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Controlling lymphatic filariasis and soil-transmitted helminthiasis together in South Asia: opportunities and challenges

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Summary

Lymphatic filariasis (LF) and the major soil-transmitted helminth (STH) infections are co-endemic in many countries, particularly in Asia. Control strategies for both groups of infections have increasingly focused on the use of mass chemotherapy. With the use of albendazole, there is now a tool that is common to both. However, there are also important differences in their modes of transmission and epidemiology, and as a result, in the overall control strategies. The Global Programme for the Elimination of Lymphatic Filariasis aims to eliminate LF through time-limited, Mass Drug Administration programmes. STH control activities are more diffuse, aiming to piggy-back de-worming onto existing services such as school health activities; controlling morbidity, rather than eliminating infection, is the stated goal. In order to maximize health benefits to communities that are endemic for one or both of these infections, it is vitally important that policy makers and programme managers have a clear understanding of both commonalities and differences, and implement control programmes that allocate available resources in an optimal manner.

Keywords

ascariasis; hookworm; trichuriasis; lymphatic filariasis; prevention; control

Introduction

The lymphatic filariases (LF, caused by *Wuchereria bancrofti, Brugia malayi* and *Brugia timori*) and the major soil-transmitted helminth infections (STHs, caused by *Ascaris lumbricoides, Trichuris trichiura, Necator americanus* and *Ancylostoma duodenale*) are essentially diseases of the poor living in tropical countries. Both groups are caused by

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nematodes which parasitise only humans, but traditional approaches to their control have been very different. This was because LF is vector-borne, and therefore dependent on the presence of suitable mosquito vectors, whereas STH transmission depends on contamination of soil with human faeces. Thus early LF control programmes relied on mosquito control activities, whereas STH control programmes concentrated on improving sanitation. Individual diagnosis before treatment was (and still is) expensive and impractical in most settings with endemic disease. Over the last decade however, the availability of highly effective, single dose drugs with excellent safety levels and low cost have meant that mass treatment without prior laboratory diagnosis has become a very good option as a tool for control or perhaps even elimination (in the case of lymphatic filariasis). As a result, control strategies for these infections have increasingly focused on the use of mass chemotherapy.

Current control programmes

The Global Programme for the Elimination of Lymphatic Filariasis (GPELF) was established in early 2000, following a World Health Assembly Resolution (no 50.29), which called on member states of the World Health Organization to eliminate the disease as a public health problem and interrupt transmission (Molyneux and Zagaria 2002). The main strategy for elimination is time-limited co-administration of two drugs through Mass Drug Administration (MDA) programmes. Entire endemic populations at risk of filarial infections are to be given annual treatments, for 4 – 6 years, with a combination of two drugs: albendazole and diethyl carbamazine citrate (DEC) or albendazole and ivermectin. Ivermectin is used instead of DEC on the African continent because DEC can cause severe reactions in individuals with onchocerciasis or loiasis.

In contrast to the stated goal of the GPELF, morbidity control is the main objective recommended by WHO with regard to STH infections (Savioli et al., 2002). This means a control strategy whereby the consequences of infection (and not infection per se*)* are reduced to a level that no longer constitutes a public health burden. Global elimination of infection through interruption of transmission is not a currently envisaged target for soil-transmitted helminthiasis. The recommended strategy for achieving morbidity control is ensuring access to anthelminthics in all health facilities, and regular de-worming of groups at risk of developing morbidity, particularly school-age children and women of child bearing age. Treatment is recommended 1-3 times a year, depending on prevalence. The drugs recommended for use are albendazole, mebendazole, levamisole or pyrantel (WHO, 2002).

In albendazole, there is now a tool that is common to both control programmes. It has been used for many years in STH control, as it is highly effective against roundworm and hookworms, and to a lesser extent, against whipworm. In the 1990s, research suggested that combination of albendazole with DEC or ivermectin enhanced suppression of microfilariaemia (Addiss et al., 1997; Ismail et al., 1998; Jayakody et al., 1993), and in 1998, the GPELF recommended MDA with the two-drug combination described above.

Thus the strategy of mass chemotherapy with albendazole is broadly common to both control programmes. However, there are some important differences too. It is vitally important that implementation of control in areas with co-endemic LF and STH take these

commonalities as well as differences into account, and complement each other in order to maximize health benefits and make optimal use of currently available tools.

Co-endemicity of LF and STH in South and South East Asia

Both LF and STH are important public health problems in the countries of South and South East Asia. STH infections are endemic in all eleven countries of the WHO's South East Asia Region, while LF is also endemic in all except Bhutan and North Korea. Within countries that are endemic for both sets of infections, co-endemicity usually occurs in confined areas. This is largely because filarial worms have specific mosquito vectors, which have very specific breeding sites. For example, *Culex quinquefasciatus* mosquitoes, which transmit *W bancrofti,* require stagnant water with a high content of organic matter, whereas *Mansonia* mosquitoes that transmit *B malayi* require the presence of floating water plants. Thus transmission is often focal in nature, in contrast to STH infections, which tend to be more widespread in their distribution. As long as faecal contamination of soil occurs, only extreme temperatures and high aridity really exclude transmission of STHs. Within co-endemic areas, levels of transmission of both groups of infections may be very high. For instance, Feni District in the plains area of Bangladesh had a STH prevalence rate of 96.8%; 60% of individuals had moderate to severe intensity levels of ascariasis. The same ecological area had microfilaraemia levels ranging from 0.2% to 16% in several foci. Similarly, high co-endemicities have been recorded in Myanmar, Nepal and Timor Leste (E.A. Padmasiri, unpublished).

At present, country-specific comparison of numbers of individuals affected by LF and STH is difficult because of the different epidemiological techniques used by researchers. LF data are presented in the form of numbers at risk of infection in IUs, i.e., individuals living in areas identified as LF-endemic (WHO, 2005), whereas STH data are in the form of estimated prevalence rates (de Silva et al., 2003a). However, WHO is currently setting up a global databank that will map current epidemiological data in each country to show prevalence and intensity of STH infections on district-by-district basis (www.who.int/wormcontrol/databank/).

In addition to the spatial distribution of infection, age-specific epidemiology must be also borne in mind. The prevalence and intensity of *A. lumbricoides* and *T. trichiura* infections tend to rise rapidly in pre-school children, peak in the primary school age group, and then slowly come down toward adulthood. Hookworm infections in contrast, rise steadily throughout childhood, reaching a peak in adulthood. The age-specific prevalence of lymphatic filarial infections also rises throughout childhood, peaking in adulthood. This age distribution is particularly important in determining cost-effective control strategies and in programme evaluation.

Operational issues and concerns

The distribution of LF is now being mapped in all nine LF-endemic countries of WHO-SEAR in order to scale up for coverage under MDA with DEC and albendazole. Such programmes have already been initiated in all LF endemic countries in the South East Asia

region. Large-scale school de-worming programmes have been launched in Nepal, Maldives and Myanmar. In co-endemic communities, LF control programmes that use combination therapy are likely to secure higher compliance than single drug therapy because of its more obvious benefits, such as visible expulsion of roundworms (Mani et al., 2002). A recently published systematic review that examined albendazole in the treatment and control of LF, concluded that the effect of albendazole against filarial parasites deserves further rigorous research, but noted that other health benefits derived from using albendazole may improve adherence to MDA for filariasis (Critchley et al., 2005). In any event, several MDA programmes that included albendazole for LF control have been shown to result in significant, sustained declines in the prevalence of STH infections (de Rochars et al., 2004; Mani et al., 2004; Oqueka et al., 2005; Rajendran et al., 2003).

School-based targeted anthelmintic treatment with albendazole in Ghana and Tanzania has been estimated to cost as little as US$0.03 per child (Guyatt, 2003). The *per capita* cost of MDA with albendazole and DEC for LF control is similar: US$0.05 per person treated, in a district-level programme carried out in India (Ramaiah and Das, 2004). Although the total cost of a MDA programme would be higher, because it requires coverage of the entire community rather than just school children, it should be remembered that those programmes that achieve high coverage of the entire population provide a population-wide benefit that would not result from a school-based deworming programme. Thus, in areas of co-endemicity where STH prevalence rates are not very high (less than 70%), albendazole used for LF control can serve as the single annual de-worming dose required for the target groups (de Silva et al., 2003b). In areas of high prevalence (>70%), one or two additional rounds of de-worming treatment with albendazole or another anthelminthic, may be required each year; this, however, is an issue that will require further testing in field studies, since there is little empirical data on the effect of LF control programmes in communities where STH prevalence rates are extremely high.

Care must be taken not to concentrate all resources for STH control in LF endemic areas alone. The more diffuse approach of piggy-backing STH control activities onto existing services, runs the risk of being overlooked while implementing time-limited LF control programmes. Those living in non-LF endemic areas must also gain the benefits of de-worming. Knowledge of pre-interventional levels of STH infections will help countries to allocate available resources in an optimal manner. This highlights the need for baseline assessment of STH infections in all ecological areas of the country, in addition to mapping of LF endemic areas, before commencement of a MDA programme.

In countries such as Nepal and Myanmar where school de-worming programmes have been started, the existing school infrastructure and schoolteachers are used to distribute anthelminthics and conduct health education (Khanal and Walgate, 2002). With proper timing and amalgamation of the two interventions, teachers already trained in de-worming can also be requested to help in drug distribution and supervision during MDA campaigns. Further, health education messages about LF can be built onto the component of health education on STH. In co-endemic areas where deworming programmes have not yet been launched, programme managers could use the filariasis programme to drive their de-worming, because albendazole is provided free to the Ministry of Health for the filariasis

programme, and the trigger for beginning MDA for filariasis is relatively low (1% infection level).

Monitoring and surveillance of drug efficacy must be built into operational programmes. As of now, no severe adverse events have been reported with co-administration of albendazole with DEC or ivermectin (Dunyo et al., 2000; Fox et al., 2005; Pani et al., 2002; Supali et al., 2002). Some have reported that addition of albendazole to DEC did not result in additional adverse reactions (Supali et al., 2002), but others have found systemic adverse reactions to be higher in children treated with DEC and albendazole, compared with those treated with albendazole or placebo alone (Fox et al., 2005).

Evaluating control programmes

It is vitally important that national control programmes should be evaluated scientifically, to demonstrate health benefits, as well as to assess cost-effectiveness. The principal issues to be considered in evaluating national helminth control programmes have been reviewed recently (Brooker et al., 2004). Targets need to be defined as precisely as possible, and the evaluation programme carefully designed to assess whether the defined aims have been reached. Targets may be based on indicators of infection (such as microfilaraemia rates for LF control, or infection intensities for STH infections) or on morbidity (e.g. anaemia in a hookworm control programme). Programme evaluation should aim to assess effectiveness (impact of the intervention in the context of programme-based evaluation) rather than to evaluate efficacy (benefits under ideal conditions such as in a randomized, double-blinded, placebo-controlled trial).

In addition to careful consideration of what is to be evaluated, similar thought must be given as to who should be evaluated. School children are the usual sentinel group in which the impact of de-worming programmes is evaluated, but with LF control, the whole community needs to be evaluated, because of the different age-specific epidemiology. Determining the appropriate sample size to detect a defined reduction in either intensity of infection or morbidity measures following treatment is also vitally important: samples that are too small may have insufficient power to detect a significant intervention effect, whereas excessively large sample sizes will waste resources. Mathematical models of transmission dynamics can provide valuable insight into the expected impact of a defined intervention (Brooker et al., 2004). Other issues that need consideration in designing an evaluation programme include the selection of study areas for evaluation, and how often to evaluate. Once again, knowledge of transmission dynamics of infection and disease is necessary, because the optimal interval between treatments must be determined by re-infection rates and bounce-back to pre-control worm burden after treatment.

We suggest that each country with co-endemic LF and STH sets up a national coordinating committee to consider all operational issues. Key members should include the focal points for both LF and STH, representatives from the National Task Force for Elimination of LF, and key public officials responsible for education, health education, and environmental sanitation. The existing National Task Force should be given a mandate to consider issues

relating to synchronization and spacing of Mass Drug Administration and de-worming, and to define areas of overlapping interventions.

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