TREATMENT OF CHILDHOOD EPILEPSY WITH DEPAKINE

R. Koinov, D. Minchev, V. Hristov

Key-words: epilepsy — children — depakine treatment — electroencephalography

Depakine or dipropyl-Na-acetate (DPA), generic term sodium valproate was first synthesized by B. S. Burton in 1981 (cited after 8). G. Carraz et al. (1964) propose the first clinical trial of its anticonvulsive effect. It causes pharmacodynamically an increase of GABA brain tissue concentration by suppressing of its physiological dissociation (7, 8).

Dipropyl acetate (DPA) (trivial term depakine) produced in 1966 by the French laboratory "Labase" was placed at our disposal in the Clinic of neurology, Higher Institute of Medicine, Varna, to be tested in clinical conditions. The main objective of the clinical experiment was to influence on the frequency of epileptic fits and EEG changes in childhood depending on duration of treatment (between 1 month and 4 years long).

Some patients aged between one year and a half and 14 years with insufficiently influenced and even untreated forms of epilepsy were selectively covered by our study. This series included 50 children (26 girls and 24 boys). On table 1 one can see patients' age, the onset of epileptic fits and of depakine therapy.

Table 1

Age in years	Patients' number depending on :	
	begin of epilepsy	begin of depakine therapy
Up to 1	3 (6 %)	—
1—3	16 (32 %)	2 (4 %)
3—5	9 (18 %)	7 (14 %)
5—7	5 (10 %)	11 (22 %)
7—10	15 (30 %)	20 (40 %)
Over 10	2 (4 %)	10 (20 %)
Total	50 (100 %)	50 (100 %)

The dosage of depakine was at the average 30 mg/kg b. w. divided into 2 till 3 times daily. The efficacy of action was clinically estimated according to the scheme: a) very good effect — 75 up to 100 per cent; b) a middle one — 74 to 50 per cent, and c) below 50 per cent becoming less frequent of epileptic fits — a poor effect. We objectified the therapeutic effect by using an EEG method. We performed background registrations with all the patients during treatment as well as after finishing the clinical trial. Standard functional loading and medicamentous sleep were applied during EEG registrations. The results obtained were processed according to the methods of variational and correlational analysis.

Results and discussion

Focal neurologic signs became apparent in 12 patients. The rest ones did not demonstrate any significant abnormalities of the neurologic state. Concerning the etiology it has to be noted that it was not clarified in 20 patients. The following main reasons were revealed in the rest 30 patients: perinatal brain damage (8 cases), postnatal labour injury (12 ones), meningoencephalitis (6 ones), and survived intoxication (4 ones). The frequency of epileptic fits varied between 1—5 daily (in 33 cases), 6—7 fits weekly (in 11 cases), and 1—4 fits monthly (in 6 patients). The structure of nosologic characteristics of different epileptic fits and their influencing by depakine is presented on table 2.

Table 2

Epilepsy form	100—75 %	74—50 %	49—0 %	Total
Grand mal	8	12	3	23
Grand mal and petit mal	1	3	0	4
Psychomotor epilepsy	4	2	1	7
Small myotonic fits	4	2	3	9
Small akinetic fits	1	3	3	7
Total	18 (36 %)	22 (44 %)	10 (20 %)	50 (100 %)

Our data showed that the preparation had a moderate therapeutic effect in cases of long-lasting drug application (at the average between 3 months and 3 years) and depending on the form of epilepsy and its etiology.

The therapeutic effect was confirmed by EEG control in all the patients. The severity of both local and general-brain epileptic bioelectrical changes was compared with the frequency and clinical results of different clinical forms. Under the influence of depakine, there was a insignificant diminishing of the frequency of convulsions ($p < 0,01$) when generalized epileptic changes or slow-wave focuses were electroencephalographically registered. However, the detection of spontaneous irritative EEG focuses of sharp waves, complexes of peaks and slow-waves was always supported by a decrease of epileptic manifestations in depakine treated patients ($p < 0,05$). Best clinical pesults on EEG registrations were related to the reduction of generalized peaks — slow-waves provoked by hyperpnea and medicamentous sleep. The correlation between EEG and clinical picture in children without any generalization of bioelectric changes before depakine treatment was statistically significant ($p < 0,01$). These clinico-EEG correlations support the moderateness of therapeutic influence of single depakine application ($r = 0,53$) as it can be seen on table 3.

It has to be noted that 10 patients without any therapeutic effect of depakine were additionally given phenobarbital (6 cases), diphenylhidantoine (2 ones) and stasepine (2 ones). No side effects and unendurability to the drug were observed.

The clinical influence of depakine was especially favourable concerning the treatment of grand mal, combined grand mal and petit mal with unclear etiology which showed on EEG some frequent discharges of sharp-slow waves spontaneous

Table 3

ECG changes	Reduction of fit frequency			
	100—75 %	74—50 %	49—0 %	Total
Generalized changes of sharp and peak waves	11	4	1	16
Slow-wave focuses	0	1	2	3
Focuses of sharp peak waves	6	3	2	11
Discharges of sharp-slow wave, both spontaneous and provoked by hyperventilation	7	1	4	12
During medicamentous sleep	10	4	4	18
Absence of response changes in functional tests	1	2	3	6
Total	35	15	16	66

or even provoked by functional loading. These data confirm the reports in the literature available (1, 2, 4, 5) but do not agree with the investigations of other authors (3, 6) according to which grand mal was activated by depakine during medicamentous sleep. The preparation had a considerably better effect in patients without any organic neurologic signs and paroxysms or slow-wave focuses on EEG registration. There was a relatively good influence in cases of psychomotor epilepsy, complicated absences, myoclonic-atactic forms, etc. with already proved brain damage. This treatment was, therefore, complex by using luminal, stasepine, diphenylhidantoine. Our results are in agreement with those of a number of authors (1, 2, 3, 8).

Our experience shows that depakine at dosage of 20—40 mg/kg b. w. daily for a period of 3 months till 3 years presents an anticonvulsive drug of choice which could be applied in clinical practice either alone or in combination with other anticonvulsants. It is especially indicated in cases of generalized tonic-clonic convulsions, of absences and of focal epilepsy with more simple symptomatology.

REFERENCES

1. Balbi, R., F. Bravaccio. *Acta Neurol. (Napoli)* 27, 1972, 479—490. 2. Barnes, S. E., D. D. Bower. *Develop. Med. Child. Neurol.*, 17, 1975, 175. 3. Carraz, C., R. Fau, R. Chateau, J. Bonnin. *Ann. Méd. Phychol.*, 122, 1964, 577. 4. Digomo, R., A. Calosimo. *Riv. Neurol.*, 43, 1973, 54—59. 5. Marlot, F. *Rev. Neuropsych. infant.*, 18, 1970, 269—278. 6. Mirribel, J., R. Marinier. *Rev. Neurol.*, 119, 1968, 313—320. 7. Roberts, C., K. Kuriama. *Brain Res.*, 8, 1968, —35. 8. Sinapas. M., M. Donner. *Acta Paediatr. Scand.*, 65, 1976, 209—215.

ЛЕЧЕНИЕ ЭПИЛЕПСИИ В ДЕТСКОМ ВОЗРАСТЕ ДЕПАКИНОМ

Р. Койнов, Д. Минчев, В. Христов

РЕЗЮМЕ

Авторы изучают эффект французского препарата Депакин при лечении пятидесяти детей, больных эпилепсией в различной форме и резистентных к предшествовавшему лечению другими медикаментами. Авторами принята оптимальная средняя дневная доза препарата — 30 мг/кг, принимаемая в два или три приема. Наблюдения показывают, что депакин может применяться с хорошим эффектом при генерализированных тонически-клонических судорогах, очаговой эпилепсии и сложных абсансах с миоклоническими, астатическими и другими проявлениями ЭЭГ картины без грубых генерализированных изменений и очагов медленноволнового характера.

Результаты наблюдений позволяют сделать вывод, что препарат, применяемый самостоятельно или в комбинации с другими антиконвульсивными медикаментами, является эффективным средством лечения эпилепсии в детском возрасте.