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# Praziquantel(Distocide®) in Treatment of *Clonorchis sinensis* Infection

Byong-Seol Seo, Soon-Hyung Lee, Jong-Yil Chai and Sung-Tae Hong
*Department of Parasitology and Institute of Endemic Diseases,*
*College of Medicine, Seoul National University*

## INTRODUCTION

In spite of the high prevalence and clinical importance of *Clonorchis sinensis* infection in endemic areas in Korea (Seo *et al.*, 1981; Kim *et al.*, 1982), no satisfactory anthelmintic, which is safe and effective, had been available for treatment of this infection. However, praziquantel (Embay 8440, Biltricide®), a new broad-spectrum anthelmintic compound, was recently introduced and proved highly safe and effective in treatment of a variety of trematode and cestode infections including human liver flukes such as *Opisthorchis viverrini* (Bunnag *et* Harinasuta, 1980 & 1981) and *C. sinensis* (Rim *et* Yoo, 1979; Soh *et al.*, 1979; Rim *et al.*, 1981b & 1982; Lee, 1983). More recently, praziquantel was synthesized independently in this country by Shinpoong Pharmaceutical Co. in technical cooperation with *KAIST, Korea. The drug is said to have been processed in particular consideration of its purity, however, studies are needed to verify the applicability for wide usage. For this reason, the present study was undertaken to evaluate the safety and efficacy of Korean product praziquantel (Distocide®) in treatment of *C. sinensis* infection.

## MATERIALS AND METHODS

A total of 55 egg positive cases of *C. sinensis* in 2 areas (Kohŭng-gun, Chollanam-do and Taegu City) were selected for this study during April-September, 1983.

The egg positive cases were treated with praziquantel (Distocide®) at the dosage regimen of 25 mg/kg t.i.d. for 1 day (total 75 mg/kg) and follow-up examination was done 2~3 weeks later. If there were any uncured cases, they were treated again with the same drug and dosage, and follow-up study was performed 2 weeks after the second treatment.

The drug efficacy was analyzed in terms of egg negative conversion (=cure) and egg reduction rates applying cellophane thick smear and Stoll's egg counting techniques. Adverse effects were checked by verbal communication with the treated patients hearing the subjective symptoms until 12 hours after the last drug administration.

In order to check any change in laboratory findings due to praziquantel treatment, 27 patients were examined their liver function(SGOT, SGPT) and blood picture(Hb, Hct,WBC count) before and 2 weeks after the treatment.

## RESULTS

After the first treatment, only 39 among 47 follow-up cases of *C. sinensis* infection were parasitologically cured and the cure rate was 83.0 % (Table 1). But all of the remaining 8 uncured cases also converted to egg negative by the second treatment, hence, the overall cure rate by one or two course treatments with praziquantel was 100 %. Although there was a

*Korea Advanced Institute of Science and Technology

**Table 1.** Cure rate of *C. sinensis* infection by praziquantel* treatment

| Treatment | No. follow-up | No. neg. conv. | Cure rate (%) |
|---|---|---|---|
| First course | 47 | 39 | 83.0 |
| Second course | 8 | 8 | 100.0 |

*Distocide® at the dose of 25mg/kg, t.i.d., for 1 day

treatment, all cases revealed no eggs and the overall egg reduction rate was 100%.

After the treatment, several kinds of side effects were complained by 26 (61.7 %) among 47 patients (Table 4). They were, in the order of frequency, dizziness (36.2% among treated), headache (27.7 %), abdominal pain (10.6 %),

**Table 2.** Distribution of treatment failure cases according to the degree of pre-treatment *E.P.G. value

| | Intensity of infection in E.P.G. value | | | |
|---|---|---|---|---|
| | Light (0~999) | Moderate (1,000~9,999) | Heavy (100,000~29,999) | Very heavy (Over 30,000) |
| No. neg. conv.(%) | 26(86.7) | 11(78.6) | 1(50.0) | 1(100.0) |
| No. failed(%) | 4(13.3) | 3(21.4) | 1(50.0) | 0 (0.0) |
| Total** | 30 | 14 | 2 | 1 |

*Eggs per gram of feces **Total No. of follow-up cases

**Table 3.** Egg reduction rate of *C. sinensis* by praziquantel treatment

| Treatment | Sum of E.P.G. | | Egg reduc. rate (%) |
|---|---|---|---|
| | Pre-treatment | Post-treatment | |
| First course | 182,500 | 1,600 | 99.1 |
| Second course | 1,600 | 0 | 100.0 |

tendency that the higher the pre-treatment egg count (E.P.G.) the lower the cure rate by one course treatment, the difference was not statistically significant ($p > 0.1$) (Table 2).

The pre-treatment total E.P.G. counts of 47 follow-up cases were 182,500(3,883 in average) and those after one course treatment were 1,600 in 8 uncured cases, hence, the egg reduction rate was 99.1 % (Table 3). After the second

**Table 4.** Number of patients who complained side effects following praziquantel treatment

| Side effects | No. cases(%) |
|---|---|
| No. follow-up | 47 |
| No. cases who complained | 29(61.7) |
| Dizziness | 17(36.2) |
| Headache | 13(27.7) |
| Abdominal pain | 5(10.6) |
| Epigastric pain | 3( 6.4) |
| Nausea | 3( 6.4) |

epigastric pain (6.4 %) and nausea (6.4 %), however, such symptoms were only mild and transient, and required no special treatment.

In 27 patients to whom praziquantel was given, no change in blood picture as well as

**Table 5.** Laboratory findings in the patients before and after treatment with praziquantel

| | | Blood picture* | | | Liver function** | |
|---|---|---|---|---|---|---|
| | | Hb | Hct | WBC count | SGOT | SGPT |
| Before tx. | No. exam. | 27 | 27 | 27 | 27 | 27 |
| | Mean | 11.6 | 36.1 | 7,881 | 15.6 | 15.7 |
| | S.D.*** | 1.6 | 6.0 | 1,943 | 10.8 | 5.5 |
| After tx. | No. exam. | 24 | 44 | 24 | 25 | 25 |
| | Mean | 11.1 | 35.8 | 7,692 | 18.8 | 15.3 |
| | S.D.*** | 1.8 | 4.6 | 2,657 | 7.7 | 6.3 |

*Hb: hemoglobin (gm/dl), Hct: hematocrit (%), WBC count: white blood cell count (/mm$^3$)
**SGOT: serum aspartate transaminase (I.U./L), SGPT: serum alanine transaminase (I.U./L)
***S.D.: standard deviation

liver function was recognizable before and 2 weeks after the treatment, except for a slight decrease of WBC count and increase of SGOT (Table 5). The difference, however, was statistically not significant ($p > 0.1$).

## DISCUSSION

The efficacy of praziquantel (Embay 8440, Biltricide®) was at first tested in treatment of schistosomes (Gönnert *et* Andrews, 1977) and cestodes (Thomas *et* Gönnert, 1977) with excellent results. Afterwards it has been extensively applied to other trematode infections such as clonorchiasis (Rim *et* Yoo, 1979; Soh *et al.*, 1979; Rim *et al.*, 1981b & 1982; Ambroise-Thomas *et al.*, 1981; Chen *et* Hsieh, 1982; Lee, 1983), opisthorchiasis (Bunnag *et* Harinasuta, 1980 & 1981; Ambroise-Thomas *et al.*, 1981), paragonimiasis (Rim *et* Chang, 1980; Rim *et al.*, 1981a; Soh *et al.*, 1981) and metagonimiasis (Rim *et al.*, 1978) also with satisfactory results.

According to the above reports, several kinds of side effects such as dizziness, headache, *etc.* were encountered during the treatment, however, they were always mild and transient. In terms of laboratory findings such as the blood picture and liver function values, there was no change before and after the treatments (Rim *et al.*, 1981b; Davis *et al.*, 1980). Some toxicological studies revealed no teratogenic, mutagenic or carcinogenic effects of praziquantel (Biltricide®) in laboratory animals (Obermeier *et* Frohberg, 1977; Bartsch *et al.*, 1978; Ambroise-Thomas *et* Goullier, 1981).

In the present study, the efficacy of the Korean product praziquantel (Distocide®) in treatment of *C. sinensis* infection was much satisfactory; 83.0~100% in cure and egg reduction rates respectively by single or two course treatments with the regimen of 25 mg/kg t.i.d. for 1 day (75 mg/kg in total). Several kinds of side effects such as dizziness, headache, *etc.* were complained but they were mild and transient, and the laboratory tests revealed no significant change in blood picture and liver function before and after the treatment. Therefore, it is concluded that Distocide® is as effective and safe as Biltricide®.

In the treatment of *C. sinensis* infection by Biltricide®, however, it is known that the therapeutic efficacy largely depends on the dosage of the drug as well as the worm burden or intensity of infection of the patients (Rim *et* Yoo, 1979; Rim *et al.*, 1981 b & 1982). In moderate (1,000~9,999 in EPG value) and heavy (10,000~29,999) infection cases, a single dose of 40 mg/kg revealed only 0~25.0% in cure rate whereas 75 mg/kg in 3 divided doses showed 83.3~85.7% of cure rate (Rim *et al.*, 1981 b). On the other hand, in light infection cases (less than 9,999 in EPG), the cure rate by 40 mg/kg in two divided doses was as high as 75 or 100% (Rim *et al.*, 1982). The majority of *C. sinensis* infections in this country are of light infections, therefore, the use of 40 mg/kg in single dose was highly recommended in mass control programme of clonorchiasis under field conditions (Lee, 1983). In this connection, if it is intended to use Distocide® in mass control, the applicability of reduced doses should be tested and re-evaluated by field studies.

## SUMMARY

Praziquantel (Distocide®), the Korean product, was tested for its safety and efficacy in treatment of *Clonorchis sinensis* infection during the period from April to September, 1983 in Korea. A total of 55 egg positive cases were selected and treated with the regimen of 25 mg/kg *t.i.d.* for 1 day (total 75 mg/kg). The follow-up stool examination was done in 47 cases by cellophane thick smear and Stoll's egg counting techniques. The 8 uncured cases were treated again with the same regimen. The laboratory tests for blood picture and liver function were done in 27 cases and compared before and after the treatment.

The results obtained are as follows:

1. After single course treatment, the cure

and egg reduction rates were 83.0 and 99.1% respectively. With the second treatment, excellent results of 100% in both rates were obtained.

2. Several kinds of side effects such as dizziness, headache, *etc.* were complained by 29 cases (61.7 %), however, those were so mild and transient that no special treatment was necessary.

3. No significant change in laboratory findings was recognizable before and after the treatment.

From the above results, it is concluded that Distocide® is as effective and safe as Biltricide® and highly recommendable in treatment of *C. sinensis* infection.

## ACKNOWLEDGMENT

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## =國文抄錄=

# 國產 Praziquantel(디스토시드®)의 肝吸蟲症에 대한 效果

서울大學校 醫科大學 寄生蟲學敎室 및 風土病硏究所

徐丙高・李純炯・蔡鍾一・洪性台

최근 開發된 國產 Praziquantel(디스토시드®)의 肝吸蟲感染에 대한 治療效果 및 安全性을 점검하기 위하여 全南 高興郡 및 大邱市의 肝吸蟲卵陽性者 55名을 색출하고 디스토시드 25mg/kg×3回×1日(총 75mg/kg)의 用量으로 投與한 뒤 2~3週후에 追跡 大便檢査를 실시하고 治癒率 및 蟲卵減少率을 구하였다. 一次 投藥後 未完治된 8名에 대해서는 同用量으로 二次投藥하고 2週후 결과를 評價하였다. 藥劑에 의한 副作用에 대해서는 患者의 個人면담으로 주관적 호소를 듣고 測定하였다.

한편, 藥劑의 毒性여부를 알아보기 위하여 全南 高興郡의 27名 蟲卵陽性者에 대하여 投藥前 및 投藥後 2週의 血液像(WBC count, Hb 및 Hct) 및 肝機能(SGOT 및 SGPT)檢査를 실시하고 결과를 비교검토하였다.

調査結果는 다음과 같다.

1. 一次投藥後 총 47名의 追跡檢査者중에서 39名이 治癒되었고(治癒率 83.0%) 投藥前 총 EPG 182,500이 投藥後 1,600으로 減少되었다(蟲卵減少率 99.1%). 未完治者에서도 二次投藥後에는 全員이 治癒되어 각각 100%의 效果를 나타내었다.

2. 藥劑에 의한 副作用은 47名중 29名(61.7%)에서 나타났으며 어지러움(36.2%), 頭痛(27.7%), 腹痛(10.6%) 등이 호소되었으나 일시적이며 가벼운 정도이었고 投藥後 4~5時間이내에 모두 자연소실되었다.

3. 投藥前後에 실시한 血液 및 肝機能檢査에서는 유의한 差異가 없었다.

이상의 결과를 보아 國產 praziquantel(디스토시드®)은 빌트리시드®와 마찬가지로 肝吸蟲感染에 대하여 매우 우수한 治療效果와 높은 安全性을 가지고 있음이 確認되었다.