Outcome in West Syndrome

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ABSTRACT

Objectives: *To assess the seizure and developmental outcome in children with West syndrome with respect to treatment lag.* ***Methods:*** *Twenty-six children satisfying inclusion criteria of West syndrome i.e., infantile spasms, psychomotor retardation and abnormal EEG pattern were prospectively evaluated. Response to treatment was assessed based on seizure control, EEG, developmental assessment and parental observations.* ***Results:*** *The time lag from onset of seizures to appropriate treatment was <1 month in 11 children; 1-6 months in 8 children; and >6 months in 7 children. Children with treatment lag <1 month fared better than those who had a large treatment lag (P<0.05). Children with good seizure control also showed better developmental improvement (P< 0.05).* ***Conclusion:*** *Children with West syndrome have better seizure control and development, if the treatment is started within 1 month of onset of symptoms.*

Key words: *Infantile spasms, Prognosis, West syndrome.*

INTRODUCTION

West syndrome consists of a characteristic triad of infantile spasms, arrest of psychomotor development, and hypsrarrhythmia; although diagnosis can be made even if one of the three elements is missing[1]. The prognosis of West syndrome is poor despite treatment[2-6]. Overall 5-12% of patients have normal mental and motor development. Approximately one-half are left with motor impairment and 70-78% are mentally retarded. The prognosis is better in the idiopathic or cryptogenic cases without known etiologic factor, and those having normal development status before the onset of the spasm, and normal neuroimaging prior to therapy. Among this group of infants, 37 to 44% are neurologically and cognitively normal at long-term follow-up. Earlier studies[3,4] observed that in the subgroup of cryptogenic patients, a delay in initiation of treatment may be associated with worse outcome. In three series[4,6,7] with larger number of patients and longer follow up time, a short time between onset and treatment correlated with a more favorable outcome than a long lag in institution of ACTH. A study[8] concluded that treatment lag is possibly a prognostic factor.

METHODS

This was a prospective study carried out in the Department of Pediatric Neurology, Kanchi Kamakoti CHILDS Trust Hospital, between January 2003 and August 2004 after seeking ethical clearance from the Institutional Ethics Committee.

All children with the classical triad of infantile spasms, psychomotor retardation and EEG pattern of hypsarrhythmia or modified hypsarrhythmia were included. Children who had received ACTH (adrenocorticotrophic hormone) injection previously were excluded. Informed consent was obtained from each child's parent or guardian after explaining the protocol. Details of history and physical examination were recorded. Baseline developmental status was assessed by CMC scale[9]. All children were subjected to complete blood count, liver function test, urine screening for inborn errors of metabolism, and EEG. Neuroimaging was done wherever feasible.

All children were started on ACTH and sodium valproate (20-40 mg/kg/day). ACTH was of synthetic origin (porcine sequence) as carboxymethylcellulose complex in water. ACTH was given

at a dose of 3 IU/kg everyday IM for the first week, followed by every alternate day for 2 weeks and then twice a week for 4 weeks, a total period of about 7 weeks and then discontinued(6). Other drugs including clonazepam, clobazam, lamotrigine, and vigabatrin were added as needed for seizure control. Response to treatment was assessed based on improvement on EEG, seizure count and developmental assessment.

All children were followed up for 12-18 months (once a week for 1 month, once a month for 3 months and once in 2 months thereafter). During follow-up, children were assessed for change in seizure status, developmental assessment based on CMC scale which included 11 parameters - attachment behavior, visual attention, auditory attention, communication, behavior, motor attention, motor functions, hand functions, play behavior, sleep pattern and feeding with individual scores for each of them. Adverse effects of the drugs were also noted. Follow up EEG was done at the end of ACTH therapy (around 2 months) and one year from the onset of treatment.

Significance of difference in continuous variables like development score, seizure control, different time lag and drugs was determined using the Mann-Whitney U test. Categorical variables like seizure control, EEG at follow up, response and relapse, were assessed by Chi-square test. Significance was determined at the 5% level, except for the different domains of the CMC scale, in which significance was determined at 0.05% level, in order to account for the multiple comparisons. Statistical analysis was performed using SPSS for Windows version 11.0.

RESULTS

Thirty two children were initially enrolled; 4 discontinued the treatment and 2 were lost to follow up. Of the remaining 26 children, there were 14 boys and 12 girls. The average age of onset was 7±3 months (range 2-18 months) and mean age of presentation was 12.2±8.9 months. Twenty-four children (93.4%) presented within first year of life; most 19 (73.1%) had flexor spasms, 6 (23.1%) had mixed spasms and only 1 (3.8%) had extensor spasm. Etiology of West syndrome was identified in

16 (61.5%) children (symptomatic) and 10 (38.5%) remained cryptogenic. The etiology of infantile spasms is depicted in *Fig.* 1. Neuroimaging (CT/MRI brain) was available for 24 children (14 normal, 4 cerebral atrophy, 4 multiple tubers, 1 periventricular leucomalacia and 1 parieto-occipital infarct).

Mean cessation time of seizures (mean±S.D) was 2±2 weeks. Twenty two (84.6%) children responded, of whom 7(31.8%) relapsed; 4 (15.2%) children did not respond. EEG at follow up at the end of 1 year was normal in 11 (42.3%) and abnormal in 15 children (57.7%). The treatment lag was classified as <1 month (*n*=11; symptomatic-7, cryptogenic-4), 1-6 months (*n*=8; symptomatic-4, cryptogenic-4) and >6 months (*n*=7; symptomatic-5, cryptogenic-2). Anticonvulsants other than ACTH and sodium valproate were required in 18 (69.2%) children for seizure control.

Table I compares seizure control, developmental progression with respect to each domain, response, relapse, number of drugs and EEG characteristics with time for treatment lag. *Fig.* 2 demonstrates that children with treatment lag of <1 month fared better in developmental score, as compared to the rest, at final follow-up. Association of seizure control (percentage reduction of seizure frequency from baseline) with change in development score is depicted in *Table* II. Children who had better seizure control fared better in development.
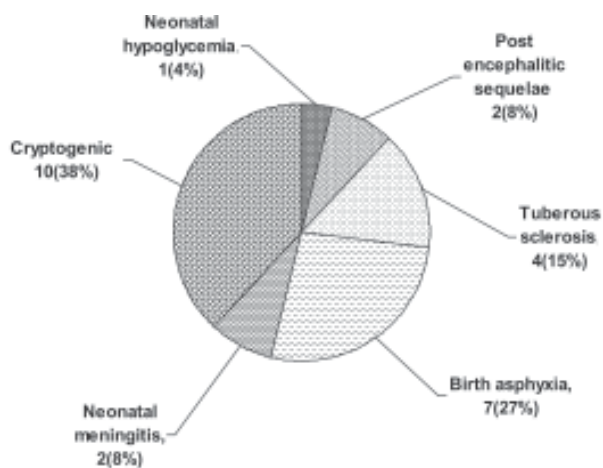

FIG. 1. *Etiology of West syndrome*[*n* (%)].

TABLE I ASSOCIATION OF TIME LAG WITH DEVELOPMENTAL SCORE, CESSATION TIME, SEIZURE CONTROL, DRUGS, RESPONSE TO THERAPY, RELAPSE AND ABNORMAL EEG AT FOLLOW-UP

Parameter	Time lag between onset and treatment			P value
	< 1 month (n=11)	1 – 6 months (n=8)	> 6 months (n=7)	
Mean ± SD Baseline developmental score	26±14	20±10	17±10	0.28*
Follow-up developmental score	72±21	50±19	24±21	0.002*
Change in developmental score	46±17	30±21	7±20	0.003*
% change in score				
Attachment behavior	40±17	27±20	13±14	0.015**
Visual attention	44±18	31±21	12±16	0.008**
Auditory attention	49±20	28±21	11±15	0.004**
Communication	49±21	31±23	14±16	0.009**
Behavior	45±16	32±22	14±18	0.011**
Motor attention	46±16	30±21	13±15	0.005**
Motor functions	41±13	30±21	12±13	0.009**
Hand functions	43±15	28±19	12±17	0.006**
Play behavior	42±11	33±21	12±14	0.005**
Sleep patterns	46±16	32±23	14±16	0.008**
Feeding	47±16	31±22	13±18	0.008**
Cessation time in weeks	2±1	3±2	2±1	0.220*
Seizure control frequencies [n %]				
0	–	1(12.5)	2 (28.6)	0.022+
50	–	–	3 (42.9)	
75	2 (18.2)	2 (25.0)	–	
100	9 (81.8)	5 (62.5)	2 (28.6)	
Drugs				
ACTH+Valproate (A+V)	6 (54.5)	1 (12.5)	1 (14.3)	0.079#
More than A+V	5 (45.5)	7 (87.5)	6 (85.7)	
Responded to therapy [N(%)]	11 (100.0)	7 (87.5)	4 (57.1)	0.047+
Relapse (among those who responded)	2 (18.2)	3 (42.9)	2 (50.0)	0.378
Abnormal EEG at follow-up	4 (36.4)	6 (75.0)	5 (71.4)	0.168+

*Mann-Whitney U test; +Chi-square test; **Mann-Whitney U test with a=0.005,*
 # Percentage reduction of seizure frequency from baseline.

Adverse events noted with ACTH during the study were–sepsis in 1 (3.4%), hypokalemia in 3 (11.4%) and 4 had weight gain above the 95th centile which returned to baseline during follow up after stopping medication. There was no mortality during the study period.

DISCUSSION

Children with West syndrome who presented within 1 month from the onset of seizures had better seizure control. Also, children who presented early and had complete seizure control showed good improvement in development. Similar findings were reported in 4 large series(2,4,6,7). EEG findings and response rate was also comparable to previous studies(11,12). In one study of 37 patients(13) normal cognitive outcome was demonstrated in 100% children with cryptogenic spasms when treatment lag was <1 month. Our results on relation of seizure control and developmental progression were also similar to

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WHAT IS ALREADY KNOWN?

• West syndrome is difficult to treat and has poor prognosis despite treatment.

WHAT THIS STUDY ADDS?

• Early diagnosis and treatment of West syndrome (starting within 1 month of onset) helps in better seizure control and improved developmental outcome.
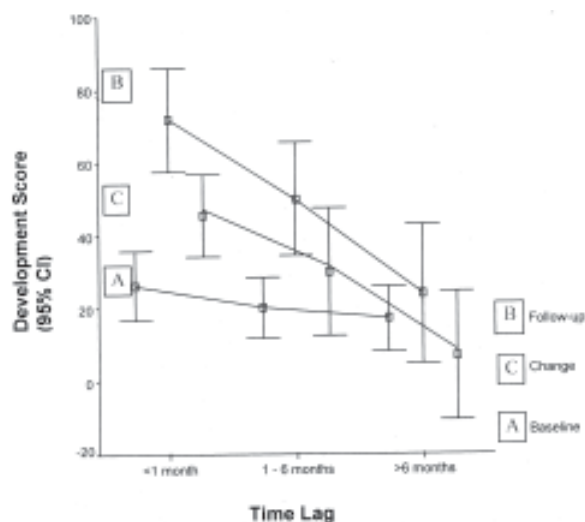

FIG. 2. *(A) Baseline development score, (B) follow up score and (C) change in score with respect to 3 groups based on treatment lag.*

TABLE II COMPARISON BETWEEN THE MAGNITUDE OF SEIZURE CONTROL WITH CHANGE IN DEVELOPMENT SCORE

Percentage reduction in seizure frequency from baseline	Change in developmental score†
0	1±2
50	14±21
75	37±5
100	37±25

† *Chi-square test, P = 0.041*

previous studies(4,6,14). Microcephaly did not affect the seizure outcome, which was also observed in another study(15).

This study emphasizes the importance of diagnosing infantile spasms early and starting appropriate treatment. Even though some would consider one month as a long time before starting

appropriate treatment for infantile spasms, these children appeared to do better than others both in terms of seizure control and developmental outcome. Interestingly in our case series, there was no significant difference in the outcome between the cryptogenic and the symptomatic group although the sample size is small and long term follow-up with detailed neuropsychological assessments is needed before one can come to definite conclusions.

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