

CASE REPORT : CARBAMAZEPINE THERAPY IN SCHIZOPHRENIA

S. S. RAJU, M.D.*

SUMMARY

9 cases of schizophrenia meeting Spitzer's Research Diagnostic Criteria and nonrespondent to conventional treatment were treated with carbamazepine, either alone or in combination with neuroleptics and 7 cases had shown improvement.

Carbamazepine has been found to be useful in the treatment of affective disorders (Okuma *et al.*, 1979; Ballenger and Post, 1980; Sethi *et al.*, 1983) and in cases of epilepsy with psychic disturbances like psychopathic behaviour, dysphoria and schizophrenia-like psychoses (Myrstener, 1968; Helmchen 1976). Carbamazepine (CBZ) is a tricyclic compound and its steric structure approaches that of psychotropic drugs such as chlorpromazine, imipramine and maprotiline, it may therefore be regarded as one of the polycyclic psychoactive drugs (Sillanapaa, 1981). It is not clear whether CBZ has any therapeutic benefits in schizophrenia. 9 cases of schizophrenia fulfilling Research Diagnostic Criteria (RDC; Spitzer *et al.*, 1978) for definite illness, nonrespondent to conventional treatment and free from major physical illness were chosen for this study. They were treated with CBZ either alone or in combination with neuroleptics, starting from October 1982. Final assessment was compiled in September 1983.

CASE REPORTS

Patient 1, born 1959, male, onset of schizophrenia in 1972, family history of psychosis and epilepsy present, had not responded to chlorpromazine, trifluoperazine and haloperidol. EEG normal. Had grossly noticeable nystagmus but no other neurological abnormality. Neurologists and ophthalmologists considered

it inexplicable and advised review at intervals. Had profound thought disorder, delusions of persecution and reference and auditory hallucinations. CBZ alone was given, starting with 400 mg/day and gradually raised to 1200mg/day. Improvement was noticed by 4 weeks time and at the end of 2 months of therapy he became asymptomatic and resumed working. Patient was maintained on the same dose for 3½ months and he remained well. His nystagmus remained same. Patient had not developed any side effects, except a subjective sense of physical weakness. Hematological investigations revealed no abnormality. Since carbamazepine itself is known to cause nystagmus and as the patient was maintaining improvement, the dosage was gradually decreased to 400mg/day and symptoms totally relapsed. Then a combination of antipsychotics with CBZ 400 mg per day was given and patient has improved again.

Patient 2, male, born 1945, schizophrenic illness commenced in 1968. After unsuccessful treatment at several psychiatric centres, underwent prefrontal leucotomy in 1976. He developed fits and was put on phenobarbitone and phenytoin sodium in addition to haloperidol and was leading a vegetative existence. CBZ was introduced in place of the previous antiepileptics and the dosage enhanced to 800mg/day. Patient had shown about 50% improvement,

*Associate Professor & Head Department of Psychiatry Kasturba Medical College Hospital Manipal, Karnataka.

which he maintained for 7 months. He then developed tubercular pleurisy for which antitubercular treatment too was prescribed. His condition deteriorated. CBZ was raised to 1000mg/day and his condition has again improved.

Patient 3, female, born 1949, schizophrenic since 1978 and patient 4, male, born 1953, schizophrenic since 1969, unresponsive to antipsychotics and electroconvulsive therapy failed to respond to CBZ alone upto 1200mg/day and in combination with antipsychotics. The latter patient developed nystagmus, diplopia and ataxia when the dosage of CBZ was raised to 1200mg/day.

Patient 5, female, born 1961, schizophrenic since 1978; patient 6, male, born 1957, schizophrenic since 1980 and patient 7, female, born 1959 schizophrenic since 1977 were treated at different centers with antipsychotics but with poor response. When CBZ was added upto 800mg/day to the antipsychotic already being received paranoid symptoms subsided and they regained interest in personal and social functioning. Their affective responsiveness improved considerably. In patient 6, when CBZ was withdrawn, symptoms relapsed and improved after reinstating CBZ.

Patient 8, female, born 1954, onset of neurotic-like symptoms in 1978, culminated in schizophrenia in 1980. Showed poor response to phenothiazines and a divorce suit was filed in the court by the husband of the patient as she was considered mentally unfit. In addition to florid schizophrenic symptoms patient complained of occasional epigastric distress with giddiness and hence an EEG was done which was normal. Patient was put only on CBZ 800/mg day and achieved over 90% improvement.

Patient 9, male, born 1938, schizophrenic illness commenced in 1974, improved with phenothiazines and E.C.T.

Had a relapse in 1981 with marked paranoid tendencies with no response to phenothiazines and was removed from his job, following which he manifested depressive symptoms in addition. When the patient was first seen in our clinic he was found to have tardive dyskinesia along with schizophrenic and mild depressive symptoms. Small dose of imipramine was added and the psychotic symptoms got further aggravated. In view of the dyskinetic movements of lips and jaw and poor response to phenothiazines all drugs were stopped and he was put on CBZ 1000mg/day with which he made a marked improvement. The dyskinetic movements were drastically reduced. But mild suspiciousness was persisting and hence a small dose of phenothiazines was added and further improvement was noticed. He has again resumed working.

COMMENT

This is the first report of the use of carbamazepine in cases of established schizophrenia. It is a preliminary clinical investigation. 7 out of 9 schizophrenics that have failed to respond to conventional treatment have improved with carbamazepine- either alone or in combination with neuroleptics. The improvement noted in the latter group may raise a doubt whether it was attributable to CBZ or antipsychotics. The very fact that these were the cases that have not responded previously to much higher dosage of the same antipsychotic points to a probable synergistic effect of CBZ and neuroleptics. Though initially reported to be beneficial in manic-depressives, the efficacy of CBZ in nuclear schizophrenics was astounding. Neuroleptics are effective both in mania and schizophrenia, and carbamazepine found to be an anti-manic agent seems to have antischizophrenic properties as

well. In addition to its efficacy against hallucinatory behaviour, paranoid delusions and thought disorder, CBZ has caused an improvement in mood in some of the withdrawn schizophrenics. It may be useful to add CBZ in cases of tardive dyskinesia, which might be beneficial in schizophrenia and in dyskinesia too, either due to its effects or consequent to reduction of dosage of anti-psychotic drugs. If there happen to be schizophrenics with post-leuctomy sequelae, a trial of CBZ seems justified. It has not produced parkinsonian symptoms in any of our patients and no prominent daytime sedation was evident. At higher dosage it produced nystagmus, diplopia, and ataxia in one case, a subjective sense of weakness in another case, but there were no other visible side effects. A better tolerance of the drug was observed if it was started at a smaller dose and then gradually enhanced. In a few cases it had produced initial worsening of symptoms followed by subsequent improvement and treatment should be given at least for 6-8 weeks before response could be assessed. Further controlled clinical trials of CBZ in schizophrenia with objective methods of evaluation are indicated as the outcome of schizophrenia still remains negative in many cases despite the introduction of a variety of antipsychotic drugs. CBZ is said to affect nor-epinephrine, dopamine,

acetylcholine, electrolyte, cyclic nucleotide and GABA systems and how exactly it helps schizophrenics remains to be seen.

ACKNOWLEDGEMENTS

Thanks are due to M/S SG Pharmaceuticals, Baroda, for the supply of carbamazepine and to Miss. Gunasagari Rao, M. S. W., M.Phil. for assistance in the collection of data.

REFERENCES

- BALLENGER, J. C., AND POST, R. M. (1980). Carbamazepine in manic-depressive illness: a new treatment. *Amer. J. Psychiat.*, 37, 782.
- HELMCHEN, H. (1976). Reversible psychic disorders in epileptic children. In: *Epileptic seizures—Behaviour—Pain.* (Ed.) Birkmeyer, W., Vienna: Hans Huber. P. 175.
- MYRSTENER, A. (1968). Carbamazepine treatment of epileptic psychosis. *Nord. Psykiat. tidskr.*, 22, 52.
- OKUMA, T., INANAGA, K., OTSUKI, S., ET AL. (1979). Comparison of the antimanic efficacy of carbamazepine and chlorpromazine: a double-blind controlled study. *Psychopharmacology.*, 66, 211.
- SETHI, B. B., TRIVEDI, J. K. AND SINGH, R. K. (1983). The use of carbamazepine in patients with manic depressive illness. *Indian J. Psychiat.*, 25, 23.
- SILLANAPAA, M. (1981). Carbamazepine. *Pharmacology and clinical uses.* *Acta Neurol. Scand. Supplement.* 88.
- SPITZER, R. L., ENDICOTT, J. AND ROBINS, E (1978). *Research diagnostic criteria (RDC) for a selected group of functional disorders.* Third Edition, Bio-metric research. New York: New York State Psychiatric Institute.