Successful Eradication of *Ascaris lumbricoides* and Hookworm Infection after Three Repeated Doses of Albendazole

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Abstract

Three repeated orally doses of albendazole 400 mg in 6 weekly intervals were evaluated in Thai hill-tribe students who had at least one kind of soil-transmitted helminths (i.e. *Ascaris lumbricoides*, hookworm and *Trichuris trichiura*). Stool examination and parasite egg count were performed using Beaver's standard direct smear method and Kato-Katz's cellophane thick smear method prior to treatment and then 1 month after the first, second and third dose of drug administrations. A single dose of albendazole was very effective against *A. lumbricoides* and hookworm infections, with cure rates of 98.68 per cent and 92.16 per cent, respectively. The second and third dosages eradicated *A. lumbricoides* and hookworm infections, respectively. Conversely, the first to third cure rates for *T. trichiura* infection were relatively low, being 37.76-58.16 per cent. Three repeated doses of albendazole proved to be beneficial in eradication of *A. lumbricoides* and hookworm infections, and decreased the prevalence of *T. trichiura* infected cases. For eradication of *T. trichiura* infection, further regimen and period of drug administration is required.

Key word : Repeated Treatment, *Ascaris lumbricoides*, Hookworm, Albendazole

SUKONTASON K, et al
J Med Assoc Thai 2000; 83: 1095-1100

Soil-transmitted helminths (STH) have been a major public health problem in human populations; 900 million cases for hookworms, 1000 million for *Ascaris lumbricoides* and 500 million for *Trichuris trichiura* were estimated worldwide[1]. STH infections depress growth, physical fitness,

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physical activity, appetite and cognitive performance in school-age children[2]. As for hookworm infection, anemia is the classical clinical manifestation while abdominal pain, diarrhea, nausea, vomiting, belching, flatulence and loss of appetite have all been associated with the presence of adult worms in the small intestine[3]. Vitamin B1, B2 and B6 deficiency was also found in schoolchildren with hookworm infection[4]. The intensity of *A. lumbricoides* infection was correlated with the level of verbal ability[5]. As for *T. trichiura* in infected children, heavy infection demonstrated a direct effect on cognitive[6] and mathematics abilities[7] whilst severe infection is associated with growth retardation, iron deficiency anemia[8], colonic obstruction and perforation[9]. Taking into account the aforementioned, children and adults who are healthy and free from these parasites can be more physically and mentally active than those who are not.

Although albendazole was found to be the most appropriate drug for mass therapy of STH[10]; the effectiveness of single dose treatment with 400 mg varied from study to study, probably attributable to the parasite load in patients[10-12]. Three repeated treatments at 6 month intervals using the same regimen for 3 consecutive days decreased the prevalence and intensity of *Ascaris* and *Trichuris* in infected persons residing in the community[13]. This repeated dosage regimen was inconvenient for mass therapy because of the relatively long period of drug administration. We reported herein the 6 weekly intervals of albendazole in a non-reinfected area for both convenient and effective control strategies, thereby, providing information for increment of the cure rate of individuals infected with STH.

MATERIAL AND METHOD

Five hundred and forty-five male hill-tribe children of Somdet Prabhudhachinnawong School, Chiang Mai province of northern Thailand, were recruited in this study for July to December 1998 after receiving complete informed consent for participation from the director of this school. All were from northern provinces of Thailand and had just enrolled for permanent stay. The school is located in the suburban area of Chiang Mai with quite a good sanitary latrine, well-prepared food and quality water supply where parasite transmission was unlikely. Prior to treatment, participating students were provided a plastic stool collection box labelled with his name and class. Stool examination was performed prior to the first treatment and 1 month after each treatment using Beaver's standard direct smear method[14,15] and Kato-Katz cellophane thick smear method[16], however, the parasite eggs per gram (EPG) were assessed using only the latter method.

Two 200 mg tablets of albendazole (Zentel®: SmithKline Beecham) were given orally to the positive cases for *Ascaris*, hookworm and *Trichuris* infections in the presence of the investigators, and this drug regimen was referred to albendazole unless otherwise stated. Stool examination was repeated in children who had been medicated 30 days after drug administration. Children still positive for STH after the first treatment were retreated and stool reexamined as the second treatment in the same manner previously described. The STH-positive children after the second treatment were provided the third treatment by the same regimen and stool-examination.

The efficacy of albendazole for the treatment STH was determined as negative for *Ascaris*, hookworm and *Trichuris* eggs in both methods. Number of cure rate was assessed and compared with the previous treatment using McNemar chi-square test (α error = 0.05). Cure rate and geometric mean egg counts followed the criteria described by Albonico et al[11]. Cure rates following drug treatment were estimated as the proportion of children excreting eggs of any particular nematode before treatment that had a zero count after treatment. Geometric mean egg counts were estimated as $\exp [(\Sigma \log_e (c+1))/n]-1$, where c was the count (eggs/g) for a particular individual and n the number of samples. Eggs per gram (EPG) of feces examined using Kato-Katz method of pretreatment, first, second and third treatments were statistically compared using Friedman's test and compared one by one using Wilcoxon Sign Rank test.

RESULTS

Prior to the treatment, 217 of 545 schoolchildren (39.82%) were infected with STH, with the number of individuals infected with *Ascaris*, hookworm and *Trichuris* being 76, 153 and 98 cases, respectively. Most were single infection (n = 132), followed by double infection (n = 60) and triple infection (n = 25). The arithmetic mean, median and geometric mean egg counts prior to treatment and

after three post-treatments egg counts examined by Kato-Katz cellophane thick smear method with percentage reduction in egg counts are shown in Table 1. After the first treatment, the number of expelled EPG was significantly reduced in *Ascaris*, hookworm and *Trichuris* infected cases, with the percentage of EPG reduction being 99.98 per cent, 97.99 per cent and 47.74 per cent, respectively. The second (59.34%) and third treatments (77.62%) enhanced the percentage of EPG reduction in *Trichuris* infected cases ($P = 0.045$ and $P < 0.001$, respectively). However, the EPG after the second and third treatments were not significantly different from the first one in *Ascaris* and hookworm infected cases.

Albendazole produced a cure rate of 98.68 per cent, 92.16 per cent and 37.76 per cent for *Ascaris*, hookworm and *Trichuris*, respectively (Table 2). Additionally, the second and third treatments eradicated *Ascaris* and hookworm infected

Table 1. Pre- and three post-treatments of schoolchildren infected with *Ascaris*, hookworm and *Trichuris* with albendazole*.

Helminth	Treatment	Arithmetic mean EPG	Median EPG	Geometric mean EPG	Percentage reduction in EPG**	
Ascaris	Pre-	12667.37	1400	750.95	-	-
(n=76)	1	4.21	0	0.08	99.98	(99.95-100.01)
	2	0	0	0	100.00	-
	3	0	0	0	100.00	-
Hookworm	Pre-	450.14	80	122.27	-	
(n=153)	1	8.11	0	0.16	97.99	(95.94-100.04)
	2	6.64	0	0.19	96.50	(92.62-100.37)
	3	0	0	0	100.00	-
Trichuris	Pre-	541.63	240	208.46	-	
(n=98)	1	213.88	40	19.27	47.74	(30.68-64.80)
	2***	145.31	0	10.97	59.34	(40.65-78.02)
	3****	94.69	0	5.64	77.62	(67.02-88.23)

* 400 mg oral administration.

** Significant tests and 95 per cent confidence intervals (in parentheses) based on differences between pre- *vs.* post-treatment EPG (eggs/gram) within individuals at $P < 0.001$. Significant differences between pre-treatment 2 *vs.* post-treatment 2, and pre-treatment 3 *vs.* post-treatment 3 were found only in *Trichuris* cases with $P = 0.045$ (***) and $P < 0.001$ (****), respectively.

Table 2. Pre- and three post-treatments of schoolchildren infected with *Ascaris*, hookworm and *Trichuris* with albendazole.

Helminth	Treatment	No. excreting eggs	Cure rate* %	P (compared with treatment 1)	P (compared with treatment 2)
Ascaris	Pre-	76	-	-	-
(n=76)	1	1	98.68	-	-
	2	0	100.00	1.0	-
	3	0	100.00	1.0	1.0
Hookworm	Pre-	153	-	-	-
(n=153)	1	12	92.16	-	-
	2	6	96.08	0.03	-
	3	0	100.00	<0.001	0.03
Trichuris	Pre-	98	-	-	-
(n=98)	1	61	37.76	-	-
	2	48	51.02	<0.001	-
	3	41	58.16	<0.001	0.0156

* All post-treatments cure rates were significantly different compared with pre-treatment of the same species at $P < 0.001$.

cases, respectively. Likewise, repeated treatment for the second and third time significantly increased the cure rate to 96.08 per cent and 100.00 per cent for hookworm (P = 0.03, P = 0.03) and 51.02 per cent and 58.16 per cent for *Trichuris*, respectively (P < 0.001, P = 0.0156). However, repeated treatments could not produce a higher significant cure of *Ascaris* infected cases.

DISCUSSION

Albendazole has been proved to be an effective anthelminthic drug for parasitic nematodes worldwide. The result of our first treatment confirmed the excellent efficacy of albendazole against *Ascaris*[10-12,17]. Additionally, two repeated doses proved to be the eradicating regimen for this parasite in Thai hill-tribe schoolchildren who had moderate infection and stayed in a non-reinfected area. Only one case was still infected after the first drug treatment, with the EPG being quite low (EPG = 320; data not shown). The existence of worms in this special case probably resulted from the sojourn of immature worms in the lung.

The cure rate of hookworm infection has increasingly been reported in Thailand after albendazole administration, i.e. 64.0 per cent (in 1982) to 84.3 per cent (in 1993) and 91.6 per cent (in 1997)[12,17,18]. In the present study, there was a 92.16 per cent cure rate after the first treatment. The reason for cure rate increment in such studies was unknown; however it was possibly due to the varied intensity of infection. Viravan et al[18] found that albendazole gave 75.0 per cent cure in low infection and only 50.0 per cent in high infection. The low infection in our study, as indicated by the EPG of 450.14, was lower than the data of Viravan et al[18]. Thus, the relatively low infection may be the explanation for the high cure rate.

Even though some locations in Thailand are endemic areas of hookworm, the worm load in infected cases may be decreased after the introduction of a latrine and footwear campaign. Reduction in EPG and efficient cure rate after the first dose of albendazole were enough for hookworm control strategy in low intensity endemic areas. The second and third treatments respectively increased the cure rate to 96.08 per cent and 100.00 per cent; however, the increased cure rate of schoolchildren with these treatments was not significantly different from the first treatment. As for individuals with heavy hookworm infection, repeated stool examination, second and/or third treatments as well as prevention from re-infection are recommended.

Albendazole yielded a lower efficacy in the treatment of *Trichuris* infection than mebendazole administered as a 500 mg single dose or 100 mg twice daily for 3 days[11,12,17], with the cure rates of those three reports using albendazole being 67.4 per cent, 10.5 per cent and 33.3 per cent, respectively. Our result revealed 37.76 per cent cure rate after the first drug administration whilst the second and third treatments significantly increased the cure rates to 51.02 per cent and 58.16 per cent, respectively. On the other hand, treatment of this parasite using mebendazole 100 mg orally in 6 repeated doses over 3 days gave a somewhat high cure rate (85.5%) than the single oral dose of 300 mg or 500 mg of the same drug (cure rate being 42.2% and 38.0%, respectively)[19]. As a result, it seems likely that the lower but repeated dosage of anthelminthic drug is required for treatment of trichuriasis. However, for the purpose of eradication, the proper dosage regimen and interval period of drug administration has not been recorded, and merits more investigation.

The relatively low effectiveness of drug treatment in trichuriasis is unknown. It may be due to biology of the worm itself, as the head penetrates into the mucosa of the large intestine. Reinfection is unlikely to be reason since the schoolchildren in the present study resided permanently in proper environmental conditions. Other confounding factors must have been involved.

In conclusion, treatment of STH depends primarily upon which species of nematode is presented in the study area. Stool examination prior to treatment is mandatory for proper drug administration. A single dose of 400 mg albendazole is adequate for treatment of *Ascaris* and hookworm infections. Stool re-examination after treatment is necessary especially in areas where *T. trichiura* is endemic; however, if that is not possible, two repeated 6 weekly doses are recommended.

ACKNOWLEDGEMENT

The authors wish to thank the school manager, head teacher and schoolchildren of Somdet Prabhudhachinnawong School, Chiang Mai Province of north Thailand, for their excellent participation and co-operation. The authors also wish to thank the staff of the Department of Parasi-

tology for their technical assistance and the Faculty of Medicine, Chiang Mai University for encouragement. This investigation received financial support from Thailand Research Fund (No. PDF/03/2541).

(Received for publication on February 24, 2000)

REFERENCES

1. Warren KS, Mahmound AAF. eds. Tropical and Geographical Medicine. New York: McGraw-Hill, 1984.
2. Stephenson LS, Latham MC, Adams EJ, Kinoti SN, 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 Nutr 1993; 123: 1036-46.
3. Migasena S, Gilles HM. Clinical features and diagnosis. In: Gilles HM, Ball PAJ, eds.: Hookworm Infection. Elsevier: Netherlands, 1991: 179-93.
4. Nontasut P, Changbumrung S, Muennoo C, et al. Vitamin B1, B2 and B6 deficiency in primary school children infected with hookworm. Southeast Asian J Trop Med Pub Hlth 1996; 27: 47-50.
5. Levav M, Mirsky AF, Schantz PM, Castro S, Cruz ME. Parasitic infection in malnourished school children: effects on behaviour and EEG. Parasitol 1995; 110: 103-11.
6. Nokes C, Grantham-McGregor SM, Sawyer AW, Cooper ES, Robinson BA, Bundy DP. Moderate to heavy infections of *Trichuris trichiura* affect cognitive function in Jamaican school children. Parasitol 1992; 104: 539-47.
7. Simeon D, Callender M, Wong M, Grantham-McGregor S, Ramdath DD. School performance, nutritional status and trichuriasis in Jamaican schoolchildren. Acta Paediatr 1994; 83: 1188-93.
8. Cooper ES, Whyte-Alleng CAM, Finzi-Smith JS, McDonald TT. Intestinal nematode infections in children: the pathophysiological price paid. Parasitol 1992; 104 (Suppl.), S91-S103.
9. Bahon J, Poirriez J, Creusy C, Edriss AN, Laget JP, Dei Cas E. Colonic obstruction and perforation related to heavy *Trichuris trichiura* infestation. J Clin Pathol 1997; 50: 615-6.
10. Pene P, Mojon M, Farin JP, Coulaud JP, Rossignol JF. Albendazole: a new broad spectrum anthelmintic. Double-blind multicenter clinical trial. Am J Trop Med Hyg 1982; 31: 263-6.
11. Albonico M, Smith PG, Hall A, Chwaya HM, Alawi KS, Savioli L. A randomized controlled trial comparing mebendazole and albendazole against *Ascaris, Trichuris* and hookworm infections. Trans R Soc Trop Med Hyg 1994; 88: 585-9.
12. Nontasut P, Waikagul J, Muennoo C, Sanguankait S, Nuamtanong S, Maipanich W. Minimum effective doses of mebendazole in treatment of soil-transmitted helminths. Southeast Asian J Trop Med Pub Hlth 1997; 28: 326-8.
13. Chan L, Kan SP, Bundy DAP. The effect of repeated chemotherapy on the prevalence and intensity of *Ascaris lumbricoides* and *Trichuris trichiura* infection. Southeast Asian J Trop Med Pub Hlth 1992; 23: 228-34.
14. Beaver PC. Quantitative hookworm diagnosis by direct smear. J Parasitol 1949; 35: 125-35.
15. Beaver PC. The standardisation of faecal smears for estimating egg production and worm burden. J Parasitol 1950; 36: 451-6.
16. Katz N, Chaves A, Pellegrino J. A simple device for quantitative stool thick-smear technique in schistosomiasis mansoni. Rev Inst de Med Trop de São Paulo 1972; 14: 397-400.
17. Jongsuksuntikul P, Jeradit C, Pornpattanakul S, Charanasri U. A comparative study on the efficacy of albendazole and mebendazole in the treatment of ascariasis, hookworm infection and trichuriasis. Southeast Asian J Trop Med Pub Hlth 1993; 24:724-9.
18. Viravan C, Migasena S, Bunnag D, Harinasuta T. Clinical trial of albendazole in hookworm infection. Southeast Asian J Trop Med Pub Hlth 1982; 13: 654-7.
19. Charoenlarp P, Waikagul J, Muennoo C, Srinophakun S, Kitayaporn D. Efficacy of single-dose mebendazole, polymorphic forms A and C, in the treatment of hookworm and *Trichuris* infections. Southeast Asian J Trop Med Pub Hlth 1993; 24: 712-6.

การให้ยาอัลเบนดาโซลซ้ำสามครั้งเพื่อกำจัดพยาธิไส้เดือนและพยาธิปากขอ

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ถึงแม้ว่ายาอัลเบนดาโซลเป็นยาฆ่าพยาธิตัวกลมในทางเดินอาหารที่ใช้ได้ผลดีโดยการให้ยาเพียงครั้งเดียว อย่างไรก็ตามยานี้ไม่สามารถกำจัดพยาธิบางชนิดเช่นพยาธิแส้ม้าให้หมดไปได้ ยาอัลเบนดาโซลได้ถูกนำมาศึกษาอีกครั้ง โดยให้รับประทานในขนาด 400 มิลลิกรัมทุก 1 $^{1}/_{2}$ เดือน รวม 3 ครั้ง ในเด็กนักเรียนชาวไทยภูเขาที่มีพยาธิตัวกลมในทางเดินอาหารอย่างน้อย 1 ชนิด (พยาธิไส้เดือน, พยาธิปากขอและพยาธิแส้ม้า) การตรวจอุจจาระและนับจำนวนไข่พยาธิในอุจจาระกระทำโดยวิธี Beaver's standard direct smear และ Kato-Katz's cellophane thick smear ก่อนการรักษาและ 1 เดือนภายหลังการรักษา พบว่าอัตราหายหลังจากการศึกษาครั้งแรกของโรคพยาธิไส้เดือน, โรคพยาธิปากขอและโรคพยาธิแส้ม้าเท่ากับร้อยละ 98.68, 92.16 และ 37.76 ตามลำดับ อัตราหายหลังจากการรักษาครั้งที่สองเท่ากับร้อยละ 100, 96.08 และ 51.02 ตามลำดับ ส่วนอัตราหายหลังจากการรักษาครั้งที่สามเท่ากับร้อยละ 100, 100 และ 58.16 ตามลำดับ การรักษาซ้ำครั้งที่สองและสามทำให้อัตราหายของโรคพยาธิปากขอและโรคพยาธิแส้ม้าเพิ่มขึ้น แต่มิได้ทำให้อัตราหายของโรคพยาธิไส้เดือนเพิ่มขึ้นอย่างมีนัยสำคัญ ส่วนการรักษาครั้งที่สามทำให้อัตราหายของโรคพยาธิแส้ม้าเท่านั้นที่เพิ่มขึ้นอย่างมีนัยสำคัญ การให้ยารักษาโรคพยาธิตัวกลมในทางเดินอาหารในเด็กขึ้นอยู่กับชนิดของพยาธิและการตรวจอุจจาระก่อนการรักษาเป็นสิ่งที่จำเป็น การให้ยาอัลเบนดาโซลหนึ่ง, สองและสามครั้งสามารถรักษาโรคพยาธิไส้เดือน, โรคพยาธิปากขอและโรคพยาธิแส้ม้าตามลำดับ

คำสำคัญ : การรักษาซ้ำ, พยาธิไส้เดือน, พยาธิปากขอ, ยาอัลเบนดาโซล

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