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PRAZIQUANTEL THERAPY IN NEUROCYSTICERCOSIS

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Abstract : Neurocysticercosis is being recognised more often now, because of advances in radio-imaging. No treatment was available for this disease till about a decade back. Praziquantel has provided new hope. From India, there are very few published reports on experience with this drug. Nine cases of neurocysticercosis are being presented, where praziquantel therapy has been tried. Five patients with tumour syndrome and one patient with a meningoencephalitic syndrome have shown a favourable response. In 3 patients with epilepsy syndrome, it is difficult to assess the role of this drug in their management. The relevant data have been presented and analysed.

Key words : praziquantel cysticercosis neurocysticercosis

INTRODUCTION

Neurocysticercosis is a disease of the developing world. Before the advent of immunological tests, the diagnosis was mainly conjectural. Stray cases were reported in the neurosurgical literature, where surgeons encountered cysticerci in the brain more as a surprise finding. Cysticerci were also seen by the pathologist occasionally in the autopsy material. As early as 1888, Armstrong (1) was the first in India to report a case of cerebral cysticercosis in a patient who died in Madras mental asylum. Ramamurthy et al (2) reported their experience from Madras with cerebral cysticercosis in 1970. This was followed by similar reports from other centres in the country (3-9).

Praziquantel (PZQ) (2 cyclo-hexul carbonyl 123671 11 B hexa-hydro-BH pyrazino 12-1a) is a pyrazoquinoline derivative, which is being specifically used in the treatment of schistosomiasis (1). Initial trials of this drug for subcutaneous nodules in cysticerosis proved very effective (10). It is this fact that actually formed the basis for its use in cerebral cysticercosis. Later *in-vitro* experiments confirmed the role of this drug in cysticercosis (11).

Since 1981, several reports have been published, defining the role of PZQ in cerebral cysticercosis (12, 13, 14). There are very few reports on PZQ therapy in India (1, 15, 16, 17).

Our initial experience with PZQ therapy in 9 cases of neurocysticercosis is being presented. The problems encountered during the treatment of this disease with PZQ have been discussed.

METHODS

In the last 18 months, nine patients with a diagnosis of neurocysticercosis were put on Praziquantel (PZQ) therapy at J.N. Medical College, A.M.U., Aligarh. Eight of them were admitted to the neurosurgical unit and one patient was admitted to medical ward and then referred. Two patients were referred to the neurosurgical unit from Gandhi Eye Hospital, Aligarh and had associated ocular cysticercosis. Once the diagnosis was established clinically and on CT Scan, patients were put on steroids. In patients with epilepsy alone, prednisolone 1 mg/kg body weight/day was given in four divided doses, whereas patients with tumour syndrome (headache,

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vomiting, blurring of vision etc.) were given Inj. Hydrocortisone (Efcorlin) 100 mg iv 6 hourly. Steroids were gradually tapered off during the course of treatment with PZQ. Twenty four hours after starting steroids, PZQ tablets were given in the dose of 50 mg/kg body weight in divided doses for 15 days.

Adverse drug reactions, if any were managed symptomatically. Adverse drug reactions of praziquantel were monitored by the Department of Pharmacology, J.N. Medical College as part of a multicentric ICMR trial.

C.T. Scan brain was advised immediately after completing PZQ therapy. Patients were discharged with advice to report with another repeat CT Scan brain 3 months following therapy. The relevant data have been analysed.

RESULTS

All patients were in the range of 15-60 years. There were five male and four female patients. Their clinical profile has been tabulated (Table I). Generalised epilepsy was the commonest symptom in all cases, except in case 4, where the patient presented with an acute stroke like picture without any convulsions.

Clinically, patients could be grouped in following categories. Three patients (cases 7, 8 and 9) presented with just epilepsy and no other symptom. One patient (case 1) presented with a meningoencephalitic picture. Patient had signs and symptoms of raised intracranial pressure with altered sensorium. Cerebrospiral fluid showed cells, that were predominantly lymphocytic. Computerised tomographic Scan revealed multiple lesions, clinching the diagnosis of neurocysticercosis. Five patients (cases 2-6) presented with a tumour like syndrome. Patients had headache, vomiting, blurring of vision, papilloedema or its after effects. One patient (case 4) presented with an acute stroke like picture without any convulsions. Computerised tomographic. Scan of the brain clinched the diagnosis in this case.

C.T. findings were as follows. Three cases (cases 6, 7 and 9) showed single lesions. Rest of the cases had multiple lesions. Only one case (case 6) showed a calcified lesion. Enhancing disc lesions (Fig. 1) were seen in 7 cases. Only two cases (cases 4 & 7) showed ring lesions.

TABLE I : Clinical profile of patients on PZQ therapy.

No.	*Age yrs*	*Sex*		*Clinical presentation*	*CT lesion*
1	25	M	Veg	Altered sensorium, generalised epilepsy, blind. Secondary optic atrophy, cysticercus seen in vitreous	Multiple enhancing lesions
2	30	M	Veg	Headache, Vomiting, blurring of vision	Multiple enhancing lesion
3	20	F	Veg	Amnorrhoea, Prim optic atrophy, hemianopia, headache general epilepsy	Multiple enhancing lesions (one lesion in suprasellar location)
4	60	F	Veg	Acute stroke like picture. No convulsions	Multiple ring enhancing lesions
5	45	M	N. Veg	Generalised epilepsy	Multiple enhancing lesions
6	15	F	N. Veg	Headache, vomiting, blurring of vision, general epilepsy	Single enhancing lesions
7	15	F	N. Veg	Headache, generalised epilepsy	Single enhancing lesion
8	40	M	N. Veg	Generalised epilepsy	Multiple enahancing lesions
9	25	F	Veg	Generalised epilepsy	Single enhancing lesion

Veg - vegetarian; N. veg - Non-vegetarian

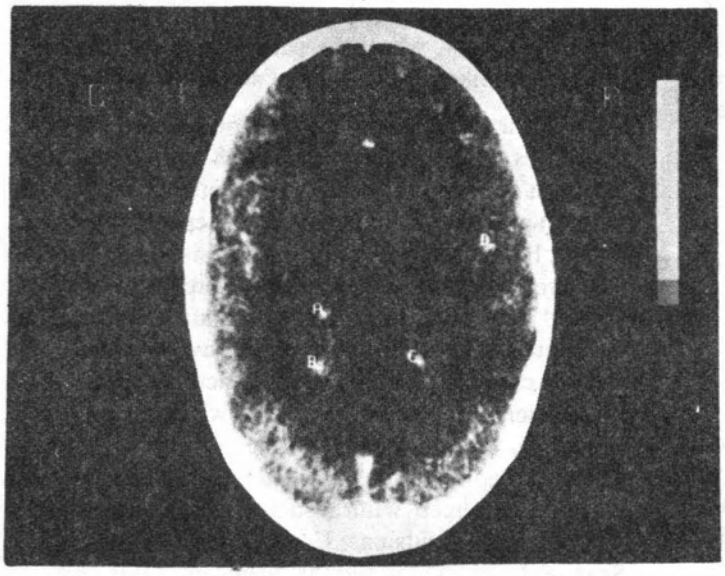

Fig. 1 : Cysticerci scattered all over the brain.

The results of PZQ thereapy were as follows (Table II). There was definte improvement in 5 cases. One case (case 5) showed no change. In three cases (cases 7, 8 & 9), it is difficult to assess the role of this drug. All these patients belonged to the epilepsy group. Since they were seizure free even before starting PZQ, it would be difficult to ascertain, if this drug has in any way helped these patients.

Maximum follow up was 6 months in one case, three months in 3 cases and 1 month in the rest. Follow up CT was available in only four cases (cases 1, 5, 6 and 9). None of the cases showed any change, where CTs were done immediatey or within 15 days following therapy. The CT scan showed a resolving lesion in one case, where it was done 3 months following PZQ therapy.

ELISA test in the serum was done in only one case (case 6) and it was positive for cysticercosis.

Adverse drug reactions were headache in all cases, vomiting in 5 cases, blurring of vision in 5 cases, diplopia in 1 case, seizure during therapy in 3 cases and skin rashes in 1 case. All these reactions were transient and occurred in the first week only.

TABLE II : Treatment profile of patients on PZQ therapy.

S. No.	*Treatment*	*Response*	*ADR*	*CT*	*Follow up*
1	EFC*+PZQ**	Seizure free, blindness persists	Headache vomiting	Lession resolving	6 months
2	EFC+PZQ	Subcut nodules disappear 2 wks symptoms subside papilloedema persists	Headache vomiting skin rashes	—	1 month
3	EFC+PZQ	Vision improved, symptom free.	Headache seizures during treatment	—	3 months
4	*ATT no response EFC+PZQ	Hemiplegia improves symptom free	Headache Nausea	No change	1 month
5	P*** PS+PZQ	Symptom free	Headache epilepsy	No change (1 month)	1 month
6	PS+PZQ	Seizure free, Symptom free	—	No change (1 month)	1 month
7	PS+PZQ	Sympton free, seizure free	Headache	—	3 months
8	PS+PZQ	Symptom free, seizure free	—	—	3 months
9	PS+PZQ	Symptom free, seizure free	—	No change (1 month)	3 months

**Efcorlin (EFC)-dose 100 mg i.v. 6 hourly gradually tapered

**PZQ-50 mg/kg body weight x 15 days

***Prednisolone (PS)-1 mg/kg body weight gradually trapered off.

DISCUSSION

In literature, results from PZQ therapy have started arriving since 1980. Robles et al (11) have reported successful results in their patients with this drug. In 1984, Sotelo et al (1) analysed their experience with 35 patients of cerebral cysticercosis. They demonstrated disappearance of C.T. lesions following PZQ therapy.

From India, Singhal et al (16) reported their experience with PZQ in cerebral cysticercosis in 1985. Kalra et al (15) published their experience of PZQ in neurocysticercosis in children. Nag (1) found complete recovery in three and partial recovery in four out of 10 cases that she reported. Varma et al (17) have dealt with adverse drug reactions of this drug during treatment of neurocysticercosis. Recently Sancheti et al (11) have reported a favourable response with this drug in 25 cases. They found complete control of seizures and intracranial tension in 7 cases and moderate improvement in 14 cases. Serial CT scans showed complete resolution in 5 cases and partial regression in 16 cases. They have also described their experience with nuclear magnetic resonance in 5 cases.

Some definite clinical syndromes seem to emerge in neurocysticercosis. There are patients, who present with just epilepsy and nothing else. C.T. Scan of the brain shows multiple lesions suggesting cysticerci. Three of our cases (cases 7, 8, & 9) belong to this group. It is difficult to assess the role of PZQ in this group. Should the patient be expected to be seizure free? If it is so, is it because of just anticonvulsants or has PZQ contributed in some way? Should the dose of anticonvulsants be reduced? One can not hazard a guess, unless a large multicentric trial is conducted over a fairly long period of time. Mani et al (6) have described this syndrome as early as 1974.

The second group of patients present with symptoms and signs of raised intracranial pressure like headache, vomiting, blurring of vision, diplopia etc. Five of our cases (cases 2-6) fall under this category. All patients in this group showed definite improvement following PZQ therapy. Symptoms generally start regressing in first week of therapy itself. One of our cases (case 5) though symptom free otherwise developed convulsions after fifteen days of completing therapy. Should recurrence of seizure within 15 days indicate that the disease is still active or is partially treated? Does PZQ therapy really alter the epileptogenecity? These are some of the questions that need answer.

The third group is the meningoencephalitic group. We had only one patient (case 1) in this group. PZQ has shown a good response and the patient is symptom free 6 months following therapy.

There is a fourth group of patients, who just complain of headaches. While investigating at some stage, CT scan reveals lesions, characteristic of neurocysticercosis. None of our patients belonged to this group. Sancheti et al (11) have reported a favourable response of this drug on this group.

Regarding disappearance of CT lesions, there seems to be no controversy. Sancheti et al (11) have clearly demonstrated that though clinical recovery occurs in 3 months time, it takes about 12-24 months for CT lesions of disappear. We had only four patients, where repeat CTs were available. In three patients where CTs were repeated immediately following therapy, there is no change radiologically. Only one patient where CT was repeated 3 months following therapy, shows a definite regression. It is obvious that we have repeated CTs rather too early. The earliest that one could find some changes in the CT would probably be 3 months time.

Ramos et al (11) have described NMR findings in neurocysticercosis. Sancheti et al (11) while describing NMR findings have clearly demonstrated degeneration and subsequent disappearance of these cysts.

It is quite clear by now that cysticerci do respond to PZQ therapy by degenerating and disappearing. But then the cysticerci die, degenerate and disappear even in their natural evolution. This is no way underscores the role of PZQ in cysticercosis. PZQ provides a unique opportunity to kill these cysts under controlled conditions rather than leave the patient to an uncertain future, where in some cases, it may become fatal (18)

As regards the adverse drug reactions of this drug, there is a word of caution while interpreting them.

Apart from skin rashes in one case (case 2), none of the other symptoms could be considered as an adverse drug reaction. These symptoms result from the disintegration of the cyst wall and the resultant inflammatory response of the brain. So, in the true sense of the term, these can not be considered as adverse reactions of the drug, but are as a result of the death of the cysticerci. Castano et al (13) and Goll (10) have suggested that appearance of these symptoms at the onset of therapy actually indicates the therapeutic efficacy of the drug in that particular individual. This is also borne by the fact that normal healthy volunteers, when given PZQ have not reported any adverse reactions (11).

REFERENCES

1. Nag D. Neurocysticercosis and its management in Proceedings of the International Seminar on Clinical Pharmacology in developing countries. Eds. Saxena, RC Gupta TK, Dixit KS. *Indian Pharmacological Society and Indian Medical Association* 1986; 2 : 170-174.
2. Ramamurthi B, Balasubramaniam V. Experience with cerebral cysticercosis. *Neurology India* 1970; 18 : 89-91.
3. Dinakar L, Mathai KV, Chand J. Cysticercosis of the brain. *Neurology India* 1971; 18 : 165-170.
4. Mehta DS, Malik GB, Dar J. Intramedullary cysticercosis. *Neurology India* 1971; 19 : 92.
5. Raja Reddy D, Shiva Reddy P, Krishnamurthy D. Reddy CS. A cause of large suprasellar cysticercus cyst with bitemporal hamianopia. *Neurology India* 1973; 21 : 44-45.
6. Mani AJ, Ramesh CK, Ahuja GK, Mani KS. Cerebral cysticercosis presenting as epilepsy. Neur*ology India* 1974; 22 : 30-34.
7. Natarajan M, Balakrishna D. Cysticercosis of the brain. *Neurology India* 1979; 18 : 171-175.
8. Shadangi TN, Abraham J. An extradural cysticercosis attached to lumbar nerve root. *Neurology India* 1977; 25 : 43-44.
9. Venkataraman S, Vijayan GP. Neurocysticercosis, clinical manifestations and problems in diagnosis. *J Ass Phys India* 1979; 543-549.
10. Groll EW. Chemotherapy of human cysticercosis with praziquantel in cysticercosis : present state of knowledge and perspectives. Eds. Flisser A. et al. Academic Press, New York 1982; 207-218.
11. Sancheti PC, Dhamija RM, Roy AK, Jena A, Venkataraman S, Krishnan NR. Praziquantel therapy in neurocysticercosis. *Neurology India* 1990; 38 *: 139-146.*
12. Botero D, Castano. Treatment of cysticercosis with praziquantel in Columbia. *Am J Trop Med and Hyg* 1982; 31 : 811-821.
13. Castano S, Botero D. Treatment of neurocysticercosis with praziquantel in Columbia. *Progress in Clinical Neurosciences* 1985; 2 : 220-231.
14. Sotelo J, Escobedo F, Rodrigne-Carbajal J. Torres B, Rubio-Donnadieu F. Therapy of parenchymal brain cysticercosis with praziquantel. *New Eng J Med* 1984; 310(16) : 1001-1007.
15. Kalra V, Deorari AK, Caulata RK. Praziquantel therapy in childhood neurocysticercosis. *Indian Paediatrics* 1987; 24 : 1095-1098.
16. Singhal BS, Sowani AM. Praziquantel in neurocysticercosis. *J of Ass of of Physician of India 1985; 35 :* 601-604.
17. Verma A, Pauranik A, Maheshwari MC. Adverse reactions during treatment of neurocystercosis with praziquantel. *Neurology India* 1987; 35 : 349-352.
18. Nash TE, Neva FA. Recent advances in the diagnosis and treatment of cerebral cysticercosis. *The New Eng J of Med* 1984; 311 : 1492-1496.