

ORIGINAL ARTICLE

Treatment of Infantile Spasms with Valproic Acid

by

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*(From the Department of Child Health, Medical School, University of Indonesia, Jakarta)***Abstract**

During 2 years (1985 - 1986), 12 patients with infantile spasms were treated at the Department of Child Health, Dr. Cipto Mangunkusumo General Hospital, Jakarta. The diagnosis of infantile spasms was based on the specific clinical manifestation and the specific EEG pattern. Head CT Scan was done to look for abnormalities of the brain.

Eleven (91.6%) of the 12 patients had suffered from neurological deficit before treatment was started. Eleven patients suffered from developmental retardation, one patient suffered from cerebral palsy, and 5 patients had microcephaly. In nine (75%) of the 12 patients, the EEG showed hypsarrhythmia, and in 3 (25%) multi focal spikes were found.

All of the 12 patients were treated with the combination of ACTH/dexamethasone and valproic acid. Excellent results were found in 8 (66.7%) patients, and good in 4 (33.3%). All of the EEG abnormalities disappeared after treatment.

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Introduction

Before 1958, infantile spasms were considered perhaps as the form of epilepsy most resistant to conventional antiepileptic therapy. The earliest form of drug treatment that appeared to be clearly effective in infantile spasms was corticotropin. Its ameliorative effects on the seizures and electroencephalographic abnormalities of patients with this disorder were first reported by Sorel and Dusaucy-Bauloye in 1958.

Equally encouraging was the suggestion of these investigators that the developmental status of such patients was also favorably affected by corticotropin administration. Since this original report, a substantial

number of additional evaluations of both corticotropin and the corticosteroids have been performed.

Matsuo (1983) had tried therapy with the combined use of ACTH and valproic acid which is said to increase the amount of GABA in the brain and to be effective in various types of seizures. In the group given only ACTH, 19 (58%) out of 33 cases showed the effectiveness, whereas in the group given a combination of ACTH and valproic acid, 16 (80.0%) out of 20 cases showed the effectiveness.

The aim of this study is to evaluate the effectiveness of valproic acid in combination with ACTH/dexamethasone for the treatment of infantile spasms.

Materials and Methods

This study is a prospective study on patients with infantile spasms treated at the Department of Child Health, Dr. Cipto Mangunkusumo General Hospital, Jakarta during 1985 and 1986.

The diagnosis of infantile spasms was based on the specific clinical manifestation and the specific electroencephalogram (EEG) pattern. Head computerized tomographic scanning (head CT scan) was done to look for abnormalities of the brain.

The treatment consisted of the combination of ACTH and valproic acid or dexamethasone and valproic acid. ACTH was given to the hospitalized patients, and after the patients was discharged this drug was substituted by dexamethasone. The result of treatment was stated as excellent (+ + +) when the reduction of seizure frequency was 90-100%, good (+ +) when the reduction of seizure frequency was 50-90%.

Results and Discussion

During 2 years, twelve patients with infantile spasms were treated at the Department of Child Health, Dr. Cipto Mangun-

kusumo General Hospital, Jakarta. The basic data of the 12 patients can be seen on table 1.

Table 1 : Basic data of 12 patients with infantile spasms

No.	Name	Sex	Age treatment/ Age onset (months)	Neurological deficit	Head CT scan	E.E.G.
1.	YS.	♂	14/11	Developmental retardation	-	Hypsarrhythmia
2.	MF.	♂	18/11	Developmental retardation	Cerebral atrophy	Hypsarrhythmia
3.	Al.	♀	4/3	Developmental retardation	Cerebral edema	Multi focal spikes
4.	And.	♂	12/5	Developmental retardation Microcephaly	Cerebral atrophy	Hypsarrhythmia
5.	Ans.	♀	12/5	Developmental retardation Microcephaly	Cerebral atrophy	Hypsarrhythmia
6.	HD.	♀	6/6	Developmental retardation	-	Multi focal spikes
7.	SS.	♀	7/2	Developmental retardation Microcephaly	Cerebral atrophy	Hypsarrhythmia
8.	K.	♀	8/7	-	Normal	Hypsarrhythmia
9.	DF.	♀	20/4	Developmental retardation Microcephaly Microphthalmia	Cerebral atrophy	Hypsarrhythmia
10.	GN.	♂	12/6	Cerebra palsy	Cerebral atrophy	Hypsarrhythmia
11.	P.	♀	15/5	Developmental retardation	-	Multi focal spikes
12.	U.	♂	6/4	Developmental retardation	Cerebral atrophy Calcification	Hypsarrhythmia

In table 1 we can see that the age at onset of spasms ranged from 2 - 11 months. This is the same as the findings of other authors (Trojaborg and Plum, 1960; Ladwing et al., 1962; Jeavons and Bower, 1964; Watanabe, 1973).

Table 1 shows that 11 (91.6%) of the 12 patients had suffered from neurological deficit before treatment was started. Eleven of the 12 patients suffered from developmental retardation, one patient suffered from cerebral palsy, and 5 patients suffered from microcephaly. Only 1 patient was without neurological deficit. This figure is very high. Gibbs et al. (1954), Druckman and Chao (1955), Kellaway (1959), Jeavons and Bower (1964), and Markham (1964) reported neurological abnormalities as high as 33 to 89%.

Head computerized tomographic scanning was done on 9 patients, and the result revealed cerebral atrophy on 6 patients, cerebral atrophy with calcification in 1 patient, cerebral edema on 1 patient, and normal head CT scan in 1 patient (Table 2).

It was very difficult to determine or to suspect the etiologic factors. Table 3 shows the possibility of etiologic factors in the 12 patients studied.

From table 3 we can see that 7 (58.3%) of the 12 patients belonged to the symptomatic group, and 5 (41.7%) of them to the idiopathic group. Lacy and Penry (1976) reviewing the studies of other authors reported that idiopathic patients represented 25 to 56% (mean 40%), and symptomatic patients 44 to 75% (mean 60%). So the distribution of our patients is not different from that of other authors.

Table 2 : Head CT scan of 9 patients with infantile spasms

Abnormality	No. of patient	%
Cerebral atrophy	6	66.7
Cerebral atrophy + calcification	1	11.1
Cerebral edema	1	11.1
Normal	1	11.1
Total	9	100

Table 3 : The possible etiologic factors in 12 patients with infantile spasms

Etiologic factors	No. of patients	%
Preterm + triplet pregnancy	2	16.7
Preterm + hyperbilirubinemia	1	8.3
Preterm + congenital toxoplasmosis	1	8.3
Sectio caesarian operation	2	16.7
Vacuum extraction	1	8.3
Unknown	5	41.7
Total	12	100

Table 4 shows the result of treatment. In 8 (66.7%) of the 12 patients the result was excellent, and in 4 (33.3%) it was good. The result of the treatment usually occurred 1 - 3 weeks after the treatment had been started.

Six of the 12 patients had been treated with other drugs previously. Lacy and Penry (1976) reviewing the work of many authors reported excellent response to treatment with corticotropin or corticosteroids in 18 - 70% (mean 44%), good 0 - 47% (mean 22%). Matsuo (1983) treated 33 cases of infantile spasms with ACTH alone found that only 19 (58%) cases showed the

effectiveness of the treatment, while 16 (80%) out of 20 cases that were treated with the combination of ACTH and valproic acid, showed an effectiveness of treatment.

In 9 (75%) of the 12 patients, the EEG showed hypsarrhythmia, and 3 (25%) showed multifocal spikes (Table 1). All of these abnormalities disappeared after treatment was given (Table 4). Jeavons and Bower (1974) found hypsarrhythmia in 153 (66%) out of 232 cases of infantile spasms on their first EEG. The incidence of hypsarrhythmia in our study was higher than that of Jeavons and Bower (1974).

Table 4 : The data about the treatment lag, drugs, and the result of treatment

No.	Name	Treatment lag (month)	Drugs	Seizure free	EEG
1.	Ys.	3	DM + VPA	++	Improvement
2.	MF	7	DM + VPA	+++	Improvement
3.	AI	1	DM + VPA	+++	Improvement
4.	And	7	ACTH + VPA DM + VPA	+++	Improvement
5.	Ans	7	ACTH + VPA DM + VPA	+++	Improvement
6.	HD	-	DM + VPA	++	Improvement
7.	SS	5	ACTH + VPA DM + VPA	++	Improvement
8.	K	1	ACTH + VPA DM + VPA	+++	Improvement
9.	DF	16	DM + VPA	++	Improvement
10.	GN	6	ACTH + VPA DM + VPA	+++	Improvement
11.	P	10	ACTH + VPA	+++	Improvement
12.	U	2	ACTH + VPA DM + VPA	+++	Improvement

DM = Dexamethasone
 ACTH = Adrenocorticotropin hormon
 VPA = Valproic acid

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