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Original Article

Treatment Outcome of West Syndrome with Low-Dose ACTH Therapy in A Tertiary Care Center in Bangladesh

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Abstract

Background: *Corticosteroids, Adrenocorticotrophic Hormone (ACTH) and vigabatrin are considered to be the first-line drug for the treatment of West Syndrome (WS). There are little consensus regarding the definitive dose, efficacy or duration of treatment of these agents in comparison to each other. So this study aimed to assess the effectiveness of low-dose ACTH in the treatment of WS.*

Materials and methods: *A prospective observational study was conducted in the Department of Child neurology of Chattagram Maa Shishu-O-General Hospital from January 2021 to December 2022. One hundered and five children with WS aged two months to two years old enrolled in the study population. Treatment was initiated with low dose ACTH (20IU-40IU/day) and clinical and Electroencephalographic (EEG) responses were assessed at two and four weeks.*

Results: *The mean ±SD age of the patients was 11.21 ± 7.86 months and 74.28% were male. The mean ±SD age of onset of epileptic spasm and time interval between the onset of the epileptic spasm and initiating ACTH therapy was at 6.00 ± 5.01 and 5.26 ± 4.36 months, respectively. Symptomatic epileptic spasm 76(72%) was the major category of spasm. Clinical cessation of epileptic spasm was found in 55(52.38%) and 71(67.61%) patients at two and four weeks follow-up, respectively. Cessation of hypsarrythmia in EEG was noticed in 24(27%) and 66(62.8%) patients at two and four weeks, respectively. Majority (65.71%) of the patients did not have any adverse effect. Irritability, sleep disturbance, infection and hypertension was found in 21(20%), 7(6.6%), 5(4.7%) and 3(2.8%) patients. Relapse after four weeks was found in 12 (11.4%).*

Conclusion: *Low dose ACTH was effective in cessation of spasm and resolution of hypsarrhythmia in with children WS.*

Key words: ACTH; Epileptic Spasm; Hypsarrythmia; West syndrome.

INTRODUCTION

West Syndrome (WS) is a specific type of infantile epileptic encephalopathy characterized by a triad of symptoms: infantile spasms, developmental regression and a distinctive EEG pattern called hypsarrhythmia.[1,2] WS usually begins between 3 to 8 months of age and can be caused by various factors, including brain injuries, genetic mutations, and metabolic disorders.[1,2]

The treatment options for WS primarily focus on controlling the seizures and addressing the underlying causes. An early diagnosis and a shorter time to start treatment still represent the golden standards for an effective response. The gold standard therapy for WS consists of the administration of ACTH, vigabatrin and corticosteroids.[1-4]

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There needs to be more consensus regarding the definitive dose, efficacy, or duration of treatment of these agents compared to each other. Some studies suggest that low doses of ACTH can be as effective as high doses for short-term seizure control. However, the evidence needs to be more conclusive, and some researchers argue that high doses may be more effective in some instances.[5-7] Therefore, this study was designed to provide an essential perspective on treating WS with low-dose ACTH as a first-line treatment in a developing country like Bangladesh.

MATERIALS AND METHODS

A prospective observational study was conducted in the Department of Child Neurology of Chattagram Maa-Shishu-O-General Hospital from January 2021 to December 2022. The study protocol was approved by the Institutional Review Board. Before enrollment, written informed consent was obtained from the parents or caregivers of the patients.

Children with WS, aged between 3 -24 months, who did not receive prior hormonal therapy were included. The diagnosis was confirmed by taking a detailed history, thorough neurological examination, and EEG. Children with the suspected neurometabolic disorder, children with a neurocutaneous syndrome like tuberous sclerosis and children who did not have a response after two weeks of low-dose ACTH therapy and needed to switch to other drugs were excluded.

Low-dose ACTH (20 IU-40 IU/day) injection started and patients were followed up at two weeks and four weeks of treatment. For patients who had undergone clinical and Electrographical remission of spasm, doses of ACTH were tapered over two weeks. Patients on only clinical remission similar doses of ACTH continued for another two weeks and tapered over the following weeks. Those who did not have clinical and electrographical remission at two weeks of treatment receiving ACTH with a dose range of 20 IU – 30 IU /day were switched to 40 IU /day and continued for two weeks, followed by tapering. If the patient did not respond to the 40 IU/day dose within two weeks of treatment, another antiepileptic drug was added and excluded from the study. Clinical and electrographic, adverse events, and relapse rates after four weeks were recorded in a case record form.

Statistical analysis was done using SPSS version 23.0. Data were expressed as mean and standard deviation or frequency and percent. Outcomes were compared between groups using the Chi-square test. $p<0.05$ was considered as statistical significance.

RESULTS

During the study period, 105 children with WS were included. The mean presentation duration was 11.2 ± 7.8 months, and 30.5% of the patients were • 6 months. The mean age of presentation was 6.0±5.0 months, and the majority (91.4%) had the onset age of • 12 months of age. Of 105 patients, 74.28% were male, with a male-to-female ratio 3:1. Time interval between the onset of spasm and starting ACTH was 5.2±4.3 months. Other clinical and radiological characteristics are shown in Table I.

Table I Baseline clinical and radiological chracteristics of the patietns with WS (n=105)

Chracteristics	Frequency	Percent
Risk factors		
History of consanguinity	3	2.9
Family history of seizure	6	5.7
History of perinatal asphyxia	67	63.8
History of prematurity	6	5.7
Clinical type		
Cryptogenic epileptic spasm	29	28
Symptomatic epileptic spasm	76	72
CT/MRI Findings		
Normal	25	23.8
Leukomalacia	42	40.0
Atrophy	19	18.1
Perinatal Stroke	14	13.3
MCDS	05	4.8

At two and four weeks, respectively, 52.3% and 67.6% of the patients had complete cessation of spasms. At two weeks, 10 (9.5%) patients were clinically non-responders. Cessation of hypsarrhythmia was found in 23.6% of the patients with complete response at two weeks and in 51.4% of the patients at four weeks (Table II).

Table II Clinical response and Electrographical response in patients with WS at 2 and 4 weeks (n=105)

Outcome paramters	Two weeks	Four weeks
Clinical Response		
Complete Cessation of Spasm	55(52.3%)	71(67.6%)
<50% Reduction	14(13.3%)	15(14.2%)
>50% Reduction	26(24.7%)	19(18.0%)
Non Responder	10(9.5%)	0(0.0%)
Cesation of hypsarrhythmia		
In complete response	21(23.6%)	54(51.4%)
In <50% reduction group	0(0.0%)	10(9.5%)
In >50% reduction group	3(3.4%)	2(1.9%)
No response	0(0%)	----

Data were expressed as frequency (%).

Table III shows that complete clinical response rates were similar between symptomatic and cryptogenic WS (p>0.01).

Table III Relation between clinical response and category of spasm at two and four weeks

Category	Clnical response (Reduction of spasm)				
	Complete	<50%	>50%	No	p Value*
Two weeks	(n= 54)	(n= 16)	(n= 22)	(n= 7)	
Symptomatic	35(33.3%)	12(11.4%)	22(21.0%)	7(6.7%)	0.186
Cryptogenic	19(18.1%)	4(3.8%)	6(5.7%)	0(0%)	
Four weeks	(n= 71)	(n=15)	(n=19)	(n=0)	
Symptomatic	47(44.8%)	13(12.4%)	16(15.2%)		0.121
Cryptogenic	24(22.9%)	2(1.9%)	3(2.9%)		

Data were expressed as frequency (%). *Chi-square test.

A complete clinical response was observed in 24 (22.9%), 14 (13.3%) and 16 (15.2%) of the patients who received 20IU, 30IU and 40IU ACTH injections. The association between the dose of ACTH injection and clinical response was not statistically significant (p>0.05). Similarly, relapse rates after four weeks were similar in patients with different doses of ACTH.

Table IV Relation of doses of ACTH with clinical response and relapse

Characteristics	Doses of ACTH			p Value*
	20IU	30IU	40IU	
Clinical responses				
Complete Response	24(22.9%)	14(13.3%)	16(15.2%)	0.371
<50% Reduction	8(7.6%)	6(5.7%)	2(1.9%)	
>50% Reduction	16(15.2%)	9(8.6%)	3(2.9%)	
No Response	5(4.8%)	1(1%)	1(1%)	
Relapse after 4 weeks				
Yes	5(4.8%)	2(1.9%)	5(4.8%)	0.161
No	48(45.7%)	28(26.7%)	17(16.2%)	

Data were expressed as frequency (%). *Chi-square test.

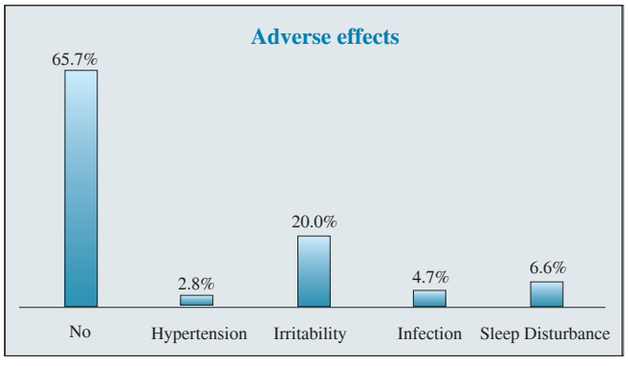

Figure 1 Adverse effect during ACTH therapy

Of 105 children treated with ACTH, 69 (65.7%) had no adverse effects. The most frequent adverse effect was irritability (20%), followed by sleep disturbance (6.6%), infection (4.7%), and hypertension (2.8%) (Figure 1).

DISCUSSION

The present study was conducted to determine whether low-dose ACTH therapy has any role in the treatment of WS, and it was found that low-dose ACTH was adequate for achieving spasm control. Male preponderance was observed in this study (74.28%), which agreed with other studies.[8,9] The mean age of onset of spasm was six months, and the mean time interval of starting treatment from the onset was 5.2 months. This delay could result from general pediatricians' unawareness of this condition and subsequent delayed referral. The symptomatic category of WS was the predominant form in this study, and these findings are consistent with other related studies in developing countries.[8,9] Hypoxic ischemic encephalopathy is one of the most typical causes of symptomatic WS in this study, which suggests inadequate or sub-optimal perinatal services in Bangladesh.

Clinical and Electrographical response was found in 52.38% and 22.8% cases respectively, at two weeks. At four weeks, it was found to be 67.61% and 62.8%. Other studies also showed similar results.[10,11] A meta-analysis compared the efficacies of low-dosage and high-dosage ACTH and did not observe any difference between the two dosages.[12] A recent cohort study also concluded that high dosages of ACTH are not more effective than low-moderate dosages in the short term for treating infantile spasms.[13]

Regarding the adverse effect profile, more than two-thirds of the patients (69%) had no adverse effect in this study. The most frequent adverse effect was irritability (20%) followed by sleep disturbance (6.6%) infection (4.7%) and hypertension (2.8%). Pronounced adverse effects of ACTH were infections and arterial hypertension observed in previous studies.[13,14]

LIMITATION

The study's limitations were that it was an observational study and was not randomized or blinded. It was conducted in a single hospital, had a limited sample and had a short follow-up period.

CONCLUSION

The treatment of WS is a major challenge due to the severity of the disease for the majority of infants. ACTH remains the treatment of choice, especially in cases with an unknown etiology. The present study showed that low dosages of ACTH are effective. Low-dose ACTH could be an option for the treatment of WS. However, considering the limitations of the present study, a multicentre prospective randomized study is needed to validate the study findings.

DISCLOSURE

All the authors declared no competing interest.

REFERENCES

1. Wheless JW, Gibson PA, Rosbeck KL, Hardin M, O'Dell C, Whittemore V, et al. Infantile spasms (West syndrome): Update and resources for pediatricians and providers to share with parents. BMC Pediatrics. 2012;12:1-9.
2. Pavone P, Polizzi A, Marino SD, Corsello G, Falsaperla R, Marino S, Ruggieri M. West syndrome: A comprehensive review. Neurological Sciences. 2020;41:3547-3562.
3. O'Callaghan FJK, Edwards SW, Alber FD, Hancock E, Johnson AL, Kennedy CR, et al. Safety and effectiveness of hormonal treatment versus hormonal treatment with vigabatrin for infantile spasms (ICISS): A randomised, multicentre, open-label trial. Lancet Neurol.2017;16:33–42.
4. Capal JK, Bernardino-Cuesta B, Horn PS, Murray D, Byars AW, Bing NM, et al. Influence of seizures on early development in tuberous sclerosis complex. Epilepsy Behav.2017;70:245–252.
5. Sahu JK, Vaddi VK, Negi S. Review of West Syndrome: Concerns on Optimum Dose of Adrenocorticotrophic Hormone. Clinical drug investigation. 2018;38:563-564.
6. D'Alonzo R, Rigante D, Mencaroni E, Esposito S. West syndrome: a review and guide for paediatricians. Clinical drug investigation. 2018;38:113-124.
7. Riikonen R, Lähdetie J, Kokki H. ACTH Treatment of Infantile Spasms: Low-Moderate-Versus High-Dose, Natural Versus Synthetic ACTH: A Retrospective Cohort Study. Pediatric Neurology. 2020;111:46-50.
8. Singhi P, Ray M. Profile of West syndrome in North Indian children. Brain and Development. 2005;27:135–140.
9. Kalra V, Gulati S, Pandey RM, Menon S. West syndrome and other infantile epileptic encephalopathies-Indian hospital experience. Brain and Development. 2001;23:593–602.
10. Hrachovy RA, Frost Jr JD, Kellaway P, Zion T. A controlled study of prednisone therapy in infantile spasms. Epilepsia. 1979 ; 20:403–407.
11. Baram TZ, Mitchell WG, Tournay A, Snead OC, Hanson RA, Horton EJ. High-dose corticotropin (ACTH) versus prednisone for infantile spasms: A prospective, randomized, blinded study. Pediatrics. 1996; 97:375–379.
12. Zeng L, Luo R, Zhang L. Efficacy of high-dose ACTH versus low-dose ACTH in infantile spasms: A meta-analysis with direct and indirect comparison of randomized trials. J Pediatr Neurol. 2011; 9: 141-149.
13. Riikonen R, Lähdetie J, Kokki H. ACTH Treatment of Infantile Spasms: Low-Moderate-Versus High-Dose, Natural Versus Synthetic ACTH : A Retrospective Cohort Study. Pediatric Neurology. 2020;111:46-50.
14. Ibrahim S, Gulab S, Ishaque S, Saleem T. Clinical profile and treatment of infantile spasms using vigabatrin and ACTH : A developing country perspective. BMC pediatrics. 2010;10:1-9.