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Change in Haematuria and Proteinuria Levels in Urinary Schistosomiasis after Treatment with Praziquantel —Population-based Study in a Kenyan Community—

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Abstract: In order to investigate efficacy of praziquantel (biltricide) on morbidity related to *Schistosoma haematobium* infection, 300 subjects of which 219 had eggs in the urine were examined for urinary eggs, blood and protein before and three months after treatment. Haematuria and proteinuria disappeared in 80.4% and 75.5% of the studied subjects respectively. The disappearance rates were not related to pre-treatment levels of haematuria and proteinuria. The rates both for haematuria and proteinuria were significantly lower in the age group 15 years and over than in the younger age group. Parasitologically, praziquantel cured 85.3% of the egg positives and reduced the mean egg count by 98.2%.

Key words: Urinary Schistosomiasis, Praziquantel, Change, haematuria, Proteinuria

INTRODUCTION

The infection of *Schistosoma haematobium* causes variety of pathological changes in the urinary system, some of which are polypoid lesions, ulcer, calcification of the bladder, deformity of the ureter. The changes may be found even among very young children of three years (Forsyth and Bradley, 1966), and the consequences must be serious if patients are left untreated for years. A significant mortality related to urinary schistosomiasis was reported (Forsyth and Bradley, 1966; Smith *et al.*, 1974; Wilkins *et al.*, 1985). The transmission of the

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disease continues as long as parasite eggs are excreted into snail habitats. Therefore, a rational chemotherapy should aim to cure the sick individuals, and to reduce egg excretion at a community level. An evaluation study of any anti-schistosomal drug should be based on these two points.

Praziquantel has been shown to be a very potent drug against *S. haematobium*. Many workers have reported high parasitological cure rate and egg reduction. However, population-based studies on the effects on morbidity are limited (Mott *et al.*, 1985). With a purpose of investigation clinical effects of praziquantel, we examined 300 subjects for urinary eggs, blood and protein, before and three months after treatment with praziquantel in a Kenyan community with a moderate infection.

Materials and Methods

A total of 915 people were examined for urinary blood and protein using Uro-Labstix Ⅲ (MILES-SANKYO CO. LTD.) This type of reagent strip could also test glucose and pH but these parameters were however not considered in this study since they did not have direct effect in diagnosis of the infection. Examination of *S. haematobium* egg was accomplished by nuclepore membrane filtration method in the months of June and July. Treatment with praziquantel as a single dose of 40mg/kg body weight was done in July and August to all egg-positive persons found in the June and July servey and egg-negative persons of age 5 to 15 years.

Three months later, urine examination was repeated and covered 635 people. The data presented in this paper is for 300 subjects of all ages who attended both urine examination before and after treatment.

Egg counts per 10 ml of urine was obtained from single random urine specimens excreted between 10.30 and 12.30 hours.

Haematuria and proteinuria were graded as −, −/+, 1+, 2+, 3+.

Haematuria −/+ up and proteinuria 1+ up were regarded as pathological and their lower levels as normal. Calculation of disappearance rates of haematuria and proteinuria was based on these criteria. For mean egg count, geometric mean of egg counts was used. To compare cure rates, chi-square test was used, and to compare reduction in egg count pre- and post-treatment by sex and age group, t-test was used.

Results

Effects of praziquantel on egg excretion

A total of 300 persons analysed consisted of 130 males and 168 females (data by sex for two individual was not available). In this group, 101 males and 116 females were egg positive. Data by age included 184 children of 0−14 years, and 115 persons who were 15 years and above (data by age for one person was not available). A hundred and thirty one persons of 0−14 years and 87 individuals in the higher age group were egg positive.

On average, the number of egg-positive persons reduced by 85.3% and there was no difference by sex and age group. The mean egg count reduced by 98.2% on the average. A significant difference ($p<0.001$) was found between subjects below 14 years and above 15 years age groups, though the difference in % reduction was very small (99.0 vs. 95.6, Table 1.).

Changes in egg counts before and after treatment are set out in Table 2. The rate of moderate- to high-count positives reduced from 71.7% before treatment to 3.2% after treatment. Cure rate of the egg positive cases increased as urinary egg excretion decreased ($p<0.005$). Only 3 out of 81 origial negatives (3.7%) turned positive after treatment.

Effects on haematuria and proteinuria

Changes in levels of haematuria before and after treatment are shown in Table 3. In

Table 1. Effects of praziquantel in reducing the number of egg-positive persons and mean egg count three months after treatment

		No. Positive	Mean egg count*
Male	Before	101	69.0
	After	13	1.3
	% Reduction	87.1	98.1
Female	Before	116	86.5
	After	19	1.5
	% Reduction	83.6	98.3
Total**	Before	217	77.9
	After	32	1.4
	% Reduction	85.3	98.2
−14 Yrs.	Before	131	141.1
	After	21	1.4
	% Reduction	84.0	99.0
15− Yrs.	Before	87	32.1
	After	11	1.4
	% Reduction	87.4	95.6
Total**	Before	218	78.1
	After	32	1.4
	% Reduction	85.3	98.2

*: Geometric mean of (egg count +1) was calculated to include the egg negatives after treatment.

**: Two persons with unknown sex and one with unknown age are excluded.

those cases with a pre-treatment haematuria of −/+ or up, the disappearance rate of haematuria was 80.4%. This rate of disappearance was irrespective of pre-treatment levels. In heavy haematuria cases (2+ up) haematuria decreased from 52.3% before treatment to 6.5% after treatment. Twelve cases or 8.2% of the original 147 haematuria negative cases turned −/+ or up after treatment.

In table 4, changes in levels of proteinuria before and after treatment are shown. Among the subjects with 1+ up before treatment, the disappearance rate was 75.0%. No difference was found in between 1+ and 2+ levels of pre-treatment proteinuria. Rate of heavy proteinuria (2+ up) decreased from 33.1% to 3.2% after treatment. Twenty five or 14.2% of the 176 original proteinuria negative cases turned 1+ up after treatment.

Table 5. shows the rate of disappearance of haematuria and proteinuria compared by sex and age group. After praziquantel administration no differences in the disappearance rate

Table 2. Change of egg counts before and three months after treatment with praziquantel

		Pre-treatment egg count/10 ml					
		0	1−25	26−100	101−500	501−	Total
Post-treatment egg count /10 ml	0	78 (96.3)	55 (88.7)	58 (95.1)	47 (82.5)	27 (69.2)	265 {88.3}
	1−25	1 (1.2)	5 (8.1)	3 (4.9)	8 (14.0)	9 (23.1)	26 {8.7}
	26−	2 (2.5)	2 (3.2)	0 (0.0)	2 (3.5)	3 (7.7)	9 {3.0}
	Total	81 {27.0}	62 {20.7}	61 {20.3}	57 {19.0}	39 {13.0}	300 {100}

( ) : Percentage of the total at each level of pre-treatment egg count.
{ } : Percentage of the grand total (300).

Table 3. Change of levels of haematuria before and three months after treatment with praziquantel

		Pre-treatment haematuria					
		−	−/+	1+	2+	3+	Total
Post-treatment haematuria	−	135 (91.8)	37 (86.0)	25 (83.3)	40 (78.4)	21 (72.4)	258 {86.0}
	−/+	6 (4.1)	5 (11.6)	0 (0.0)	4 (7.8)	2 (6.9)	17 {5.7}
	1+	3 (2.0)	1 (2.3)	3 (10.0)	3 (5.9)	2 (6.9)	12 {4.0}
	2+up	3 (2.0)	0 (0.0)	2 (6.7)	4 (7.8)	4 (13.8)	13 {4.3}
	Total	147 {49.0}	43 {14.3}	30 {10.0}	51 {17.0}	29 {9.7}	300 {100}

( ) : Percentage of the total at each level of haematuria.
{ } : Percentage of the grand total (300).

Table 4. Change of levels of proteinuria before and three months after treatment with praziquantel

		Pre-treatment proteinuria			
		negative	1+	2+up	Total
Post-treatment proteinuria	negative	151 (85.8)	66 (79.5)	27 (65.9)	244 {81.3}
	1+	23 (13.1)	15 (18.1)	12 (29.3)	50 {16.7}
	2+UP	2 (1.1)	2 (2.4)	2 (4.9)	6 {2.0}
	Total	176 {58.7}	83 {27.7}	41 {13.7}	300 {100}

negative: Proteinuria − and −/+ are combined.
( ) : Percentage of the total at each level of proteinuria.
{ } : Percentage of the grand total.

Table 5. Comparison of disappearance rates in haematuria and proteinuria after treatment with praziquantel according to sex and age group

	Sex		Age group		
	Male	Female	−14 Yrs.	15− Yrs.	Total
Haematuria % Cured	79.7	80.5	88.1**	64.7**	80.4
(No. subject)	(64)	(87)	(101)	(51)	(153)
Proteinuria % Cured	76.4	73.1	81.2*	60.5*	75.0
(No. subject)	(55)	(67)	(85)	(38)	(124)

**: Difference significant at 1% level
*: Difference significant at 5% level.
Two persons with unknown sex and one with unknown age are excluded.

of haematuria and proteinuria was noted between sex. When compared by age there was a significant difference of haematuria between the older age group (15 years & over) and the younger group (14 years & below) ($p<0.01$) with the older group showing 64.7% as compared to 88.1% in the younger age group. Proteinuria disappeared in 75.0% of the studied subjects. Again, a significant difference was found by age group, with older age group showing 60.5% compared to 81.2% of the younger age ($p<0.05$).

Discussion

The present study confirmed the efficacy of praziquantel on parasitological indices, that is, very high cure rate (85.3%) and egg reduction rate (98.7%), in a Kenyan community three months after treatment. However, there was no difference in cure rate between the young and older age groups in their pre-treatment averages of egg count. Both sexes had similar

cure rate. The percentage reduction in egg count was found to be very high (98.7%). No difference was noted between sex or age. These findings are largely in accordance with the past data (Davis *et al.*, 1979; McMahon and Kolstrup, 1979; Ejezie and Okeke, 1987), although much lower cure rates were reported by some authors (Pugh and Teesdale, 1983; Wilkins and Moore, 1987).

Haematuria and proteinuria disappeared in 80.4% and 75.0% of subjects after treatment respectively. The disappearance was not related to pretreatment levels of urinary blood and protein, or sex. However, the disappearance rates both in haematuria and proteinuria were significantly lower in the older age group than in the 0−4 years group. In a similar study by Mott *et al*, (1985), haematuria and proteinuria by reagent strips disappeared respectively in 65−73% and 69−72% of subjects after treatment, and the rates of improvement were similar in all pre-treatment age group. Haematuria was found to be associated strongly with hyperaemia and ulcer of the urinary bladder (Abdel-Salam and Ehsan 1978). Different stages of ulcers of the bladder (Lichtenberg, *et al.*, 1971) and urolithiasis will also cause haematuria. Urinary protein was reported to be of postrenal origin (Doehring *et al.*, 1985), but the kidney might be also involved (Edington *et al.*, 1970; Lehman *et al.*, 1970; Greenham and Cameron, 1980). Direct relationship between severity of pathology and intensity of infection was shown (Forsyth and McDonald, 1965; Lichtenberg *et al.*, 1971, Abdel-Salam and Ehsan, 1978; Warren *et al.*, 1979). The disappearance or reduction in urinary blood and protein, together with the marked reduction of egg counts, following praziquantel treatment indicate overall improvement of the pathological changes. Several radiological and ultrasonographical studies which showed rapid disappearance of abnormality after treatment support his findings (Oyediran *et al.*, 1975; Farid *et al.*, 1984; Doehring *et al.*, 1985).

The clinical improvement was particularly good in children with high egg counts when treated at early stages of the disease (Lehman *et al.*, 1973). On the other hand, these changes might become irreversible if patients were left untreated for many years (Forsyth and McDonald, 1966; McDonald *et al.*, 1968). Therefore, treating patients at early stages of pathological changes must have substantial benefit, and our study showed praziquantel was sufficiently effective.

Significantly lower rates of disappearance in haematuria and proteinuria in the older age group were observed in our study. Lehman *et al.* (1973) reported the linear increase of obstructive uropathy, bladder calcification, ureterolithiasis and bladder retention by age. Lichtenberg *et al.* (1971) observed much higher egg deposition in the bladder tissue in adults than in children. More irreversible nature of adult pathology seems to be relate to our results.

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