기 생 충 학 잡 지 제23권 제 1 호
The Korean Journal of Parasitology
Vol. 23, No. 1, 7-17, June, 1985

Effect of anthelmintics on the early stage of *Enterobius vermicularis*

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INTRODUCTION

When antipinworm drug therapy was tried once in heavily infected population of *Enterobius vermicularis*, the egg positive rate dropped to its lowest for a certain period, then returned to pre-treatment level. The interval between the day of treatment and returning to pre-treatment level varied by drug. After pyrantel treatment, for example, the rate returned within 24 days whereas it did within 30 day after mebendazole or pyrvinium treatments (Cho *et al.*, 1977).

To confirm the above findings morphologically in expelled worms, Cho *et al.* (1981) undertook the following observation; heavily infected groups were treated once with piperazine, pyrantel, pyrvinium and mebendazole respectively. Twenty days later the first treatment, the second one was done to collect the expelled *E. vermicularis*. The groups treated initially with mebendazole and pyrvinium expelled shorter worms (8.6 mm long) than those treated with pyrantel and piperazine (10.6 mm long) in terms of their maximum length.

According to the life span of *E. vermicularis* (=days from ingestion of infective eggs to anal migration of gravid females), we can interprete the above findings in two different ways. Firstly, if the span is postulated to be shorter than 20 day, the difference between length of pinworms after different drug treatment should indicate different prophylactic effects between drugs.

Secondly, if we postulate that the span is longer than 20 days, as ranging 45~50 days, the different length of the longest females between drug-treated groups can be interpreted as differences in anthelmintic activities, especially on the early stages of development. The longest worms were considered as those which resisted the first treatment, and had grown for 20 days. In other words, mebendazole and pyrvinium removed completely the earlier developmental stages of pinworms than pyrantel and piperazine did. In this connection, there were some supporting reports that piperazine and pyrantel were less active in rat against the early stages of *Syphacia obvelata* (Brown *et al.*, 1954; Kagei and Kihata, 1971).

Even though the second interpretation was considered as more realistic, we still could not fully accept it because the life span itself was not settled yet, and diversely stated as 15~50 days (Cram, 1943; Davis, 1973; Muller, 1975; Beaver *et al.*, 1984). Therefore we do not know at present which of the first or second postulation is correct. Furthermore, even if the second postulation is correct, we do not know at what age of *E. vermicularis* they actually became susceptible to different anthelmintics.

The objective of the present study is to determine the age of *E. vermicularis* to become susceptible to antipinworm drugs, pyrantel and mebendazole. Throughout this study, our hypothesis was that the life span was longer than 40 days. By sequential anthelmintic treatment of volunteers after experimental infection, and by collecting the expelled pinworms after each

** This research was supported by the Research Grant from the Asan Social Welfare Foundation (1982).

treatment, we observed the chronologic growth pattern as well as the susceptible age of *E. vermicularis*.

MATERIALS AND METHODS

The experiments were duplicated in this study. At first, we postulated that the drug-susceptible age was in the range of 4～16 days of infection. However, the results of the experiment suggested that the susceptible age might be in later than 16 days. Therefore, the second experiment was undertaken again to cover the age range of 20～28 days.

Hereafter, in every section, we separately describe the first and second experiments to indicate the difference in experimental condition.

1. Infective eggs of *E. vermicularis*:

Gravid females were collected from naturally infected children of orphanages in Anyang City, Kyunggi Do. At night, the migrating females were picked up at anus.

The collected worms were kept at room temperature overnight; most eggs were naturally released, but some were harvested by teasing the body. Then the eggs were incubated at 36°C in humid vials up to 5 days.

In the first experiment, about half of the eggs contained larva at the third day of incubation, with rapid revolving movements within the shell; some began to hatch naturally as described by Hsü (1951). The 3-day incubated eggs were used in the first experiment.

In the second experiment, the eggs which were collected again, had larva after 3 days of incubation. However, the larva inside the shell did not move until the 5th day of incubation. These eggs with not-moving larva were used in the second experiment.

2. Human volunteers:

Three faculties, 4 laboratory technicians, 7 medical and biology students of Chung-Ang University, all males, aged 17～45 years, were explained the details of necessity and importance of the study, possible hazards and clinical symptoms due to infection and safety of our experimental design. Ethical aspects in human experiments were considered and complied. Five volunteers participated in both experiments.

3. Infection procedure:

The amount of egg emulsion was measured to pick up about 500 eggs once. Then the actual number of eggs in measured emulsion was counted using a slide chamber.

In the first experiment, only the eggs with moving larva were counted excluding morphologically immatured; each volunteer was infected with 484～580 of good eggs. In the second experiment, each volunteer was infected with 461～550 eggs which were incubated for 5 days (Tables 1 & 2).

The volunteers were infected by licking the chamber first, then by drinking cups of water which washed the egg counting chamber. The last drops in the cup, and in counting chamber were examined under microscope to count the remaining eggs.

4. Schedule of anthelmintic treatments:

In the first experiment, 9 volunteers were divided into 3 groups; 4 cases of pyrantel-treated and mebendazole-treated in respect, and 1 case of control. In pyrantel- and mebendazole-treated groups, each case took the drug once on the 4th, 8th, 16th and the 32nd day respectively. The dose of pyrantel pamoate was 10 mg/kg of body weight and that of mebendazole was 100 mg irrespective of the body weight.

On the 40th day of experimental infection, all volunteers were treated with pyrvinium pamoate (in dose of 5 mg/kg) to terminate the experimental infection and to evaluate the effect of previous treatment.

In the second experiment, 10 volunteers were divided into 3 groups again; 5 cases of pyrantel-treated, 3 cases of mebendazole-treated and 2 controls. Each case of pyrantel group was treated on the 4th, 16th, 24th, 28th and the 35th day of experimental infection and that in mebendazole group was treated on the 20th, 24th and the 28th day. Again all volunteers were treated on the 40th day as in the first experiment.

5. Collection and observation of

expelled worms:

After each treatment, all volunteers collected their 3-day stools from which worm parasites were collected as described by Cho *et al.*(1981).

The numbers of collected *E. vermicularis* were counted. After clearing them in lactophenol, and mounting on a slide glass, the length of each worm was measured because it has been regarded as a most reliable indicator of development in female *E. vermicularis* (Cho *et al.*, 1982). The developmental status of sex organs were observed.

RESULTS

1. Clinical symptoms in experimental infection:

None of our volunteers, including control cases, complained of any overt symptoms related or non-related to the experimental infection. Specifically no one complained of anal itching throughout the whole period of experiment.

2. Results of the first experiment:

(1) Worm collection during 4th-32nd day of

Table 1. Results of the first experiment in volunteers

Case No.	Volunteer		No. of eggs taken	Days between infection & 1st treatment	Drug used	No. of worms collected at	
	Name	Age(yr)				1st treatment	40th day*
1	BJC	20	534	4	Mebendazole	0	15
2	JYC	22	532	4	Pyrantel	0	0**
3	CYC	18	503	8	Mebendazole	0	1
4	SKL	17	578	8	Pyrantel	0	10
5	HSK	26	500	16	Mebendazole	0	27
6	JJK	18	580	16	Pyrantel	0	0**
7	YK	28	531	32	Mebendazole	7	0
8	HY	23	487	32	Pyrantel	43	2
9***	SIK	28	494	(−)	—	—	40

* : Terminating treatment with 5mg/kg of pyrvinium pamoate
** : Performed again in the second experiment
*** : Control

Table 2. Results of the second experiment in volunteers

Case No.	Volunteer		No. of eggs taken	Days between infection & 1st treatment	Drug used	No. of worms collected at	
	Name	Age(yr)				1st treatment	40th day**
10	CYC*	18	552	4#	Pyrantel	0	34
11	SKL*	17	528	16#	Pyrantel	0	17
12	SHP	21	479	20	Mebendazole	3	0
13	KHK	26	461	24	Mebendazole	54	0
14	JHS	23	483	24	Pyrantel	24	3
15	JYC*	22	530	28	Mebendazole	1	0
16	CYS	45	531	28	Pyrantel	53	1
17	JJK*	18	490	35	Pyrantel	69	11
18***	SIK*	28	542	(−)	—	—	72
19***	SYC	41	525	(−)	—	—	3

* : Participated in the experiments twice
** : Terminating treatment with 5mg/kg of pyrvinium pamoate
*** : Control
# : Performed again to confirm the results in the first experiment

infection:

From 6 cases who were treated with pyrantel or mebendazole, on the 4th, 8th and 16th day of infection respectively, no worms were found in 3-day stools.

However, the case treated with pyrantel on the 32nd day passed 43 females; the case treated with mebendazole on the same infection day expelled 7 female *E. vermicularis*.

(2) Worm collection on the 40th day of infection:

One control case (Case 9), who did not take any drug before, passed 40 females after the terminating treatment with pyrvinium.

The cases previously treated with pyrantel on the 4th, 8th, 16th and 32nd day expelled 0, 10, 0 and 2 females respectively after the 40th day treatment.

The cases who were previously treated with mebendazole passed worms on the 40th day after pyrvinium treatment as follows; 15 females from the 4th day treated, 1 female from the 8th day

Table 3. Distribution of female *Enterobius vermicularis* by total body length which were collected on different days after the experimental infection. Out of 490 worms collected, 411 were measured

Age of worms (days)	Case No.	No. of worms		No. of worms in total body length (mm) of													
		collected	measured*	2.0 ≀ 2.4	2.5 ≀ 2.9	3.0 ≀ 3.4	3.5 ≀ 3.9	4.0 ≀ 4.4	4.5 ≀ 4.9	5.0 ≀ 5.4	5.5 ≀ 5.9	6.0 ≀ 6.4	6.5 ≀ 6.9	7.0 ≀ 7.4	7.5 ≀ 7.9	8.0 ≀ 8.4	8.5 ≀ 8.9
20	12	3	3	1	1	1	—	—	—	—	—	—	—	—	—	—	—
24	13	54	36	—	3	11	13	5	4	—	—	—	—	—	—	—	—
	14	24	19	2	5	9	1	2	—	—	—	—	—	—	—	—	—
Subtotal		78	55	2	8	20	14	7	4	—	—	—	—	—	—	—	—
28	15	1	1	—	—	—	—	—	—	1	—	—	—	—	—	—	—
	16	53	49	—	2	4	11	15	12	5	—	—	—	—	—	—	—
Subtotal		54	50	—	2	4	11	15	12	6	—	—	—	—	—	—	—
32	7	7	7	—	—	—	—	1	0	3	3	—	—	—	—	—	—
	8	43	35	—	—	1	2	10	14	5	3	—	—	—	—	—	—
Subtotal		50	42	—	—	1	2	11	14	8	6	—	—	—	—	—	—
35	17	69	57	—	—	—	—	—	2	5	23	17	8	2	—	—	—
40	1**	15	15	—	—	—	—	—	—	—	—	—	—	3	9	2	1
	3**	1	1	—	—	—	—	—	—	—	—	—	—	1	—	—	—
	4#	10	6	—	—	—	—	—	—	—	—	3	2	1	—	—	—
	5**	27	26	—	—	—	—	—	—	—	1	2	6	6	8	3	—
	8#	2	2	—	—	—	—	—	—	—	1	—	—	1	—	—	—
	9##	40	36	—	—	—	—	—	—	1	1	12	13	5	3	1	—
	10#	34	24	—	—	—	—	—	—	—	3	7	7	6	1	—	—
	11#	17	11	—	—	—	—	—	1	4	3	3	—	—	—	—	—
	14**	3	3	—	—	—	1	—	—	1	—	1	—	—	—	—	—
	16#	1	1	—	—	—	—	—	—	1	—	—	—	—	—	—	—
	17#	11	11	—	—	—	—	—	—	—	1	—	5	5	—	—	—
	18##	72	65	—	—	—	—	—	—	—	10	20	22	12	1	—	—
	19##	3	3	—	—	—	—	—	—	—	3	—	—	—	—	—	—
Subtotal		236	204	—	—	—	1	—	1	7	23	48	55	40	22	6	1

* : Broken and degenerated worms were excluded

** : Treated previously with mebendazole

\# : Treated previously with pyrantel pamoate

: Control

treated, 27 worms from the 16th day treated, and 0 worms from the 32nd day treated.

3. Results of the second experiment:

(1) Worm collection during 4th-35th day of infection:

The cases treated with pyrantel on the 4th, 16th, 24th, 28th and 35th day of infection passed out 0, 0, 24, 53 and 69 females on corresponding days.

The cases treated with mebendazole on the 20th, 24th, and the 28th day of infection expelled 3, 54 and 1 females in respect.

(2) Worm collection on the 40th day of infection:

Two control cases (Cases 18 & 19) expelled 72 and 3 females in respect on the 40th day by pyrvinium treatment.

The cases who were previously treated with pyrantel on the 4th, 16th, 24th, 28th and the 35th day expelled 34, 17, 3, 1 and 11 females respectively in 3-day stools by terminating treatment on the 40th day. On the other hand, the cases who were previously treated with mebendazole on the 20th, 24th and 28th day expelled no worms at all on the 40th day.

4. Growth of female *E. vermicularis* by infection day:

All of 490 collected *E. vermicularis* were females without exception. Other than *E. vermicularis*, we collected one female *Trichuris trichiura* from Case 17 after pyrantel treatment on the 35th infection day. No other helminthes were collected.

Total body length was measured in 411 worms after excluding broken and degenerated females out of 490 collected. The distribution of total body length was presented in Table 3 by 0.5 mm interval; the mean, standard deviation and ranges of length were in Table 4.

Total body length was in normal distribution either by case or by infection day. The length of worm increased consistently by infection day in terms of mean length; 2.69±0.31 mm in 20-day old females, 3.56±0.77 mm in 24-day old, 4.21±0.60 mm in 28-day old, 4.73±0.59 mm in 32-day old, 5.99±0.55mm in 35-day old and 6.69±0.75mm in 40-day old females (Fig. 1). By infection case, the standard deviations of total body length were around 0.5mm (Table 4).

Table 4. Total body length of female *E. vermicularis* (mean, standard deviation and range) as presented by infection day and by individual case

Age of worms (days)	Case No.	No. measured	Total body length (mm)		
			Mean	Std. Dev.	Range
20	12	3	2.69	0.31	2.47~3.04
24	13	36	3.74	0.54	2.53~4.82
	14	19	3.12	0.57	2.08~4.25
28	15	1	5.10	(—)	(—)
	16	49	4.19	0.60	2.94~5.35
32	7	7	5.26	0.43	4.49~5.80
	8	35	4.65	0.56	3.47~5.76
35	17	57	5.99	0.55	4.66~7.39
40	1	15	7.73	0.42	7.13~8.64
	3	1	7.00	(—)	(—)
	4	6	6.57	0.40	6.22~7.16
	5	26	7.28	0.65	5.98~8.43
	8	2	6.53	1.30	5.61~7.45
	9	36	6.69	0.60	5.15~8.25
	10	24	6.66	0.69	5.55~7.96
	11	11	5.64	0.61	4.55~6.49
	14	3	5.08	1.26	3.75~6.25
	16	1	5.41	(—)	(—)
	17	11	6.86	0.48	5.70~7.43
	18	65	6.51	0.49	5.51~7.84
	19	3	5.68	0.16	5.51~5.80

The control cases No. 9 and No. 18 were same individual. In this case, mean and standard deviation of female length in both experiments were very similar each other. The worms collected on the 40th day were always longer than those collected in previous treatments when compared in same volunteers (Cases 14, 16 and 17). Mean length of females which were collected from cases treated before the 35th day varied less between cases than those from 40th day.

The differences in total body length in 40-day old females between control, pyrantel-treated and mebendazole-treated groups were not tested

for their statistical significance. All of the pyrantel-treated cases showed that the expelled females on the 40th day were in same length distribution with control cases; females from mebendazole-treated cases showed more variations in lengh by individual case on either sides of control (for example, Cases 1 and 14). Therefore the deviations in body length in mebendazole-treated cases were not considered to be caused by the drug.

5. Development of sexual organs in female *E. vermicularis* by infection day (Table 5):

(1) 20-day old females:

In one female, the sexual organ was 0.23mm long from anterior to posterior tips of ovarian strands around vagina and sac-like structure. Vulva opened at 1.02mm from anterior and of body. No worms had uterus. Those worms were corresponded to the "youngest females" described by Hulinska (1968).

(2) 24-day old worms:

The sexual organs were 0.57±0.23mm long in 43 worms from anterior tip of ovarian loops to posterior end of posterior uterine loop. Vulva opened at 1.13±0.21mm from anterior end of body. Uterine loops were observed in 20.9% of worms, and 0.36±0.30mm long.

(3) 28-day old worms:

The sexual organ was 0.94±0.39mm long as measured in 27 worms. Vulva opened at 1.31±0.21mm from anterior end of body. Uterine loops were observed in 63% of worms and were 0.74±0.32mm long. No worms had eggs in their uterine loops yet.

(4) 32-day old worms:

The sexual organ was 1.91±0.45mm long in 18 measured worms. Vulva opened at 1.30±0.31mm from anterior end (4 out of 5 measured worms shrinked their anterior body in certain degrees). All worms had uterine loops of 1.42±0.28mm long. Out of 48 observed, 39 worms (81.6%) had empty uterus, 4 worms (8.3%) just began to have eggs, and 5 worms (10.1%) filled one side of uterine loops with eggs. The posterior end of uterine loop was far anterior to the anal pore.

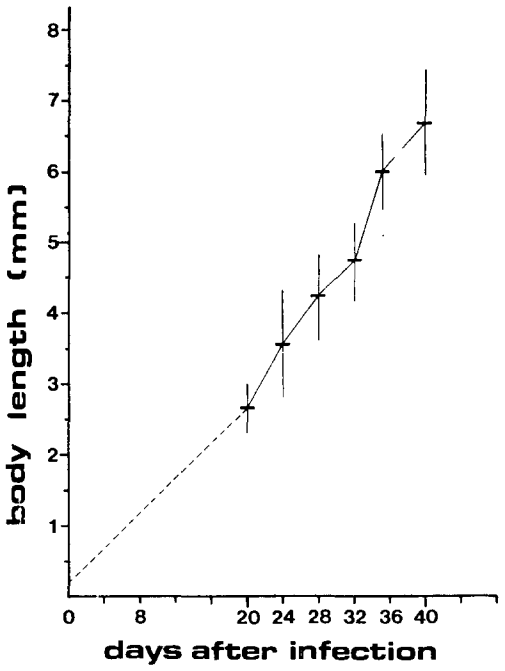

Fig. 1. Mean and standard deviation of total body length of female *E. vermicularis* collected on 20-40 days after the experimental infection. Length on the 0th day was that of naturally hatched larva from the shell (0.173mm in average).

(5) 35-day old worms:

The sexual organ was 2.99±0.57mm long in 52 measured worms. Vulva opened at 1.69±0.30mm from anterior end of body. Uterine loop was 2.17±0.46mm long. Out of 67 observed worms, 15 worms (22.4%) had empty uterus, 4 worms (6.0%) began to have eggs, 13 worms (19.4%) filled one side of uterine loops with eggs, 24 worms (35.8%) filled uterus with eggs but not yet fully, 11 worms (16.4%) filled uterus with eggs in full. The posterior uterine loop may reach the anal level.

(6) 40-day old worms:

The sexual organ was 3.79±0.79mm long in 165 measured worms. Vulva opened at 1.83±0.33mm from the anterior end of body. Uterine loop was 2.89±0.76mm long in 182 measured worms. Out of 236 observed, 13 worms (5.5%) had empty uterus, 1 worm (0.4%) began to

Table 5. Developmental status of uterus in *E. vermicularis* by infection day

Age of infection (day)	No. of worms observed	No. of worms in developmental stage of						
		1*	2*	3*	4*	5*	6*	7*
20	3	3	0	0	0	0	0	0
24	43	34	9	0	0	0	0	0
28	27	10	17	0	0	0	0	0
32	48	0	39	4	5	0	0	0
35	67	0	15	4	13	24	11	0
40	236	0	13	1	9	32	161	20

*1: Females without uterus 2: Females with empty uterus 3: Females which began to produce eggs 4: Females which filled eggs in one side of uterine of uterine loops 5: Females with uterus which were not completely filled with eggs yet 6: Females with egg-laiden uterine loops extending from vulva to anal level 7: Females with egg-laiden uterine loops extending anterior to vulva level

have eggs, 9 worms(3.8%) filled one side of uterine loop with eggs, 32 worms(13.6%) did not fill uterus fully with eggs yet, and 181 worms(76.7%) filled uterus with eggs in full. Out of 236 worms 20(8.4%), which were longer than 7.5mm in body length, began to extend their egg-laiden uterine loops anterior to vulva.

DISCUSSION

There are no available laboratory methods predicting that a person is *not* infected with *E. vermicularis*. In this study, therefore, much efforts were not paid to select the non-infected persons as volunteers. The only consideration was the selection from social class which showed the lowest egg positive rates by anal swab in epidemiologic point of view. Our volunteers were urban dwellers, 17-28 years old unmarried or 41-45 year-old married men with grown up children. By national survey(Ministry of Health and Social Affairs and Korea Assoc. for Parasite Eradication, 1981), those male population showed 2~4% of egg positive rates in contrast to average 12% in general population.

The data of worm measurements in this study indicated that our volunteers were not naturally infected prior to or during the experiments because the collected worms were all comparable each other in growth and development. All worms were in their range of normal distribution of body length. Therefore, the collected worms by antipinworm therapy were concluded to be derived from the experimental infection.

In control cases, the infection rates(No. of worms harvested/No. of eggs given) were 8.1% in the first and 0.6~13.2% in the second experiments. Except for the cases who were firstly treated with mebendazole(in whom 3-day stools were insufficient to collect all expelled worms; Comley, 1980), the rates in pyrantel-treated cases were similar with control in both experiments. However, the actual infection rates may be about double of our data(1~25%; about 14% in average) because male *E. vermicularis* were not detected throughout the study.

It was very interesting that we could not collect any male in the experiment. Cho *et al.* (1981) reported that males were harvested in cases who were treated with mebendazole, pyrantel, pyrvinium and piperazine as much as 770 out of 78 cases in heavily endemic orphanages. Retrospectively, those males may be discharged naturally rather than removed by anthelmintics.

One of the differences in our duplicated experiments was whether the larva inside the egg shell showed active movement. Our data of worm collection indicated that the larval movement was of negligible importance in determining the infectivity. The larval development to maturity in 3-5 days seems to be more important.

The life span of female *E. vermicularis* has been variously stated by different authors. The

reports can be categorized into two; the shorter life span ranging 13-30 days, and longer life span ranging 35-93 days. The former was reported by Grassi (1881) as 15-30 days and by Hall and Cram (1939) as 13-28 days. However, others reported the longer span; 37-65 days by Leuckart (1868), 37-93 days by Schueffner (1947), 45-62 days by Akagi(1973) and 35-75 days by Kozlov(1982).

The life span of female *E. vermicularis* so far reported was measured by the interval between the days of swallowing infective eggs and migration of gravid females. Due to this experimental method, those who favoured the shorter span may have thought that the reports of longer span were, in fact, results of intraintestinal development as proposed by Koch(1925), which was denied later by Skrjabin and Schults(1928). Such confusion on the life span may be due to the lack of acceptable descriptions on the chronologic growth of *E. vermicularis* by day. Therefore, the theory of shorter life span could not be denied.

Our results on the chronologic growth of females strongly indicated that the gravid females could not migrate out of the anus in 13～30 days after infection, when the developmental patterns of females were considered. Rather, the results suggested the longer span, 45～50 days, because a part of 40-day old worms were in their early gravid stages. Furthermore, many of females showed delayed growth even until 40th day, which supported the reports of the prolonged migrations of gravid females up to 62～93 days(Leuckart, 1868; Schueffner, 1947; Akagi, 1973; Kozlov, 1982). From our observation, we accepted our hypothesis that the life span of female *E. vermicularis* was longer than 40 days.

Fig. 2 summarized the results of anthelmintic effects on different developmental stages of *E. vermicularis*. The drug resistance was different by age of infection; evidently the worms younger than 16 days were fully susceptible to neither mebendazole nor pyrantel. Fig. 2 also showed that 4-day old and 16-day old worms were more resistant to both drugs than 8 day old

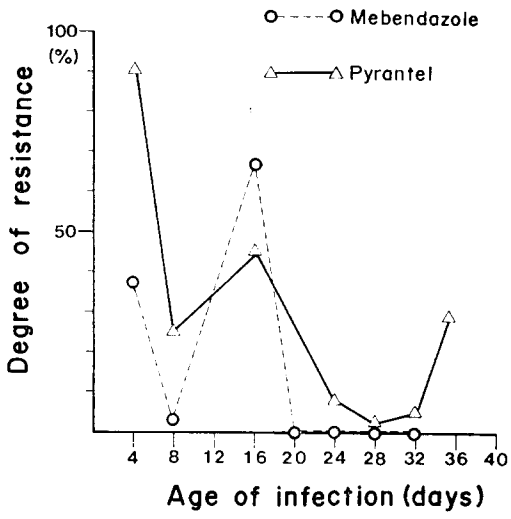

Fig. 2. Degree of drug resistance according to age of infection in *Enterobius vermicularis*. The degree of resistance was calculated by the formula:

$$\frac{\text{No. recovered in 2nd treatment on 40th day}}{\text{Mean No. from control cases}} \times 100$$

worms were. Such fluctuation of drug resistance by age is hardly interpretable at present. It is necessary to confirm whether it was consistent finding. Even though the cases who were treated before 20 days passed a fair number of females by the treatments on 40th day their numbers were always smaller than those of controls. It suggested that some of young worms in resistant age may be susceptible in a certain degree to antipinworm drugs.

We do not know at present by what kind of mechanism the young *E. vermicularis* showed different susceptibility to drug therapy. Probably, the larval development of *Aspiculuris tetraptera* in crypt of small intestine (Anya, 1966) may be a mechanism of evasion from drug action also in *E. vermicularis*(Beaver *et al.*, 1984).

The susceptibility of *E. vermicularis* after the age of 20 days to mebendazole explained very well the findings that the egg positive rate of anal swab returned to pre-treatment level within 30 days(Cho *et al.*, 1977). If the life span is in 45～50 days, the resisted females (=younger than 16 days) grew again in later 30 days to migrating gravid females which detected by anal

swab. The results of Cho *et al.* (1981) were also comparable with results of present study.

Anyway, this report made it clear that the objectives and reasons for repetition of chemotherapy in control of hyperendemic population are not only the reinfection but also the apparent limitation of anthelmintics efficacy on early stages of *E. vermicularis*. The reports of Matsen and Turner(1969) provided a nice model in control of enterobiasis in families; but its rationale in aspects of life span and reasons were not necessarily correct in view of our study results.

SUMMARY

In order to determine the susceptible age of *Enterobius vermicularis* to anthelmintics and to observe the chronologic growth of female *E. vermicularis* in man, experimental infections were done. About 500 eggs were challenged to 19 volunteers. After 4, 8, 16, 20, 24, 28, 32 and 35 days of infection, each case was treated by either mebendazole or pyrantel pamoate. On the 40th day of infection all cases including control were treated again to terminate the experimental infection and to evaluate the effect of previous treatment. Each case collected 3-day stools to harvest the expelled worms. The results could be summarized as follows:

1. The infection rates of females were in range of 0.6~13.1% in control cases. Because the collected worms showed comparable growth and development by day, the worms were concluded to be derived from experimental infection.

2. Cases that were treated with mebendazole on 4, 8 and 16 days after infection expelled 37.5%, 2.5% and 67.5% of the number expelled by a control case on the 40th day. Cases treated thereafter expelled no worms on the 40th day.

3. Cases that were treated with pyrantel pamoates on 4, 8, 16, 24, 28, 32 and 35 days, expelled 90.7%, 25%, 45.3%, 8%, 2.7%, 5% and 29.3% of the number collected from control cases in respect.

4. All the worms collected were females. The total body length increased consistently and comparably from the 20th day of infection. Those collected on the 20th day were 2.5~3.0 mm long with vagina, sac-like structure and strands of ovaries; 24 day-old worms may have short uterus, 28 day-old worms had long uterus without eggs, 32 day-old worms began to produce eggs, 35 day-old worms showed wide variations in egg deposit in uterus, and 40 day-old worms had uterus filled with eggs from vulva to anal levels.

From the above results, it was inferred that the life span of female *Enterobius vermicularis* was longer than 40 days, and the developmental stages of worms younger than 16 days resisted considerably to both mebendazole and pyrantel pamoate.

ACKNOWLEDGMENT

The authors of the present study would like to express their thanks to following persons for their understanding and willingly participation in this experiment: Mr. Ju Young Choi, Mr. Chan Young Chung, Mr. Hyung Se Kim, Mr. Jung Jin Kim, Mr. Sang Kuk Lee, Mr. Byung Joon Chung, Mr. Ki Hyung Ko, Mr. Yoon Kong, Mr. Jung Hwan Seo, Mr. Hyung Yoo and Mr. Sung Hoon Park of Chung-Ang University. Miss H.S. Kang prepared and measured the worm specimens for us. This research was supported by the Research Grant from the Asan Social Welfare Foundation, Korea (1982).

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=우리말요약=

요충 초기 발육단계에 대한 구충제의 효과

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이 실험의 목적은 요충감염에 있어 감염 일자별 충체의 구충제 감수성, 특히 초기단계 충체의 감수성을 관찰하는 것이다. 이와함께 각 감염 일자별로 배출되는 충체의 발육상태를 관찰하여 감염기간별 발육 양상을 관찰하는 것도 이 실험의 또 다른 목적이다.

경기도 안양시 소재보육원 원아에서 살아있는 요충 암놈을 수집, 충란을 분리하고 부란기에서 3~5일이 경과하여 유충이 형성된 충란을 약 500개씩 세었다. 이 실험의 대상으로 자원한 남자 19명(17~45세)에게 세어 놓은 충란을 투여하였다. 감염자는 "피란텔"치료군, "메벤다졸"치료군 및 대조군으로 나누었다. 각 치료군에 대해서는 감염후 4일, 8일, 16일, 20일, 24일, 28일, 32일 및 35일에 각 구충제를 투여하였다. 실험감염후 40일째 되는 날 대조군을 포함한 대상자 모두에게 "퍼르비늄"을 투여하여 감염을 완전히 중단시켰다. 각 약제 투여후에는 그후 3일간의 대변을 수집하고 배출되는 요충충체를 수집하였다. 그 숫자를 세고, 충체의 발육정도를 관찰하였다. 그 결과를 요약하면 다음과 같다.

1. 이 실험에서 감염율은 대조군에서 0.6~13.1%이었다. 감염 일자별로 수집한 충체의 발육단계가 모두 일정한 단계의 범위안에 있어 이번 실험에서 얻은 충체는 모두 실험감염의 결과 감염되어 발육한 충체라고 판단하였다.

2. "메벤다졸"을 감염후 4일, 8일, 16일에 투여한 예에서는 대조군에서 배출한 충체수의 37.5%, 2.5%, 및 67.5%가 40일째에 배출되었다. 그 이후에 투약한 예에서는 투약 직후에는 충체가 배출되었으나 감염 40일째에 투약한 후에는 충체배출을 하지 않았다.

3. "피란텔"을 감염후 4일, 8일, 16일, 24일, 28일, 32일 및 35일에 투여한 예에서는 대조군에서 배출한 충체수의 90.7%, 25%, 45.3%, 8%, 2.7%, 5% 및 29.3%를 배출하고 있었다.

4. 배출된 충체는 모두 암놈이었다. 충체의 길이는 일자별로 20일에서 40일째까지 일정한 양상으로 발육하고 있었고, 각 일자별, 증례별로 충체 길이는 정규분포 형식으로 분포하고 있었다.

이상의 소견에서 요충 암놈의 인체내 발육기간은 40일 이상이고 감염후 16일째까지의 어린 충체는 "메벤다졸"이나 "피란텔"에 대해서 정도의 차이는 있으나 치료에 저항한다고 결론을 내린 수 있었다.