



HEALTH OF SCHOOL CHILDREN
TREATMENT OF INTESTINAL HELMINTHS AND SCHISTOSOMIASIS

SUMMARY

School children harbour some of the most intense helminth infections with adverse effects on health, growth and school performance. Treatment of this group achieves the maximum return in terms of reduction of morbidity. School children are also one of the most accessible groups for treatment, and health care can be efficiently integrated with education programmes. High prevalence of mixed infections of intestinal helminths and schistosomiasis justify integrated control programmes including chemotherapy. Safe and highly effective single dose drugs such as the benzimidazoles (albendazole and mebendazole) and praziquantel are now available permitting integrated interventions. The frequency, intensity and reinfection pattern of multiple infections may vary considerably requiring careful monitoring to determine the value and methodology of integrated programmes based on chemotherapy. Joint administration of drugs may offer improvement of logistics, may reduce delivery costs and improve patient compliance. Joint administration of praziquantel with albendazole has been shown to be safe and effective. In areas where high prevalence of both intestinal helminths and schistosomiasis are present and joint administration is appropriate, post treatment surveillance is encouraged.

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Introduction

The success of global programmes to reduce infant morbidity and mortality has created new opportunities and new challenge for WHO. The opportunities are in the increasing size of the school age group. The challenge is how improve their health status. Keeping this age group healthy to bring children into a productive adulthood is an added guarantee on the long term return of the educational investment of developing countries. Progressive urbanization of the developing world has increased the proportion of school enrolled children, but also created conditions for more favourable transmission of helminths due to overcrowding, contamination of the soil of shanty towns by human excreta and environmental degradation.

The situation

School age children: Among the 1.2 billion school age children, 700 million are registered in a school and each day it is estimated that 400 million are present. However school enrollment is presently increasing.

Helminthic infections negatively affect school performance, cognitive processes and nutritional status and justify programmes to improve the health of school age children by control of helminthic infections.

The first initiative in this direction was taken by a United Nations Administrative Committee on Nutrition recommending treatment of intestinal parasites integrated with food and vitamin A supplementation (United Nations, 1989). More recently, the Partnership for Child Development in collaboration with WHO is investigating how a package of interventions, including distribution of anthelmintics and micronutrient supplements, can be delivered through the educational system.

The WHO Expert Committee on Control of Schistosomiasis (WHO, 1993) has emphasized that the target groups for chemotherapy will depend upon infection and morbidity patterns as well as budgetary and operational feasibility. In many cases, schoolchildren will be the most easily accessible target group, and they generally belong also to the most heavily infected age group. However, in some areas school attendance rates are low, and precisely those children who do not attend school may be the most at risk of heavy infection. Thus, treatment of children slows the onset or development of morbidity and even reverses morbidity which is present at the time of treatment.

Intestinal helminths: About 400 million school-age children are infected with intestinal helminths. Ascaris lumbricoides and Trichuris trichiura infect one quarter of the world's population. School-age children harbour both the highest prevalence and intensity of these helminthic infections. Small hookworm loads may precipitate severe anaemia in children and in adolescent girls of childbearing age.

Infection with Ascaris lumbricoides can be responsible for a decrease in growth rate, nitrogen absorption and retention, fat absorption, D-xylose absorption, and mucosal lactate activity and can also cause structural abnormalities of the mucosa of the small intestine in malnourished children. Deworming of children can lead to increased growth rates and in physical and

mental improvements.

Hookworms (*Necator americanus* and *Ancylostoma duodenale*) are responsible for decreased physical fitness and activity, work capacity and productivity by loss of blood, even without overt anaemia, and a decrease of appetite.

Infection with *Trichuris trichiura* may be responsible of loss of blood, growth retardation and impairment of school performance: treatment may reverse these effects with a very fast return to normality.

Schistosomiasis: Over 200 million persons residing in 74 countries are infected, of which approximately 88 million are under fifteen years of age. In heavily infected children, growth may be dramatically retarded. This effect is completely reversed by treatment of schistosomiasis. In Cambodia, Sudan, and Madagascar, severe disease (hepatosplenic enlargement with portal hypertension) due to different types of intestinal schistosomiasis is frequent in children under fifteen years of age. Blood loss in urinary schistosomiasis substantially augments the anaemia caused by hookworm infection.

Foodborne trematodes: Some 40 million persons are infected with these parasites which affect the liver, lungs and gastrointestinal tract and at least 15 million children are infected (WHO,1995).

Epidemiological characteristics

The interaction between these helminthic diseases is determined by their focal distribution and clustering at all levels. If both schistosomiasis and intestinal helminths are present, the prevalence and intensity of each may be different even in localities in close geographical proximity. The pattern of reinfection after treatment is different and may not be constant. These epidemiological differences necessitate prior surveys or investigations in the field in which the presence of both infections can be determined to decide if intervention for both schistosomiasis and intestinal helminths is warranted. Rapid, low-cost methods of identifying schools with a high risk of morbidity associated with *S. haematobium* infection have been developed, and are currently being tested for *S. mansoni* and other intestinal helminthic infections.

Drugs of choice

Intestinal helminths: Albendazole (400 mg single dose), levamisole (2.5 mg/kg single dose), mebendazole (500 mg single dose), piperazine (75mg/kg single dose) and pyrantel (10 mg/kg single dose) are all effective in producing cures in nearly 100% of cases of *Ascaris lumbricoides* infection (WHO, 1990).

The two benzimidazole derivatives, albendazole and mebendazole, have recently been compared by the Programme of Intestinal Parasitic Infections of the Division of Communicable Diseases of WHO (IPI/CDS/WHO) (Albonico et al, 1994). Both drugs were highly effective against *Ascaris*. Against hookworms the geometric mean egg count was reduced by 98% by albendazole compared to 82% by mebendazole. Neither drug was very effective in clearing *Trichuris* but

both reduced the egg count by 70% and mebendazole was significantly more effective than albendazole. After four months the differences in efficacy between the two drugs for hookworm and *Trichuris* were no longer apparent, suggesting that cost may be the major determinant for the choice of the drug to be used in large scale disease control programmes.

Levamisole and piperazine are very effective against *Ascaris*. The former has also some effect, mostly on intensity of infection of *Necator americanus* and *Ancylostoma duodenale*. Pyrantel, apart from being extremely effective against *Ascaris*, has been demonstrated highly effective in some community based control programmes against hookworms, with a significant reduction in the intensity of infection.

Side effects: Most side effects with all these drugs are mild and transient. The benzimidazole derivatives (albendazole and mebendazole) are teratogenic and embryotoxic in some species of experimental animals. On balance, it appears that species differences in pharmacokinetics and metabolism afford protection against teratogenic and genotoxic effects in humans during the vulnerable stages in early pregnancy. Single dose, oral anthelmintic treatment for hookworm infection is recommended also for pregnant and lactating women, using one of the following four drugs: albendazole, levamisole, mebendazole and pryzantel. As a general rule, in the case of pregnant women, treatment should not be given in the first trimester unless there is specific medical need to do so.

Schistosomiasis: Praziquantel has broad spectrum effectiveness against all forms of schistosomiasis (in a single dose of 40mg/kg), other trematode and cestode infections at other dose levels (WHO, 1990). Oxamniquine is effective in a single dose (15 mg/kg or higher) against *S. mansoni* infection only. When only urinary schistosomiasis is present, metrifonate is also effective in three doses, at two week intervals, thus requiring an efficient primary health care system or full collaboration of the school system. The low cost of metrifonate may favour its use in these areas.

Side effects: Thirty percent of children treated with praziquantel have transient abdominal pain 1-2 hours after treatment. Generalized allergic reactions have been reported from West Africa and Madagascar. Blood in the stool has occurred occasionally after treatment.

Drugs with multiple anthelmintic effects. Metrifonate has a significant effect on *Ascaris* and hookworm infections as well as urinary schistosomiasis. Long term single dose treatment at short intervals - monthly or bimonthly - has not been tested.

Combination of drugs and joint drug delivery: The formulation of praziquantel and one or more anthelmintic drugs into a single preparation is not recommended. Differences in recommended doses and regulatory requirements make this approach unpractical. On the other hand, The potential advantages for combined drug delivery include,

- lower cost of drug delivery due to logistic advantages
- simplification of therapy resulting in improved patient compliance and improved efficacy by potentiation of therapeutic effect.

There is no evidence from controlled trials of adverse effects from combining anthelmintic treatment with albendazole and praziquantel. A potential disadvantage due to the known interaction of the two active components may include the accumulation of adverse reactions.

Studies on joint drug delivery. It is prudent to consider the interactions if praziquantel and intestinal anthelmintics are coadministered, especially in endemic countries where poor levels of nutrition and general health might be expected to exacerbate any untoward drug interactions.

The UNDP/WORLD BANK/WHO Special Program for Tropical Diseases (TDR) undertook a series of studies on the concomitant administration of the albendazole and praziquantel. No difference in acute toxicity have been observed in animal studies where combinations of albendazole or mebendazole have been compared to single drug administration.

Phase I clinical studies have revealed a four-fold increase in the bioavailability of albendazole in the presence of praziquantel but the significance of this is not known. The bioavailability of praziquantel was unaffected by the administration of albendazole.

Phase II studies on the safety and efficacy of combined treatment with praziquantel and albendazole have shown neither increased adverse effects nor diminished efficacy. The half life of praziquantel is 2.1 hours and all the drug is eliminated in 24 hours. For albendazole the figures are 10.1 and 48 hours, respectively. Thus, if blood levels of only one drug are desirable, albendazole could be administered 24 hours after praziquantel.

The recommendation of the WHO Informal Consultation on Intestinal Helminth Infections (1990) was that if combined chemotherapy is desirable and justifiable on epidemiological grounds, the two drugs should be spaced by one week in community control activities. However after the results of the TDR trials concurrent administration is now acceptable, if justified epidemiologically.

Treatment approaches

Intestinal helminths: WHO emphasizes the importance of targeting treatment to the school-age children since they harbour the most intense infections with Ascaris, Trichuris and other helminth infections. Treatment of this group achieves the maximum return in terms of reduction of morbidity. In addition, children in school are one of the most accessible groups for treatment.

Schistosomiasis: WHO also emphasizes the importance of treatment of school-age children with oral antischistosomal drugs. Programmes to reduce morbidity should orient their operations to achieve complete coverage of the section of the population of school age. These can be integrated with other operational programmes of high priority such as control of intestinal parasitic infections, immunization, nutritional programmes, maternal and child health activities, tuberculosis, leprosy and sleeping sickness surveys as well as the control of diarrhoeal diseases.

Retreatment of schistosomiasis is not recommended more than once a year and may be required only once every five years (WHO, 1993). Thus, the epidemiological criteria for retreatment need to be established in every area.

Integrated approaches: Partnership between the health and education sectors will be the basis of future control of helminthic infections in school age children. WHO intends to promote school health programmes using deworming as an entry point and emphasizing personal hygiene. School and community based chemotherapy integrated into the primary health care system will improve coverage and achieve optimal retreatment schedules. Experience in this area is growing and in line with the commitment of Member States to promote the capacity of peripheral health services to control communicable diseases. The major potential benefit of integrated helminth control is the strengthening of the health services by training of the peripheral health care personnel, and developing activities based on disease-specific (reduction in prevalence of infection and morbidity) and operational (coverage of schools and localities) objectives.

Field quantitative parasitological screening techniques are simple to perform and low cost, but are time consuming and need an experienced microscopist. Treatment without prior individual screening of the whole population is recommended where surveys of school-age children indicate the prevalence of intestinal helminths or schistosome infection exceeds 50%. Periodic monitoring of appropriate samples of the treated population will ensure effective evaluation of the programme. On the other hand indirect screening techniques for haematuria are highly reliable to identify children for treatment against S. haematobium.

The available data now permits greater flexibility in integrating national intestinal helminth and schistosomiasis control programmes allowing coordination of diagnosis and treatment activities as part of comprehensive control strategies. Programmes targeting the health of the school-age child can utilize combined treatment schedules at appropriate intervals. In all circumstances, chemotherapy is one aspect of control which will have even greater success if health education, improved water supplies and sanitation and environmental management are integrated control activities.

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