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Review

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Current status of the treatment of paragonimiasis

Joachim Richter

Institute of Tropical Medicine and International Health, Charité Universitätsmedizin, Corporate Member of Freie Universität and Humboldt Universität Berlin and Berlin Institute of Health, Berlin D-13353, Germany.

Correspondence to: Prof. Joachim Richter, Institute für Tropenmedizin, Charité, Campus R. Virchow, Augustenburgerplatz 1, Berlin D-13353, Germany. E-mail: jockelri@gmail.com

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Abstract

Paragonimiasis, a foodborne trematodiasis is caused by various Paragonimus species endemic in Asia, Africa, and the Americas. Human infection occurs through consuming improperly cooked freshwater crustaceans, crabs or crayfish, eating raw meat of paratenic hosts or by ingesting metacercariae from contaminated hands and cooking utensils. More than 292 million persons worldwide are at risk. The morbidity associated with paragonimiasis includes acute febrile illness and chronic pleuro-pulmonary manifestations which may be confounded with tuberculosis or lung cancer. Ectopic manifestations mostly involve the central nervous system, heart, or subcutaneous tissues. **Objectives:** to evaluate the efficacy and safety of currently available drugs praziquantel (PZQ) and triclabendazole (TCZ). **Methods:** a PubMed and Google Scholar search and reference selection was performed according to the the Preferred Reporting Items for Systematic Reviews protocol using a combination of the terms "paragonimiasis" AND "treatment" OR "therap*" from 01/2000 to 02/2022. **Results:** no randomized controlled trials were identified. Five open trials on 487 patients treated with PZQ showed 81%-100% parasite clearance depending on dosage and duration. Three open trials on 226 patients with TCZ showed a 99.6% efficacy. A quantitative comparison was not applicable to retrospective analyses of hospital records, case series and case reports because of surgical interventions, various co-morbidities and -medications and definitions of cure. Some patients treated with PZQ required multiple courses or re-treatment with TCZ, whereas one patient treated with TCZ required re-treatment with PZQ. **Conclusions:** PZQ and TCZ are usually effective for treating paragonimiasis. Controlled randomized trials are required to compare the safety, efficacy and applicability of PZQ versus TCZ and to evaluate combined PZQ-TCZ therapy.

Keywords: Paragonimus, paragonimiasis, lung fluke, praziquantel, triclabendazole

INTRODUCTION

Paragonimiasis belongs to the family of foodborne trematodiases and is a neglected tropical disease. Paragonimiasis is caused by various species of the genus *Paragonimus*. Out of the 50 different species isolated from freshwater crabs or crayfish in Asia, Africa and the Americas, a dozen species are known to cause disease in humans[1].

Human infection occurs through consuming improperly cooked freshwater crustaceans, crabs or crayfish, eating paratenic hosts such as wild boar and deer or by ingesting metacercariae from contaminated hands and cooking utensils[2,3]. Metacercariae may also be present in raw juice extracted from crabs/crayfish. Traditionally, in Korea and Japan the juice is used as traditional medicine for humans and in some African societies raw crabs are thought to increase fertility[2].

In subtropical and tropical countries paragonimiasis occurs especially in marginalized populations. In Africa and in the Americas, the disease is frequently associated with a low standard of living and insufficient or irregular food supply, causing people to catch and eat freshwater crabs. In Asia, raw or undercooked crabs are regarded as a delicacy including "drunken crab" in China, "Kung Ten" and "Nam Prik Poo" in Thailand, "Ke Jang" in Korea and "Kinilao" and "Sinugba" in the Philippines[2].

By consequence, paragonimiasis is expected to occur in settings where people do not have sufficiently to eat and/or where people consider eating raw crabs/crayfish as a delicacy. Other risks to take into account include eating undercooked paratenic host meat and traditional beliefs about eating raw crab meat or juice[2,3].

Approximately one million people are infected every year. Human infections have been reported from 39 countries and areas, although the major endemic areas are in Asia. More than 20 million persons are infected and 292.8 million persons are at risk[4,5]. Paragonimiasis has always been a serious medical problem in some countries, such as China, Japan, Korea, the Philippines, Cameroon; Nigeria and Ecuador[5,6]. The number of patients decreased in Japan and Korea over the last decades. In the meantime, new endemic foci have emerged, raising the necessity for effective treatment[6,7].

The morbidity associated with paragonimiasis is directly related to the development of ingested metacercariae in the final host. Metacercariae released from ingested crabC flesh develop into juvenile worms which penetrate the intestinal wall and then follow a complex migration route through the peritoneum, the diaphragm and the pleura to finally reach the lung parenchyma. Typically, adult flukes encapsulate within the pleura or in the lung parenchyma. In the former case pleuritis or pleural thickening will develop. In the latter case eggs are released into bronchioles, coughed up, mixed with sputum, and are either expectorated or swallowed for later excretion via feces. The clinical picture (cough, hemophthysis, fever, asthenia, pleura effusions, pulmonary masses, lung cavernae) is very similar to tuberculosis (TB)[8]. Therefore, paragonimiasis in Vietnam is also called "eosinophilic TB" (Richter 2002, personal observation, unpublished). In endemic areas paragonimiasis may also be associated with TB or it may be confused with lung cancer[8-10].

Symptoms of pulmonary paragonimiasis are results of pleuritis and pneumonia/bronchitis. Pleuritis is caused by worms present in the pleural cavity inducing pleural effusion with massive eosinophil infiltration[11].

Extrapulmonary localization occurs in about 1% of all patients, its frequency depending on the *Paragonimus* species[1]. The most frequent ectopic localization is in the brain with 30%-60% of all extrapulmonary localizations[1]. Other ectopic localization are: spinal cord, eyes, subcutaneous tissues, heart muscles, mediastinum, breast, bone marrow, liver, spleen, pleural cavity and pericardial cavity and scrotum[1]. Globally, the disability weight of paragonimiasis is high[12].

This review aims to provide an update on how to treat paragonimiasis with either triclabendazole or praziquantel, the two drugs currently available.

SEARCH STRATEGIES AND SELECTION CRITERIA

This study is reported according to the Preferred Reporting Items for Systematic Reviews[13].

The PUBMED database was searched using a combination of the terms "paragonimiasis" AND "treatment*" OR "therap*" from 01/2000 to 02/2022. Since a tentative search did not show any randomized controlled trial (RCT), in the final search, open clinical trials, case reports, case series and retrospective analyses of hospital records were looked for as well.

Additional searches were undertaken in Google Scholar, and reference lists of included papers were manually searched. After duplicates were removed, the titles and abstracts of the records were screened for relevance and the full-text articles were reviewed for eligibility. Due to the small number of publications on the topic, all publications describing at least one case of paragonimiasis treated with praziquantel or triclabendazole were included regardless of study population, intervention type, outcome measures, and duration of follow-up. The non-RCT studies were analyzed and summarized to provide a comprehensive profile on the treatment of paragonimiasis.

Data extraction and analysis

Data extracted included study origin, type of study, study inclusion and exclusion criteria, patient characteristics, disease diagnoses, treatment details, study outcome measures, and results. All analyses that were made are summarized in Tables 1-3 and narratively described in the text.

RESULTS

No randomized controlled trials were identified. Therefore, open clinical trials, retrospective analyses of hospital records, cases series and case reports were analyzed. The open trials with praziquantel are summarized in Table 1. All trials were performed between 1981 and 1989, a couple of years after the introduction of praziquantel into the market. The five studies on 487 patients aimed to identify the optimal dosage for paragonimiasis in the lungs. Most studies performed in South Korea and China showed that in 81%-100% of patients treated with 3 × 25 mg/kg/d for three days no eggs were detected in sputum after three months[14,15]. Lower doses, such as 3 × 20 mg/kg/d for 2 days, were less effective. Radiological findings, such as cavities, nodular opacities, pleural effusion diminished in size, but remained visible after 90 days post-treatment[15]. According to Rim *et al.*, all patients improved clinically, and radiological findings reversed to normal after one year[14].

Table 1. Open clinical trials with praziquantel

Country/region	Paragonimus species	Organ affected	Study design	Number of patients	Dosage (mg/kg/d)	Outcome measure	Outcome	Reference
South Korea	*P. westermani*	Lungs	Open trial Comparing 3 doses of praziquantel	52	3 × 25 for 1 day 3 × 25 for 2 days 3 × 25 for 3 days	Presence of eggs in sputum, disappearance of haemoptysis; regression/disappearance of radiological findings	No eggs in sputum after 3 × 25 mg/kg/d for 3 days independent of the intensity of paragonimiasis; almost all patients improved clinically. In all cases X-ray was normal after 1 year; 3 × 25 mg/kg single dose, 3 × 25 mg/kg/d for 2 days less effective	[14]
China	*P. westermani*	Lungs	Open trial Comparing 3 doses of praziquantel	40	3 × 20 for 2 days 2 × 15 for 5 days 3 × 25 for 3 days	Presence of eggs in sputum	In 91% of patients no eggs detected 90 days after treatment with 3 × 35 mg/kg/d for 3 days 3 × 20 mg/kg/d for 2 days, 2 × 15 mg/kg/d for 5 days less effective	[15]
Ecuador	*P. mexicanus*	Lungs	Open trial Comparing 2 doses of praziquantel	43	3 × 25 for 1 day 3 × 25 for 2 days	Decrease of IgG- and IgE-antibodies	IgE-antibodies decreased more rapidly than IgG-antibodies	[16]
Nigeria	*P. utero-bilaterialis*	Lungs	Open trial Comparing 3 doses of praziquantel	322	3 × 15 for 2 days 3 × 20 for 2 days 3 × 25 for 2 days	Presence of eggs in sputum	In 87% no eggs detected after 3 × 25 mg/kg/d for 1 day 3 × 15 mg/kg/d and 3 × 20 mg/kg/d for 2 days were less effective; cure rate seemed to be higher in children and young adults	[17]
Cameroon	*P. africanus*	Lungs	Open trial	30	3 × 25 for 3 days	Presence of eggs in sputum; symptoms and signs; regression/disappearance of radiological findings	Absence of eggs in sputum, disappearance of symptoms and signs in all patients 2 months after treatment; partial regression of radiological findings	[18]

The efficacy of the treatment with praziquantel did not seem to depend on the *Paragonimus* species.

In three open trials on 226 patients triclabendazole was used [Table 2]. The two studies performed in Ecuador were designed to identify the optimal dosage. 5 mg/kg/day for three days cleared eggs from the sputum more rapidly than 5 mg/kg/d in a single dose. Similarly, 2 × 10 mg/kg on one day cleared eggs from the sputum more rapidly than 10 mg/kg in a single dose [Table 2][19,20]. Calvopiña *et al.* reported a similar efficacy of triclabendazole (5 mg/kg/d for 2 days) and praziquantel (3 × 25 mg/kg/d for 3 days). However, the study was not designed to allow a comparison of the efficacy of both drugs[19].

Retrospective analyses of hospital records, case series and case reports is shown in Table 3. Of the 558 cases described, 425 were from China, 52 from Ecuador, 33 from South Korea, 24 from Columbia and 12 from the USA. From the remaining countries, only single cases were reported. Since the great majority of patients were from Asia, the dominant parasite species was *P. westermani* in 160 cases, followed by *P. skrjabini* (71 cases) and *P. heterotremus* (9 cases). On the

Table 2. Clinical trials with triclabendazole

Country/ region	Paragonimus species	Organ affected	Study design	Number of patients	Dosage (mg/kg/d)	Outcome measure	Outcome	Reference
Ecuador/ Amazon region	*P. mexicanus*	Lungs	Clinical trial using praziquantel as "therapeutic control"	62	Triclabendazole 5 single dose for 3 days Praziquantel (3 × 25 for 3 days)	Presence of eggs in sputum; disappearance of symptoms + signs	Complete recovery in all patients; eggs were cleared from sputum more rapidly with 3 doses of triclabendazole; no difference between triclabendazole and praziquantel	[19]
Ecuador	*P. mexicanus*	Lungs	Open clinical trial Comparing 2 doses of triclabendazole	154	10 2 × 10 on one day	Presence of eggs in sputum; disappearance of symptoms + signs; regression/disappearance of radiological findings	Eggs were cleared from sputum in all patients (disappearance occurred more rapidly with 2 × 10 mg/kg); symptoms + signs regressed in 10% to 35% of patients; radiological findings diminished in size, but remained visible in up to 83%	[20]
Cameroon	*P. utero-bilateralis*	Lungs	Open clinical trial	10	10 single dose	Presence of eggs in sputum; disappearance of symptoms + signs	In 9/10 patients eggs were cleared from sputum 11 months after treatment; 7/10 patients fully recovered	[21]

American continent, patients were infected with *P. mexicanus* (74 cases) or *P. kellicotti* (12 cases). The great majority of the patients had paragonimiasis of the lungs and/or the pleural cavity. In Chinese patients the brain, the pericardium and the liver were also affected.

544 cases were treated with praziquantel and 14 cases with triclabendazole. Usually, praziquantel was administered in a dose of 3 × 25 mg/kg/d for three days and triclabendazole in a dose of 10 mg/kg/d for one or two days. Since the definition of improvement and cure varied greatly between the studies, a quantitative comparison of the efficacy of the different treatments was not possible. To indicate the outcome of the treatment in a narrative manner, the terms "improvement" and "recovery" were therefore used.

After treatment with praziquantel (3 × 25 mg/kg/d) recovery was reported in 147 cases and improvement in 66 cases. In the 244 cases from the retrospective analysis of hospital records either improvement or recovery were noted. In a substantial number of patients full recovery needed additional treatment courses with praziquantel.

All cases of paragonimiasis caused by *P. mexicanus* (Ecuador, Columbia) and *P. kellicotti* (USA) were cured after praziquantel (3 × 25 mg/kg/d) except for a single case with a chronic disease[7,10,48,50-52]. In 9 patients infected with *P. skrjabini* and treated with triclabendazole recovery was reported[24].

Since the patients differed regarding to organ manifestation, disease duration, stage and severity, co-morbidity (such as TB) and other host-related factors, no conclusion can be drawn on the efficacy of praziquantel for the treatment of paragonimiasis in general. Particularly, it is impossible to determine the efficacy of praziquantel in the treatment of brain paragonimiasis. Many patients were operated and/or received additional medications such as methylprednisolone or

Table 3. Retrospective analysis of hospital records, case series and case reports

Origin of patients	Type of study	Number of patients (age years)	Paragonimus species	Affected organs/concomitant disease	Treatment TCZ = triclabendazole PZQ = praziquantel	Dosage (mg/kg/d)	Outcome	Reference
China	Case report	4 (1-38)	*P. skrjabini*	Lungs, pleural cavity, brain, subcutaneous tissue	TCZ	10 for 3 days	Recovery	[22]
China	Retrospective analysis of hospital records	94 (2-53)	*P. westermani*	Lungs, pleural cavity, brain, liver, subcutaneous tissue	PZQ	150-250 for 2-3 days[a]	Improvement/ recovery[b]	[23]
China	Case report	5 (?)	*P. skrjabini*	Lungs	TCZ	10 for 3 days	Recovery	[24]
China	Retrospective analysis of hospital records	89 (2-64)	*P.* not specified	Brain	PZQ (72 patients)	Dosage not specified	?	[25]
China	Retrospective analysis of hospital records	27 (?)	*P. westermani* or *P. skrjabini*	Brain	PZQ	3 × 25 for 3 days	Improvement/ recovery[c]	[26]
China	Case report	1 (12)	*P.* not specified	Lungs/pleural effusion	PZQ	3 × 50 for 3 days; 2 further courses during 12 months	Recovery	[27]
China	Retrospective analysis of hospital records	123 (1-13)	*P.* not specified	Lungs/pleural effusion; tuberculosis	PZQ	3 × 25 for 3 days[d]	Improvement/recovery	[28]
China	Case reports	2 (21, 27)	*P. skrjabini*	Scrotum	PZQ	3 × 25 for 3 days	Recovery	[29]
China	Case report	1 (5)	*P.* not specified	intra-orbital, brain	PZQ + corticosteroids[e]	Dosage not specified	Recovery	[30]
China	Retrospective analysis of hospital records	57 (3-14)	*P. skrjabini*	Pericardial effusion/pericardial tamponade	PZQ[f]	3 × 25 for 3 days; 1-3 repetitions[g]	Improvement	[31]
China	Case report	3 (8,12,23)	*P. skrjabini*	Brain	PZQ	3 × 25 for 3 days, 1-2 repetitions	Recovery	[32]
China	Retrospective analysis of hospital records	8 (49-61)	*P. heterotremus*	Lungs	PZQ	3 × 25 for 3 days	Recovery	[9]
China	Retrospective analysis of hospital records	11 (3-12)	*P.* not specified	Lungs, pleural effusion, brain, liver	PZQ followed by TCZ	3 × 25 for 3 days; 1-2 repetitions[h]	8 patients recovered; 3 improved	[33]
Japan	Case report	1 (45)	*P. miyazakii*	Lungs	PZQ	3 × 25 for 3 days	Recovery	[34]
Japan	Case report	1 (38)	*P. miyazakii*	Pleural cavity/pleural effusion	PZQ	3 × 25 for 3 days	Recovery	[35]
Japan	Case report	1 (66)	*P. westermani*	Lungs	PZQ	3 × 25 for 3 days	Improvement	[36]
Japan	Case report	1 (42)	*P. westermani*	Lungs/familial mediterranean fever	PZQ	3 × 25 for 3 days	Improvement	[37]
Japan	Case report	1 (43)	*P. westermani*	Lungs/pleural effusion	PZQ	3 × 25 on 1 day	Improvement	[38]
Japan	Case report	1 (47)	*P. westermani*	Pleural cavity	PZQ	3 × 25 for 3 days	Recovery	[39]

South Korea	Retrospective analysis of hospital records	32 (28-63)	*P. westermani*	Lungs/pleural effusion	PZQ	3 × 25 for 3 days	Recovery in all patients after 2-3 courses	[11]
South Korea	Case report	1 (46)	*P. westermani*	Lungs, pleural cavity/pleural effusion	TCZ; followed by PZQ[i]	10 single dose (3 × 25)	TCZ no effect Recovery after PZQ	[40]
Taiwan	Case report	1 (94)	*P. westermani*	Colon	PZQ	3 × 25 for 2 days	Recovery	[41]
Malaysia	Case report	1 (46)	*P.* not specified	Lungs	PZQ	3 × 25 for 2 days	Recovery	[42]
Thailand	Case report	1 (39)	probably *P. heterotremus*	Lungs/tuberculosis	PZQ	3 × 25 for 3 days	Recovery	[43]
Nepal	Case report	1 (48)	*P. westermani*	Lungs	PZQ	3 × 25 for 3 days	Recovery	[44]
Nepal	Case report	1 (45)	*P.* not specified	Pericardium/pericardial tamponade	PZQ	3 × 25 for 3 days	Recovery	[45]
Ecuador	Retrospective analysis of hospital records	45 (3-45)	*P. mexicanus*	Lungs	PZQ	3 × 17.5 for 3 days	Recovery	[46]
Ecuador	Case report	3	*P. mexicanus*	Lungs	TCZ	5 for 3 days	Recovery	[47]
Ecuador	Case series	?	*P. mexicanus*	Lungs	PZQ	3 × 25	95%-100%	[7]
Ecuador	Case report	1 (30)	*P. mexicanus*	Lungs	PZQ	3 × 25 for 3 days	Improvement	[46]
Columbia	Case series	24 (3-50)	*P. mexicanus*	Lungs	PZQ	3 × 25 for 3 days	Recovery	[48]
Peru	Case report	1 (7)	*P. mexicanus*	Lungs	TCZ	2 × 10 on 2 subsequent days	Improvement	[49]
USA	Case series	9 (10-32)	*P. kellicotti*	Lungs	PZQ	3 × 25 for 2-3 days	Recovery	[50]
USA	Case report	1 (29)	*P. kellicotti*	Lung/pleural effusion	PZQ	3 × 25 for 2 days	Improvement	[51]
USA	Case report	1 (46)	*P. kellicotti*	Lungs	PZQ	3 × 25 for 4 days	Recovery	[52]
USA	Case report	1 (56)	*P. westermani*	Lungs	PZQ	3 × 25 for 3 days	Recovery	[10]

[a]5 patients received a second course; [b]depending on organ manifestation, only a subgroup of 15 hospitalized patients was analyzed; [c]all patients were treated neurosurgically; [d]24% of the patients needed more than 1 course for improvement; [e]surgery, PZQ + corticosteroids, [e]to mitigate immune response; [f]all patients were operated; [g]some patients received a second course; [h]some patients failed to respond to 3 doses of praziquantel, one patient was eventually cured after treatment with triclabendazole 10 mg/kg; [i]patient failed to respond to 3 doses of triclabendazole, but was cured after treatment with praziquantel. Since the patient was allergic against praziquantel the patient received increasing doses from 30 to 1200 mg in a desensitization procedure.

anti-epileptics. Two larger case series with cerebral paragonimiasis from China, however, indicate that the great majority of patients improved[25,26].

Two case reports merit to be discussed in detail. Qian *et al.* reported that in some patients with paragonimiasis in the brain multiple courses of praziquantel (3 × 25 mg/kg/d for 3 days) did not result in improvement[33]. These patients were cured after an additional treatment with 10 mg/kg triclabendazole. In contrast, Kyung *et al.* observed no effect of triclabendazole as the primary treatment of a patient with lung paragonimiasis. The patient was cured after treatment with praziquantel[40].

None of the studies was designed to allow the comparison of the efficacy of praziquantel and triclabendazole.

DISCUSSION

Paragonimus species develop in a broad range of specific snail (= first intermediate host) and crab/crayfish species (= second intermediate hosts). The final host encompasses many different species of wild and domestic mammals which consume freshwater crabs/crayfish, such as mink bobcat, raccoon, civet, coyote, fox, dog, skunk, weasel, badger, marten, boar, pig, deer, guinea pig, tiger, leopard, panther, and cat[1-4]. Since paragonimiasis is a zoonosis with many animal reservoirs it is impossible to eradicate, and new cases will continue to occur as long as people consume fresh/undercooked crab/crayfish. Early diagnosis and effective treatment are therefore the mainstay to avoid the development of debilitating, and in the case of brain paragonimiasis, life-threatening disease.

In the open clinical trials, praziquantel (3 × 25 mg/kg/d for 3 days) cleared eggs from the sputum taken 90 days post-treatment in all patients with pulmonary paragonimiasis[14,15]. Symptoms and signs disappeared, and radiological findings reversed to normal after one year[14]. However, it cannot be excluded that the true cure-rate was lower: The sensitivity of the detection of eggs in sputum is not known, the method has never been standardized, and day-to-day-variation of release of eggs into the bronchi may have an impact on the diagnostic precision of the method.

In the open clinical trials with triclabendazole, it was shown that 5 mg/kg/d were needed to rapidly clear eggs from the sputum[19,20]. None of the studies allowed to compare the efficacy of praziquantel with that of triclabendazole. Of the 558 cases identified in retrospective analyses of hospital records, case series and case reports, 544 were treated with praziquantel and only 14 with triclabendazole. Since 2003 only a few cases treated with triclabendazole have been reported.

After treatment with praziquantel (3 × 25 mg/kg/d) recovery was reported from 147 patients and improvement from 66 patients. In the 244 cases from the retrospective analysis of hospital records either improvement or recovery were noted. Similar results were reported also in case series and case reports on patients published earlier than 2000[17,53-67] In 9 patients infected with *P. skrjabini* and treated with triclabendazole and recovery was reported. Since the patients differed with regard to organ manifestation, disease duration, stage and severity, co-morbidity (such as tuberculosis), other therapeutic interventions such as surgery and other host-related factors, no conclusion can be drawn on the efficacy of praziquantel compared to that of triclabendazole. For instance, in areas where tuberculosis and paragonimiasis overlap and patients are treated with antibiotics for long periods, the efficacy of the treatment of paragonimiasis may be impaired[46]. Rifampicin, for example, induces degrading enzymes and thereby reduces the plasma level of praziquantel to zero[8].

In 11 patients with cerebral paragonimiasis multiple courses of praziquantel (3 × 25 mg/kg/d for 3 days) did not result in improvementl[33]. These patients were cured after an additional treatment with 10 mg/kg triclabendazole. In a report of a case with lung paragonimiasis, the treatment with triclabendazole remained without effect. The patient was cured after treatment with praziquantel[40]. Whether these findings indicate that in the first case praziquantel, and in the second case triclabendazole was not sufficiently absorbed or rapidly degraded, remains to be elucidated. The findings, however, underline that the characteristic pharmacokinetics of praziquantel and triclabendazole have to be understood to guarantee that the medication is effective[68].

Since schistosomiasis and paragonimiasis overlap in many countries in Africa and Asia, and because praziquantel is administered to school-age children as preventive mass chemotherapy in all schistosomiasis-endemic areas, it has been suggested that the regular treatment with praziquantel may have an additional benefit on the incidence of paragonimiasis in children and adolescents[69].

However, experimental studies show that a 10-fold higher concentration of praziquantel is required to paralyze the small liver fluke *Clonorchis sinensis*, another member of the family of food-borne trematodes, than to paralyze *Schistosoma mansoni*[4].

On the other hand, in areas endemic for *Taenia (T.) solium* infection and possible unrecognized cerebral cysticercosis, the activity of praziquantel against *T. solium* metacestodes and the consequent immune response could possibly cause cerebral edema and epilectic attacks which is not expected for triclabendazole which is apparently not active on cysticerca[70,71]. Furthermore, TCZ is not only active against small liver flukes but also against the large liver fluke *Fasciola hepatica*[68,21,44,72]. Although TCZ is a well investigated and safe drug higher daily TCZ dosages and co-medication of PZQ and TCZ of unresponsive cases has apparently never been tried.

CONCLUSION

Both, PZQ and TCZ are usually effective for treating paragonimiasis. In some cases not responding to one of the drugs, the other has proven effective, so far. Either drug has its advantages depending on the clinical and epidemiological context. PZQ is effective against a large range of plathelminthes including schistosomes, small liver flukes and taeniae. This effect can be advantageous in areas where these infections are co-endemic. TCZ has the advantage of requiring lower dosages and fewer treatment courses, being effective also against Fasciola spp. as well as apparently not being active on unrecognized cysticercosis co-infection, which might pose problems in areas where *Taenia solium* is co-endemic. For comparison of the efficacy of PZQ versus TCZ double blinded, controlled randomized investigations are required. Furthermore, trials are warranted to find out the ideal medication (single dose versus multiple dose-therapy schemes, TCZ-PZQ combination-therapy for a given setting taking into account co-infections and logistic issues.

DECLARATIONS

Author's contribution

The author solely contributed this article.

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Not applicable.

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Conflicts of interest

The author declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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