Original Article

Six−monthly De−worming in Infants to Study Effects on Growth

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Abstract. Objective : The study was conducted to assess the effectiveness of six monthly albendazole (ABZ) for improving the weight and height of preschool children when initia ted at 0.5−1 year of age in populations with a high transmission rate of intestinal roundworm, Ascaris lumbricoides. It was a cluster randomized trial in the urban slums of Lucknow, North India. Methods : Control children received 2 ml (1 ml to infants) of Vitamin A every six month whereas those in the ABZ areas received, in addition, 400 mg of ABZ suspension (Zentel, SKB) every six month. Sixty−three and sixty−one slum areas were randomized to albendazole (ABZ) or to control groups, respectively. Children aged 0.5−1 year were recruited in April 1996 and followed up for 1.5 years. Of 1022 children recruited from control and 988 from ABZ areas, the loss to follow−up at 1.5 year was 15.6% and 14.6% respectively. Mean (± SE) weight gain in Kg in control versus ABZ areas was 3.04 (0.03) versus 3.22 (0.03), (p=0.01). Results : After controlling for the presence of weight−for age z−score <−2.00 at enrollment in the ordinary least square's regression model, the extra weight gain in 1.5 years in those who received ABZ plus vitamin A was 0.13 Kg (95% CI: 0.004 to 0.26 Kg., p value=0.043) when compared to those who received only vitamin A; underweight children at enrollment benefiting more than the normal ones. Conclusion : It was concluded that there was an improvement in weight with six monthly ABZ over 1.5 years. However, a much larger trial would be needed to determine whether there is any net effect of improvement in weight on under five mortality rate. [Indian J Pediatr 2001; 68 (9) : −827]

Key words : *De−worming; Albendazole; Growth; Underweight; Infant*

It has been estimated that more than one third of the world population is infected with one or several species of parasitic worms.1 One decade ago, it was estimated that in the Indian subcontinent, there were 160 million cases of ascariasis and hookworm infestation each.1 The consequences of such infestations are malnutrition and anemia.1,2 Infestation in children begins from the time weaning is started, around the age of six months, and by the time they reach the school going age, helminths are the leading cause of disability3. Several studies have also reported association between low vitamin A intake and impaired growth4,5. Decreased absorption of vitamin A has been reported in enteric as well as other infections6,7. A few randomized controlled trials have shown improvement in ponderal and linear growth,8,9 but others have shown no association10. Concomitant administration of vitamin A and deworming results in increased vitamin A absorption and serum retinol levels11. Thus, vitamin A deficiency as well as worm infestation are both associated with malnutrition. The critical period to tackle malnutrition, and thereby reduce malnutrition related mortality, is in the preschool age group. Our study hypothesis was that albendazole administration six monthly, as a single 400 mg dose in syrup, could be linked with the six monthly vitamin A administration and may result in improvement in the nutritional status of the children. The objective was to study the impact of four doses of albendazole and vitamin A administration between 6−12 months of age on weight gain after 1.5 years. **Materials and Methods** The study was conducted in the slums where an anganwadi centers (AWC) was established under the Integrated Child Development Services (ICDS) Scheme in urban Lucknow, North India. The population of such slums is of about 1000, which includes about 100 children less than 5 years of age. The crude birth rate is 30.13 The family income is below the proverty line and there are suboptimal living conditions. The AWC is a small room within the slum and an anganwadi worker (AWW) is appointed for each AWC. The primary job responsibilities of the AWW are to run a creche and provide primary health care and supplementary nutrition for children less than six years of age and pregnant and lactating women. She also maintains a survey register on the entire population with their ages.

This study was a randomized, community based trial. Cluster randomization was done to have about 60 slums, with about 15 children, aged 0.5−1year, within each cluster, in each arm. From 200 slums with a functional AWC in urban Lucknow, 124 were randomized to receive either vitamin A (100,000 unitis) alone or albendazole (400 mg suspension) and vitamin A (100,000 units) every six

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mg suspension) and vitamin A (100,000 units) every six months for 1.5 years. Included were children living in the slum area designated for the AWC and whose age was between 0.5−1 years only, with written and informed consent of the parents. The children were given vitamin A as well as albendazole from 6 months of age.

The slums were visited by the project teams, eligible children identified and their homes marked in a map of the slum prepared by the staff. The field staff had master's degree in social work. They were supervised by a retired, registered nurse. The supervisor validated 15% of the data collected by the field staff within one week. The author (VKP) independently validated 5% of all the data collected within 3 days. Date of birth was abstracted from the register maintained by the AWW and reconfirmed by asking the mother. At enrollment, in a few randomly selected slums within the two groups, stool examination was done by direct fecal smear examination.14 History of passage of roundworms in the preceding six months before enrollment or between 2 consecutive visits was asked from the mother. The weight and height were measured at enrollment and thereafter for every six months. Each child was given the intervention after the measurements were taken. Death was noted among the children.

The project team trained to measure weight and height and the inter−observer and intra−observer coefficient of variation was of less than 5%. For those who could not stand, lying down weight was measured on a Braun infant weighing spring scale with a precision of 50 GMs and length was measured in a rigid infantometer with a precision of 1 mm. For those who could stand weight was measured on a spring scales with a precision of 100 GMs and height was measured in a stadiometer with a precision of 1 mn.

Analysis was done using EPI6 statistical software.15 Chi square test was used for comparison of categorical variables and student's t test for continuous variables. A two tailed chi square and t−test distribution was used and a p value of <0.05 was considered to be statistically significant. An intention to treat analysis was done. Ordinary least squares regression was done to find the association between weight gain and height gain after controlling for initial weight or height for age and sex and the treatment type given.15

ResultsThe study began in April 1996 and lasted for 1.5 years. There were 63 slums with 988 children in the albendazole plus vitamin A group and 61 slums with 1022 children in the vitamin A group. The male to female ratio was 0.88 and 0.98 in the albendazole plus vitamin A and vitamin A alone slums, respectively. The baseline anthropometric characteristics are given in Table 1. The number of children contacted at each follow−up visit is given in Table 2. At enrollment stool examination was done in randomly selected 12 slums (n=196 children) which received

Table 1. Number of Subjects Enrolled and Contacted at Each Visit

	Albendazole +Vitamin A	Vitamin A	P value
Number of Slums	63	61	
Number of children	988	1022	
Number of males	528	501	0.1
Number underweight	471 (47.2%)	480 (47.1%)	0.9
Number stunted	622 (66.3%)	609 (59.7%)	0.3
Number wasted	174 (17.6%)	166 (16.2%)	0.5
	Mean, SE	Mean, SE	
Age (months)	9.4, 0.69	9.6 0.58	
Weight (KG)	6.97, 0.14	7.03, 0.15	0.3
Height (CM)	64.9, 3.25	65.63, 3.17	0.4
WAZ	−1.98, 0.13	−1.99, 0.13	0.8
HAZ	−2.43, 0.21	−2.44, 0.2	0.9
WHZ	−0.07, 0.25	−0.09, 0.24	0.8

Abbreviations:
WAZ: Weight−for−age z−score HAZ: Height−for−age z−score WHZ : Weight−for−height z−score

Table 2. Number of Children Enrolled and Contacted at Each Follow−up

	Albendazole +Vitamin A	*Vitamin A*	*P value*
Enrolled	988	1022	
After 6 months	941	968	
After 12 months	832	831	
After 18 months	832	840	
Loss to follow−up*	13.9%	16.2%	0.6%
Dead over 1.5 years	21	20	0.7

albendazole with vitamin A and in 11 slums (n=161 children) which received vitamin A alone. The baseline prevalence of infestation with Ascaris lumbricoides was 8.16% in the albendazole plus vitamin A slums and 9.32% in vitamin A slums (p value=0.2). At enrollment, 8 and 10 mothers from the albendazole plus vitamin A group and vitamin A group, respectively, gave history of passage of round−worms. At the second, third and fourth visits after 6 months, 12 months and 18 months the percentages in the albendazole plus vitamin A versus vitamin A groups were 2.7% (n=25) vs. 0.93% (n=9) (p=0.006), 2.31% (n=19) vs. 0.36% (n=3) (p=0.001) and 36.2% (n=301) vs. 17.0% (n=143) (p=0.0001).

The mean weight gain in 1.5 years in the albendazole plus vitamin A group was 5.57% greater than that in the vitamin A group alone (3.22 KG(SD: 2.03, SE: 0.26) vs. 3.05KG (SD: 1.47 SE: 0.19)P value=0.01) (Table 3). The mean height gain in 1.5 years was similar in both the groups (Table 3). Those who gave history of passage of round worms at the 18 month visit had a 13.1% greater weight gain in the albendazole plus vitamin A group as compared to those in the vitamin A group and the difference was statistically significant (p=0.007) (Table 3).

There was a statistically significant association between treatment type and weight gain after controlling for presence of underweight at recruitment (Table 4).

Table 3. Anthropometric Characteristics of Children in Both the Group at 18 months

	Albendazole +VitaminA	*Vitamin A*	*P value*
	n Mean, SE	n Mean, SE	
Age after 18 month	832 27.5, 2.88	840 27.39, 2.78	0.5
Weight at 1.5 years (KG)	832 9.94, 0.02	840 9.87, 0.02	0.3
Height at 1.5 years (CM)	832 81.75, 0.5	840 81.60, 0.5	0.6
WAZ	832 −2.23, 0.94	840 −2.25, 0.91	0.6
HAZ	832 −1.89,1.49	840 −1.89, 1.45	0.9
WHZ	832 −1.28, 0.76	840 −1.31, 0.76	0.5
Number underweight	552 (66.3%)	580 (69.1%)	0.2
Number stunted	455 (54.7%)	441 (52.5%)	0.3
Number wasted	123 (14.8%)	133 (15.8%)	0.5
Weight gain (KG) at 1.5 years and stratified by sex and history of passage of round worms at the fourth follow−up and changes in weight for age−zscores			
	n Mean, SE	n Mean, SE	
Over−all	832 3.22, 0.26	840 3.05, 0.19	0.01
Stratified by sex			
In males	444 3.31, 0.18	405 3.14, 0.19	0.08
In females	388 3.11, 0.18	435 2.96, 0.31	0.1
(P value)	(0.04)	(0.08)	
Stratified by history of passage of round worms at 4th follow−up			
H/O roundworms	301 3.28, 0.17	143 2,90, 0.17	0.007
No (H/O) roundworms	531 3.18, 0.18	697 3.08, 0.18	0.2
(p value)	(0.7) (0.2)		
Change in weight−for−age			
z−score	832 −0.22, 0.15	840 −0.25, 0.16	0.7
Height gain (CM) at 1.5 years stratified by sex and history of passage of round worms at the forth follow−up and changes in height for age−z−scores			
	n Mean, SE	n Mean, SE	
	n Mean, SE	n Mean, SE	
Overall	832 16.5, 0.82	840 16.1, 0.83	0.2
Stratified by sex			
In males	444 16.72, 0.76	405 16.34, 0.83	0.7
In females	388 16.31, 0.76	435 15.94, 0.84	0.6
(p value)	(0.4) (0.4)		
Stratified by history of passage of round wormd at 4th follow−up			
H/O roundworms	301 16.10, 0.79	143 15.36, 0.78	0.1
No H/O roundworms	531 16.77, 0.83	697 16.29, 0.84	0.1
(p value)	(0.4) (0.3)		
Change in height−for−age			
z−score	832 0.67, 0.26	840 0.48, 0.26	0.05

Abbreviations: WAZ: Weight−for−age z−score HAZ: Height−for−age z−score WHZ: Weight−for−height z−score

Table 4. Ordinary Least Squares Regression for Association Between Weight Gain in Kg. over 1.5 Years and Underweight Status at Enrollment and Treatment Type

	Coef. SE	95% CI	P	Coding
Under weight (at enrollment)	0.94 0.06	0.81 to 1.06	<0.0001	0=Normal, 1=Underweight
Treatment type	0.13 0.06	0.004 to 0.26	0.043	0=Vit A, 1=ABZ+Vit A
Constant	2.38 0.05	2.27 to 2.49	<0.0001	
Number of observations	= 1672			
F (2, 1670)	= 109.06			
Prob> F	= 0.0000			
R−squared	= 0.1155			
Adjusted R−squared	= 0.1145			

Abbreviations : Coef = Coefficient SE=Standard Error CI: Confidence Interval
ABZ=Albendazole Vit A: Vitamin A

Discussion

Since malnutrition and worm infestation both begin between the ages of 6 to 12 months, this was taken as the age of recruitment. Recruited infants were contacted once every six months and followed up for 1.5 years. This trial was conducted on children between the ages of 6−12 months using cluster randomization. Asignificant improvement in weight was observed in the children who were de−wormed every six months for 1.5 years at the end of the study period. Intestinal helminths are know to cause malnutrition due to impaired absorption of nutrients from the alimentary tract and improvements in weight have been documented after deworming by various workers.1,16,17 However, most of the studies have been done in school age children.18,20 There are a few studies in the preschool children too showing similar effects.16,21,22

The current trial has recruited the youngest subjects with reference to all other published studies. Mothers of about one−fourth of the children between the age of 1.5−2 year gave history of passage of roundworms. This is indicative of high transmission rates within the community. High transmission rates are found in areas where there is improper handling of human excreta, which is the case in most of the urban slums of Lucknow. There was a significantly greater weight gain but no height gain in the de−wormed children in 1.5 years as compared to those who were not. Similar findings have been reported in another study in older children from the Lucknow slums.23

The recruited subjects included those with normal weight−for age as well as underweight.15 In the ordinary least squares regression model it was noted that the mean weight gain was greater by 0.98 Kg in the underweight as compared to normal weight children. Controlling for this, treatment with albendazole plus vitamin A demonstrated an additional increase in weight gain in all. Thus, while treatment with albendazole and Vitamin A is of benefit to all, but is likely to be more so to the underweight.

Over a period of 18 months, there was a similar increase in the proportion of underweight children in both the arms. However, the proportion of stunted and wasted children was reduced in both the arms. There was an incremental reduction in the proportion stunted (4.9%) and wasted (2.4%) with albendazole and vitamin A when compared to vitamin A alone. Similar findings have been reported in another study in a different set of children from the urban slums of Lucknow.16 The children in the earlier study received 600 mg of powdered albendazole or powdered placebo and were 1.5−3.5 years of age at inclusion.24

The limitations of the study are that the worm burden and plasma retinol levels were not estimated. Also the trial was not blinded and hence this may have biased the results if the investigators knew the study hypothesis. Also concomitant co−intervention of deworming medications in the vitamin A alone group may have resulted in making the differences in weight and height gain with albendazole plus vitamin A less. History of passage of roundworms was asked from the mothers, even though no clear association between this and slide positivity has been established. It was found that at each visit a statistically significantly higher proportion gave history of passage of roundworms in the albendazole plus vitamin A group. This can be attributed to albendazole. This could also make blinding very difficult, hence it was not done in the current trial. Estimation of the intensity of infestation was not a part of this study and therefore the characteristics of infants who are likely to be benifited by early routine deworming could not be determined. Also a longer follow−up could have determined if the growth benefits exist into preschool age and validated the findings of earlier study from the same area reporting this.23 Since there was an improvement in weight gain over 18 months in children recruited in infancy, further studies with longer follow−up are needed to see the effects in later ages as well in under five mortality rates.

Acknowledgement

This study was funded by International Clinical

Epidemiological Network (INCLEN) Inc., USA and Clinical Trials Unit (CTSU), Oxford, UK.

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