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Efficacy of Praziquantel (Cesocide® injection) in Treatment of Cestode Infections in Domestic and Laboratory Animals

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Abstract: Efficacy of praziquantel (Cesocide® injection) by intramuscular (I.M.) route against cestode infections was evaluated. Total 93 domestic or laboratory animals such as dogs, cats, rats, mice, goats, deers and chickens were used. Animals were infected with *Dipylidium caninum*, *Spirometra* sp., *Taenia pisiformis*, *Taenia taeniaeformis*, *Hymenolepis nana*, *Moniezia expansa*, *Moniezia* sp. or *Raillietina* sp.

A single dose of praziquantel, 6 mg/kg of body weight, was highly effective (97.9%) against cestodes of various kinds disregarding the host species or their intensity of infection. At higher dose above 6 mg/kg, the cure rate was 100%. All the cestodes treated were expelled from the host within 48 hours. The discharged proglottides were damaged severely except *Hymenolepis nana* and *Moniezia expansa*. Intramuscular injection of this drug evoked a brief pain response in a dog, but no other side reactions were observed.

Key words: praziquantel, intramuscular injection, animals, tapeworms, cestodes

INTRODUCTION

Praziquantel has been developed for the treatment of various trematode infections, which is also useful for intestinal or systemic cestodiases (Andrews *et al.*, 1983; Rim *et al.*, 1981; Thomas and Gönnert, 1978; Eslami and Bazargani, 1986). Many drugs such as bithionol, niclosamide, dichlorophen, paromomycin, bunamidine hydrochloride have been developed for the treatment of cestode infections (Yokogawa *et al.*, 1962; Nagahana *et al.*, 1966; Burrows and Lillis, 1966; Poole *et al.*, 1971; Seaton, 1956; Salem and El-Allaf, 1969; Botero, 1970; Wescott, 1967). These drugs are currently used widely. But they may not damage the scolex or neck region of cestodes, so that the worms may regenerate occasionally. On the contrary, praziquantel induces vacuolization of the tegument around neck region of cestodes (Becker et al., 1981) and the cestodes lose their ability to resist digestion by the host enzyme. Oral administration of praziquantel is a common route for human intestinal cestode infections but subcutaneous as well as oral route is also used in animals. Praziquantel is the first injectable cestocide and this easy mode of administration is of particular interest in veterinary practices (Andrew *et al.*, 1983). Thomas and Gönnert (1977 & 1978) reported that oral and subcutaneous injection have the same effect for animal cestodes such as *Taenia taeniaeformis*, *T. pisiformis*, *T. hydatigera*, *Mesocestoides corti*, *Echinococcus multilocularis*, *Dipylidium caninum*, *Moniezia* sp. in dogs, cats, rats, mice and

sheeps.

Since little information is available on the use of intramuscular injection of praziquantel, we evaluated the efficacy of injection by intramuscular route for the treatment of animal cestode infections.

MATERIALS AND METHODS

During May 1st, 1986, to July 25th, 1988, total 483 animals were examined for intestinal cestode infections. Among them, 93 animals were found to pass proglottides and/or eggs in their feces. They were 28 male and female mongrel dogs (weighing from 6 to 18.5 kg), 4 cats (1.0～4.1kg), 18 Sprague-Dawley rats (180.0～230.0 g), 29 ICR mice (25.0～33,0g), 10 goats (3.0～7.0 kg), 2 deers (10.0～30.0kg) and 2 chickens (1.3～2.2 kg).

Before treatment their stools were examined by direct smear, brine floatation, cellophane thick smear, scotch tape anal swab, or tube rectal swab. Proglottides in stool were examined by the naked eye after sieving the stool through No. 18～35 mesh (diameter 1.0～0.5 mm).

Subjected parasites were *Dipylidium caninum* (20 dogs), *Spirometra* sp. (3 dogs), *Taenia pisiformis* (5 dogs), *T. taeniaeformis* (4 cats), *Hymenolepis nana* (18 rats and 29 mice), *Moniezia expansa* (10 goats), *Moniezia* sp. (2 deers), and *Raillietina* sp. (2 chickens). All infections were natural ones except *T. pisiformis* and *H. nana*. *T. pisiformis* was infected experimentally with 1～5 cysts orally, which were obtained from viscera of rabbits. *H. nana* was infected experimentally by rearing mice in a cage which was contaminated with *H. nana* eggs. Rats and mice were given commercial pellets.

Composition of praziquantel injection (Cesocide® injec.; commercial product of Shin Poong Pharm. Co. Ltd., Seoul, Korea), was 56.8 mg of active ingradient in propyleneglycol as a solvent, N′, N-dimethylacetamide as a detergent, with 0.075 ml benzyl alcohol, 5 mg chlorobutanol. Praziquantel, acylated isoquinoline-pyrazine, has following structural formula: 2-(cyclohexylcar bonyl) -1, 2, 3, 6, 7, 11b-hexahydro-4H-pyrazino [2, 1-a] isoquinolin-4-one. This clear solution has been formulated for subcutaneous or intramuscular use. The tested dosages were 12.0 mg, 9.0 mg, 6.0 mg, 3.0 mg, and 1.5 mg/kg body weight. In rats and mice, diluted praziquantel (1.2 mg/ml) was used. The injection site was thigh muscle for all animals. Animals were not starved before injection of praziquantel and were kept in individual cage.

All of the injected animals were observed during the next 72 hours after praziquantel administration to check any expelled proglottides in their stool. Then they were sacrificed at the 14th day to examine the intestine, or kept alive to observe proglottis discharge between 60 days and 90 days after the drug injection.

E.P.G. (Eggs per gram of feces) of cestodes were calculated as follows: add 0.5ml saline to one pellet of mouse stool in a tube, then emulsify and take 0.03 ml from the tube to count the whole number of eggs.

E.P.G.=number of eggs per $0.03(\text{ml}) \times \frac{(0.5+0.02^*)}{0.03}$, where 0.02* is the average weight (g) of one pellet of mouse stool.

RESULTS

1. Dosage regimens for the treatment

In 21 animals that were injected with 9 or 12 mg/kg body weight of praziquantel, the percentage of worm elimination was 100% in both 12 mg/kg (8/8) and 9 mg/kg (13/13) groups (Table 1).

Forty seven animals given 6 mg/kg body weight, showed the cure rate of 97.9%. In *Spirometra* sp., one out of three dogs was not cured with 6.0 mg/kg. The dog (b.w. 12kg) discharged *Spirometra* eggs at the 7th and 15th day after the administration of praziquantel. It was the only exception which was not cured with the dose of 6 mg/kg among all tested animals.

Twenty five animals were given 3 or 1.5

Table 1. Efficacy of praziquantel injection for treatment of cestode infections in animals

Hosts	Parasites	No. cured/no. tested at dosages (in mg/kg) of				
		12	9	6	3	1.5
Dog	*D. caninum*	1/1	3/3	12/12	1/2	0/2
	Spirometra sp.			2/3		
	T. pisiformis			4/4	0/1	
Cat	*T. taeniaeformis*			4/4		
Rat	*H. nana*	2/2	2/2	6/6	3/5	0/3
Mouse	*H. nana*	3/3	3/3	11/11	5/8	2/4
Goat	*M. expansa*	1/1	3/3	6/6		
Deer	*Moniezia* sp.	1/1		1/1		
Chicken	*Raillietina* sp.		2/2			
	Total	8/8	13/13	46/47	9/16	2/9
	Cure rate (%)	100	100	97.9	56.3	22.2

mg/kg body weight of praziquantel. The percentage of worm elimination was 44.0% in average. In 3 mg/kg, *D. caninum* was cured in 50%(1/2), *T. pisiformis* 0%(0/1), *H. nana* in rat 60%(3/5), and *H. nana* in mice 62.5% (5/8), with average cure rate of 56.3%. In 1.5 mg/kg, none of *D. caninum* (0/2), *H. nana* in rat (0/3), and 50% (2/4) of *H. nana* in mice were cured (average cure rate of 22.2%).

In dogs infected with *D. caninum*, all of the worms including scolices and proglottides discharged in stool were damaged severely, and each proglottis passed out separately, which was found only with care. But the worms such as *M. expansa* in goat and *H. nana* in rats or mice, were discharged in strobilate state without severe morphological changes as viewed by the naked eye. In chickens, 9 mg/kg of praziquantel showed 100% (2/2) cure rate for *Raillietina* sp.

Intramuscular administration of praziquantel (Cesocide® injection) produced a brief pain response as shown by limping in the leg in a dog but no other special reactions were detected in dog or other animals.

2. Expulsion of strobilae and eggs

When a single I.M. dose of praziquantel, 6 mg/kg body weight, was given, strobilae with scolices were expelled between 3 and 5 hours in mice infected with *H. nana*. The E.P.G. increased after two hours, reached maximum (approximately five times of pretreatment level) at five hours in most mice. Twenty four hours after injection, eggs were not detected from the stool of mice. No worms were found in the intestine of all tested mice when necropsied after 14 days.

Mice injected with a single dose of 1.5 mg/kg showed increased E.P.G. after 2 hours, maximum E.P.G. at $3^1/_2$ hours. The egg discharge continued during 4 days after the injection without expulsion of *H. nana*.

In goat injected with a single dose of praziquantel 6 mg/kg, all the proglottides of *M. expansa* were expelled between 7 and 11 hours. Eggs were discharged until 26 hours after the praziquantel administration. In mice and goats, *H, nana* and *M. expansa* were not severely damaged.

3. Time needed for expulsion of whole worm

The majority of cestodes were expelled completely between 12 and 24 hours after praziquantel injection. *H. nana* needed 6 hours, while *T. taeniaeformis* needed as long as 48 hours for expulsion of their strobilae (Table 2).

In dogs, *D. caninum* proglottides were expelled in 12 hours but a few residual proglottides

Table 2. Expulsion of proglottides after injection of praziquantel

Parasite	Hours after injection				
	0	6	12	24	48
D. caninum					
Spirometra sp.					
T. pisiformis					
T. taeniaeformis					
H. nana					
M. expansa					
Raillietina sp.					

were discharged in 24 hours after administration of 6 mg/kg praziquantel. The most of egg capsules of *D. caninum* were broken, and the eggs were scattered in the damaged proglottides.

DISCUSSION

Various dosages of praziquantel for the treatment of cestode infections were reported by different authors in cases of oral or subcutaneous administration. Single dose of 0.5~5 mg/kg was used against *Taenia* species, *Dipylidium*, and *Mesocestoides* in dogs and cats, and single dose of 5~15 mg/kg was used against *Moniezia* and *Avitellina* in sheep (Andrews *et al.*, 1983).

Our study showed that praziquantel injection was effective against all of 8 tapeworm species when tested with a minimum dose of 6 mg/kg. With this dose, almost complete cure was achieved disregarding the host species, parasite species or their intensity of infection. Only one exception with this dose, a treatment failure was observed in a dog infected with *Spirometra* species. On this regard, Sakamoto (1977) reported that the treatment of diphyllobothriid cestodes in cats or dogs require higher oral doses of praziquantel (25 to 35 mg/kg×1) than cyclophyllidean tapeworms.

Thomas and Gönnert (1977 & 1978) reported that the age, sex, and strain of mice, or intensity of infestation of *H. nana*, showed no influence on the efficacy of praziquantel. Both oral and subcutaneous routes were equally effective with the same dose. The intramuscular injection was also found to be effective against various intestinal cestodes of animals in our results.

Becker *et al.* (1981) showed the effect of praziquantel on the ultrastructure of the tegument of *H. nana in vitro*. Numerous vacuoles were formed on the tegument that finally bursted up. The tegument of neck region was most vulnerable, while the tegument of mature proglottides was not affected by praziquantel. In our macroscopical observation, *H. nana* and *M. expansa* were less damaged than other cestodes when observed after expulsion from the hosts. The majority of other tapeworms were almost digested to pieces, so that they were found with difficulty in feces. The damaging effect of praziquantel seems to become stronger according to the time duration of cestode species to retain in intestine of host after praziquantel injection.

Underdose of praziquantel (1.5 mg/kg) did not affect *H. nana* to death though the egg discharge increased temporarily after praziquantel injection. Egg capsules of *D. caninum* in the dog became fragile after the administration of praziquantel.

In conclusion, praziquantel injection is highly effective and safe in the treatment of cestode infections of animals. The cure rate was 97.9% with the dosage of 6 mg/kg by injection.

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=국문초록=

가축 및 실험동물의 조충류 감염에 대한 프라지콴텔(Cesocide®注) 주사제의 치료효과

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프라지콴텔 주사제의 조충류 치료 효과를 평가하였다. 개, 고양이, 산양, 사슴, 닭, 쥐 및 마우스 등 총 93마리 동물의 장관내에 기생하는 조충류 *Dipylidium caninum*, *Taenia pisiformis*, *Spirometra* sp., *Taenia taeniaeformis*, *Moniezia expansa*, *Moniezia* sp., *Raillietina* sp. 및 *Hymenolepis nana*에 체중 kg당 프라지콴텔 12 mg, 9 mg, 6 mg, 3 mg, 1.5 mg을 대퇴부에 근육주사한 후 치료효과를 판정하였다. *H. nana*에 감염된 마우스는 6 mg/kg 투여 후 3시간부터 6시간 사이에 충체를 배출하였다. 다른 조충류도 약제투여 48시간 이내에 모두 체외로 배출되었다. *H. nana* 및 *M. expansa*를 제외한 모든 충체는 체외 배출시 심하게 손상되어 있었으며, *D. caninum*의 충란낭은 붕괴되어 충란이 분리되었다.

조충의 종류와 감염강도 등에 따른 숙주 체중 kg당 투여 용량의 차이는 관찰되지 않았으며 *Spirometra* sp.에 감염되었던 한 마리의 개를 제외하고는 프라지콴텔 6 mg/kg 1회 용량으로 완치되어 97.9% (46/47)의 치유율을 보임으로써 우수한 치료 효과를 나타내었다.