

Haematological and Biochemical Morbidity of *Schistosoma Haematobium* in School Children in Sudan

*Elagba HA Mohammed¹, Mohamed Eltayeb², Hikmat Ibrahim¹

أثر الإصابة بالبلهارسيا البولية على بعض مكونات دم تلاميذ المدارس الإبتدائية في السودان

المخلص: الهدف: تحديد معدل الإصابة بمرض البلهارسيا وأثر ذلك على بعض مكونات الدم لأطفال المدارس. وكذلك تقييم العلاج بعقار البرازيكوانتل في العلاج وتحسين مكونات الدم إلى المعدلات الطبيعية. الطريقة: تم مسح عينة مكونة من 346 تلميذا بعمر (7-13) سنة من مدرسة الكرياب الإبتدائية بالقرب من مشروع السليط الزراعي شرق مدينة الخرطوم. تم الكشف على 136 (80 تلميذا و 56 تلميذة) مصابا بالبلهارزيا (بنوعيهما). وفحصهم. ومعالجتهم بجرعة واحدة من البرازيكوانتل (40 جم/ كجم من وزن الجسم). النتائج: وجد أن 28% (64 تلميذا و 33 تلميذة) مصابون بالبلهارسيا البولية. وفي 74% منهم فاق عدد البيض 500 بيضة / 10 مل من البول. ارتبطت حدة الإصابة بارتفاع عدد كريات الدم البيضاء. و بروتينات مصل الدم و القلوبولين والكالسيوم وانخفاض الألبومين والبوتاسيوم. كانت نسبة الشفاء 58%. مع انخفاض في عدد البيض (98%) وتحسنت الحالة الصحية للأطفال بعد 6 أسابيع. الخلاصة: أثبتت الدراسة تأثير حدة الإصابة بالبلهارسيا البولية على الصحة العامة للأطفال وفعالية عقار البرازيكوانتل في العلاج. توصي الدراسة بالاستخدام الدوري للبرازيكوانتل ضمن برنامج الرعاية الصحية الأولية بالإضافة إلى التثقيف الصحي وتوفير الماء النقي ووسائل الصرف الصحي في المنطقة.

المفردات المفتاحية: دم . حساب البيض . برازيكوانتل . انتشار . البلهارزيا البولية . السودان.

ABSTRACT Objectives: To determine the prevalence and intensity of infection with schistosomiasis among school children and to evaluate the efficacy of praziquantel in normalizing the levels of some haematological and biochemical blood constituents. **Methods:** A total of 346 school children, aged 7-13 years, from El-Kriab primary school, near the El-Seleit irrigation scheme east of Khartoum, Sudan, were screened for schistosomiasis. All 136 children infected with *Schistosoma haematobium* and/or *S. mansoni* were clinically investigated and treated with a single oral dose of praziquantel (40 mg/kg body weight). **Results:** In 74% out of 97 children infected with *S. haematobium* the egg count exceeded 500 eggs/10 ml of urine and they had high level of eosinophilia and leukocyte counts, high globulin and calcium levels and low potassium. The serum total proteins, globulins, albumin and urea showed statistically significant differences between control and patients and between patients before and after treatment, although the levels were within the normal reference range. Praziquantel treatment was highly effective as proved by a (58%) cure rate, a (98%) reduction in egg count and normalization of the examined blood parameters six weeks post-treatment. **Conclusion:** Infection with *S. haematobium* influenced the normal levels of certain blood constituents and treatment with praziquantel normalized the physiological conditions. According to WHO guidelines, regular mass treatment with praziquantel and health education are recommended as part of the primary health care programme in areas of high prevalence and intensity of *S. haematobium* infection.

Keywords: Blood, egg count, electrolytes, praziquantel, prevalence, *Schistosoma haematobium*, Sudan.

SCHISTOSOMIASIS IS A SERIOUS PUBLIC HEALTH and socio-economic problem in Sudan.¹ Infection with *Schistosoma haematobium* and/or *S. mansoni* is widespread among the entire population, with a prevalence range of 57-79%.² The spread of the disease is associated with the establishment of irri-

gation schemes and the flow of migrant labourers in the country.²⁻³ Praziquantel was introduced in Sudan in the early 80s to treat patients infected with urinary and/or intestinal schistosomiasis in Gezira and proved to be an efficient drug.⁴⁻⁵⁻⁶ In 1992, a new focus of *S. haematobium* was reported as a public health prob-

¹Natural History Museum, Faculty of Science, University of Khartoum. P. O. Box 321, Khartoum, Sudan. ²National Health Laboratory, Ministry of Health, Sudan. P. O. Box 22, Khartoum, Sudan.

*To whom correspondence should be addressed. Email: elagba2000@yahoo.com

lem after the establishment of the El-Seleit irrigation scheme in Eastern Khartoum State. Although a high prevalence of *S. haematobium* infection was recorded among school children in the area (unpublished data), no effective control measures were taken by the authorities. The epidemiology of urinary schistosomiasis in the Sudan was extensively studied, but the clinical, haematological and biochemical aspects of the disease have received little attention.² Haematological and biochemical morbidity studies are needed to understand better the public health significance of urinary schistosomiasis. Accordingly, this study was conducted to determine the prevalence of *S. haematobium* among the pupils of El-Kriab primary school, aged (7-13) years, who live near El-Seliet agricultural scheme. The other objectives of this study were to investigate the clinical, haematological and biochemical effects of *S. haematobium* before and six weeks after treatment with praziquantel. Since praziquantel has been established as an efficient drug for treatment of schistosomiasis in Sudan, it was thus used in the present study.

METHODS

STUDY AREA AND SUBJECTS

This study was carried out in El-Kriab village, 20 km east of Khartoum in El-Seleit agricultural scheme on the Blue Nile. Most of the residents had originally come from an endemic schistosomiasis area in western Sudan. The environmental sanitation and health services are below standard in the village, where more than 50% of the villagers have no latrines at home and 10% of them depend completely on the irrigation canals for their water supply. Both *S. haematobium* and *S. mansoni* were first reported a few years after the establishment of El-Seleit and other agricultural schemes in the area. The pupils of El-Kriab primary school were selected in the present study.

CLINICAL AND PARASITOLOGICAL EXAMINATION

A total of 346 students were screened with the filtration technique⁷ or stool examination for *S. haematobium* and *S. mansoni*, respectively. Ninety seven children (64 males and 33 females) infected with *S. haematobium* only were selected for pre- and post-treatment analysis.

The initial screening survey of infected children included a clinical examination according to standard protocols⁸ as well as grading and measuring of liver

and spleen sizes. Abdominal pain and headache were reported and urinary blood was detected by chemical reagent strips.⁹ Concurrent bacterial or parasitic infections (chest infection, malaria, typhoid...etc) were also reported. Urine was collected from patients shortly before midday. The number of eggs per 10ml urine was determined for each patient.¹⁰

HAEMATOLOGICAL AND BIOCHEMICAL EXAMINATION

A blood sample was taken from each patient, as well as a control group of 20 non-infected school children. Half of each sample was kept in a tube containing an anticoagulant and used for a full blood analysis including haemoglobin, haematocrit and differential and total leukocyte counts.¹¹ The other half was used to determine the serum levels of total proteins, albumin, globulin, urea, uric acid, sodium, potassium and calcium.¹²

All patients were treated with a single oral dose of 40 mg/kg body weight of praziquantel, according to WHO guidelines¹³, under the supervision of a medical doctor and after family consent was obtained. None of them has had a previous history of antischistosomal therapy. For no obvious reason, 47 of the *S. haematobium*s patients, previously treated did not come for follow up examination, so only 50 were considered in this study. Clinical, parasitological, haematological and biochemical examinations were repeated six weeks after the treatment with praziquantel.

STATISTICAL ANALYSIS

Data analysis was carried out by the statistical package for social sciences (SPSS/PC, Ver. 4.1). All continuous data are represented as mean \pm standard deviation (SD). For comparisons of means Students *t*-test was used.

RESULTS

The children examined, including the control group, were 7 to 13 years old, with a mean body weight of 20 kg (range: 15-45 kg). Clinical examination revealed a wide spectrum of the clinical forms of the disease. Thirty-four percent of the children complained of abdominal pain, while 30% had haematuria and 9% had dysuria and/or diarrhea. Hepatomegaly was not encountered in any of the patients and splenomegaly was detected in three females only.

Table 1 shows significant increase ($p < 0.01$) in eosinophilia and leukocyte counts in *S. haematobium* in-

ected children and a haemoglobin level below 12 g/dl for both the patients and the control group. There was no relationship between the level of haemoglobin and the intensity of the infection. Haematocrit was within the normal range. Elevated levels of serum total protein and globulin and decreased serum albumin were observed in infected children. No significant change in the level of urea and uric acid or sodium content was observed. Serum potassium was significantly decreased and calcium was significantly increased ($p < 0.01$).

A cure rate of 58 % (56 % of the males and 61 % of the females) was obtained. Although 42 % (66.7 % of the males and 33.3 % of the females), including 76.2 % of the age group ≤ 10 years, had some schistosome eggs after treatment, a 98 % reduction in the intensity of infection (egg output) was recorded ($p < 0.01$). Both sexes followed the same pattern of improvement independent of the intensity of infection. A significant improvement ($p < 0.05$) in most of the clinical symptoms was observed six weeks after treatment. This was associated with an improvement in the levels of all the

tested blood parameters [Table 1].

DISCUSSION

Clinical observations noted among the *S. haematobium* infected children agreed with some authors.⁸ Haematuria and dysuria are common clinical consequences of urinary schistosomiasis.⁹ Hepatomegaly and splenomegaly were not common among our patients. Relationships between hepatomegaly and splenomegaly with *S. haematobium* infection and regression in both organs after treatment were previously documented.¹⁴ The absence of enlarged liver and spleen in our patients is not surprising, because the prevalence of these clinical forms of the disease was found to be associated with the intestinal rather than urinary schistosomiasis.¹⁵

The biochemical results indicated that eosinophilia and raised leukocyte counts were related to the intensity of infection, while haemoglobin level was not. Low haemoglobin concentrations were observed, a cut-off point suggested for anaemia.¹³ This corresponded with the findings of some authors,¹⁶⁻¹⁷ but differed from

Table 1: Biochemical and haematological features of blood from children infected with *S. haematobium*, before and after praziquantel treatment (mean \pm Standard Deviation)

Blood Indices	Control Group (N=20)	Infected Subjects (N = 50)		(p value)*
		Before Treatment	After Treatment	
Haemoglobin(g/dl)	11.2 \pm 0.2	10.7 \pm 0.2	11 \pm 0.2	NS
Haematocrit	33 \pm 0.7	31 \pm 0.5	33 \pm 0.5	NS
Leukocytecount(/mm3)	5100 \pm 82	10184 \pm 30	5260 \pm 95	p<0.01
Lymphocytes(/mm3)	2096 \pm 58	321 \pm 61	2374 \pm 74	p<0.01
Neutrophils(/mm3)	2454 \pm 76	3886 \pm 89	3645 \pm 53	p<0.01
Eosinophils(/mm3)	359 \pm 82	1572 \pm 90	435 \pm 50	p<0.00
Monocytes(/mm3)	103 \pm 27	363 \pm 59	139 \pm 7	p<0.01
Total Protein(g/dl)	6.8 \pm 0.1	7.6 \pm 0.1	7.4 \pm 0.1	p<0.05
Globulin(g/dl)	3.4 \pm 0.1	4.4 \pm 0.1	3.7 \pm 0.1	p<0.05
Albumin(g/dl)	3.8 \pm 0.1	3.2 \pm 0.1	3.6 \pm 0.1	p<0.05
Urea(mg/dl)	22 \pm 0.7	26 \pm 0.9	22 \pm 0.8	p<0.05**
Uric acid(mg/dl)	3.5 \pm 0.1	3 \pm 0.1	3 \pm 0.1	NS
Sodium(meq/l)	138 \pm 0.6	137 \pm 0.7	138 \pm 0.	NS
Potassium(meq/l)	4 \pm 0.1	3.7 \pm 0.1	4.5 \pm 0.1	p<0.05
Calcium(mg/dl)	9 \pm 0.2	9.7 \pm 0.2	8.8 \pm 0.2	p<0.01

NS: Not significant

* Infected vs. control & infected vs. treated

** Statistically significant, but clinically below the normal clinical range

those of others.¹⁴ In Kenyan school children infected with *S. haematobium*, the low level of haemoglobin did not recover until six weeks after treatment,¹⁸ despite its significant relationship to the intensity of infection and there was no significant difference between infected and non-infected or treated children with *S. haematobium* infection from East Cameroon.¹⁹ Heavy infections with *S. haematobium* are known to cause iron deficiency anaemia due to urinary iron loss and red cells haemolysis by the spleen.¹⁴⁻¹⁸ Treatment of the infection was expected to result in a significant increase in haemoglobin levels of anaemic children, but no improvement was noted. Interestingly, haemoglobin in the control group was also below the normal limits. This could probably be due to malnutrition and/or poor quality of food for the whole community of children in the area and not necessarily due to *S. haematobium* infection. In addition, treated children were not given any supplementary food or iron therapy.

A significant rise in the level of total leukocyte counts could be attributed to the rise in eosinophils, but likewise a significant rise was encountered in monocytes, lymphocytes and neutrophils. This indicated a general immunological response. A number of systems employing antibodies and/or eosinophils, neutrophils, monocytes were produced to kill schistosomes. A significant relationship was observed between the degree of eosinophilia and the intensity of infection.¹⁶ However, the significant reduction observed in the circulating leukocytes and eosinophils after treatment indicates that this immunological cell response was due to *S. haematobium* infection, as the level remained high in the patients still passing eggs after treatment, unlike patients with other parasitic infections.

We found significant abnormalities in serum total protein, albumin, globulin, urea, potassium and calcium ions in infected subjects ($p < 0.05$). Serum sodium and uric acid levels were normal. The increase of serum total proteins and globulin and the decrease of serum albumin may have been due to liver dysfunction or to a poor nutritional status or both. The increased levels of serum total proteins and globulin, associated with the intensity of infection, could also have been due to immunological reactions and the production of immunoglobulin, which occurred before treatment. The low level of serum albumin could also be explained by high protein loss due to heavy infection.

Urinary protein excretion is known to interfere with the concentration of serum proteins, which may contribute to hypoproteinemia in cases of marginal protein supply.²⁰ It was obvious, following treatment, that there was a significant improvement in the levels of these indices, which indicates recovery of some liver functions. Low levels of serum proteins and albumin in *S. mansoni* infection, but no change in pure *S. haematobium* infection was observed.²¹ Low levels of serum total proteins and albumin in *S. haematobium* patients was observed by some authors,²² while others²³ found normal level of serum proteins before and after treatment. The significant increase in urea with intensity of infection contrasted with some researchers,²²⁻²³ who found urea to be within the normal limits for both *S. mansoni* and *S. haematobium* infected subjects. The increase found in our study could be explained either by an excessive production of amino acids, due to an increased breakdown of proteins and the production of urea, and/or an abnormal function of the kidneys and their inability to excrete urea. Uric acid decreased slightly after treatment, but did not show a significant difference between pre- and post-treated subjects.

The change observed in the serum electrolytes could be due to their influence in cellular metabolism, particularly in enzyme regulation. The decrease in potassium level of infected children might be due to an excessive urinary and gastric excretion of potassium (gastro-intestinal disorder) and/or decreased gut potassium absorption.²⁴ The significant increase in calcium level before treatment could be explained by an increased intestinal absorption of dietary calcium and/or by a decreased urinary excretion. Increased resorption of calcium from bone could be another cause. Elevated calcium is believed to result from an increase of vitamin D, $1/25-(OH)_2$ Vit D, which is necessary for the response of the gut to the parathyroid hormones. This in turn promotes calcium absorption from the gut and increases its resorption from bone.²⁵ Macrophages and other cells associated with granulomatous deposits are believed to synthesize $1/25-(OH)_2$ Vit D, and schistosome eggs initially evoke a granulomatous response, which probably caused elevation in serum calcium in our subjects. Hypercalcemia might also alter the renal function due to calcium deposits in renal tubules and interstitial areas of the kidneys.²² All electrolytes normalized in both sexes after treatment.

CONCLUSION

This study showed that *S. haematobium* infection can influence the normal levels of some haematological and biochemical constituents of the blood and treatment with praziquantel proved to be effective in normalizing these parameters. We recommend the following control strategies: community-based screening, large-scale treatment with praziquantel and health education, as well as permanent improvement in water supply and sanitation. Previous studies on schistosomiasis among school children in Sudan produced the same recommendations.

ACKNOWLEDGEMENTS

The authors would like to thank the Postgraduate College, University of Khartoum for financing this work. Our thanks also go to the technical staff of the National Health Laboratory, Ministry of Health, Sudan. Our gratitude is also due to Dr. E. Scrimgeour, Department of Medicine, College of Medicine and Health Sciences, Sultan Qaboos University for valuable comments on the manuscript.

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