ACTA VET. BRNO, 47, 1978: 87–90

THE EFFECT OF PRAZIQUANTEL (DRONCIT) ON CYSTICERCUS PISIFORMIS IN RABBITS

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Received February 21, 1978

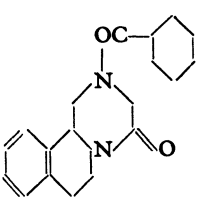
Abstract

Koudela B., H. Schanzel: *The Effect of Praziquantel (Droncit) on Cysticercus pisiformis in Rabbits.* Acta vet. Brno, 47, 1978: 87–90.

Rabbits experimentally infested by *Cysticercus pisiformis* were treated by different single doses of praziquantel (Droncit-Bayer). The drug was administered orally at successive stages of development of cysticerci. The dosage tested of about 8 and 15 mg kg^{-1} and no effect on number, size and vitality of cysticerci.

Experimental infection, chemotherapy, oral administration.

A new highly efficient cesticidal compound has been developed recently 2-(cyclohexylcarbonyle)--1,3,4,6,7,11b-hexahydro-2H-pyrazino/2,1-a/isoquinolin-4-one, with the following structural formula:



The short term for the compound is praziquantel, and the producer, Bayer, delivered it to the market under the name Droncit.

The drug is very well tolerated, as has been shown by Mürmann et al. (1976). In mice and rats, LD_{50} ranged from 2,000 to 3,000 mg kg^{-1} after oral administration and was even higher when administered parenterally. The LD_{50} for dogs could not be determined, since doses from 200 mg kg^{-1} resulted in vomiting. Praziquantel showed neither skin-sensibilizing nor embryotoxic and teratogenic effects. Andrews (1976) demonstrated very rapid absorption of praziquantel from duodenum and very rapid distribution to organs CNS included. The drug is rapidly metabolized, probably in the liver, and eliminated.

The efficacy of praziquantel on adult tape-worms has been tested mainly in dogs and cats (Güralp et al. 1976; Rommel et al. 1976; Dey-Hazra 1976). Like with other cesticides, largely different doses were needed depending upon the species of tapeworm involved. Dey-Hazra (1976) achieved complete expulsion of *Echinococcus granulosus* by a single dose of 5.0 mg kg^{-1} administered to experimentally and naturally infested dogs. A single dose of 2.5 mg kg^{-1} was perfectly effective against *Dipylidium caninum*, 2.0 mg kg^{-1} against *Taenia hydatigena*, and, as little as 1.0 mg kg^{-1} against *Taenia pisiformis* in dogs and *Taenia taeniaeformis* in cats. Referring to the fact that field results are usually a little worse than experimental results, the author recommended an uniform dose of 5.0 mg kg^{-1}.

Another matter were the results concerning the effect of praziquantel on larval stages of tapeworms, reported by Thomas et al. (1975a, b, 1977), Thomas and Andrews (1977) Lang-

nes (1976), Hörchner et al. (1976), Thomas and Gönnert (1976, 1978). Langnes (1976), and Hörchner et al. (1976), observed a very good effect on *Cysticercus tenuicollis* in pigs and a satisfactory result with *Cysticercus pisiformis* in experimentally infested rabbits after 50 mg kg^{-1} for 5 days: 60% of cysticerci were found dead. They started their treatment 8 weeks after infestation, thus at a time when the cysticerci were settled, developed and surrounded by their protective cuticula. Having in mind the importance of the right moment for chemotherapy emphasized by Hinz (1961, 1964) particularly for measles of the cysticercus type, we decided to investigate whether even lowered doses of praziquantel would not act efficiently as long as the larvae had not finished migration or the cysticerci missed protection by the outer cuticular layer.

Material and Methods

Rabbits of different breeds, sex (9 males and 18 females) and age (2.5–4.2 kg) were infested by administering a ripe proglottis of *Taenia pisoformis* orally to each animal. At the day of infestation one animal was treated by half a tablet of Droncit, one by a whole tablet, while a third rabbit remained untreated. At intervals of one week, three more rabbits were treated in the same way. The mean doses of praziquantel were 7.82 ± 0.71 mg kg^{-1} and 14.86 ± 2.62 mg kg^{-1}, respectively. After 10 weeks of trial, the rabbits were weighed, killed, dissected and examined for number, size and vitality (microthermal test) of cysticerci. Limits of confidence were calculated for statistical evaluation of results.

Results

The results are summarized in Table 1:

Table 1

Effect of a single dose of praziquantel on Cysticercus pisiformis in experimentally infested rabbits

Treatment days p. i.	Group I		Group II		Group III	
	dose mg/kg	No. of cysticerci	dose mg/kg	No. of measles	dose mg/kg	No. of cysticerci
0	9.6	76	17.2	1	–	11
7	8.8	12	22.8	112	–	7
14	8.7	2	15.6	9	–	26
21	7.4	4	12.5	16	–	2
28	7.3	9	12.0	3	–	64
35	6.7	3	12.8	8	–	2
42	7.2	2	13.8	4	–	4
49	7.2	6	12.8	4	–	9
56	7.5	11	14.3	1	–	3
$\bar{x}$	7.82	13.9	14.86	17.9	–	14.2
$\pm s_{\bar{x}} \cdot t$	±0.71	±18.1	±2.62	±27.3	–	±15.5

It is obvious that there was no significant difference between the three groups. At no stage of larval development the tapeworm was affected by praziquantel. The cysticerci were equal in size and vitality in both treated and control animals. No side effects were observed.

Discussion

The negative result of our trial is in accordance with the findings reported by Hörchner et al. (1976). Though they consider oral administration as less effective than the parenteral way, we do not assume the failure of our treatment was due to the oral way of administration we used. Pharmacokinetical studies performed by Andrews (1976), demonstrated that praziquantel is equally efficient after oral and parenteral administration.

Neither location and structure of the cysticerci is likely to respond for the failure of treatment. Hörchner et al. (1976), who described a very good effect of praziquantel on *C. fasciolaris* in mice and *C. tenuicollis* in pigs, met no satisfactory result with *C. pisiformis* in rabbits. They concluded that the effect depends rather upon the host species than upon the species of tapeworm.

Compared with our dosage, the doses used by Langnes (1976), and Hörchner et al. (1976), were considerably higher. They administered 50 mg kg^{-1} for 5 consecutive days and even 100 mg kg^{-1} for 14 days. On the other hand, they treated rabbits not earlier than 8 weeks after infestation, while in our trial praziquantel was administered at different and earlier stages of larval development. Though Thomas and Gönnert (1978), observed in mice that developed larval stages of *C. fasciolaris* were susceptible to praziquantel while younger stages were not, we feel a new trial would be appropriate, with doses of praziquantel as high and/or repeated as Langnes (1976) and Hörchnes et al. (1976) used, but with a timetable and sequence of treatment described in our report.

Účinek praziquantelu (Droncitu) na Cysticercus pisiformis u králíků

Praziquantel (Droncit-Bayer) se aplikoval v různých dávkách králíkům, experimentálně invadovaným *Cysticercus pisiformis*. Jednorázová orální dávka kolem 8 mg/kg a 15 mg/kg se podávala za různou dobu po invazi. Při těchto dávkách se neprojevil žádný účinek na počet, velikost a životnost boubelů.

V literatuře byl popsán 60% účinek praziquantelu na *Cyticercus pisiformis* po dávce 50 mg/kg, podávané po 5 dní, a aplikované za 8 týdnů po invazi králíků.

Soudíme, že v příštím pokuse bude nutno vyzkoušet vyšší, případně opakované dávky praziquantelu, avšak v časovém sledu, který jsme dodržovali v této práci.

Воздействие празиквантела (Дронцита) на Cysticercus pisiformis у кроликов

Празиквантел (Droncit-Bayer) применяли в различных дозах кроликам, экспериментально зараженным *Cysticercus pisiformis*. Однократная доза через рот около 8 мг/кг и 15 мг/кг применялась по истечении различного времени после инвазии. Эти дозы не оказывали никакого воздействия на количество, величину и выживание цистицерков.

В литературе указывается 60% воздействие празиквантела на *Cysticercus pisiformis* после 5-дневного применения дозы 50 мг/кг, которое производили через 8 недель после инвазии кроликов.

Мы полагаем, что в следующих опытах испытаниям подлежат более высокие и м. б. повторяющиеся дозы празиквантела, однако, в той же временной последовательности, которая соблюдалась в нами предлагаемой работе.

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