 (36%)	38 (32%)
Hydronephrosis	n = 23	n = 41	n = 9	n = 73
Regression	22 (95,5%)	25 (61%)	6 (66,5%)	53 (73%)
No Regression	1 (4,5%)	16 (39%)	3 (33,5%)	20 (27%)

We notice that the older the patients, the less lesions regress (Wilcoxon test: $p < 0.001$).

No significant difference in regression of renal lesions between men (33/50) and women (20/23) was observed ($\chi^2 = 3.46$, $p < 0,1$).

The more important the initial urinary egg count, the less regression is observed (Wilcoxon test: $p < 0.04$ for lesions stage I).

Regression of stage I (43/56) is slightly better than regression of stage II (10/17) but with no statistical significance ($\chi^2 = 2.02$ $p < 0.2$).

Among twenty patients with stage I and II hydronephrosis that did not regress after treatment we observed, before therapy, in 15 of them (75%), the presence of major bladder lesions, associated with a preponderance of major irregularities.

Evolution of stage 0 cases

Among 6 patients out of 76 stages 0 becoming stage I, we notice significant higher egg outputs (Wilcoxon test: $p < 0.001$) with no relation to age or sex.

3. Discussion

The efficacy of the treatment on egg count depended on whether the initial urinary egg count was less or greater than 100 eggs/10 ml. As observed by others authors (15, 17, 22), with praziquantel the total reduction in egg count, was very important.

This study confirms the findings of other studies using intravenous urography (1, 19, 20, 21, 23, 27), and 2 recent studies using ultrasonography (9, 11), showing the regression of bladder lesions after antischistosomal treatment.

The 87% parasitological cure rate of praziquantel, was higher than the 68% rate of regression of bladder lesions. Several hypotheses can be considered to explain this difference:

a) In spite of the treatment, the thickening of the wall (between 6 and 10 mm) may be due to a persistent inflammatory mucosa.

b) The images of thickening and irregularity of the mucosa, although very suggestive of schistosomiasis in endemic area, can be observed in other bladder pathologies, especially in bladder infections, often associated to schistosomiasis and that can persist after the treatment of the disease.

Doehring suggested this hypothesis for 3 out of 4 patients presenting a thickening of the bladder wall after treatment (9).

c) Despite the treatment whose efficiency is proved by the parasitological examination, some patients present evolutive bladder lesions which do not decrease. They could be considered as a risk-group for bladder cancer and should ideally be regularly examined (cystoscopy and anatomopathology).

d) Other treated patients go from stage 0 to stage 1 or 2. This could be due to the difficulty in using and reading ultrasonography.

Although it is possible, albeit rare in light of the results, to obtain false negatives, it is nearly impossible to obtain false positives.

Ultrasonography also proved to be an interesting tool for the follow-up on renal lesions. A 73% regression rate was observed in our study. This rate appears low in comparison to the one found in another ultrasonography study (9), in which only one person presented persistent dilatation after treatment. This is probably due, according to the author, to the young age of the patient studied.

Renal lesions and their regressions after treatment depend on several factors:

1) The more important the initial egg count, especially among children aged between 5 and 9, the more severe the renal lesions, and the less numerous the regressions.

2) It depends also on age, as other authors already noticed (12, 20, 25). We notice a much better cure among children between 5 and 9 compared to older patients. This could be due to the appearance among adolescents and adults of fibrosis in the lower ureter or in the intravesical portion of the ureter (5, 6, 12, 13, 19, 20), generating an evolving stenosis and/or an aperistalsis (23, 28) which could produce a serious renal insufficiency.

3) The type of underlying bladder lesion seems important in our study, major irregularities of bladder mucosa generate less effective regressions of renal lesions after treatment.

The relationship between bladder and renal lesions due to schistosomiasis is still under discussion (4, 10, 18, 23).

Ultrasonography is therefore an excellent means of detection of morbidity due to schistosomiasis. It is also an uncomparable tool of follow-up of the treatment.

In order to restrict false negatives with this technique it is necessary that a well experienced echographer repeats the examinations himself operating on full bladders.

It appears important, regarding our results, to treat bilharziasis as soon as possible in order to act with efficiency on renal lesions that affect the patient's vital prognosis.

In the future, ultrasonography could be introduced as a mean of diagnosis and of supervision within the framework of a national bilharziasis control program.

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Evaluation échographique de la régression des lésions vésicales et rénales dues à *Schistosoma haematobium* après traitement par le praziquantel.

Résumé — Cette étude, réalisée au Niger dans une communauté où la bilharziose sévit à l'état endémique, a permis d'observer en échographie, 10 mois après traitement par le praziquantel, l'état des lésions vésicales et rénales chez les 149 patients.

L'échographie s'est avérée un excellent moyen de surveillance thérapeutique, fiable, rapide, bien accepté des populations, permettant de définir un indice de régression des lésions. Cet indice est de 68% au niveau vésical et de 73% au niveau rénal, 10 mois après traitement.

La présence de lésions vésicales a une influence négative sur la régression des lésions rénales. Presque toutes les lésions rénales, sans présence de lésions vésicales, ont régressé au cours des 10 mois d'observation.

Cette étude a permis de dégager un groupe de patients dont les lésions vésicales n'ont pas régressé, et qui pourrait constituer un groupe à risque pour l'apparition de cancer de la vessie, ce qui nécessiterait un suivi à long terme.

Echografische evaluatie van de regressie van de blaas- en nierletsels veroorzaakt door *Schistosoma haematobium* na behandeling met praziquantel.

Samenvatting — Het effect van praziquantel op de letsels van de urinewegen veroorzaakt door *Schistosoma haematobium* werd met echografie in een endemisch dorp in Niger nagegaan. Bij de 149 patiënten werden tien maanden na toediening van praziquantel de blaas- en nierletsels geobserveerd. Parasitologische genezing werd vastgesteld bij 87% van de patiënten.

Echografie bleek een uitstekende manier te zijn om pathologische veranderingen te meten. Het is betrouwbaar, snel uitgevoerd, goed ontvangen door de bevolking en laat een definitie toe van de graad van regressie van pathologische letsels. Tien maanden na behandeling bedroeg deze regressiegraad bij blaasletsels 68% en bij nierletsels 73%.

De aanwezigheid van blaasletsels had een negatieve invloed op de regressie van de nierletsels. Haast alle nierletsels, zonder blaasaantasting, kenden een regressie binnen de tien maanden durende periode van de observatie.

Deze studie liet de identificatie toe van een groep personen wiens blaasletsels niet regresseerden en die mogelijk meer vatbaar zijn voor de ontwikkeling van blaaskanker en dus een langdurige follow-up vereisen.

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