

## Effect of Oxantel/Pyrantel Pamoate Tablets against Intestinal Nematodes in Korea

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### INTRODUCTION

Multiple helminthic infections are very frequently encountered in the Korean populations. Routine stool examinations revealed over 80 per cent of the population to be infected with one or more of the following nematodes: *Ascaris lumbricoides*, *Trichuris trichiura*, hookworms, *Enterobius vermicularis* and *Trichostrongylus orientalis* etc. Among these infections, *T. trichiura* has been shown the highest prevalence rate.

In view of the frequency of multiple nematode infections in the rural areas, safe and effective broad-spectrum anthelmintics are greatly needed. Rim et al. (1972, 1973) and other many workers have shown that pyrantel pamoate is very effective against *A. lumbricoides*, hookworms, *T. orientalis* and *E. vermicularis*, but it has no significant effect against *T. trichiura*. However oxantel pamoate appears to be an efficient drug against *T. trichiura* (Park et al., 1973; Lim, 1974; Rim et al., 1974). In the previous paper we reported high cure rates with the combined drug of pyrantel/oxantel pamoate suspension in the infections of *A. lumbricoides*, *T. trichiura*, hookworms and *E. vermicularis* (Rim et al., 1975).

The present study was undertaken to determine the efficacy of oxantel/pyrantel mixture tablets in cases of multiple infections with *T. trichiura* together with either *A. lumbricoides*, *E. vermicularis* and/or *A. duodenale*, and also to determine the incidence and severity of side effects at the dosage used.

### MATERIALS AND METHODS

A total of 48 subjects, of all age groups consisting of 42 orphanage children (males 11, females 31) and 6 adults (males 4, females 2) were included in this study.

The incidence of multiple helminthic infections in the present study is shown in Table 1. Of 48 patients, 45 were infected with *T. trichiura* and 44 children with *E. vermicularis*, 37 with *A. lumbricoides*, 8 with *A. duodenale*, 1 with *T. orientalis* and 2 with *Clonorchis sinensis*. The majority of this group harboured three species of worms: *T. trichiura* with *A. lumbricoides* and *E. vermicularis* and/or *A. duodenale*.

All the 48 patients were given a single dose of 20 mg per kg body weight each of oxantel/pyrantel pamoate tablets (100 mg/tablets each) in the following dosage schedule: 3 tablets for under 15 kg body weight, 4 tablets for between

Table 1. Incidence of multiple helminthic infections in 48 subjects

Helminths	No. of infecting helminths per subject			Total No. of cases
	Double	Triple	Quadruple	
<i>Trichuris trichiura</i>	8	34	3	45
<i>Ascaris lumbricoides</i>	1	33	3	37
<i>Ancylostoma duodenale</i>	2	3	3	8
<i>Enterobius vermicularis</i>	8	33	3	44
<i>Trichostrongylus orientalis</i>		1		1
<i>Clonorchis sinensis</i>	1	1		2

15 to 20 kg, 5 for 20 to 25 kg, 6 for 25 to 30 kg, 7 for 30 to 35 kg, 8 for 35 to 40 kg, 9 for 40 to 45 kg, 10 for 45 to 50 kg, 11 for 50 to 55kg, 12 for 55 to over 60 kg body weight.

The criteria of assessment of the drug efficacy against intestinal nematodes were by 24 hour stool egg counts using Stoll's method with the specimens of stool obtained on three occasions prior to treatment; and the same examinations repeated twice in each on the 10 to 11th day and 20 to 21st day after treatment. When the egg count was zero, at least further two stool examinations were performed by the formalin-ether sedimentation method in order to exclude false negatives. In patients with hookworm infection, the species of hookworm was identified by coproculture prior to treatment and this examination was repeated twice in each on the 10 to 11th day and the 20 to 21st day after treatment. The patients were rated as cured if the fecal egg count were zero on the 20 to 21st post-treatment days and either formalin-ether or zinc sulfate floatation methods were negative and whenever it was performed coproculture being negative. The adult worms were also collected from 24 hours stool for 3 successive days after drug medication.

In *E. vermicularis* infection, the Scotch-tape swab tests were performed to establish the assessment of diagnosis and cure. The Scotch-tape swabs were taken on 3 occasions at the

morning prior to treatment, and on the 1st to 6th days, the 10 to 11th days and the 20 to 21st days after treatment.

The subjects were carefully observed to ascertain the type and severity of side effects. However hematological and blood biochemical examinations and routine urinalysis were not undertaken in this study.

## RESULTS

As shown in Table 2, a total of 48 subjects harbouring *T. trichiura*, *A. lumbricoides*, hookworm and/or *E. vermicularis* were treated with oxantel and pyrantel pamoate in the form of tablet (100 mg of each) in a single dose of 20 mg base per kg of body weight of each.

In all 37 cases of *A. lumbricoides* with an average EPG of 2,560 (200-19,067), complete cure was obtained on both the 10 to 11th and the 20 to 21st days after treatment. Examination of stools for adult worms could be carried out in all cases. The mean recovered worm-load was 3.8 with a range of 1 to 21 worms. Eight cases of *A. duodenale* infection with an average EPG of 742 (67-3,600) were treated. All cases had negative stool examinations. The mean recovered worm load was 5.8 with the range from 3-9 worms during 3 consecutive days after treatment. In *T. trichiura* infection, a total of 45 cases with an average EPG of 861 (67-

**Table 2.** Effect of a single dose of oxantel/pyrantel pamoate tablets against intestinal nematode infections (20mg/kg body weight each)

Name of helminths	No. of subject	Pre-Treat. EPG: mean (range)	Post-Treat. EPG(D+20, 21)		Egg reduction rate(%)	No. of cured (%)	Mean No. recovered worms
			No. of posit.	Mean EPG (range)			
<i>Trichuris trichiura</i>	45	861 (67~4, 533)	13	79 (0~750)	90.8	71.1	14.6 (1~77)
<i>Ascaris lumbricoides</i>	37	2, 560 (200~19, 067)	0	0	100.0	100.0	3.8 (1~21)
<i>Ancylostoma duodenale</i>	8	742 (67~3, 600)	0	0	100.0	100.0	5.8 (3~9)
<i>Enterobius vermicularis</i>	44	—	17	—	—	61.4 (84.1)*	17.7 (1~62)
<i>Trichostrongylus orientalis</i>	1	133	0	0	100.0	100.0	—

\*Cure rate on the 10 to 11th days after treatment

4, 533), the cure rate on the 20 to 21st days after treatment was 71.1 per cent, and the average egg reduction rate was 90.8 per cent. The mean recovered worm-load was 14.6 with a range of 1-77 worms.

In *E. vermicularis* infection, of the 44 patients who were positive by Scotch-tape method, 37 (84.1%) were negative on the 10 to 11th days and 27 (61.4%) on the 20 to 21st days after treatment. In detailed analysis on the anthelmintic effect of a single dose of oxantel/pyrantel pamoate tablets against *E. vermicularis*, 27 (61.4%) patients out of 44 treated orphanage children were negative throughout the post-treatment observation period and were considered to have been cured. On the other hand 5 (11.4%) patients of 44 cases remained positive throughout the course of the study, and the other 2 cases initially negative at the 4 to 6th days after treatment proved positive again through the 2 post-treatment tests on the 10 to 11th days and the 20 to 21st days after treatment. Therefore 7 (15.9%) out of 44 cases were considered as failure. However 10 (22.7%) of 44 cases who were initially negative on the 4 to 6th days and the 10 to 11th days after treatment and later shown to be positive on the 20 to 21st post-treatment days were thought to have had relapse or to have been

reinfected.

Only one patient with *Trichostrongylus orientalis* treated with a single dose of oxantel/pyrantel pamoate tablets at a dosage of 20 mg base per kg showed no eggs in their stools throughout the post-treatment examinations. However this drug showed no therapeutic response in 2 patients with *Clonorchis sinensis*.

Side effects were not noted in all treated cases.

## DISCUSSION

Many investigators proved that pyrantel pamoate was highly effective against a wide range of human parasitic nematodes. A single dose of pyrantel pamoate has been shown highly effective against human ascariasis, enterobiasis and hookworm infections. Rim et al. (1972, 1973) have earlier shown that pyrantel pamoate is very effective against *A. lumbricoides*, hookworms, *T. orientalis* and *E. vermicularis*, but has no significant effect against *T. trichiura*.

Recently oxantel pamoate appears to be efficient and well tolerated drug against *T. trichiura* (Park et al., 1973; Lim, 1974; Rim et al., 1974), but this drug has no significant effect

against *A. lumbricoides*, hookworms and *E. vermicularis* infections and will be unsuitable for treatment of multiple infections.

Intestinal helminth infections have been a major medical problem in this country, because of their high incidence and difficulty of effective mass treatment. In view of the frequency of multiple helminthic infections in Korean populations, the combination of oxantel pamoate and pyrantel pamoate should be considered as a drug of choice in multiple infections of the common intestinal nematodes.

In the previous paper, Rim et al. (1975) reported high cure rates with the combined drug of oxantel/pyrantel pamoate suspension in the infections of *A. lumbricoides*, *T. trichiura*, hookworms and *E. vermicularis*.

The present study was undertaken to determine the efficacy in tablet form of oxantel/pyrantel mixture in the cases of multiple infections with *T. trichiura* together with either *A. lumbricoides*, *E. vermicularis* and/or *A. duodenale*.

The drug combinations as anthelmintics in intestinal nematode infections were used by many workers. Beck (1966) reported on the combination of pyrvinium and piperazine in a few patients given as a single dose on two successive days. In the result, 21 out of 24 cases of *Ascaris* infection achieved 100% egg reduction and 10 of 11 cases of enterobiasis became negative. These findings were confirmed by Santos and Noseñas (1968) who gave a single dose on 2 consecutive days to 103 children with enterobiasis of whom 98 also has ascariasis. Cure rate were estimated at 84% for ascariasis and 73% in enterobiasis. Atra et al. (1965) used a tablet form of a combination of pyrvinium and thiabendazole and gave either a 6 day or a 12 day course in 50 assorted parasitic infections. They obtained cure rates of 86% in trichuriasis, 100% in ascariasis, 90% in hookworm,

and experienced some 21% of side effects. Filho et al. (1971) tested a formulation containing thiabendazole and piperazine in 41 patients with hookworm, *Ascaris* and/or *Strongyloides*. A three day course of treatment was used and the mixture was given twice daily. An overall figure of 63% were cured; for individual parasites 89% in *Ascaris*, 97% in *Strongyloides* and 66% in hookworm infections were cured.

Above combined drugs have shown only moderate effectiveness against intestinal nematode infections, and they are always needed to apply these remedies with higher dosages of longer courses and it is difficult to eradicate completely in mass treatment.

Recently Rim et al. (1975) used a paratable suspension of oxantel/pyrantel pamoate mixture (50 mg of each per ml) in 56 subjects with multiple nematode infections with *T. trichiura*, *Ascaris*, hookworms and *Enterobius*. A single dose of 10mg per kg body weight in each cured 100% of 54 subjects with *Ascaris*, 97.1% of 35 subjects with hookworms, 77.8% of 36 subjects with *Enterobius* and 73.2% of 56 subjects with *T. trichiura* infection. Similar results were obtained in the present study. A total of 48 subjects harbouring *T. trichiura*, *A. lumbricoides*, *A. duodenale* and/or *E. vermicularis* were treated with oxantel/pyrantel pamoate tablets (100mg of each) in a single dose of 20 mg base per kg of body weight. In all 37 cases of *A. lumbricoides* and 8 cases of *A. duodenale* infections complete cure was obtained on both the 10 to 11th and the 20 to 21st days after treatment. Cure rates were estimated at 71.1% for trichuriasis and 61.4% in enterobiasis on the 20 to 21st days after treatment. There was no significant differences in the efficacy between the oral suspension and tablet forms of oxantel/pyrantel pamoate mixture. However the tablet formulation is more convenient than the suspension in mass treatment. An interesting findings

was that there was no significant differences in the dosage of 10mg base (suspension) and 20 mg base (tablet) per kg of body weight in the cure rates of trichuriasis and enterobiasis. These findings were also observed by Lee and Lim (1977). When oxantel/pyrantel suspension was administered at a single dose of 20 mg/kg, 100 % cure rate was obtained in *Ascaris*, but the cure rate and egg reduction rate were 70% and 96.1% respectively in the treatment of *Trichuris* infection. Lim(1977) experienced similar results. A single dose of 10 mg/kg body weight each of oxantel and pyrantel pamoate syrup mixture were given to 80 subjects, cure rates were obtained as 77.3% for *Trichuris*, 97.3% for *A. lumbricoides*, 95.5% for hookworm and 84.9% for *Enterobius* infections. However, of 78 subjects with multiple helminth infections given a single dose of 15 to 20 mg/kg body weight each of oxantel/pyrantel pamoate tablets, the cure rates were obtained 78.2% for *Trichuris*, 100% for *Ascaris*, 100% for hookworm and 77.8% for *Enterobius* infection. On the other hand, Lee et al. (1977) treated 34 subjects with the mixed infections in a single dose of 15 mg/kg body weight of oxantel/pyrantel pamoate tablets, the cure rates and egg reduction rates were 85.3% and 97% in trichuriasis respectively, but 100% each in ascariasis and ancylostomiasis. Similarly they also used a single dose of 15 mg/kg of oxantel/pyrantel suspension, and found 100% for *Ascaris* infection and 90% for *Trichuris* infection with 100% of egg reduction rate. With regard to dosage, a single dose of 15 mg/kg body weight of oxantel/pyrantel pamoate in either suspension or tablet forms seems like to be more effective than that of 20 mg/kg body weight in the treatment of multiple infections of intestinal nematodes.

In the enterobiasis, of 44 children treated with oxantel/pyrantel pamoate in this study, 37 (84.1%) were negative eggs on the 10 to

11th days and 27 (61.4%) on the 20 to 21st days after treatment. But 10 (22.7%) of 44 cases who were initially negative on the 4 to 6th days and the 10 to 11th days after treatment and later shown to be positive on the 20 to 21st post-treatment days. This was considered to be relapsed or reinfected. Kagei and Kihata (1971) reported that pyrantel pamoate did not show therapeutic action against larval worms of *Syphacia obvelata* at the doses 50, 25, 12.5 and 6mg/kg body weight in mice. Yamamoto et al. (1971) and Cho and Kang (1975) agreed that pyrantel pamoate at the dose of 10 mg/kg did not expell completely the immature and/or larvae of *E. vermicularis*. On the other hand, Cram (1943) stated that the migration out of gravid female worms occurs from 15 to 43 days after the ingestion of infective stage of pinworm eggs. In this connection, the cure rate for enterobiasis in the present study, 84.1% should be evaluated at the dose of 20 mg/kg oxantel/pyrantel pamoate tablets.

## SUMMARY

A total of 48 subjects harbouring *Trichuris trichiura*, *Ascaris lumbricoides*, hookworm and/or *Enterobius vermicularis* were treated with oxantel/pyrantel pamoate tablets (100 mg of each) in a single dose of 20 mg base per kg of body weight.

In all 37 cases of *A. lumbricoides* and 8 cases of *A. duodenale* infections cured completely, and the mean recovered worm-load was 3.8 with a range of 1-21 and 5.8 with a range of 3-9 respectively. In *T. trichiura* infection, 32 (71.1%) of 45 cases cured completely and the average egg reduction rate was 90.8 per cent. The mean recovered worm-load was 14.6 with a range of 1-77 worms. On the other hand, in *E. vermicularis* infection, 37 (84.1%) of 44 patients were negative eggs by anal swab tests

on the 10 to 11th days and 27 (61.4%) on the 20 to 21st days after treatment. The mean recovered worm-load was 17.7 with a range of 1-62. Only one patient with *Trichostrongylus orientalis* treated with this drug showed no eggs in his stools throughout the post-treatment examinations. Side effects were not noted in all treated cases.

These findings demonstrate that a single dose of oxantel/pyrantel pamoate tablets can be considered a drug of choice for multiple infections with these nematodes.

### REFERENCES

- Atra, E., Vilela, M.P. & Zucas, A.W. (1965). Terapêutica da tricocéfaliase. Hospital (Rio de J.), 68:217-224. (cited from Davis, 1972)
- Beck, J.W. (1966). The treatment of *Ascaris lumbricoides* and *Enterobius vermicularis* with combination drug composed of pyrvinium pamoate and piperazine. Acta méd costarric., 9:9-11.
- Cho, S.Y. and Kang, S.Y. (1975). Significance of Scotch-tape anal swab technique in diagnosis of *Enterobius vermicularis* infection. Korean J. Parasit., 13(2):102-114.
- Cram, E.B. (1943). Studies on oxyuriasis. XXVIII Summaries and conclusion. Am. J. Dis. Child, 65:46-59.
- Davis, A. (1972). Drug treatment in intestinal helminthiasis. WHO/HELM/72.1, 100pp.
- Filho, F.F., Duarte, G.G., Teruel, J.R. & Franco, A.R. (1971). Estudo de uma associação antihelmintica em parasitoses intestinais múltiplas. Rev. Soc. bras. Med. trop., 5:209-212.
- Kagei, N. and Kihata, M. (1971). Anthelmintic effects of pyrantel pamoate against *Syphacia obvelata* and *Aspicularis tetraoptera*. Jap. J. Parasit., 20(3):228-234.
- Lee, S.H. and Lim, J.K. (1977). A comparative study of the anthelmintic effects of oxantel/pyrantel suspension and mebendazole in mixed infection of *Ascaris* and *Trichuris*. Program & abstracts of Pfizer Forum on common parasitic diseases, Manila, 1977.
- Lee, S.H., Song, C.Y. & Lim, J.K. (1977). Anthelmintic effect of oxantel and oxantel/pyrantel tablets against intestinal nematode infections. Korean J. Parasit., 15(2):121-126.
- Lim, J.K. (1974). Anthelmintic effect of oxantel pamoate against *Trichocephalus trichiurus* infection. Korean J. Pharmacol., 10:97-101.
- Lim, J.K. (1977). Effect of oxantel and oxantel/pyrantel against intestinal nematode infections. Program & abstracts of Pfizer Forum on common parasitic diseases, Manila, 1977.
- Park, C.W., Lim, J.K., Shim, S.J., Kim, M.S. and Chung, M.H. (1973). Anthelmintic effect of trans-1, 4, 5, 6-tetrahydro-2-(3-hydroxy-styryl)-1-methyl-pyrimidine (CP-14, 445) on *Trichocephalus trichiurus*. Seoul J. Med., 14: 228-232.
- Rim, H.J. and Lim, J.K. (1972). Treatment of enterobiasis and ascariasis with combantrin (pyrantel pamoate). Trans. Roy. Soc. Trop. Med. & Hyg., 66(1):170-175.
- Rim, H.J., Lim, J.K. and Seo, B.S. (1973). The effect of pyrantel embonate (Combantrin) against hookworm and other intestinal nematodes in Korea. Asian J. Med., 9:393-396.
- Rim, H.J., Won, C.Y., Lee, S.I. and Lim, J.K. (1975). Anthelmintic effect of oxantel/pyrantel suspension against intestinal nematode infections. Korean J. Parasit., 13:97-101.
- Rim, H.J., Chang, Y.S., Ha, J.H. and Lim, J.K. (1976). Anthelmintic effect of oxantel pamoate (CP-14, 445) against trichuriasis. Korea Univ. Med. J., 13:205-211.
- Santos, A.T.Jr. & Noseñas, J.S. (1968). Pyrvinium pamoate with piperazine in the treatment of enterobiasis and ascariasis. J. Philipp.

med. Ass., 44:33-38.  
Yamamoto, H., Hayashi, S., Motoyoshi, K.  
and Mori, Y. (1971). Anthelmintic effect of

pyrantel pamoate against *Enterobius vermicularis*. Jap. J. Parasit., 20(5):359-365.

≡국문초록≡

腸內線蟲類에 對한 Oxantel/Pyrantel 合錠劑의 驅蟲效果

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Oxantel 및 Pyrantel을 각각 100mg씩 함유된 경제분 사용하여 48명의 장내선충류 감염자에게 20 mg/kg의 용량으로 단회 투약함으로써 그 구충효과를 검토하였다.

투약전 3회의 대변검사로서 평균 EPG를 구하고 투약후 10, 11일 및 20, 21일에 각각 대변검사를 실시하여 비교함으로써 구충효과를 판정하였다.

요충에 대하여는 항문주위도말법을 사용하여 투약전 3회, 투약후 6일간 계속 검사하고 투약 10, 11일과 20, 21일에 각각 검사하여 요충 구충효과를 검토하였다.

한편 투약후 3일간 전량의 대변을 수집하여 배출된 충체를 집계하였다.

복약자 48명중 회충감염자가 37명, 편충감염자는 45명, 요충감염자 44명, 구충감염자 8명 및 동양모양선충 감염자 1명이었다.

본 정제의 단회 투약으로 회충 및 구충은 100%의 음전율을 얻었고 편충에서는 45명중 32명이 완전 구충되어 71.1%의 음전율을 얻었으나 90.8%의 충난 감소율을 얻었다.

요충감염자에 있어서 투약 10, 11일에 있어서 44명중 37명에서 음전되어 84.1%의 음전율을 얻었으나 투약 20, 21일에 있어서 27명만이 요충란이 음전하여 61.4%의 음전율을 얻었다.

단 1예의 동양모양선충 감염자에 있어서는 본제 단회 투약으로 완전 구충되었다.

본제는 전예에서 부작용이 전혀 없었으며 투약은 간편하였다.