

# Effects of single-dose praziquantel on morbidity and mortality resulting from intestinal schistosomiasis

M.M. Kheir,<sup>1</sup> O.Z. Baraka,<sup>1</sup> I.A. El-Tom,<sup>2</sup> M.M. Mukhtar<sup>3</sup> and M.M.A. Homieda<sup>4</sup>

تأثير الجرعة الوحيدة من البرازيكنواتيل على مراضة البلهرسيات المعوية ووفياتها  
موسى محمد خير وعمر زايد بركة وعصام عبد الله التوم ومعاوية محمد مختار ومأمون محمد علي حميدة

خلاصة: في العامين 1987 و1994 أُجري مسحان لدراسة التأثير الطويل الأجل للجرعة الوحيدة من البرازيكنواتيل على مراضة البلهرسيات المعوية ووفياتها في وسط السودان. لقد انخفض معدل انتشار العدوى من 53% إلى 34%، كما انخفضت كثافة المعوى (≥ 400 بيضة في كل غرام من البراز) من 31% إلى 18%. وانخفضت حالات ضخامة الكبد وضخامة الكبد والطحال، وإن كانت ضخامة الطحال وحده لم تتغير. وانخفض انتشار التليف حول البائي من 14% إلى 10%. وقد أظهر التنظير الداخلي للمرضى ذوي التليف انخفاضاً في دوالي المريء من 47% إلى 30%. وكان معدل الوفاة بسبب نزف دوالي المريء مرتفعاً (حتى 11 من كل مئة مريض مصاب بالعدوى والنزف على صعيد المجتمع كله). إن المعالجة الجموعية بالبرازيكنواتيل يمكن أن توزع على فترة زمنية أطول، وهكذا تقل تكاليف العلاج وإتاحته وتوزيعه.

**ABSTRACT** The long-term effect of single-dose praziquantel on morbidity and mortality from *Schistosoma mansoni* was investigated in surveys in 1987 and 1994 in central Sudan. Prevalence of infection dropped from 53% to 34%, and intensity of infection (≥ 400 eggs/g of faeces) from 31% to 18%. There was a reduction in hepatomegaly and hepatosplenomegaly, although splenomegaly alone was unchanged. Prevalence of periportal fibrosis decreased from 14% to 10%. Endoscopic investigation of patients with fibrosis showed a reduction in oesophageal varices from 47% to 30%. Mortality due to bleeding varices was high (community-wide, up to 11/100 infected patients with bleeding). Thus praziquantel mass treatment can be spaced to a much longer period, reducing the expense of treatment, delivery and distribution.

## Effets d'une dose unique de praziquantel sur la morbidité et la mortalité imputables à la schistosomiase intestinale

**RESUME** Les effets à long terme d'une dose unique de praziquantel sur la morbidité et la mortalité dues à *Schistosoma mansoni* ont fait l'objet d'investigations durant des enquêtes en 1987 et 1994 dans la région centrale du Soudan. La prévalence de l'infection chutait de 53% à 34%, et l'intensité de l'infection (≥ 400 œufs/g de matières fécales) de 31% à 18%. Il y a eu une réduction de l'hépatomégalie et de l'hépatosplénomégalie, bien que la splénomégalie seule fût inchangée. La prévalence de la fibrose périportale a diminué, passant de 14% à 10%. L'investigation endoscopique des patients ayant une fibrose a montré une réduction des varices œsophagiennes, passant de 47% à 30%. La mortalité due aux hémorragies des varices était élevée (dans toute la communauté, jusqu'à 11 sur 100 de patients infectés ayant des hémorragies). Le traitement de masse par praziquantel peut donc être espacé pour une période beaucoup plus longue, réduisant les frais de traitement, de fourniture et de distribution.

<sup>1</sup>Faculty of Medicine; <sup>2</sup>Institute of Endemic Diseases, University of Khartoum, Khartoum, Sudan.

<sup>3</sup>Department of Pathology, University of Alabama, Birmingham, Alabama, United States of America.

<sup>4</sup>Academy of Medical Sciences, Khartoum, Sudan.

Received: 09/12/99; accepted: 01/06/00

## Introduction

Schistosomiasis affects 200 million people worldwide, 20 million of whom have advanced disease. Despite its magnitude, little is known about the pattern of schistosomiasis mortality in endemic areas [1]. While there are many clinical manifestations of the disease, the morbidity and mortality caused by *Schistosoma mansoni* infection is usually secondary to Symmers periportal fibrosis of the liver, and subsequent portal hypertension and oesophageal varices [2,3]. In Sudan, schistosomiasis is endemic, especially in areas where gravity irrigation schemes have a major socioeconomic impact. Available control measures include health education, mollusciciding and mass treatment with praziquantel. The primary objective of any schistosomiasis control programme is to reduce and prevent disease morbidity through these measures [1].

Assessment of the impact of mass treatment with praziquantel is usually by determining the prevalence of infection and presence of periportal fibrosis. Most of the studies on the long-term effects of praziquantel have been performed on animals, with very few studies on humans. A study in Sudan found that praziquantel treatment could lead to a reduction in egg excretion and reversibility of sonographically proven early periportal fibrosis 7 months after treatment [4]. In another study, both annual and biennial treatment with praziquantel also led to a reduction in periportal fibrosis [5]. In Brazil, mass chemotherapy has also been reported to reduce mortality, from 0.67 to 0.47 pcr 100 000 in some areas [1]. However, no study has collectively used the four parameters of evaluation—parasitological, clinical, sonographic and endoscopic.

In 1987, in a village endemic with schistosomiasis in the Gezira area of Sudan, a

survey involving combined parasitological, clinical, sonographic and endoscopic examination was conducted. Following the survey, the whole population received mass treatment with single-dose praziquantel. No mass treatment was again offered to the villagers until 1994. The opportunity was thus available to assess the long-term impact of this single-dose mass chemotherapy with praziquantel, administered 7 years previously, on disease prevalence, intensity of infection, and the presence of periportal fibrosis and oesophageal varices.

## Materials and methods

### Study area

The study was conducted in the village of Abu Jin in central Sudan, 150 km south of Khartoum. The area is known to be endemic for both *S. mansoni* and *S. haematobium* (prevalence 70% and 15% respectively) [6–10]. Following mass chemotherapy, health education and monthly mollusciciding by the Blue Nile Health Project, which operated in parts of the endemic area, the prevalence of *S. mansoni* infection dropped to less than 10% [6]. The Blue Nile Health Project had not covered the village at the time of our first survey in 1987.

The Medical Research Board, Faculty of Medicine, University of Khartoum approved the study. The study plan and objectives were explained to the villagers and informed consents obtained

### Surveys

Two surveys were carried out in 1987 and 1994. Baseline data were gathered and parasitological examination carried out for all village inhabitants. In both surveys, the prevalence and intensity of *S. mansoni* infection were determined by stool examination using the Kato–Katz method. Villagers whose stools had an egg load of  $\geq 400$

eggs/g faeces were considered heavily infected. Approximately 20% of the village population were randomly selected for clinical examination and ultrasonography. Clinical histories were recorded, including symptoms of intestinal and urinary schistosomiasis, jaundice and haematemesis, past history of haematuria and schistosomiasis, and history of schistosomal therapy. Villagers were examined for palpation of the liver and spleen, and the presence or absence of ascites. Abdominal ultrasound examination was conducted for evidence and grading of periportal fibrosis. Upper gastrointestinal endoscopy was carried out on 32 villagers with different grades of periportal fibrosis to detect and grade oesophageal varices. All villagers who were parasite-positive received medically supervised treatment of praziquantel (dosage 40 mg/kg body weight). The exclusion criteria for treatment were noted. The same groups were re-examined in 1994. Data obtained in the two surveys were recorded and analysed.

### Statistical analysis

The chi-squared test was used to compare morbidity parameters, prevalence, hepatosplenomegaly, periportal fibrosis and oesophageal varices obtained in the two surveys.

## Results

### Demographic findings

In 1987, the total population in Abu Jin was 1080. By 1994, it had increased to 1190. The estimated mid-term population was 1135. There was no significant population movement, apart from 5–10 Bedouin families, who were not included in either survey. The mid-term distribution of Abu Jin's population was not significantly different from that of other regions in Sudan. During the period of the study, 165 children were

born in the area, a birth and fertility rate of 29 and 123 per 1000 population per year respectively [1].

### Morbidity indices

By 1994, 7 years after the initial single-dose mass chemotherapy, overall prevalence of infection in Abu Jin's total population of 1190 (none of the inhabitants refused stool examination) had decreased significantly, from 53% to 34% ( $P < 0.05$ ). Prevalence in the 10–19-year-old age group had decreased from 73% to 51%. The intensity of infection ( $\geq 400$  eggs/g of faeces) had dropped from 31% to 18%.

The incidence of hepatomegaly and hepatosplenomegaly had also fallen significantly ( $P < 0.05$ ), from 50% and 34% to 20% and 10% respectively. However, there was no significant difference in the incidence of splenomegaly (41% in 1987, 37% in 1994) (Figure 1). Ascites was not detected in any patient from the study sample in either survey.

Ultrasound examination showed a reduction in the overall prevalence of periportal fibrosis from 14% to 10%. The incidence of oesophageal varices dropped significantly, from 47% to 30% ( $P < 0.05$ ) (Table 1). During the study period, two patients died, one due to massive haematemesis, and the second to heart failure resulting from rheumatic heart disease.

## Discussion

The study provided a unique chance to study and investigate the effect of a single dose of praziquantel treatment 7 years after treatment. In our 1994 survey, the studied village was not part of the activities of the Blue Nile Health Project. No control measures were in place during the period 1987–94, something confirmed by villagers and health workers. Furthermore, there was no

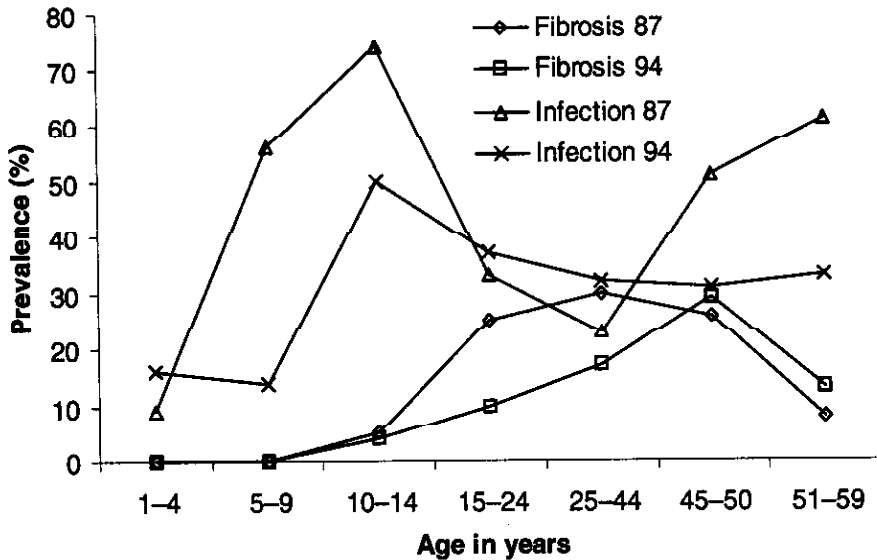


Figure 1 Prevalence of infection with *Schistosoma mansoni* and periportal fibrosis by age 7 years after single-dose mass chemotherapy in a village endemic for schistosomiasis in Sudan.

Table 1 Grades of oesophageal varices in patients with schistosomal periportal fibrosis examined by fiberoptic endoscopy in 1987 and re-examined in 1994

Endoscopy result	1987 (n=32) No.	1994 (n=30) No.
Grade 0*	17	21
Grade 1	7	5
Grade 2	7	3
Grade 3	1	1
Total	32	30

\*Grade 0 = no oesophageal varices.  
Two patients were not found in 1994.

observable change in the system of water supply or sanitation.

The initial survey and the investigations carried out in the second survey in 1994 showed a significant reduction in both prevalence and intensity of infection ( $\geq 400$  eggs/g of faeces). Interestingly, schistosomal morbidity levels among children < 5 years of age remained high, indicating the active transmission of the parasite. Since the exposure to infection in 1994 was comparable with that of 1987, and since the only intervention over the study period was the single-dose mass chemotherapy with praziquantel, we attribute the reduction in prevalence and intensity of infection to the single-dose praziquantel treatment. Farghaly and his group found that in experimental animal

studies, praziquantel can improve immunity and resistance to reinfection [12]. Moreover, on direct questioning, only three villagers were found to have received hospital-based, repeated treatment with praziquantel.

The sonographic investigations showed a significant improvement in the grade of periportal fibrosis, indicating the beneficial effect of single-dose praziquantel treatment on reducing the progression of morbidity. It is known that annual application of praziquantel to patients with periportal fibrosis is associated with a significant reduction in the prevalence and intensity of the pathology [5,7,8]. This observation was confirmed by Doehring-Schwerdtfeger et al. in 1991, who also found, after 7 months treatment, significant reduction of egg excretion and reversibility of sonographically proven early periportal fibrosis [4].

The study showed that there is a change in the prevalence and grade of oesophageal varices, which can be attributed to the effect of praziquantel on the reduction of infection intensity as determined by egg-load, and that this may halt development or progression of periportal fibrosis. There is no similar study for oesophageal varices. However, since oesophageal varices are the result of periportal fibrosis, the reversibility of early periportal fibrosis might therefore lead to reversibility of the oesophageal

varices [7]. Interestingly, our study showed a significant ( $P < 0.05$ ) reduction in both hepatomegaly and hepatosplenomegaly, but not splenomegaly alone. The finding might be due to the prevalence of other causes of splenomegaly. In fact malaria is known to be endemic in the studied area.

Despite the reduction in several schistosoma morbidity parameters, mortality due to schistosomiasis did not change [1]. Little data are available on mortality in the village prior to praziquantel treatment. In Brazil, mass chemotherapy has been reported to reduce mortality from 0.67 to 0.47 per 100 000 in some areas [1]. In addition, antagonists of beta receptors have shown promising results in reducing the mortality of advanced cases of periportal fibrosis [13]. Making these drugs available at an affordable price, together with other public health measures, remains a high priority in areas endemic for schistosomiasis.

## Acknowledgements

We thank the staff of the Bilharzia Research Unit, National Health Laboratory, Medical Research Centre, Khartoum, Sudan for their excellent technical help. This work was funded by the joint EMRO/TDR/CTD small grants programme for control-oriented research in schistosomiasis (grant number: TDR 8/22 T5/72/6).

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