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Epidemiological study of clonorchiasis and metagonimiasis along the Geum-gang (River) in Okcheon-gun (County), Korea

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Abstract: The endemic status of clonorchiasis and metagonimiasis along the Geum-gang (River) in Okcheon-gun (County) in Korea was examined. From February to December 2000, stools of total 1,081 inhabitants living in 5 villages were examined. Each stool specimen was examined by both the cellophane thick smear method and the formalin-ether sedimentation technique. Egg-positive cases were further analyzed by Stoll's egg-counting technique, and praziquantel was administered to positive cases. The egg-positive rates for *Clonorchis sinensis* and *Metagonimus* species were 9.3% and 5.5%, respectively, and the double infection rate was 3.5%. The numbers of eggs per gram (EPG) of feces of *C. sinensis* and *Metagonimus* sp. were 918±1,463 and 711±947, respectively. The egg-positive rates for *C. sinensis* and *Metagonimus* sp. in the riverside area were 14.2% and 8.4%, respectively, which were significantly higher than those of the inland area (3.2% and 1.7%, respectively). The egg-positive rates of *C. sinensis* and *Metagonimus* sp. in males (16.7% and 10.0%) were significantly higher than those of females (3.5% and 1.8%). However, there were no significant differences of EPG values between localities and sexes. The prevalence of clonorchiasis and metagonimiasis in this survey was significantly lower than that in the previous reports. However, there is still a high prevalence of infection with *C. sinensis* and *Metagonimus* sp. in this region, especially in the riverside area.

Key words: *Clonorchis sinensis*, *Metagonimus* sp., epidemiology, Okcheon-gun

INTRODUCTION

In the past, parasitic infections were regarded as a major public health problem in Korea. Over the past three decades, the prevalence of such infections has been decreasing rapidly, accompanied by an increase in the GNP, improvements in sanitation and hygiene, changes in agricultural management, and a nationwide control plan (Cho, 1994; Rim, 1997). Infection by soil-transmitted helminths, such as *Ascaris* and *Trichuris*, decreased dramatically: the egg-positive rates for these parasites were 13.0-23.4% in 1981 and 0.04-0.06% in 1997 (MHW and KAH, 1997). However, the pattern of prevalence of snail-transmitted trematode infections seems to be quite different from that of soil-

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transmitted helminth infections. The nationwide egg-positive rates for *Clonorchis sinensis* and *Metagonimus* sp. were 2.6% and 1.2% in 1981, and 1.4% and 0.3% in 1997, respectively (MHW and KAH, 1997). These data show that clonorchiasis and metagonimiasis are still common parasitic diseases in Korea.

C. sinensis, the liver fluke, is a well-known parasite that is of major public health importance in Korea and several other Asian countries. Infection with *C. sinensis* occurs by eating uncooked freshwater fish that harbors the metacercariae. In Korea, human infection has been shown to have a high prevalence along several major Korean rivers (Seo et al., 1981; Kim et al., 1994; Rim, 1997). The Geum-gang (River) basin is a well-known endemic area, where the prevalence of clonorchiasis over the last two decades has been in the range of 30.8 to 50.7% (Chang, 1979; Seo et al., 1981; Kim et al., 1994). Metagonimiasis is a fish-borne trematodiasis that is also of medical importance in Korea; it is endemic along the southern and eastern coasts (Seo et al., 1981; Kim et al., 1987; Chai et al., 1993 and 2000). In addition to these areas, the Geum-gang (River) basin, western coastal areas, and the Namhan-gang (River) basin have also been reported to be endemic areas (Kim 1980; Chai et al., 1993; Kim et al., 1994).

Even today, snail-transmitted trematodes infections are the most significant parasitic diseases in Korea, especially in rural and riverside areas, and the Geum-gang basin is an endemic area for clonorchiasis and metagonimiasis. Although there have been a few surveys of the prevalence of snail-transmitted trematode infection in this area in the past (Chang, 1979; Kim, 1980; Seo et al., 1981; Kim et al., 1987; Kim et al., 1994), there is no up-to-date survey reports. Therefore, we examined the endemicity and intensity of infection by *C. sinensis* and *Metagonimus* sp. in inhabitants of Okcheon-gun (County) living near the Geum-gang (River), and also obtained the follow up results after treatment of *C. sinensis*-positive cases with praziquantel.

MATERIALS AND METHODS

Area surveyed and population

This epidemiological study was undertaken during the period of February to December

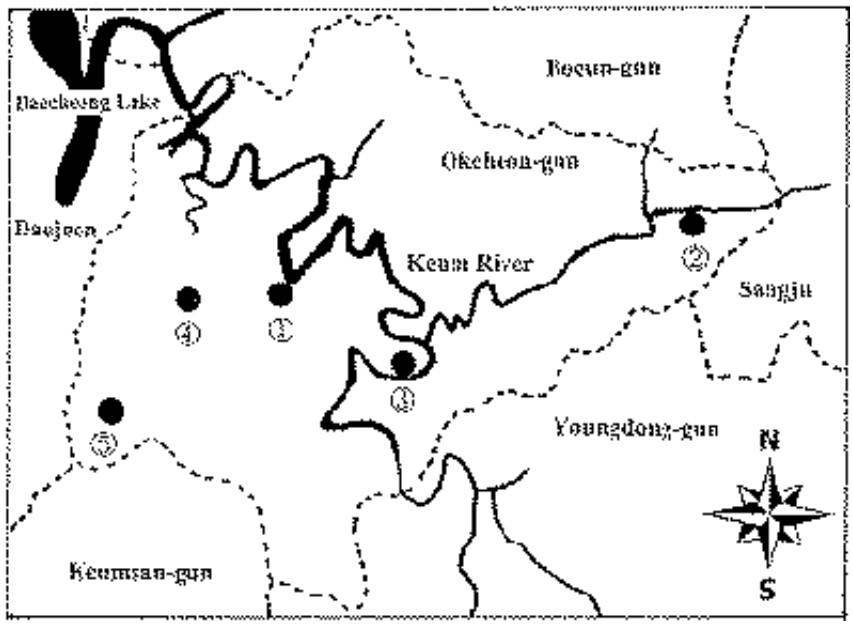

Fig. 1. Map of the areas surveyed in Okcheon-gun, Chungcheongbuk-do, Korea. ①, Subug-ri Okcheon-eup; ②, Yegog-ri Cheongsan-myeon; ③, Usan-ri Dongyi-myeon; ④, Okgag-ri Okcheon-eup; ⑤, Eunhaeng-ri Gunseo-myeon.

2000. Total of 1,081 inhabitants (479 males, 602 females) of 5 villages in Okcheon-gun in Chungcheongbuk-do (Province), Korea, were examined. The subject villages were divided into riverside and inland areas. Subug-ri Okcheon-eup, Yegog-ri Cheongsan-myeon, and Usan-ri Dongyi-myeon belonged to the riverside area, which is within 2 km of the main channel of the Geum-gang. Okgag-ri Okcheon-eup and Eunhaeng-ri Gunseo-myeon were in the inland area which is farther than 5 km from the main channel of the river (Fig. 1). The age of the subject population ranged from 7 to 88 years, and the average age was 56.9± 15.2 years (Table 1).

Stool examination and treatment of *C. sinensis* egg-positive cases

Fecal specimens were collected during the period of February and April 2000 from 1,081 inhabitants, including both sexes and all age groups, residing in the five villages (Table 1). The specimens were examined once each by the cellophane thick smear method (Kato's method) and the formalin-ether sedimentation (FES) technique.

After the fecal examination, Stoll's egg-counting technique was applied to specimens that were positive for the eggs of *C. sinensis* or *Metagonimus* sp.. Based on the eggs per gram of feces (EPG), the specimens were classified as Grade I (EPG 100-900), Grade II (EPG 1,000-4,900), Grade III (EPG 5,000-9,900) and Grade IV (EPG over 10,000) as described in previous reports (Cho 1994). *C. sinensis* egg-positive inhabitants were treated with 75 mg/kg praziquantel, administered as three 25-mg/kg doses on a single day in August 2000. Stool samples of those treated were collected in November 2000, and the infection status of clonorchiasis was again examined by both the cellophane thick smear method and the FES technique.

Statistical analysis

We used SPSS 10.0 software to analyze the data from these experiments. The chi-square test and Student's t-test were used to check

Table 1. Locality, sex and age distribution of surveyed population in Okcheon-gun, Chungcheongbuk-do, Korea

Localities	Sex	No. of exam.	Age group (year)								
			0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-
Subug-ri	Male	130	2	2	3	5	17	27	40	26	8
Okcheon-eup[a)]	Female	157	1	3	4	9	20	29	56	29	6
	Subtotal	287	3	5	7	14	37	56	96	55	14
Yegog-ri	Male	103	-	10	1	3	15	17	35	17	5
Cheongsan-myeon[a)]	Female	122	-	3	-	2	18	29	45	22	3
	Subtotal	225	-	13	1	5	33	46	80	39	8
Usan-ri	Male	35	-	4	1	3	9	5	12	1	-
Dongyi-myeon[a)]	Female	58	2	3	4	10	12	11	10	6	-
	Subtotal	93	2	7	5	13	21	16	22	7	-
Okgag-ri	Male	120	3	7	3	7	19	23	33	23	2
Okcheon-eup[b)]	Female	158	10	10	5	8	20	29	41	27	8
	Subtotal	278	13	17	8	15	39	52	74	50	10
Eunhaeng-ri	Male	91	-	2	2	9	21	22	19	14	2
Gunseo-myeon[b)]	Female	107	-	-	1	9	19	22	43	13	-
	Subtotal	198	-	2	3	18	40	44	62	27	2
Total	Male	479	5	25	10	27	81	94	139	81	17
	Female	602	13	19	14	38	89	120	195	97	17
	Total	1,081	18	44	24	65	170	214	334	178	34

[a)]Riverside area; villages within 2 km from the main stream of Geum-gang (River).
[b)]Inland area; villages 5 km apart from the main stream of Geum-gang (River).

Table 2. Number of egg-positive cases and their EPG counts of *C. sinensis* and *Metagonimus* sp. depending on localities in Okcheon-gun, Chungcheongbuk-do

Localities	No. of cases Examined	*C. sinensis*		*Metagonimus* sp.	
		Egg-positive cases[a](%)	EPG counts of positive	Egg-positive cases (%)	EPG counts of positive
Riverside areas	605	86 (14.2)[b]	967 ± 1,565[c]	51 (8.4)	760 ± 1,010
Subug-ri Okcheon-eup	287	35 (12.2)	582 ± 516	20 (7.0)	520 ± 119
Yegog-ri Cheongsan-myeon	225	33 (14.6)	1,260 ± 2,002	24 (10.7)	841 ± 1,126
Usan-ri Dongyi-myeon	93	18 (19.4)	1,177 ± 1,913	7 (7.5)	1,171 ± 1,782
Inland areas	476	15 (3.2)[b]	640 ± 561	8 (1.7)	400 ± 151
Okgag-ri Okcheon-eup	278	9 (3.2)	688 ± 609	3 (1.1)	400 ± 200
Eunhaeng-ri Gunseo-myeon	198	6 (3.0)	566 ± 527	5 (2.5)	400 ± 141
Total	1,081	101 (9.3)	918 ± 1,463	59 (5.5)	711 ± 947

[a]Egg positive cases of stool examination were found eggs either by formalin-ether sedimentation technique or cellophane thick smear method (Kato's method).

[b]The difference of egg positive rates between the riverside and inland areas was statistically significant ($p<0.05$).

[c]Mean±SD of EPG counts of egg positive cases.

Table 3. Egg-positive cases of *C. sinensis* and *Metagonimus* sp. according to age group in Okcheon-gun, Chungcheongbuk-do, based on stool examination

Age group	No. of cases examined			Egg-positive cases of *C. sinensis* (%)			Egg-positive cases of *Metagonimus* sp.(%)		
	Riverside areas	Inland areas	Sub-total	Riverside areas	Inland areas	Sub-total	Riverside areas	Inland areas	Sub-total
0-9	5	13	18	1 (20.0)	-	1 (7.6)	-	-	-
10-19	25	19	44	3 (12.0)	1 (5.3)	4 (9.1)	1 (4.0)	-	3 (6.8)
20-29	13	11	24	1 (7.6)	1 (9.1)	2 (8.3)	-	1 (9.1)	1 (4.1)
30-39	32	33	65	1 (3.1)	1 (3.0)	2 (3.1)	-	-	-
40-49	91	79	170	17 (18.8)	2 (2.5)	19 (11.2)	12 (13.2)	1 (1.3)	13 (7.6)
50-59	118	96	214	23 (19.5)	2 (2.1)	25 (11.7)	9 (7.6)	2 (2.1)	11 (5.1)
60-69	198	136	334	25 (12.6)	5 (3.7)	30 (9.0)	19 (9.6)	2 (1.5)	21 (6.3)
70-79	101	77	178	10 (10.0)	5 (6.5)	15 (8.4)	6 (5.9)	2 (2.6)	8 (4.5)
80-	22	12	34	3 (13.6)	-	3 (8.8)	2 (9.1)	-	2 (5.9)
Total	605	476	1,081	86 (14.2)	15 (3.2)	101 (9.3)	51 (8.4)	8 (1.7)	59 (5.5)

for statistical differences. Differences between two groups were considered significant when the p value was < 0.05.

RESULTS

Analysis of positive cases for eggs of *C. sinensis* or *Metagonimus* sp.

The results obtained from the stool examinations are summarized in Tables 2 and 3. The overall egg-positive rates for *C. sinensis* and *Metagonimus* sp. were 9.3% (101 cases) and 5.5% (59 cases), respectively. The rate of double infection with both parasites was 3.5% (38 cases). Among the 101 *C. sinensis*-positive cases, 99 were identified by the FES technique, 94 were detected by the cellophane thick smear method, and 92 were identified by both methods. In the 59 cases positive for eggs of *Metagonimus* sp., 58 cases were identified by the FES technique, 51 were identified by the cellophane thick smear method, and 50 were identified by both methods. Beside clonorchiasis and metagonimiasis, three cases positive for eggs of *Ascaris lumbricoides*, two positive for *Trichuris trichuria*, and one cyst-

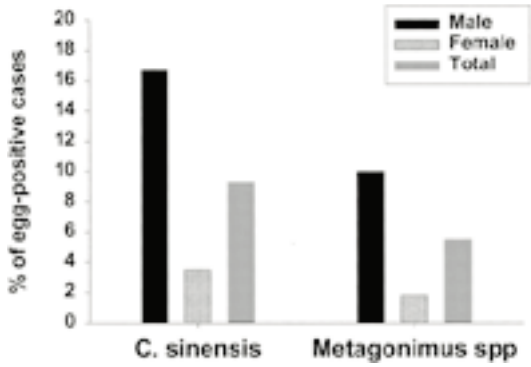

Fig. 2. Egg positive rates of *C. sinensis* and *Metagonimus* sp. based on stool examination according to sex in Okcheon-gun, Chungcheongbuk-do

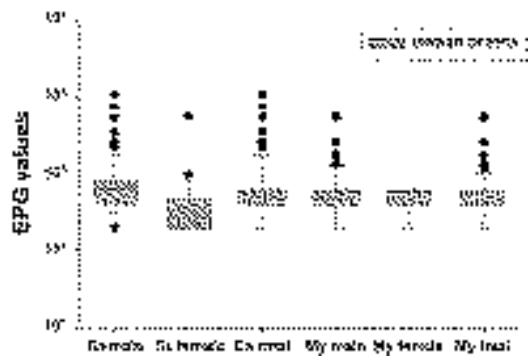

Fig. 3. EPG counts of egg positive cases of *C. sinensis* and *Metagonimus* sp. according to sex in Okcheon-gun, Chungcheongbuk-do. Cs males of *C. sienesis* egg positive cases; Cs female, females of *C. sinensis* egg positive cases; Cs total, both sexes of *C. sineneis* egg positive cases; My male, males of *Metagonimus* sp. egg positive cases; My female, females of *Metagonimus* sp. egg positive cases; My total, both sexes of *Metagonimus* sp. egg positive cases.

positive case of *Entamoeba histolytica* were also found.

As shown in Table 2, the egg-positive rates for *C. sinensis* by locality ranged from 3.0% in Eunhaeng-ri Geunseo-myeon to 19.4% in Usan-ri Dongyi-myeon. The highest egg-positive rate for *Metagonimus* sp. was 10.7% in Yegog-ri Cheongsan-myeon, whereas the lowest was 1.1% in Okgag-ri Okcheon-eup. When we divided the subject areas by distance from the main channel of the Geum-gang (River), 14.2% of 605 inhabitants in the riverside area showed egg-positive for *C. sinensis*, whereas 3.2% of the inland residents examined were infected. The difference in the *C. sinensis* egg-positive rates between the two areas was significant ($p < 0.0001$). Similarly, a significant difference between the riverside and inland areas was also observed in the egg-positive rates for *Metagonimus* sp. (8.4% vs 1.7%, $p < 0.0001$).

In Fig. 2, the egg-positive rates for *C. sinensis* and *Metagonimus* sp. were significantly higher in males than in females (16.7% vs. 3.5% for *C. sinensis* infection; 10.0% vs. 1.8% for *Metagonimus* infection). The egg-positive rates for *C. sinensis* by age group ranged from 3.1 to 11.7%, and was the highest in subjects in their fifties (11.7%), followed by subjects in their forties (11.2%) (Table 3). In the cases of *Metagonimus* infection, subjects in their forties showed the highest egg-positive rate (7.6%).

EPG counts of cases positive for eggs of *C. sinensis* and *Metagonimus* sp.

The EPG counts of the 101 *C. sinensis* egg-positive cases ranged from 200 to 10,800, and the mean EPG was 918±1,463 (Table 2). The mean EPG for *C. sinensis* egg-positive cases in the riverside area was 967±1,565, whereas it was 640±561 in the inland area (p=0.426). When EPG values were classified by grade, 82.2% were Grade I, 13.9% Grade II, 3.0% Grade III, and 1.0% Grade IV (Table 4). The proportions of each EPG grade in males and females were 80.0% and 90.5% in Grade I, 16.3% and 4.8% in Grade II, 2.5% and 4.8% in Grade III, and 1.3% and 0.0% in Grade IV, respectively. The mean EPG of males was 1,005±1,535, whereas that of females was 590±1,121, and the difference was not significant (p=0.249) (Fig. 3).

In cases positive for the eggs of *Metagonimus* sp., the mean EPG was 711±947 (range, 200 to 5,400) (Table 2). The mean EPG of inhabitants of the riverside area was 760±1,010, which was higher than that of inhabitants of the inland area (400±151) (p=0.321). The proportions of Grade I, II, and III EPGs were 89.8, 6.8, and 3.4%, respectively (Table 4). In males, the proportions of Grade I,

Table 4. EPG grade of *C. sinensis* and *Metagonimus* sp. egg-positive cases of surveyed population according to sex in Okcheon-gun, Chungcheongbuk-do

EPG grade[a)]	Egg-positive cases of *C. sinensis* (%)			Egg-positive cases of *Metagonimus* sp. (%)		
	Male	Female	Subtotal	Male	Female	Subtotal
Grade I	64 (80.0)	19 (90.5)	83 (82.2)	42 (87.5)	11 (100.0)	53 (89.8)
Grade II	13 (16.3)	1 (4.8)	14 (13.9)	4 (8.3)	-	4 (6.8)
Grade III	2 (2.5)	1 (4.8)	3 (3.0)	2 (4.2)	-	2 (3.4)
Grade IV	1 (1.3)	-	1 (1.0)	-	-	-
Total	80 (100.0)	21 (100.0)	101 (100.0)	48 (100.0)	11 (100.0)	59 (100.0)

[a)]Grade I, EPG 100-900; Grade II, EPG 1,000-4,900; Grade III, EPG 5,000-9,900; Grade IV, over 10,000

II, and III EPGs were 87.5, 8.3, and 4.2%, respectively. However, all the infected females had Grade I EPG. The mean EPGs of males and females were 775±1,040 and 436±150, respectively (p=0.289) (Fig. 3).

Follow up results of *C. sinensis* egg-positive cases after treatment

The 101 *C. sinensis* egg-positive inhabitants were administered an one-day oral dose of 3x25 mg/kg praziquantel. Three months later, stool samples were obtained from 85 of these cases. The samples were again examined by both the cellophane thick smear method and the FES technique. Five cases had *C. sinensis* eggs in their stools, while no parasites were found in the other 80 cases. The five positive cases were all male, and all had eaten raw freshwater fish after the praziquantel treatment.

DISCUSSION

Okcheon-gun lies in the Geum-gang (River) basin in Chungcheongbuk-do, Korea. Among the 1,081 inhabitants surveyed in this area, we found overall egg-positive rates of 9.3% for *C. sinensis* and 5.5% for *Metagonimus* sp.. The mean EPG counts for egg-positive cases were 918±1,463 and 711±947, respectively. The egg-positive rates for both snail-transmitted trematodes were significantly higher in both males or inhabitants of the riverside area than in other groups. These data show that the egg-positive rates for both parasites were significantly lower than those reported earlier in similar regions. However, this area still has a high prevalence of infection with these parasites.

The prevalence of soil-transmitted helminth infections in Korea has sharply decreased over the last three decades. The overall helminthes egg-positive rate was 84.3% in 1971, 41.1% in 1981, 3.8% in 1992, and 2.4% in 1997 (MHK and KAH, 1997). We also confirmed very low egg-positive rates of soil-transmitted helminthes; among the 1,081 subjects surveyed, only five cases of soil-transmitted helminthes were found. The egg-positive rates for *C. sinensis* decreased steadily from 4.6% in 1971, 2.6% in 1981, and 2.2% in 1992, to 1.4% in 1997 (MHK and KAH, 1997). A nationwide survey of clonorchiasis showed that endemic areas were scattered throughout the country along several major rivers, including the Geum-gang (River), and the most intensive endemic regions were mainly found along the Nakdong-gang (Seo et al., 1981; Rim, 1997). Clonorchiasis is a common infectious disease in Korea. For example, the yearly egg-positive rate for *C. sinensis* among outpatients nationally ranged from 2.3 to 3.9% between 1984 and 1992 (Lee et al., 1994), indicating the infection of this trematode infection in the general population.

The Geum-gang basin is one of the endemic regions for snail-transmitted trematode infections in Korea. The egg-positive rate for *C. sinensis* in Okcheon-gun was 50.7% in 1979 (Chang, 1979), 40.4% in 1994 (Kim et al., 1994), and 9.3% in the present study, confirming that the local prevalence of clonorchiasis has significantly decreased over the past 6 years. Whereas Kim et al. (1994)

previously surveyed the riverside within 1 km of the main channel of the river, the present study examined both the riverside and the inland areas within 5 km from the main channel. Generally, the prevalence of *C. sinensis* is higher in males and in inhabitants living in rural areas, and increases with age (MHW and KAH, 1997; Rim, 1997). We also found that egg-positive rates were higher among inhabitants of the riverside area than in those of the inland area, and also higher in males than in females. Although the fifties were the highest egg-positive rates for *C. sinensis* in both riverside and inland areas, there were no significant differences of egg-positive rates among age groups, except the thirties. However, the egg-positive rates of the fifties or forties were significantly higher rates than that of the other age groups in the riverside areas, except age group of 0-9 years. The EPG counts were also much lower than those previously reported. In the Geum-gang basin, the mean EPG value was 5,760 (range, 100-26,600) in 1981 (Seo et al., 1981), whereas it was 918±1,463 in this study. The low EPG counts in this area may be due to the government-supported control program, which includes praziquantel treatment and health education. However, these EPG counts may not be enough to develop apparent clinical features in humans, thus they may have repeated to eat the raw fish. The EPG for *Clonorchis* in most cases with clinical symptoms and abnormal liver function tests is more than 10,000 (Rim et al., 1981).

Three species of *Metagonimus* are known to occur in Korea; *M. yokogawai* (Chai and Lee, 1990), *M. miyatai* (Kim et al., 1987; Chai et al., 1993), and *M. takahashii* (Chai and Lee, 1990). *M. yokogawai* is widely distributed in large and small rivers of the southern and eastern coasts of Korea (Seo et al., 1981; Chai et al., 2000). According to a previous survey along the Geum-gang basin, human infections with *Metagonimus* sp. different from *M. yokogawai* were first noticed by Kim (1980), and Kim et al. (1987) later reported it as *Metagonimus* Miyata type. In this study, we did not classify the species of *Metagonimus*. In the Geum-gang basin in Okcheon-gun, the egg-positive rate for *Metagonimus* sp. was 25.9 % in 1979 (Chang 1979) and 9.8% in 1994 (Kim et al., 1994). In this study, the egg-positive rate and EPG count for *Metagonimus* sp. were 5.5% and 711±947, which are lower than those observed in the previous reports (Chang, 1979; Kim, 1980; Seo et al., 1981; Kim et al., 1994).

Praziquantel is a very well tolerated drug; occasional side effects consist of mild and transient headache and dizziness. In this study, *C. sinensis*-positive cases were given 3x25 mg/kg in one day at the Okcheon-gun Public Health Center. Five of the 85 specimens collected after praziquantel treatment were positive for *C. sinensis* eggs. Treatment failure in these 5 cases was thought to be due to either an insufficient treatment dosage of the drug or reinfection after treatment. The most practical method of preventing human reinfection is to avoid eating raw or under-cooked freshwater fishes. All five treatment failure cases had eaten raw freshwater fishes after praziquantel treatment.

Human infection with *C. sinensis* and *Metagonimus* sp. is usually acquired by eating uncooked fishes containing infectious metacercariae. The intensity of human infection is dependent upon the eating habits of the population. In rural and riverside areas of Korea, eating raw fish is a deeply rooted traditional custom. The results described in this study indicated that the overall prevalence for *C. sinensis* and *Metagonimus* infections in Okcheon-gun was significantly lower than that in the previous reports. However, this area still has high prevalence of clonorchiasis and metagonimiasis. Therefore, practical prevention or health education programs as well as mass chemotherapy are needed to reduce the prevalence of snail-transmitted trematodiasis in endemic areas.

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