

Foreword

In the following INCLLEN monograph, Dr. Shally Awasthi, an Indian pediatrician working with the INCLLEN Clinical Epidemiology Unit at King George's Medical College, Lucknow, India, has devised an inexpensive and highly effective strategy for addressing the problem of childhood worm infestation. Dr. Awasthi and her collaborators designed a study to measure the impact on preschool children's weight gain of a regular dose of albendazole given each six months. Albendazole, a known effective treatment for worm infestation in school age children, was given to preschool children, under 5 years of age, in conjunction with the Indian Government's regular program of bi-annual Vitamin A supplements for children. The results of the 1994-95 study are very encouraging, and justify the need for a simple, large community trial to identify an effective, low-cost treatment for a health problem that afflicts more than one third of the world's population, and as many as 160 million people in India alone.

Robert Fletcher, MD
(Chairman of the Board)
Harvard Medical School
Boston, Massachusetts

Claire Bombardier, MD
Faculty of Medicine
University of Toronto
Toronto, Canada

David William Fraser, MD
International Health Consultant
Yardley, Pennsylvania

Julio Frenk, MD, PhD
Fundacion Mexicana para la Salud
Mexico City, Mexico

Ronald Gebert, MD
Universidad de la Frontera
Temuco, Chile

Joyce C. Lashof, MD
Dean Emerita
School of Public Health
Univ. of Calif. at Berkeley

James McCord
President
OACIS Health Care Systems
Greenbrae, California

Charas Suwanwela, MD
Chulalongkorn University
Bangkok, Thailand

Arturo Morillo, MD
(ex-officio)
Executive Director
INCLLEN

Shelly Kessler
(Secretary to the Board) (ex-officio)
Deputy Executive Director
INCLLEN

INCLLEN, INC. EXECUTIVE OFFICE 3600 MARKET STREET SUITE 380 PHILADELPHIA PA 19104-2644 USA
PHONE: 215.222.7700 FAX: 215.222.7741 EMAIL: INCLLEN@MCIMAIL.COM

CONTROLLING PARASITIC INFESTATION IN CHILDREN UNDER FIVE YEARS OF AGE: GIVING ALBENDAZOLE IN CONJUNCTION WITH AN INDIAN GOVERNMENT VITAMIN A SUPPLEMENT PROGRAM

Shally Awasthi, M.D.¹, Richard Peto², Robert Fletcher, M.D.³, Henry Glick⁴

Introduction

It is estimated that more than one third of the world's population is infected with one or several species of parasitic worms.¹ Ten years ago, it was estimated that in India alone, there were 160 million cases each of ascariasis and hookworm infection.¹ The consequences of such infections include, among a number of symptoms, malnutrition and anemia.^{1,2} For children, these consequences can be especially devastating. Children typically become infected after weaning has begun, around the age of six months. By the time children reach school age, helminths are the leading cause of illness in countries like India.³ The critical period for the incidence of malnutrition, especially in regard to physical development and growth, is between six months and twenty-four months of age. Unfortunately, this is the time period when most infections begin.

The most critical period then, in terms of early childhood development, to prevent malnutrition, and thereby reduce malnutrition related mortality, is in the preschool age group. The hypothesis of this study is that administering a single 400 mg dose of albendazole, in syrup form, through the existing Indian health care delivery system, is a practical and effective way to achieve mass deworming of preschool children. The albendazole can accompany the pre-existing, UNICEF, Vitamin A dosage schedule that begins at nine months of age, and is repeated every six months for preschool children. A logical extension of this hypothesis is that this treatment with albendazole will result in a demonstrable improvement in the nutritional status of preschool

¹ Department of Pediatrics, King George's Medical College, Lucknow, India.

² Department of Clinical Medicine, Nuffield College, Oxford University, UK.

³ Department of Ambulatory Care & Prevention, Harvard University Medical School, Boston, USA.

⁴ Department of Biostatistics & Clinical Epidemiology, University of Pennsylvania, Philadelphia, USA.

children. Specifically, the impact of two doses of albendazole, given at six month intervals, will be studied to measure the impact on weight gain in children at this critical stage in their development.

The Study

The site of this study was fifty urban slums, chosen at random from 203 slums in and around Lucknow, India. All of the children residing in the chosen slums and under five years of age were included in this study, a total of 4003 children, after obtaining written consent from their parents. The age of the children, in months and years, was noted from the register maintained by the slum health worker and the date of birth, correct to the nearest month, was then confirmed while interviewing the mothers.

Data was collected on the age, sex, history of passage of worms in the preceding six months, and any history of hospitalization for respiratory or diarrheal diseases in the preceding six months. The weight of each child was measured in kilograms to the nearest one hundred grams and the standing height was measured in centimeters to the nearest millimeter. The main outcome measure was weight gain in one year's time. The purpose of the weight measurement of the first visit was to establish a base line weight or value for each child. The weight measurement at the second visit was to study the effect of one dose of albendazole, and the measurement during the third visit was to study the effect of two doses of albendazole. A third dose of albendazole has been given, and its effects are yet to be studied.

Weight gain, during the year long study period, between the first and third visits, was compared in all of the six age categories. The fact that at the beginning of the study, some of the children were underweight and some were not, was factored into the measurement of weight gain in all of the six age categories. Based on the fact that the critical period for malnutrition is in the first two years of life⁴, the children in the study were placed into two groups: those two years of age or less and those more than two years of age. The group of children who received albendazole was also studied to determine whether or not each six month deworming was effective, and whether a second dose was really required.

The Results

In the study, 1996 children received only the dose of Vitamin A, while 2007 received doses of both Vitamin A and albendazole. There were equal proportions of girls and boys in each of the two groups. There were equal proportions of each sex in each age category for the study: children under one year of age, children one to two years of age, children two to three years of age, children three to four years of age, and children four to five years of age.

Compared with children who received only Vitamin A, children who received albendazole had 25% greater weight gain in one year's time. This difference was obvious after the first six months and was maintained at the end of one year of follow up study. Critical to the importance of this study was the fact that the significant difference in weight gain in each group was maintained after controlling for

differences in weight of the children at the beginning of the study, and for a number of other variables present in the study. After six months, the relative weight gain for the albendazole group was 10.2%, and for the children who received only Vitamin A, the gain was 6.9%. After twelve months, the relative weight gains for the albendazole and Vitamin A groups were 19.1% and 14.8% respectively. It was also noted that each dose of albendazole was effective in deworming the children in the study, and that the prevalence of worm infestation increased with the age of the children, the evidence for this being a greater proportion of children passing worms with each successive dose of albendazole.

Summary

By the time they are five years of age, two-thirds of Indian children are stunted by conventional standards.⁵ In this study, 61.2% of the children were found to be stunted by these same standards. Intestinal helminthic infestation begins in preschool age children. Of the Lucknow preschool children who participated in this study, 15.4% were infected with worms at the beginning of the study. These worms were most likely ascaris, one of the two most widely prevalent geohelminths, the other being hookworm. The peak incidence of ascaris is between the ages of one to six years.

Worm infested children are prone to protein energy malnutrition, manifesting as underweight, stunting, and wasting.^{1,2,6,7} The World Bank notes that by the time children go to school, helminths are the leading cause of childhood disability. In addition to malnutrition and anemia, studies have shown that worm-infested children do worse in cognitive function tests when compared to their uninfested school age counterparts.^{8,9} When children are dewormed there is a marked improvement in physical fitness, growth and cognitive functioning.^{10,11}

Improvements in sanitation and water supply will greatly reduce worm infestation in all developing countries. But these kinds of improvements are contingent upon economic growth and a political commitment to address these problems. In lieu of these preconditions, the next best strategy for reducing worm infestation is drug therapy. In fact, well targeted mass chemotherapy can now be shown to be a practical, cost-effective strategy.

Albendazole has been shown to be effective in school-based deworming programs, with the primary measure of effectiveness being weight gain. We can now demonstrate that using albendazole in preschool age children can be of critical value for child survival and ensuring normal development growth. Weight gain is an important indicator of normal child development and good health, however, weight gain is of greater importance to preschool children than for school age children, as there is a direct correlation between mortality and weight. The relative risk of death from common childhood diseases is doubled in a mildly malnourished child, tripled for a moderately malnourished child, and increases by more than ten times for a

severely malnourished child. Remarkably, 80% of the deaths in children under five years of age occur in those who are only mildly malnourished. Hence, the importance of controlling worm infestations, which can rob a child of badly needed nutrients, can be easily seen.

Administering 400 milligrams of albendazole every six months, in coordination with the pre-existent Vitamin A program and necessitating no increase in the existing Indian health care infrastructure, is an effective way of improving the nutritional status of preschool children. A subsequent study will measure the effect of albendazole on maintaining weight gain and in reducing all causes of child mortality.

References

1. Warren, KS, Bundy DAP, Anderson RM, Davis AR, Henderson DA, Jamison DT, Prescott N, Senft A. "Helminthic Infections." In *Disease Control Priorities in Developing Countries*. Eds. Jamison DT, Mosley WH, Meashom AR, Bobadilla JL. Oxford University Press, New York, 1993, 131-160.
2. Kazura JW, Mahm AAF. "Intestinal Nematodes." In *Nelson's Textbook of Pediatrics*. Eds. Behrman RE, Kliegman RM, Nelson WE, Vaughan VC. 14th Edition, WB Saunders Co., Philadelphia, Pa. 1992, 896-899.
3. *World Development Report 1993: Investing in Health*. N.Y.U. Press, 204-222.
4. *Newsletter of the Survival of Women and Children (SWACH) Foundation*, Volume III, July, 1994.
5. Grant JP. *The State of the World's Children, 1994*. UNICEF, Oxford University Press.
6. Egger RJ, Hofhuis EWH, Bloen MW, Chusilp K, Wedel M, Intrakhao C, et. al. "Association between intestinal parasites and nutritional status in 3-8 years old in northeast Thailand." *Trop Geogr Med*, 1990, 42: 312-323.
7. WHO Expert Committee. "Public health significance of intestinal parasitic infections." *Bulletin of the World Health Organization*, 1987; 65: 575-588.
8. Nokes C, Grantham McGregor SM, Sawyer AW, Cooper, et. al. "Parasitic helminth infection and cognitive function in school children." *Proc R Soc Lon B*, 1992; 247: 77-81.
9. Kvalsvig JD, Cooppan RM, Connolly KL. "The effects of parasite infections on cognitive processes in children." *Ann Trop Med Parasitol*, 1991; 85: 551-568.
10. Stephenson LS, Latham MC, Adams EJ, Kinoti SN, Peter A. "Physical fitness, growth and appetite of Kenyan school boys with hookworm, *trichuris trachyris* and *ascaris lumbricoid* infections are improved four months after a single dose of albendazole." *J Nutrition*, 1993; 123: 1038-1046.
11. Stephenson LS, Latham MC, Adams EJ, Kinoti SN, Perter A. "Weight gain of Kenyan school children infected with hookworm, *trichuris trachyris* and *ascaris lumbricoid* following once or twice yearly with albendazole." *J Nutrition*, 1993; 123: 656-665.