Poor Patient Compliance Reduces the Efficacy of Metrifonate Treatment of *Schistosoma haematobium* in Somalia

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Summary. The degree of compliance during metrifonate therapy of *Schistosoma haematobium* infection has been evaluated together with its impact on drug efficacy in two rural villages in Somalia. Drug treatment was offered to all subjects with *S. haematobium* infection. 243 subjects were screened for the presence of eggs in the urine using a sensitive Nucleopore filtration method and 211 were positive. All infected patients were put on a treatment schedule of 3 doses of metrifonate 7.5 mg/kg at fortnightly intervals. Drug efficacy was evaluated 6, 12 and 32 weeks after treatment.

Only 48% of the patients took all 3 doses, 15% took 2 doses and 37% only took 1 dose. The cure rate was maximal in Week 6 at 60, 44 and 30% in those who took 3, 2 and 1 dose, respectively. Corresponding egg reduction rates were 98, 90 and 84%, respectively. Drug efficacy throughout the follow up period was much greater in patients who complied with all 3 doses.

It is unlikely that the goal of mass treatment programmes for endemic *S. haematobium* in villages in Africa will be realized due to poor compliance with the current dosage schedule for metrifonate of 3 doses of 7.5 mg/kg at fortnightly intervals.

Key words: metrifonate, *Schistosoma haematobium*, compliance, cure rate, egg reduction rate, filtration

Poor compliance is a common problem in the treatment of chronic diseases, such as hypertension, schizophrenia, epilepsy, cardiac arrhythmias and asthma, and is frequently seen in developed countries [1]. Treatment of several parasitic diseases in the tropics, e.g. leishmaniasis, filariasis and trypanosomiasis, requires complicated dosage schedules, but little is known about how this affects compliance and thus the outcome of treatment [2]. Drugs such as diethylcarbamazine, melarsoprol, pentamidine, suramin and tuberculostatic drugs must be given according to complicated dose schedules, which limit their efficacy at the community level.

In schistosomiasis, drug treatment has been shown to be the easiest and cheapest way to reduce and prevent morbidity [3]. Mefronate is a cheap, safe and effective drug, and for these reasons it is still regarded as the drug of choice where *S. haematobium* is the only common species, as in Somalia [4]. However, the drug has a complicated dose schedule, which requires several visits to the village by the health team, with a consequential high delivery cost, and there is a large proportion of drop-outs.

Studies evaluating the degree of compliance with metrifonate treatment in endemic areas in rural Africa are rare. Compliance in metrifonate therapy during a large scale treatment scheme has been examined and its possible consequences on drug efficacy evaluated in two rural villages in Somalia.

Materials and Methods

Study Area

The study took place in two villages along the Shabelle river, in the southern part of Somalia. Isgoyska is situated about 50 km north of Mogadisho, and
Waagaadi is located about 150 km south of the capital. They have estimated populations of 2500 and 1500 inhabitants, respectively. The people depend on subsistence farming and animal rearing. The prevalence of *S. haematobium* infection in this area is around 8–18%, one of the highest in Somalia [5]. *S. haematobium* is the only species of schistosome found in the country [6].

**Patient Recruitment**

At a prior meeting with the leaders of the villages, the purpose of the survey was explained and they were informed about schistosomiasis (its life cycle, transmission, prevention and means of control). The information was communicated to the people through the leaders. All subjects in the two village were offered urine examination for *S. haematobium*, and anyone with an infection was offered treatment. At the start of the clinic a clarion call was always made by driving the car around the village to announce our arrival.

On presentation the patient’s name, age and weight were taken. His/her urine was examined and the egg count recorded. Anyone without eggs in the urine was informed that treatment was not needed. Otherwise he/she was treated on the same day after receiving a full explanation of the treatment schedule. All possible efforts were made to locate the patients on the 2nd and the 3rd treatment days and during the follow-up period. For example, if it was learnt that someone was staying behind at home, or taking care of animals nearby or in the fields despite the call, the individual was visited to persuade him/her to take the drug, with the help of the village leaders and the traditional healer.

**Parasitological Examination**

Single, mid-day urine samples were collected in 200 ml plastic containers before treatment and 6, 12 and 32 weeks after treatment. Urine samples collected before treatment were examined in the villages. All other samples were transported in a cool box to the Medical Faculty in Mogadisho, where they were processed. Egg counting methodology was similar in both instances. Urine 10-ml was drawn randomly into a 10-ml syringe after careful mixing and the eggs were counted by the Nucleopore filtration technique [7].

**Drug and Dosing**

Metrifonate (Bilarcil, Bayer AG, Leverkusen, FRG) as 100-mg tablets was used in a regimen of 3 doses of 7.5 mg/kg metrifonate at fortnightly intervals. All doses were rounded to the nearest 25 mg. The drug was swallowed in front of us on all 3 occasions, and the mouth was checked after drug intake.

**Trial Procedure**

The treatment team consisted of a physician, a laboratory technician, a driver and a traditional herbalist, who was trusted by the villagers and the community leaders. A central location in each village (huts used by the Ministry of Agriculture) was used for the work. Children at the Quranic schools were examined, treated and followed up at those sites. At the

**Statistics**

The comparability of the patients regarding age, weight, egg output before treatment and drug efficacy (cure and egg reduction rates) were evaluated by the Kruskal-Wallis test [8].

**Definitions**

cure absence of ova in the urine after treatment
relapse appearance of schistosome eggs in the urine at Week 12 in a patient diagnosed as cured in Week 6 after treatment [9].
re-infection appearance of schistosome eggs in Week 32 in the urine of a patient diagnosed as cured in Weeks 6 and 12 after treatment [9].

**Results**

A total of 243 subjects from the two villages volunteered to be examined for *S. haematobium* (less than 7% of the total population). Of them 211 had a positive urine test for *S. haematobium* and were recruited into the trial. Details of the patients are shown in Table 1. The numbers of patients who took 1, 2, or 3 doses are also listed there. The subjects were comparable in age (*P* > 0.25), weight (*P* > 0.5) and egg output (*P* > 0.75). 101 patients took 3 doses; they represented 48% of the population treated (Table 2). The therapeutic results in the 211 patients 6, 12 and 32 weeks after the third dose are shown in Table 3. The cure rate was maximal in Week 6 at 30, 42 and 60% in those who had taken 1, 2 and 3 doses, respectively. The