ROUTINE INTERMITTENT ANTHELMINTH THERAPY IN DISADVANTAGED POPULATIONS [PROTOCOL]

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BACKGROUND

Drawing on prevalence data from studies in developing countries, some authorities estimate that one third of the world's population is infected with one or more species of intestinal helminth (Warren 1993). Whilst these infections have occasional acute clinical effects, it is the impact on long term health status that is of particular concern to policy makers and health professionals. Helminth infections have been associated with malnutrition, anaemia, iron deficiency, poor performance at school, and absenteeism from school (Evans 1995). There have therefore been attempts since the 1920s to eradicate intestinal helminths from populations where they are endemic in order to improve nutrition and general health status, particularly in children.

The biological relationship between malnutrition and anaemia and helminth infection is consistent with our understanding of worm infections: they can interfere with food consumption by causing anorexia or nausea; decrease food absorption by increasing nutrient loss through vomiting and diarrhoea or decreasing the absorptive activity of the intestinal tract; and some helminths cause mild blood loss from the gut (Stephenson 1987). So it is credible that helminth infections actually cause both malnutrition and anaemia (Warren 1984). On the other hand, poverty is also closely linked to malnutrition and anaemia, particularly in children (Warren 1993). The association between poverty, anaemia and helminth infection could be important in assessing the effectiveness of interventions for two reasons.

-Eradication of worms will have little effect on malnutrition or anaemia if they are all independent consequences of poverty.

-The environmental and economic circumstances leading to endemic worm infection in the community could mean that the population will remain vulnerable to helminth infection, even if targeted drug programmes decrease them for a time.

Programmes designed to address the problem of intestinal helminths focus on two areas. The first aims to decrease transmission through a reduction in environmental excreta contamination. These programmes concern sanitation and handling of human waste. Such interventions require infrastructure investment, and can be costly, but result in a longer term reduction in the risk of infection. The second set of interventions aim to reduce human infections through chemotherapeutic treatment. The potential advantage is a rapid impact on infection, but the risk is of rapid re-infection of the treated population (WHO 1996).

Early combined and independent sanitation and drug treatment programmes aimed to eradicate intestinal helminths. Results of programmes implemented as early as 1913 indicated that this goal was unrealistic (Warren 1993, Cort 1922). These early attempts at helminth control were impaired by ineffective and/or toxic drugs and the difficulty in improving environmental conditions and sanitation especially in developing countries.

Continued research has provided effective, broad spectrum, single-dose chemotherapeutic agents that are relatively safe (Warren 1993). The difficulty in the design of programmes that use these agents relates to the rapid re-infection rates of treated individuals. The drugs eliminate the adult parasites, but without changes in sanitation and food handling, transmission of new infections is difficult to curtail. The problems of control are related to the difficulty in establishing long term programmes that integrate the use of chemotherapeutic agents and environmental and sanitation programmes. Results of such combined programmes implemented in Japan after the Second World War indicate that comprehensive programmes can be effective in controlling infection rates and transmission of infections. However, these programmes are time and resource intensive (Yokogawa 1985).

Current international anthelminth programmes focus on a chemotherapeutic approach. The programme designers use elaborate mathematical models based on prevalence and treatment studies in developing countries (Anderson 1991). These models indicate that infections are aggregated. That is, a small proportion of the population harbour a large proportion of the worm burden. Children commonly carry the heaviest worm burdens. These models also indicate re-infection patterns and have provided information for decision makers on the frequency of repeat treatment programmes.

Given these infection patterns and the availability of broad spectrum, effective and safe drugs, children are the target of chemotherapeutic control programmes advocated by the WHO (1990 and 1996). The aim of these programmes is to treat all children to reduce the worm and egg burdens. The secondary aim is to improve their nutritional status and cognition and learning (Nokes 1992, Stephenson 1993). Although studies have shown the effectiveness of available chemotherapeutic agents to decrease parasite rates, not all researchers agree that these treatment programmes have an impact on measures of nutritional status and cognition (Greenberg 1981, Lai 1995). Therefore, this treatment strategy needs to be examined by systematic review of the literature that uses nutritional status and cognition measures as outcomes of the assessment of effectiveness.

A second chemotherapeutic strategy utilised in the control of helminth infections is one in which entire populations or segments of populations are treated with intermittent drug therapy (Guyatt 1993). The goal of these programmes has been to decrease the prevalence and intensity of helminths in the overall population and interrupt the transmission cycle (Bundy 1990). Again mathematical models related to aggregation of infections have helped to direct these programmes. However, the effectiveness and long term impact of this strategy have not been examined.

The World Development Report (1993) highlighted population interventions for intestinal helminth control as a cost-effective way to improve health. With the increased emphasis on helminth control as a cost-effective public health intervention, funds and resources are being channelled into these programmes in a number of developing countries. The limited resource base in developing countries means that when funds are utilised in anthelminthic programmes, other programmes may be compromised.

The purpose of this review is to systematically examine the available evidence to assess the effectiveness of anthelminthic

chemotherapeutic programmes aimed at improving nutrition and learning in children; and those aimed at decreasing prevalence and intensity of infection within populations or communities.

OBJECTIVES

1. To determine the effectiveness of chemotherapeutic helminth therapy in children on their nutritional status and cognition.

2. To determine the effectiveness of chemotherapeutic helminth therapy, either given to the whole population or a targeted subgroup, on prevalence and intensity of intestinal helminths in that population.

Hypotheses tested:

1. Anthelminth chemotherapy treatments in children have no effect on nutritional status or cognition.

2. Anthelminth chemotherapy treatment of populations is not effective in decreasing helminth prevalence and intensity in that population.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All randomised controlled trials in which individuals or groups were treated with drug interventions for intestinal helminths. Trials which used pseudo-randomisation techniques or alternate allocation to treatment or control groups are also being considered.

Types of participants

Children who participated in chemotherapeutic control programmes.

Adults and children residing in areas where mass community chemotherapeutic treatment programmes were conducted.

Types of interventions

Chemotherapy treatment programmes for children within schools or communities.

Community-based chemotherapy programmes where mass treatment of the population or a subgroup of the population was carried out.

The review was limited to treatment with the most common drugs (mebendazole, piperazine, albendazole, levamisole, pyrantel, piperazine, praziquantel, niclosamide, bephenium, tetracholroethyline, thiabendazole, and ivermectin).

Types of outcome measures

Objective 1

Trials that reported on the treatment of children were included if they reported clinical outcomes such as, nutritional status, growth and development or measurements of cognition or learning. Data related to anaemia, iron deficiency and parasite measures (prevalence rates, worm and egg counts) were extracted if they were available in the study. Studies that reported only parasite measures were excluded from the review.

Abstracted data includes:

Laboratory markers:
Infection prevalence rates
Worm counts
Egg counts
Iron status including haemoglobin, serum ferritin, erythrocyte protoporphyrin
Vitamin A status

Anthropometric/nutrition measures:
Weight
Height
Body mass index
Arm circumference
Skin fold measures

Activity levels:

Cognition/learning measures:
Any test of cognition in children
School absenteeism

Objective 2

Trials that reported on community-based chemotherapeutic programmes were included if they reported parasite measures, other laboratory markers or clinical measures of nutritional status as listed above.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

The trials register of the Cochrane Infectious Diseases Group (CIDG) was searched for relevant trials. The topic terms used were Ancylostoma duodenale/Necator americanus, Ascaris lumbricoides, Enterobius vermicularis, Trichinella spiralis, Trichuris trichiura, hookworm, roundworm, pinworm, trichinosis and whipworm. Full details of the CIDG methods and the journals searched are published in The Cochrane Library in the section on "Collaborative Review Groups".

A second search strategy is being developed to cross check the first and will identify relevant work from nutrition-based studies.

The reviewers searched The Cochrane Controlled Trials Register, published on the Cochrane Library (Issue 2, 1997). This is a compilation of over 130,000 published trials identified by handsearching within The Cochrane Collaboration. Full details of the sources and methods used are published in The Cochrane Library.

MEDLINE was also searched (1966-present). The topic search terms were used in combination with the Cochrane highly sensitive search strategy for identifying trials. This strategy is outlined in The Cochrane Handbook, Appendix 5, Section 5.

Organisations and individuals working in the field will be contacted. A panel of individuals supporting this review and the external referees have checked the completeness of the search strategy and the efforts made to identify unpublished, ongoing and planned trials.

The reviewers will also draw on existing reviews of the topic and check the citations of all the trials identified by the above methods.

METHODS OF THE REVIEW

All identified trials are being entered in a trial register. The inclusion criteria are being independently applied to all trials by two reviewers. If disagreement occurs the review editor will be consulted and a consensus reached.

Quality assessment of included trials

The methodological quality of each trial is being independently assessed by two reviewers using the guidelines of the Cochrane Infectious Diseases Group. Trials will be classified according to allocation of concealment, generation of allocation sequence and inclusion of all randomised participants.

Data will be abstracted independently by two reviewers on to previously designed and tested data abstraction tables. Data will be double-checked and discrepancies settled through discussion.

Data analysis

For each outcome specified, a pooled estimate of treatment effect across the studies will be calculated (odds ratio for dichotomous outcomes, weighted mean difference for continuous outcomes). A chi-square test for homogeneity will be applied and if significant, possible causes of heterogeneity will be investigated.

Percentage reduction in egg counts and mean values of skewed data will be used with care, and a statistician (member of the review panel) will work with the reviewers at all stages of the review.

POTENTIAL CONFLICT OF INTEREST

None

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REFERENCES

Additional references

Anderson 1991
Anderson R, May R. Infectious diseases in humans: dynamics and control. :dynamics and control. Oxford, Oxford University Press; 1991.

Bundy 1990
Bundy D, Wong M, Lewis L, Horton J. Control of geohelminths by delivery of targeted chemotherapy through schools. Trans R Soc Trop Med Hyg 1990;84:115-120.

Cort 1922
Cort W. A graphic analysis of certain factors in hookworm control. Am Jour Trop Med 1922;2:449-63.

Evans 1995
Evans DB, Guyatt HL. The cost effectiveness of mass drug therapy for intestinal helminths. PharmacoEconomics 1995;8:14-22.

Greenberg 1981
Greenberg B, Gilman R, Schapiro H, Gilman J, Mondal G, Madsud M, Khatoon H, Chowdhury, J. Single dose piperazine therapy for

Ascaris lumbricoides: an unsuccessful method of promoting growth. Am J Clin Nutr 1981;34:2508-2516.

Guyatt 1993

Guyatt H. Bundy D, Evans D. A population dynamic approach to cost-effectiveness analysis of mass anthelmintic treatment: effects of treatment frequency on Ascaris infection. Tran R Soc Trop Med Hyg 1993;87:570-575.

Jamison 1993

Jamison D, Mosley W. Measham A, Bobadilla J. (eds). Disease control priorities in developing countries. :Oxford Medical Publications, 1993.

Lai 1995

Lai K, Kaur H, Mathias R, Ow-Yang C. Ascaris and trichuris do not contribute to growth retardation in primary school children. Southeast Asian J Trop Med Public Health 1995;26(2):322-328.

Nokes 1992

Nokes C, Grantham-McGregor S, Sawyer A, Cooper E, Bundy S. Parasitic helminth infection and cognitive function in school children. Proc R London B 1992;247:77-81.

Stephenson 1987

Stephenson L. The impact of helminth infections on human nutrition. ;1987.

Stephenson 1993

Stephenson L, Latham M, Adams E, Kinoti S, Pertet A. Physical fitness, growth and appetite of Kenyan school boys with hookworm, Trichuris trichiura and Ascaris lumbricoides infections are improved four months after a single dose of albendazole. J of Nutr 1993;123(6):1036-1046.

WHO 1990

WHO. Informal consultation on intestinal helminth infections. WHO/CDS/IPI/90.

WHO 1996

WHO. Report of the WHO informal consultation on the use of chemotherapy for the control of morbidity due to soil-transmitted nematodes in humans. WHO/CTD/SIP/96.

Warren 1984

Warren K , Mahmoud A. Tropical and geographical medicine.

Warren 1993

Warren K, Bundy DAP, Anderson R, Davis AR, Henderson DA, Jamison DT, Prescott N, Senft A. Helminth Infection in Jamison DT, Mosley W, Measham A, Bobadilla J.(eds). Disease control priorities in developing countries. :Oxford Medical Publications, 1993.

World Bank 1993

World Development Report 1993: Investing in health. :Oxford University Press, 1993.

Yokogawa 1985

Yokogawa M. JOICFP's experience in the control of ascariasis within an integrated programme. In Crompton DWT, Neisheim MC, Pawlowski ZS. Ascariasis and its public health significance. :265-78.