

SHORT COMMUNICATION

EFFECT OF COMMON ANTI-EPILEPTIC DRUGS ON COGNITION
IN SCHOOLCHILDREN WITH EPILEPSY

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Abstract : This study was conducted to observe the effect of some commonly used anti-epileptic drugs (AEDs), on cognition, in 118 school going children with epilepsy, in an age range of 9-12 yrs., (Mean 10.4 ± 1.7 yrs.). For comparison, 28 healthy, age and sex matched schoolchildren served as controls. After a clinical, electrophysiological and radiological evaluation, the cognitive functions were assessed in both groups, using a modified Wechsler's Intelligence Scale. It was observed that cognition was impaired in only 2.5% of children with epilepsy, there being no relationship between cognitive performance and the type of AED used. It is concluded that cognitive functions are impaired in only a limited number of children with epilepsy and effect of phenobarbitone and phenytoin on cognitive functions is comparable to carbamazepine and sodium valproate, particularly when demand of task is not very high.

Key words : cognition anti-epileptics

INTRODUCTION

Cognitive function has been reported to be impaired in children with epilepsy, compared with age matched controls. Multiple factors influence cognition in such patients including underlying brain pathology, inherited tendencies, psychosocial factors, antiepileptic medication etc (1, 2) and, it is difficult to evaluate their individual significance (3).

Epileptologists now monitor cognition with a view to offering excellent seizure control with minimal possible negative impact (4, 5).

This study was conducted to determine the effect of commonly used anti-epileptic drugs (AED) on cognitive function in children having well controlled epilepsy. The changes, if any, with the type of AED used, were also evaluated.

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METHODS

This prospective case controlled study was conducted on 118 (78 male and 40 females) school going children selected from 212 patients with epilepsy. Their ages ranged from 9–12 years (mean age 10.4 ± 1.7 yrs). They had primary generalised seizures (ILAE) classification) and were fully controlled on monotherapy with either of the AEDs viz. Phenobarbitone (PB)-38 patients, Phenytoin (PHT)-34 patients, Carbamazepine (CZ)-26 patients and Sodium Valproate (VPA)-20 patients. The control group consisted of 28 (20 male, 8 female) school children.

Children having epilepsy secondary to Intracranial space occupying lesions, head injury, cerebral anoxia, cerebrovascular accidents were excluded. Children with mental retardation, cerebral palsy, and those on polytherapy were not included. Intellectual capability of subjects and control were tested and found to be adequate for understanding the mental test being performed (IQ- 80 and above). After detailed clinical and neurological examination relevant radiological (cranial CT and MRI) and electrophysiological investigation were done to fulfill selection criteria and exclude secondary causes. The children were evaluated at the time of entry into study and at three month intervals. Cognition in patients and control was measured using Wechsler's intelligence scale test which had to be partly modified to suit the Indian children (6). This was a written format and comprised of simplified and common questions as tests of orientation, attention, memory (immediate, recent and remote), calculation and comprehension. Evaluation

was done with the help of clinical psychologist in morning hours just before the first dose since the children were more alert at that time. Teachers were informed about the seriousness of this study and regularly interviewed by investigators and/or parents regarding the scholastic performance and behavioural changes. The assessment result cards of patients and control were regularly checked and graded from A-J (A = 100% and J = 10%). Decrease in scholastic performance was defined as decrement by 2 grades (20%) or more. Compliance was ensured by observing the seizure diary, maintained by parents. The period of follow up of each patient was 1.5 years and the total period of study was 3.5 years. Estimation of drug level was done only in children with epilepsy, by Fluorescence Polar Immunoassay Analyser (FPIA) at each follow up.

Statistic analysis was done using students 't' test.

RESULTS

While cognition was normal in control subjects, significant impairment was observed in only 3 (2.5%) of 118 patients, one each on PHT, PB and CZ. Complaints of increased sleeping hours (more in day time) and excessive drowsiness were reported in 12 (32%) patients on PB, 10 (30%) on PHT but only 4 on CZ and VPA (16% and 20% respectively Table I). Five (19%) children with epilepsy showed significant improvement in immediate recall on CZ and 3 (15%) on VPA, while 6 revealed a tendency towards improvement in attention and immediate recall both on PHT (18%) and PB (16%). The serum levels of all

TABLE I: Comparison of common AED and their effect on cognition

	PB	PHT	CZ	VPA
No. of Patients	38	34	26	20
Price/day (in Rs.)	0.5	0.6	6.0	7.0
Increased sleep (day time)	32%	30%	16%	20%
Improvement in immediate recall	16%	18%	19%	15%
Deterioration in Attention	2.6%	2.9%	3.8%	-
Decrement in immediate recall	2.6%	2.9%	3.8%	-
Decrement in recent memory	2.6%	2.9%	3.8%	-
Decrement in long term memory	Nil	Nil	Nil	Nil
Serum Level ug/ml	38±2.6	18.4±3.6	7.4±1.4	6.2±12.6

the AED were within therapeutic range. In only 2 patients, one each on PB and CZ, the drowsiness persisted after 6–8 months, while others adjusted to a normal sleep pattern after an initial period of 2–6 weeks. School performance as observed by teachers in terms of day to day class work and grades achieved in assessment result cards remained essentially unaltered except deterioration by 2 grades (20%) in only three children, one each on PB, CZ and PHT. Most of subjects (95%) maintained their grade between F and D (50%–70%). Though formal testing was not done, no significant behavioral or mood alteration were observed in these patients by teachers or parents.

DISCUSSION

Thus, in this the two important observations were that in well controlled patients of epilepsy on AED in therapeutic non toxic monotherapy, the Cognitive function remained unaltered and secondly, there is no significant difference in cognitive performance amongst various AED's. Surprisingly, improvement was observed in 20 (18%) patients which may be attributed

to better seizure control and proper dose adjustment rather than to individual psychotropic effect (4, 7, 8). Thus only a limited number of children have cognitive deficit while on AEDs and after discontinuation (9). This is in line with reports that the major factor contributing to quality of life is seizure control (10, 11). In India, where epilepsy continues to be a social stigma, its control instills confidence in the child which may account for the improved cognition (7, 10).

VPA and CZ are known since long to cause negligible impairment in cognition, while PHT and PB have been notorious in causing abnormalities in cognition (12). We observed that PB and PHT do not cause significant cognitive impairment so as to cause serious concern, especially in daily activities where demand of task is not very high (4, 13). While there are reports to document that cognitive impairment in epileptics may be temporary, no difference on cognitive measures between children on AED and control have been reported, especially if seizures are controlled (9, 11). Their use should be encouraged without

hesitation since they are less expensive and there is no appreciable difference in cognition, toxicity, school performance or efficiency between these common AED.

That cognitive abnormalities occur at higher dose and after prolonged use of PHT and PB (5, 14). So is likely our conclusions which are based on a study limited to well controlled rather "benign" epileptics, cannot be generalised. Larger neuropsychiatric (cognitive, behavioral and mood) studies incorporating larger number of control subjects and with emphasis on two key

points: 1. Effect of higher dose (hence higher serum levels) of AED on cognition in epileptics. 2. The impact of AED on cognitive function in uncontrolled epileptic syndromes like West and Lennox etc; refractory to AEDs are required.

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