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A COST-EFFECTIVENESS ANALYSIS OF ANTHELMINTHIC INTERVENTION FOR COMMUNITY CONTROL OF SOIL-TRANSMITTED HELMINTH INFECTION: LEVAMISOLE AND *ASCARIS LUMBRICOIDES*

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ABSTRACT: A study to compare effects of mass, targeted, and selective chemotherapy with levamisole as an intervention for the control of *Ascaris lumbricoides* was carried out in 3 communities in rural Oyo State, Nigeria. Selective treatment was applied in 1 village by treating the most heavily infected 20% of the inhabitants, targeted treatment in the second village involved children aged 2–15 yr, whereas mass treatment was offered to all inhabitants in the third village, excluding infants under 1 yr and pregnant women. Intensity (eggs per gram,) of *A. lumbricoides* infection was determined immediately before and 3 mo after the period of intervention as a means of assessing the relative efficacy of the treatment regimes. During the field study, information on resource use was also collected for a retrospective cost analysis of the 3 strategies. Resources used included manpower, materials, drugs, and transport. The results of the parasitological evaluation on the effect of treatment on egg intensity were then combined with the cost analysis to provide an overall measure of the cost-effectiveness of mass, targeted, and selective interventions. The results were expressed in terms of the cost per 1,000 egg reduction in intensity and the cost per person treated. The results showed the mass and targeted approach to be considerably more cost effective than the selective approach.

Soil-transmitted gastrointestinal nematodes infect in excess of 1 billion people per year. Recent research has focused upon their impact on host nutritional status (Stephenson, 1987), cognitive development (Nokes et al., 1992), and epidemiology (Anderson, 1986). As evidence accumulates about their public health significance, the need to design appropriate and cost-effective strategies for treatment and control increases. Despite the availability of safe, effective anthelminthics, control activities remain rare in developing countries largely because of costs (Walsh and Warren, 1979).

Control can be viewed in terms of long-term and short-term objectives (WHO, 1987). Long-term objectives, which would constitute a sustained reduction in prevalence and intensity of soil-transmitted helminths, involve the improvement of sanitary facilities, the provision of safe water supply, the promotion of personal and food hygiene through education, and the safe disposal of waste. In the short term, the objective of a control intervention would be the rapid reduction of morbidity and mortality. Community-based chemotherapy remains the principal way to achieve these short-term objectives (Davis, 1985). Repeated treatment ensures that even if rapid reinfection occurs, intensity is maintained below the level associated with morbidity (Savioli et al., 1992).

The crucial factor in community-based chemotherapy is the need for epidemiologically accurate information (Trainer, 1989). A community-based study was undertaken in 4 Nigerian villages to assess the relative efficacy of 3 chemotherapeutic regimes against common soil-transmitted helminths, with particular emphasis upon *Ascaris lumbricoides* (Asaolu et al., 1991). During this study, information on resource use was collected for a retrospective cost analysis and linked to effectiveness in order to compare alternative strategies of chemotherapeutic control against ascariasis.

MATERIALS AND METHODS

Village selection and intervention procedures

Four villages near the town of Ile-Ife, Nigeria were selected on the basis of similar socioeconomic profile and their cooperative residents (Asaolu et al., 1991). A campaign phase was instigated in order to explain the control program in each village and to secure cooperation. Subsequently, pretreatment fecal samples were collected from willing participants in village during January and February 1989 to assess the prevalence (%) and intensity (mean egg count ± SD) of soil-transmitted nematode infection. Intensity was assessed indirectly by counting eggs per gram (epg) of feces using the Kato–Katz procedure (WHO, 1985). Average pretreatment epg values for the 4 villages can be described as moderate according to WHO cut-offs for *A. lumbricoides* (WHO, 1987). Anthelminthic treatment with levamisole (Ketrax, CAPL/Lagos, Zeneca, U.K.) was provided to each intervention village at 3-mo intervals in March, June, September, and December 1989 according to the following procedures: (a) selective treatment was provided at Alakowe where the 20% most heavily infected individuals were treated; (b) targeted treatment was provided at Iyanfoworogi for all children aged from 2 to 15 yr, regardless of infection status; (c) mass treatment was provided at Akeredolu where willing residents were treated, but infants under the age of 1 yr and pregnant women were excluded; (d) Iloba village acted as a control, with no treatment. In March 1990, a post-treatment fecal sample was collected and mass treatment was then offered to all participants.

Statistical analysis

The difference between pretreatment and post-treatment mean parasitic intensity was assessed by means of paired *t*-tests on the log(x + 1) transformed data (epg of feces) for each village. Given the number of *t*-tests employed, the confidence level was adjusted and was set at the 99.7% level (Asaolu et al., 1991).

Calculation of costs

Manpower, materials, drugs, and transport were chosen as resources for study; information was enumerated and quantified during each stage of the treatment process for each village. Costs were retrospectively assigned to each item of resource use, thereby allowing a total program cost to be estimated for each of the 3 treatment villages. Valuation of

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TABLE I. Pretreatment and post-treatment intensity of *Ascaris lumbricoides* among the inhabitants of the study villages.

Village	n*	Pretreatment (mean epg ± SD)	Post-treatment (mean epg ± SD)	Paired *t*-value (*P* value)
Iloba (control)	288 (523)	7,542 ± 11,785	4,735 ± 8,137	0.62 $P \leq 0.5383$
Alakowe (selective)	185 (334)	6,775 ± 10,790	4,259 ± 2,579	1.63 $P \leq 0.1045$
Iyanfoworogi (targeted)	211 (445)	9,057 ± 15,797	2,579 ± 6,529	9.01 $P \leq 0.0001$
Akeredolu (mass)	224 (595)	11,906 ± 17,219	1,489 ± 5,165	12.97 $P \leq 0.0001$

* Number of individuals who provided pretreatment and post-treatment fecal samples. Numbers in brackets refer to population size of each village. Adapted from Asaolu et al. (1991).

resource use is in terms of Nigerian Naira, with more emphasis placed on comparative aspects of the analysis than on actual monetary values. This approach was adapted to adjust for the instability of the Nigerian currency and the difficulty of interpreting money values over time in a volatile exchange rate regime. Costs for the individual resources were calculated as follows. Labor costs were calculated for the time spent by a supervisor and a number of technicians, which ranged between 2 and 4 depending on the task and village involved. Transport costs were calculated for each visit based on vehicle hire, distance travelled, and the cost of petrol. Treatment costs in the villages were made up of the labor time of those administering the treatment and the cost of the drugs consumed. The calculation of the latter is based on the number of doses provided, multiplied by the cost of each tablet administered per dose. The cost of labor and consumables for laboratory analysis was estimated for the pretreatment phase for the selective village only.

Results of the the effect of treatment on egg intensity were combined with the cost analysis to give an overall cost-effectiveness measure for each of the 3 interventions. Results are expressed in terms of the cost per 1,000 epg reduction in intensity and the cost per person treated. The results are based on the number of people presenting for treatment who subsequently provided pre- and post-treatment samples. An intermediate measure of output was used to measure overall effectiveness. The focus is upon the relationship between treatment regime and reduction in epg of feces. The assumption is that there is a link between egg reduction and the subsequent quality of life of recipients of the treatment. Because more detailed information on the health impact of infection, in terms of their affect on quality of life, was not available, the derivation of a more complete output measure was not possible. This is the reason why this study, in common with other work in the area (Polderman, 1984; Prescott, 1987; Guyatt et al., 1993), is limited to a cost-effectiveness analysis.

RESULTS

Parasitological impact of the treatment strategies

An analysis of the impact of the 3 treatment regimes on helminth parasite intensity is given in detail by Asaolu et al. (1991). The most significant impact on post-treatment intensity of *A. lumbricoides* was found in the mass village, Akeredolu (Table I). In the targeted village, Iyanfoworogi, a significant reduction in the mean intensity of *A. lumbricoides* was also found within the community after treatment. A significant reduction in parasite intensity was observed in both the target group and in the untreated adults. Analysis revealed a highly significant reduction in the child age class ($t = 9.93$, $P \leq 0.0001$) (2–15 yr: n = 105) as expected, but in the adult age classes a significant reduction in intensity was also observed (7,742 ± 9,782 pretreatment versus 4,561 ± 8,798 post-treatment) ($t = 3.71$, $P \leq 0.0003$) (≥16 yr: n = 94) despite the fact that these individuals deliberately did not receive treatment. In contrast, in the village that received selective treatment, Alakowe, no significant reduction in intensity was observed in the village as a whole, although the selected individuals did show a significant reduction in intensity of infection.

It is unclear why a reduction in *Ascaris* intensity was observed in the control village, which received no anthelmintic treatment. In a subsequent study that compared the impact of different frequencies of targeted chemotherapy to Nigerian school-age children, a similar reduction in *Ascaris* intensities was also observed in the control village (Holland et al., 1996). An analysis was undertaken with regard to compliance by the villagers for fecal collection and its impact on the observed patterns. Compliance was found to vary from village to village. It was generally higher for the pretreatment sample and this trend was particularly pronounced for the control village. Furthermore, compliance was generally lower for the provision of both pre- and post-treatment samples and was lowest in the control village. This analysis indicates that subject compliance may also be a contributory factor to the unexplained reduction in *Ascaris* intensity in the control village after treatment in the present study.

Cost effectiveness of the treatment strategies

Costs for each stage of the treatment regime are shown in Table II. Mass treatment was found to be the most cost-effective regime on the basis of 1,000 egg reduction per g of feces (Table III). The targeted approach was also relatively cost effective, with a cost only slightly above that for mass. Selective treatment was judged to be the most expensive strategy under the conditions of this study. The differences among the 3 options are more obvious when the relative effectiveness of each treatment is compared using mass intervention as the base unit of comparison. For the number of people treated, the selective approach is over 17 times more expensive than mass treatment (Table III). Targeted treatment is only twice the cost per person treated relative to the mass approach. The cost-effectiveness results show that both mass and targeted chemotherapy are considerably more cost effective than the selective approach. These results closely mirror the effectiveness of the different interventions in terms of the parasitological findings shown in Table I.

TABLE II. The cost of each treatment regime.

Costs	Selective Alakaowe	Targeted Iyan-foworogi	Mass Akeredolu
Campaign phase, labor and transport	2,175.6	2,260.8	2,196.3
Sample collection, labor (distribution and collection)	627.8	627.8	627.8
Treatment			
Drugs	76.8	406.2	891.6
Labor	389.4	661.3	985.2
Pretreatment examination, consumables and labor	9,221.20	N/A	N/A
Total: Naira	12,490.80	3,956.10	4,700.90

TABLE III. Measures of cost effectiveness.

Effectiveness measures	Selective Alakowe	Targeted Iyan-foworogi	Mass Akeredolu
Total cost	12,490	3,956	4,701
Reduction (eggs per gram)	2,496	6,478	10,417
Number treated	36	194	455
Cost per 1,000 egg reduction per gram	5,004	611	451
Cost per person treated	347	20.4	10.3

DISCUSSION

Control of soil transmitted helminthiases in developing countries requires the deployment of scarce resources. Optimal choice of treatment strategy must be based on analysis of the financial costs of each type of intervention, as well as on public health significance. Although chemotherapy is recognized as a safe and highly effective method for initiating helminth control, the most effective form of treatment may be beyond the economic resources of developing countries. The design of more cost-effective methods of intervention remains an area of operational research.

Targeted treatment involves a group application whereby membership of the group may be defined by age, sex, religion, or other characteristics (Anderson, 1989). Age has been a particularly useful characteristic for selection, specifically 2–15-yr-old children who are found on average to harbor the heaviest infections of *A. lumbricoides* and *Trichuris trichiura* a pattern that has been reported worldwide (Anderson, 1986; Bundy, 1988: Asaolu et al., 1992). In the present study, the targeted approach was found to be effective in reducing intensity in the treated children but also in untreated adults. In addition, targeted chemotherapy was found to be almost as cost effective as mass chemotherapy and considerably cheaper than selective. The targeted approach carries other significant advantages, including the ease of reaching children through attendance at school (Stephenson et al., 1980), the reduced possibility of disrupting acquired immunity in the adult classes (Keymer and Pagal, 1990), and the avoidance of concern over teratogenic effects (Bundy and Cooper, 1989).

Selected chemotherapy has been defined as an individual application where selection is based upon the intensity of current or past infection (Anderson, 1989). Heavily infected individuals are selected on the basis of the aggregated distribution of worm numbers of *A. lumbricoides, T. trichuira,* and hookworms within a community. This pattern is well documented from many different populations, as is the observation that individuals are predisposed to harbor heavy or light infections of 4 helminth species (Keymer and Pagal, 1990). The selection of such individuals is based upon this assumption of predisposition to infection status, hence their subjection to repeated treatment without assessment of parasite status at each round of treatment. Theory (Anderson and Medley, 1985) indicates that such an approach could be effective in reducing intensity of infection in the community as a whole, but there are practical and other difficulties associated with this strategy (Keymer and Pagal, 1990; Asaolu et al., 1991). In particular, the selection of people for treatment is a time-consuming and expensive process. Findings from the present study indicate that compared to other forms of intervention selective treatment is an expensive option. In addition, selectivity may cause resentment, particularly in endemic communities where the need for treatment is a general perception.

Reduction in egg intensity is the measure of effectiveness used in this study. There are inherent difficulties in using egg counts as measures of change in intensity in treated individuals. The high variability in egg production coupled with our lack of precise understanding of their relationship with worm burden and hence as measures of morbidity make interpretation difficult. Practical considerations determine that they will continue to be used particularly in field-based evaluations of control strategies. The use of egg counts is an intermediate measure of output. For a more complete measurement, we would need to consider quality adjusted life year (QALY) indicators, which are concerned with both the quantity and quality of life gained as a result of a health care intervention. A number of different approaches can be used to elicit information about health status, including categorical scaling, time trade-off, and standard gamble methodologies. Unfortunately, general health classification systems (Rosser and Watts, 1972; Drummond et al., 1987) are unlikely to be suitable for measuring quality of life following the treatment of helminth infection in developing countries. Instead, program specific measures may be necessary in order to capture the particular morbidity patterns, and their impact on quality of life, associated with helminth infections (Guyatt and Evans, 1992). Information on health outcomes is generally scarce, partly because these infections have tended to be underestimated in terms of their public health significance.

There are difficulties in assessing morbidity associated with infection and, therefore, in being able to show quantitative improvements in quality of life after treatment (Guyatt and Evans, 1992). It is difficult to demonstrate that helminth infections contribute to large-scale economic losses. Endemic regions often lack the specific epidemiological information needed to identify high-risk groups and morbidity associated with heavy infections (Holland and Asaolu, 1990). Therefore, there have been few attempts to develop a QALY measure based on a disease of this sort (Prescott et al., 1984). The absence of good outcome measures has prevented analysts from being able to offer advice about the relative merits of alternative courses of action for the control of helminth infection (Mills, 1985). Reliance on intermediate measures of output, for want of a better alternative, has occurred. Where benefit evaluation has been attempted, the definition, measurement, and valuation of outcome are often so restricted or misspecified as to make interpretation difficult and meaningless (Dunlop, 1984). This has led to evaluation studies having had only a weak influence on the decisions of health officials and planners. The restrictiveness of the analysis, particularly in the absence of costings, provides the perfect excuse for government inaction in this area, leading to the general neglect of helminth control programs. More research is, therefore, urgently required on both costs and outcomes in the evaluation of helminth infections.

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