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Reduced Single Dose of Mebendazole in Treatment of *Ascaris lumbricoides* Infection

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INTRODUCTION

The efficacy of mebendazole in the treatment of *Ascaris lumbricoides* infection has been studied by many workers with excellent results (Pena Chavarria et al., 1973; Wolfe and Wershing, 1974; Soh et al., 1974 and Seo et al., 1977). The recommended dose of mebendazole in this infection is total 600mg, divided in 6 doses for 3 days. This dose schedule was primarily designed on the multiple infection of certain nematodes such as hookworms and *Trichuris trichiura* rather than the single infection of *A. lumbricoides*.

Although the schedule of 3-day treatment is known to be very effective in such multiple infections, it is still hardly feasible to undertake the mass chemotherapy and field control of soil-transmitted nematodes. This schedule is rather complicated to be used in the field, too repetitive to accept the full course treatment.

Furthermore, if the mass chemotherapeutic control programme is concerned mainly with *Ascaris* infection, the single, minimal dose without repetition will be more convenient to achieve the economic and acceptable mass chemotherapy. As already studied by Pena Chavarria et al. (1973) in Costa Rica, some of the single regimens of mebendazole were equally effective as repeated doses. But further data supporting the above finding were rather scarce except for the report of Partono et al. (1974) which agreed to the result of Pena Chavarria et al. (1974).

The present observation was made to find out the effectiveness of single doses of mebendazole in the treatment of *Ascaris* infection which will make this drug more practicable in the mass chemotherapy and field control.

MATERIALS AND METHODS

1. Subjected cases:

Two rural Korean populations in Hwaseong Gun, Kyunggi Do and Kangjin Gun, South Cholla Do were selected for this observation, and surveyed during the period from December 1977 to March 1978. Out of 472 subjected cases, 191 were found to be infected with *A. lumbricoides*. The infected cases were divided into five groups according to dosage schedule of mebendazole and in each group, the same doses were administered regardless of the age and sex of the subjected cases.

2. Stool examination and follow-up:

Both in selection of infected cases and in follow-up evaluation, two kinds of stool examination technique were employed in every cases; the cellophane thick smear technique and Stoll's dilution egg counting technique. Follow-up examination was performed on the 21st day from the last day of the drug administration.

Adverse effects during and after the treatment were observed only upto 24 hours after the

last administration of the drug with verbal communication.

RESULTS

The results of stool examination undertaken before treatment were presented in Table 1. The inhabitants in Kangjin Gun showed the higher prevalence of infection both in soil-transmitted and snail-transmitted helminthic infections. *A.lumbricoides* infections were more prevalent and heavier in the inhabitants of Kangjin Gun.

As shown in Table 2, the negative conversion rates by the various dosage regimens in two subjected populations were rather proportionate with the increase of total doses: 89.7 percent in 100mg single dose, 93.8 percent in 200mg single dose, 96.7 percent in 300mg single dose, 100 percent both in 400mg (200mg/day, # 2, for 2 days) and in 600mg (200mg/day, #2, for 3 days). The cases from Hwaseong Gun, where *Ascaris* infection was less endemic and relatively lower in worm burden, showed 100 percent of negative conversion rates (=cure rates) regardless of the dosage used. However in cases from Kangjin Gun, whose worm burden was almost always much higher than in Hwaseong Gun, the negative conversion rates were lower in single minimal dose; 87.5 percent in 100mg single dose, 92.0 percent in 200 mg single dose and 94.1 percent in 300mg single dose.

Table 2. Cure rate of *Ascaris lumbricoides* infection by dosage schedules of mebendazole

Dosage schedule	Area	No. treated	No. followed	No. neg. conv.	Cure rate (%)
100mg, single	Hwaseong	9	7	7	100
	Kangjin	36	32	28	87.5
200mg, single	Hwaseong	9	7	7	100
	Kangjin	32	25	23	92.0
300mg, single	Hwaseong	15	13	13	100
	Kangjin	19	17	16	94.1
400mg, in 4 doses	Hwaseong	12	8	8	100
	Kangjin	21	17	17	100
600mg, in 6 doses	Hwaseong	10	10	10	100
	Kangjin	28	20	20	100

The cause of failure in complete cure was analyzed in aspect of age of subjected cases and presented in Table 3. Six out of 7 failed cases in complete cure were adults over 25-year-old. Among children and young adults upto 24-year-old, only one case was failed to achieve the complete cure.

The egg reduction rates by the dosage shedule were presented in Table 4. The number of

Table 1. Results of stool examination in two surveyed inhabitants revealed by cellophane thick smear method

	Hwaseong Gun		Kangjin Gun		Total	
	No.	Perent	No.	Percent	No.	Percent
No. examined	207		265		472	
No. helminths posit.	109	52.7	233	87.9	342	72.5
Ascaris lumbricoides	55	26.6	136	51.3	191	40.5
Trichuris trichiura	90	43.5	193	72.8	283	60.0
Hookworm	15	7.2	0	—	15	3.2
Trichostrongylus orientalis	1	0.5	0	—	1	0.2
Enterobius vermicularis	0	—	4	1.5	4	0.8
Metagonimus yokogawai	1	0.5	71	26.8	72	15.3
Clonorchis sinensis	1	0.5	36	13.6	37	7.8
Taenia spp.	0	—	7	2.6	7	1.5
Hymenolepis nana	0	—	1	0.4	1	0.2

Table 3. Distribution of failed cases in complete cure according to the age band of subjected cases by doses

Doses	Age band(in years)							
	0~7		8~14		15~24		25 or over	
	No. exam.	No. fail.	No. exam	No. fail.	No. exam.	No. fail.	No. exam.	No. fail.
100mg	4	1	9	0	9	0	17	3
200mg	2	0	7	0	5	0	18	2
300mg	5	0	12	0	2	0	11	1
400mg	2	0	6	0	6	0	11	0
600mg	8	0	8	0	6	0	8	0

Table 4. Egg reduction rates of *Ascaris lumbricoides* according to doses of mebendazole

Doses	Before treatment			After treatment		Egg reduction rate
	No. exam.	Sum of E.P.G.	Mean	No. posit.	Sum of E.P.G.	
100mg single	38	347,300	9,140	4	4,900	98.6
200mg single	30	102,500	3,420	2	1,400	98.6
300mg single	30	259,800	8,660	1	300	99.9
400mg in 4 doses	24	148,400	6,180	0	—	100
600mg in 6 doses	25	288,200	11,530	0	—	100

Table 5. Distribution of failed cases in complete cure according to the pre-treatment E.P.G.

Doses	100~5,000		5,100~10,000		10,100~50,000		Over 50,000	
	No. cases	No. failed	No. cases	No. failed	No. cases	No. failed	No. cases	No. failed
100 mg	22	2	9	1	5	1	2	0
200 mg	24	1	4	1	2	0	0	—
300 mg	18	1	3	0	8	0	1	0
400 mg	18	0	2	0	4	0	0	—
600 mg	18	0	2	0	3	0	2	0
Total	100	4	20	2	22	1	5	0

followed-up cases were smaller than in followed-up cases of qualitative stool examination because some of cases were dropped out in quantitative stool examination. But the results of egg reduction were also satisfactory in any dosage schedules and the rates ranged from 98.6 percent in 100 and 200mg single dose groups to 100 percent in 300mg single dose and multiple dose groups. The failed cases in complete cure also showed remarkable egg reduction and it seemed that the vast majority of the worms had been cleared from the intestine.

As presented in Table 5, the failed cases in complete removal of infected *Ascaris* were distributed rather evenly in each category of egg counts. It seemed that there were no difference between the rate of failure in complete cure and pre-treatment worm burden which was revealed by the egg counting.

During the course of treatment, severe adverse effects were hardly encountered even in the cases treated with 300mg single dose of meben-

dazole. Side effects observed during the treatment were mild and transient gastrointestinal troubles, diarrhea and abdominal discomfort in only 3 cases. Two cases who were children and whose E.P.G. were 700 and 3,600 respectively discharged the adult *Ascaris* worm through mouth and nasal opening.

DISCUSSION

As shown in Table 2 and Table 4 in this observation, the single dose regimens were proved to be effective as much as multiple doses of mebendazole against *A. lumbricoides* infection. The results in this study almost completely agreed to the results of Pena Chavarria et al. (1973); the cure rate of 100 percent in 200mg single dose, 93.3 percent in 300mg single dose and 90.0, 90.9 and 100 percents with 400mg, 600mg and 800mg in multiple doses of mebendazole. The single dose treatment was also tried by Partono et al. (1974) in Indonesia and reported 94 percent of cure rate when the infected cases were treated with 100mg single dose and 100 percent with 200mg.

As discussed by Brugmans et al. (1971) and Pena Chavarria et al. (1973), the efficacy of mebendazole is not dependent on the age and weight of subjected cases and worm burden, but the availability of mebendazole in the host intestine. By the result, as shown in Table 3 and Table 5, the failed cases in complete cure were distributed not unevenly in any category of age and the degree of pre-treatment E.P.G.

In this respect, the minimal dose for the successful treatment of *Ascaris* infection seemed to be 100mg or 200mg in single dose to achieve the satisfactory result in mass control.

Adverse effects encountered in this observation were so mild that no special problem would be met.

SUMMARY

The efficacy of reduced single doses of mebendazole against *Ascaris lumbricoides* infection was evaluated by cellophane thick smear and egg counting techniques, in two rural populations from December 1977 to March 1978.

Total 191 infected cases were divided into five dose groups; 100mg single dose, 200mg single dose, 300mg single dose, 400mg and 600mg in repeated doses.

The cure rate of mebendazole in the treatment of *Ascaris* infection was remarkably high and satisfactory in every dose groups. The egg reduction rates were all over 98 percent in every dose groups.

Side effects were observed during the treatment, mainly mild and transient gastrointestinal troubles, and not exacerbated by the increase of doses upto 300mg in single dose.

Above results confirmed that in case of mass chemotherapy of *Ascaris* infection, 100mg or 200mg of single dose treatment is sufficient to achieve the economic and acceptable method of treatment.

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=국문초록=

蛔蟲感染의 治療에 있어서 메벤다졸의 減量 및 單回 服用效果

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蛔蟲感染에 있어서 減量 및 單回의 메벤다졸 服用效果를 調査하기 위하여 1977年 12月부터 1978年 3月까지 京畿道 華城郡 住民 및 全羅南道 康津郡 住民 472名을 대상으로 投藥前 및 投藥後 21日의 大便檢査 結果에 의하여 蟲卵陰轉率 및 蟲卵減少率을 구하고 1回의 多量服用으로 인한 不作用이 나타나는지를 관찰하였다.

蛔蟲卵陽性者는 472名 중 191名(40.5%)이었고 이들을 메벤다졸의 용량에 따라 5群으로 나누어 각각 100mg 1회, 200mg 1회, 300mg 1회 및 400mg(100mg, 1日 2回, 2일간), 600mg(100mg, 1日 2回, 3일간)씩을 투여하였다. 그 結果는 다음과 같다.

1. 蟲卵陰轉率은 위 각 群에서 모두 만족할만 했다 : 화성군—모두 100%, 강진군—위 각 群에서 각각 87.5%, 92.0%, 94.1%, 100% 및 100%.

2. 蟲卵減少率은 화성군에서는 역시 모두 100%, 강진군에서는 모두 98,6% 이상이었다.

3. 치료 실패자 7명 중 6명은 成人이었으나 統計學的으로 연령별 치료효과의 차이는 인정할 수 없었으며, 치료전 E.P.G의 정도에 따른 치료실패의 차이도 없었다.

4. 심한 不作用을 나타낸 사람은 없었으며 단지 3名에서 가벼운 정도의 腸症狀이나 혹은 蛔蟲의 成蟲이 입이나 코로 기어나오는 일이 있었으나 곧 소실되었으며 별 문제를 일으키지 않았다.

이상의 結果는 Pena Chavarria등(1973)이나 Partono등(1974)이 報告한 減量 메벤다졸의 蛔蟲에 대한 구충효과와 거의 一致하였고, 완전치료에 실패한 者는 치료전의 感染負荷나 연령의 차이에 의한 것이 아니고, 藥 服用時 개개인의 腸의 狀態(예, 설사 등)에 따라 치료효과가 달라질 수 있는 것으로 생각되었다.

따라서, 蛔蟲症의 集團治療 및 集團管理를 위해서는 100mg 또는 200mg의 메벤다졸을 單回에 服用하는 것이 가장 경제적이고 편리한 用量인 것으로 判斷할 수 있었다.