INTESTINAL GEOHELMINTHIASIS AND GROWTH IN PRE-ADOLESCENT PRIMARY SCHOOL CHILDREN IN NORTHEASTERN PENINSULAR MALAYSIA

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Abstract. A cohort of one hundred 8-9 year old school children in Northeastern Peninsular Malaysia underwent stool examination, weight and height measurements. Seventy-three children were infected with *Ascaris lumbricoides* and/or *Trichuris trichiura*. All infected children were treated with albendazole at baseline, 6 months and 9 months. Measurements were repeated on all but 2 children at 1 year. Repeat stool examination (n = 94) at 1 year revealed a marked reduction in the level of *Ascaris* infection and a modest reduction in *Trichuris* infection. There was no difference in net growth between treated children and uninfected controls. Post-hoc analysis by gender however revealed that infected girls (n = 33) experienced significantly higher increments in weight, height and weight for age. Furthermore, children found to be infected at baseline level but worm free at follow-up, were observed to have experienced greater increments in height and height for age. The evidence suggests that periodic antihelminthic treatment may have a positive effect on the growth of subsets of pre-adolescent children but it is emphasised that further work is required to validate these findings.

INTRODUCTION

It is estimated that the global prevalence of human infection with the intestinal geohelminths *Ascaris lumbricoides* and *Trichuris trichiura* is more than a billion (Warren *et al*, 1993). A significant proportion of those infected are children of primary school going age, despite which published studies on the effect of infection on growth are relatively few in number and from a geographical point of view have focused on only a few population groups (Stephenson *et al*, 1989; 1993a; 1993b; Adams *et al*, 1994; Thein-Hlaing *et al*, 1991; Simeon *et al*, 1994; Lai *et al*, 1995; Watkins and Pollit, 1996; Hadju *et al*, 1996; Koroma *et al*, 1996). The reported studies on the effect of antihelminthic treatment on growth parameters of primary school children have yielded divergent findings which may have resulted from variations in the spectrum and intensity of helminthiasis as well as confounding factors such as the prevailing levels of malnutrition, age characteristics of the children studied and a myriad of other socio-economic factors. Cross-sectional and longitudinal observations of two cohorts of primary school children in Northeastern Peninsular Malaysia, revealed a reasonably consistent association between ascariasis, particularly heavy *Ascaris* infection and growth stunting (Mahendra Raj *et al*, 1997). A longitudinal interventional study was conducted on one of these cohorts to determine if the relationship between helminthiasis and growth impairment was more than incidental. While it is acknowledged that a randomized double blind placebo controlled treatment study would have been the ideal design for a study of this nature, there were reservations on the acceptability of such a design to the community. All helminth infected children were therefore treated and uninfected children served as a compromise control group. The design was based on the assumption that if helminthiasis was an important determinant of growth, removal of the infection would result in some degree of "catch-up growth" in the infected group (Tanner, 1981).

METHODS

The study cohort consisted of 100 children attending the third grade of Tawang primary school on the outskirts of Kota Bharu which is the major town in the state of Kelantan in Northeastern Peninsular Malaysia. Small scale agriculture is the main economic activity of the area. The cohort were the subject of a previous study on helminthiasis and had last received a round of anti-helminth treatment

17 months previously. Stool specimens were examined for helminth eggs at baseline and at 1 year and quantified by a modified Stoll count (Garcia and Bruckner, 1988). Height and weight were also measured at baseline and at 1 year. Measurements were taken in school uniform without shoes using a stadiometer and platform health weighing scales. The accuracy of the measurement devices were checked periodically with standard weights and lengths. Although the graduations on the scales were 0.5 cm and 0.5 kg respectively, the observer was asked to record to the nearest 0.1 cm and 0.1 kg, respectively. Despite the need for a degree of estimation, the coefficients of variation between 2 independent observers were in the order of 0.1-0.2% for both height and weight measurements. Infected children were treated with single supervised 400 mg doses of albendazole at baseline, 6, and 9 months. Weight for age (WA), height for age (HA), and weight for height (WH) were expressed as percentages of the median reference values and computed using the Epilnfo version 6 software package (CDC, Atlanta, USA and WHO, Geneva, Switzerland), which is based on reference curves developed by the National Center for Health Statistics (NCHS) and Centers for Disease Control (CDC), USA.

Ethical approval was granted by the Research and Ethics Committee of the School of Medical Sciences, University Science Malaysia and informed parental consent was obtained for all children.

Statistical analysis

Quartile deviation (QD) was used to indicate the degree of dispersion if the distribution was skewed. Non-parametric statistical tests were generally used and computed with the aid of Epilnfo version 6 (CDC, Atlanta, USA and WHO, Geneva, Switzerland). The worm negative control group was compared separately against the worm positive group and against the subset of children with heavy *Ascaris* infection.

RESULTS

Demographic data, infection prevalence rates and intensities.

Seventy-three children were infected with either *Ascaris lumbricoides* or *Trichuris trichiura*, all of whom were treated. Sixteen children had heavy *Ascaris* infection as defined by a count of more than 50,000 eggs per gram (*epg*) of feces. Hookworm infection was absent. The worm positive group (n= 73) was comparable to the worm negative control group (n = 27) in terms of age and sex ration (Table 1). Mean age of the heavy *Ascaris* subset was marginally but statistically significantly higher than controls. Follow-up measurements were available on all but two children. Six children did not hand in follow-up stool samples. As Table 1 illustrates, the *Ascaris* burden had been considerably reduced by the end of 1 year. The reduction in the level of *Trichuris* infection was less substantial. The prevalence and intensity of *Trichuris* infection remained significantly higher in the treated group at follow-up.

Weight and height in relation to baseline infection status

Twenty percent (20/100) of all children were below 90% height for age. None were below 80% weight for height. Table 2 summarizes the data on nutritional indices at baseline and at follow-up in relation to the baseline infection status. Children with heavy *Ascaris* infection were clearly of shorter stature and lighter than controls both at baseline and at follow-up. Although increments of weight for age and weight for height were greater in the infected groups than worm negative controls, the differences were someway from being statisically significant (Table 2). There was clearly no difference in linear growth between infected and uninfected groups. Regression analysis revealed no correlation between baseline worm intensities and increments in any of the growth indices used; nor was there any correlation between fall in egg counts and change in growth indices ($R < 0.1$, $p > 0.05$). Repeat analysis after log transformation of egg counts did not improve the correlation coefficients.

Post hoc analysis

Analysis by gender revealed divergent results. As Table 3 shows, infected girls (n = 33) experienced greater increments in weight, height and weight for age when compared to uninfected girls and infected boys. Infected boys and girls had

Table 1

Demographic data, infection rates and intensities.

Baseline status	Worm negative (controls)	Worm positive	Heavy *Ascaris* subset
No. of children[a]	27	73	16
Mean age (SD) years	9.0 (0.3)	9.1 (0.3)	9.3 (0.3)[c]
Gender, % boys	54	53	50
Prevalence rate, (%):			
Ascaris -baseline	-	56/73 (77)	16/16 (100)
Ascaris -final	9/26 (35)	11/68 (16)	3/16 (19)
Trichuris -baseline	-	56/73 (77)	14/16 (88)
Trichuris -final	6/26 (23)	37/68 (54)	14/16 (88)
Intensity[b]:			
Ascaris -baseline	-	17.0 (22.1)	71 (16.6)
Ascaris -final	0.0 (1.0)	0.0 (0.0)	0.0 (0.0)
Trichuris -baseline	-	1.2 (1.9)	3.6 (3.0)
Trichuris -final	0.0 (0.0)	0.4 (1.8)	3.7 (2.7)

[a] Follow-up stools unavailable from 6 children
[b] Median (Quartile deviation in parentheses), eggs per gram $\times 10^3$
[c] Significantly higher than control group ($p = 0.05$)

similar levels of infection at baseline (data not shown). Subset analysis was also done in relation to final infection status and is summarized in Table 4. Children who were infected at baseline but worm free at follow-up (n = 27) fared the best particularly in terms of increments in height and height for age (Table 3). The median baseline *Ascaris* intensity of this group was 12,800 *epg* (QD 0.8) and the median *Trichuris* intensity was 800 *epg* (QD 1.2). The median baseline height for age of this subset was similar to the group of children who were worm negative at both evaluation points but was somewhat higher than that of children who were found to be infected at follow-up (data not shown).

DISCUSSION

Treatment essentially resulted in a marked reduction in the *Ascaris* load in treated children and a modest reduction in *Trichuris* infection. The limitations of the non-randomization design notwithstanding, a number of trends emerge. When the cohort was considered as a whole there was no detectable benefit of antihelminth treatment on growth rates. The possibility cannot be excluded that the period of study was not long enough to detect the beneficial effects of treatment. In a large study from Myanmar (Thein-Hlaing *et al*, 1991) it took 18 months to detect again in height and 2 years to detect a gain in weight among 6-10 years old. Previous observations in Northeastern Peninsular Malaysia showed a consistent association between heavy ascariasis and relative stunting (Mahendra Raj *et al*, 1997). Treatment of this group did not result in any appreciable reduction in the growth deficits except perhaps for a trend towards an improvement in weight for height (Table 2). It could equally be argued that there was at least no deterioration in the growth indices of this subset compared to controls. It has to be noted also that the level of *Trichuris* infection in the subset at follow-up had hardly changed from the pre-treatment level (Table 1).

Table 2

Weight and height at baseline and at follow-up in relation to baseline infection status.

Baseline status	Worm negative (controls)	Worm positive	p-value[c]	Heavy *Ascaris* subset	p-value[d]
No. of children[a]	27	73		16	
WA:					
baseline[b]	82.8 (7.2)	80.6 (6.3)	0.25	72.3 (5.2)	0.007
final[b]	81.7 (6.3)	80.7 (6.8)	0.58	73.4 (6.0)	0.02
HA:					
baseline[b]	94.0 (1.7)	93.2 (2.7)	0.64	90.3 (2.3)	0.03
final[b]	94.1 (1.7)	93.5 (2.5)	0.52	91.2 (1.6)	0.03
WH:					
baseline[b]	97.0 (8.2)	96.1 (4.4)	0.48	94.0 (4.2)	0.17
final[b]	96.4 (5.4)	97.5 (4.6)	0.64	96.0 (3.0)	0.76
δWA[b]	- 0.6 (1.9)	0.1 (2.3)	0.24	0.4 (2.0)	0.41
δHA[b]	0.3 (0.5)	0.3 (0.6)	0.50	0.2 (0.7)	0.87
δWH[b]	-0.1 (2.4)	1.0 (3.4)	0.13	2.4 (2.9)	0.15
δwt, kg[b]	2.5 (0.5)	2.8 (1.0)	0.44	2.9 (0.8)	0.93
δht, cm[b]	5.2 (0.5)	5.4 (0.9)	0.61	5.1 (0.8)	0.93

WA = weight for age, HA = height for age.
WH = weight for height.
wt = weight, ht = height.
δ denotes increase in the parameter between baseline and 1 year follow-up.
[a] Follow-up measurements not done on 2 children
[b] Median (quartile deviation in parentheses), %
[c] Worm positive group compared to controls
[d] Heavy *Ascaris* subset compared to controls

Table 3

Change in nutritional indices in relation to baseline infection status and gender.

	Girls		Boys		
Baseline status	Worm negative n = 13	Worm positive n = 33	Worm negative n =13	Worm positive n = 39	p-value
δWA[a]	-1.8 (1.0)	1.0 (2.3)	0.9 (0.9)	-0.4 (2.1)	0.05
δHA[a]	-0.2 (0.5)	0.3 (0.7)	0.4 (0.3)	0.3 (0.3)	0.60
δWH[a]	-1.4 (2.0)	1.4 (3.9)	1.1 (2.6)	0.8 (2.3)	0.21
δwt, kg	2.6 (0.5)	3.4 (0.9)	2.5 (0.4)	2.2 (0.6)	0.01
δht, cm	5.1 (0.5)	6.1 (0.8)	5.3 (0.4)	5.0 (0.6)	0.01

[a] Median (quartile deviation in parentheses), %
δWA = increase in weight for age between baseline and follow-up
δHA = increase in height for age between baseline and follow-up
δWH = increase in weight for height between baseline and follow-up
δwt = increase in wight between baseline and follow-up
δht = increase in height between baseline and follow-up

Table 4

Change in nutritional indices in relation to baseline and follow-up infection status.

Baseline status	Worm positive		Worm negative		
Follow-up status	negative n = 28	positive n = 39	negative n =15	positive n = 11	p-value
δWA[a]	0.6 (3.4)	0.1 (1.9)	-1.2 (1.9)	0.4 (2.2)	0.31
δHA[a]	0.6 (0.7)	0.3 (0.6)	-0.1 (0.5)	0.5 (0.3)	0.02
δWH[a]	0.3 (3.0)	2.0 (3.0)	-0.1 (1.9)	1.2 (3.1)	0.23
δwt, kg	3.0 (1.5)	2.5 (0.8)	2.4 (0.5)	2.5 (0.8)	0.26
δht, cm	6.1 (0.8)	5.1 (0.6)	5.1 (0.5)	5.5 (0.8)	0.005

[a] Median (quartile deviation in parentheses), %
δWA = increase in weight for age between baseline and follow-up
δHA = increase in height for age between baseline and follow-up
δWH = increase in weight for height between baseline and follow-up
δwt = increase in weight between baseline and follow-up
δht = increase in height between baseline and follow-up

While post hoc analyses should always be interpreted with caution, they may provide some insight and cannot be entirely ignored. The finding that infected girls experienced greater increments in weight, height and weight for age is intriguing and may relate to complex socio-cultural as well as pathophysiological factors. It is conceivable that deworming girls during the phase of the pre-adolescent growth spurt accentuates the beneficial effect. No less intriguing is the observation that the rate of linear growth was highest in the subset of infected children who were worm free at follow-up. This may have been as much due to efficacy of treatment as to the possibility that the subset represented a more advantaged group to begin with and were subjected to less exposure not only to recurrent worm infections but also to other associated adverse factors. It is plausible that removal of even moderate levels of infection in the absence of other adverse factors permits a degree of growth acceleration. While some of the trends appear at first sight contradictory, they fit with the unifying hypothesis that helminthiasis exerts a modest independent effect on growth. If it was a major determinant, a significant effect would have been detected on analysis of the group as a whole and the subset with the heaviest intensity of infection would have been expected to benefit most. Conversely, if helminthiasis had no effect whatsoever on growth, it would be difficult to explain the positive effect observed in certain subsets. Further work is obviously required to validate the findings of this study.

In summary, the results of this study undertaken in Northeastern Peninsular Malaysia, suggest that periodic antihelminthic treatment may have a beneficial effect on the growth of certain subsets of pre-adolescent school children; findings which clearly require confirmation by repeated interventional studies.

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