The efficacy of artesunate in the treatment of urinary schistosomiasis in ogoja, Cross river state, nigeria

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Citation

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Abstract

The efficacy of artesunate in the treatment of urinary schistosomiasis was investigated among 250 randomly selected subject aged 6 – 50 years in Ogoja, Nigeria. In the parasitological examination, infection was confirmed in 25 (10%) of the 250 subjects screened. Artesunate were administered orally at 4mg/kg body weight. Adverse effects due to drug reactions were assessed 3 days after medication and all perceived symptoms of illness were treated. The cure rate was evaluated after 2 weeks of treatment. There cure rate was 16 (64.0%) after treatment. There was a significant reduction in prevalence from a pre-treatment value of 10% to a post-treatment value of 3.6%. The intensity of infection also reduced significantly (p<.001) from 17.2% -3.1% for pre-treatment and post-treatment respectively giving a reduction rate of 82.1%. This study has shown that artesunate is effective in the treatment of schistosomiasis. It is recommended that a combination of artesunate and praziquantel, might produce a more effective treatment than the separate use of either drug.

INTRODUCTION

Human schistomiasis remains one of the most important parasitic diseases in the tropics for which there are no vaccines[1]. Chemotherapy with praziquantel currently offers the most feasible means of controlling human schistosomiasis, at least in the short term[2,3]. There are concerns however that schistosoma haematobium the aetiologic agent of urinary schistosomiasis is developing resistance to praziquantel or at least have the tendency to do so[4,5]. Studies conducted elsewhere have associated praziquental with low cure and egg production rates after the administration of a single dose of the drug[6,7,8]. Subsequently, communities in a very intense focus of S. mansoni infection in Senegal showed unexpectedly low rate following treatment with praziquantel[9,10]. Perhaps the best evidence so far of resistance to praziquantel is the failure of Ismail et al.[11] to cure some natural S. mansoni infection in some Egyptian patients with three doses of the drug.

The potential problem of praziquantel resistance led to a search for alternative drug for the treatment and control of schistosomiasis[12,13]. Although artemisinin and it derivatives such as artesunate, arteether, artemether and dihydroartemisinin were originally developed for the treatment of malaria, they have antischistosomal activity[13,14]. In vitro treatment of adult schistosomes with artemether, for example led to a significant reduction in the glycogen content of the worms and extensive tegumental damage[15].

For more than a decade, evidence has been accumulating of the effect of treating S. japoniucum and S. mansoni infections with one of the artemisinins[16]. Artemether appears to exhibit maximum activity against the liver stages and adult worms being less susceptible[15]. In human trials, administration of artemisinin derivatives (artesunate, artemeter) at a dose of 6mg/kg every 15 days during the S. japonicum transmission season resulted in the effective control of schistosomiasis in highly endemic areas in China[17]. Recently, treatment of schistosomiasis with the combination of artesunate and praziquantel show that more than 80% curative[18,19]. Artesunate not only exhibits antimalaria properties, but also possesses strong activities against schistosomes.

The objective of our present research is to determine the efficacy of artesunate in the treatment of urinary schistosomiasis in patients attending the General Hospital, Ogoja in the Cross River State of Nigeria.

MATERIALS AND METHODS

SAMPLE COLLECTION

The General Hospital, Ogoja in Cross River State of Nigeria was chosen for this study because a cross section of

members of this community often visit the Hospital to sort out their health needs. Ogoja is in Cross River State, Nigeria, which lies between latitude 5°32' and 4°27' North and longitude 7°50' and 2°20' East. There are two different climatic seasons in the area, the rainy season from March to October and the dry season from November to February. Majority of the people in Ogoja are rural farmers and fishermen.

ETHICAL CLEARANCE

The Cross River State Ministry of Health approved the study. Consent was sought and obtained from all the subjects that took part in the study. In the case of children, permission was granted from their parents. The objectives, significant and benefits of the study were explained to the subject.

COLLECTION OF URINE SAMPLES

Urine samples were collected from each patient attending the Hospital from May 2006 to October 2006. These samples were used to determine the prevalence and intensity of urinary schistosomiasis among patients attending the Hospital. All the samples were collected between 12.00 and 14.00 hours, the period when maximum egg excretion occurs[20] from patients.

10ml of urine samples were collected twice from each patient throughout the duration of the study. The samples were collected before and after treatment with artesunate. Patients were monitored for two weeks after treatment before the second samples were collected.

URINALYSIS

The 10ml of urine sample obtained form each patient was preserved in four drops of commercial bleach. This was poured into a centrifuge tube and spun at 5000 rpm for five minutes. The supernatant were decanted leaving the deposits at the bottom of the tube. The deposits were shaken properly with the remaining urine before transferring to the microscope slide using Pasteur pipette and covered with coverslip. Positive result shown ova of Schistosoma haematobium in the urine. A tally counter was used to count the eggs as the microscope field was moved. The total number of eggs found in each 10ml of urine samples were recorded[21].

SOURCES OF DRUG

Artesunate (50mg) manufactured by Mekophar, HO ChI Minh City Vietnam.

TREATMENT OF INFECTED PATIENTS

Only the pupils found positive for S. haematobium eggs in the initial screening were treated. Each pupil was given a single oral dose of artesunate (4mg/kg) body weight with the help of a physician. Two weeks after treatment with artesunate, the treated pupils were screened again for S. haematobium ova. A subject was only considered cured if no ova was detected in her urine sample collected after treatment (post-treatment).

ADVERSE EFFECT MONITORING

All treated subjects were carefully monitored by a physician for up to 3 days post-treatment. Any adverse effects were noted and treated accordingly.

RESULTS

Of the 250 pupils (129 males and 121 females aged 6 – 50 years) initially screened for the presence of Schistosoma haematobium ova in the urine, 25 (10%) pupils were found positive and therefore included in the treatment plan (Table 1).

The frequency of parasitological cure (as estimated two weeks after treatment) is summarized in Table 1. Out of the 25 patients who each received a single dose of artesunate, 16 (64.0%) were cured after treatment. The prevalence of the infection was reduced from 10% pre-treatment to 3.6% post-treatment following the administration of artesunate ($P<0.05$) (Table 1). There was a drastic and significant ($P<0.001$) reduction in mean egg count after treatment mean egg count drastically reduced by treatment. The value fell from 17.3% to 3.1% post-treatment. The overall percentage reduction in intensity was 82.1 (range 64.0 – 90.2) (Table 2).

Figure 1

Table 1: Age related, prevalence of infection before and after treatment with artesunate

Age range (Years)	No. of patients examined	No (%) prevalence before treatment	No (%) cured after treatment	No (%) infected after treatment
6 - 12	55	7 (12.7)	6 (71.4)	2 (28.6)
13 - 19	35	3 (8.6)	1 (33.3)	2 (66.7)
20 - 26	64	9 (14.1)	7 (77.8)	2 (22.2)
27 - 33	52	5 (9.6)	3 (60.0)	2 (40.0)
34 - 40	18	1 (5.6)	0 (0.0)	1 (100.0)
41 - 50	26	0 (0)	0 (0.0)	0 (0.0)
TOTAL	250	25 (10.0)	16 (64.0)	9 (36.0)

Figure 2

Table 2: Age related intensity of infection before and after treatment with artesunate

Age range (Years)	No infected before treatment	No infected after treatment	Mean ova/10ml of urine		% reduction
			Before treatment	After treatment	
6 – 12	7	1	10.5± 2.1	2.5 ± 1.1	76.2
13 – 19	3	2	25.0 ± 1.1	4.0 ± 0.9	84.0
20 – 26	9	2	12.5 ± 3.1	4.5 ± 1.7	64.0
27 – 33	5	2	25.5 ± 1.1	2.5 ± 2.2	90.2
34 – 40	1	0	8.0 ± 2.2	2.0 ± 1.4	75.0
41 – 50	0	0	0.0	0.0	0
TOTAL	**25**	**7**	**17.3 ± 2.1**	**3.1 ± 1.5**	**82.1**

DISCUSSION

This study has assessed the efficacy and tolerability of oral artesunate for the treatment of urinary schistosomiasis.

From the result of the investigation, a single dose of oral artesunate appeared to cure 64% of those treated and also reduced significantly the intensities of infection in those not cured from 17.2 mean ova/10ml urine to 3.1 mean ova/10ml urine. In Senegal, De Clercq et al.[22] also found artesunate to be effective against S. haematobium, although the result they obtained with praziquantel were consistently better. Inyang-Etoh et al.[23] found artesunate to be effective against S. haematobium as 70% of those treated were found cured in Admin Community, Nigeria.

In the present study, 36% of the patients treated were not cured probably due to resistance of the patients to artesunate. Borrmann et al.[18] found that only 27% of the subjects they treated with artesunate in Gabon were cured. However, Borrman et al.[18] thought that their disappointing results might be as a result of an inherent resistance to artemisinin or its derivatives in S. haematobium in addition.

Even though 36% of the patients in the present study were not completely cured, there was a drastic reduction in the intensity following the administration of the single doses of artesunate from 17.3 mean ova/10ml to 3.1 mean ova/10ml. There was probably inherent resistance of this individual to artemisinin.

Based on the cure rate of 64% established in the present study, artesunate was said to be effective. Similarly, Ejezie et al.[24] recorded a cure rate of 67% using praziquantel. This indicated that there was no significant difference between the two results even though praziquantel is widely recognized as a major drug of choice in the treatment of urinary schistosomiasis. Artesunate was also established as a widely used antimalarial drug in the tropics and thus can similarly treat urinary schistosomiasis. However, the 3.6% that were not cured might be acting as a veritable sources of re-infection, thereby becoming a public health problem.

The use of combination therapy as a safeguard against the rapid development of drug resistance by schistosomes has been advocated by several authors[11,25]. The enhanced cure rate obtained by these workers suggest that combination therapy may be an effective strategy of combating drug resistance in schistosomiasis infection. Borrmann et al.[18] recorded that the combination of artesunate and praziquantel gave a cure rate of 81% in Garbon while Inyang-Etoh et al.[19] recorded a cure rate of 88.6% in their study in Nigeria using artesunate and praziquantel combination.

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