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Cumulative Response of High Dose Steroids and Sequentially Added Vigabatrin in Patients of Infantile west Syndrome in A Resource Constrained Setting.

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Abstract
Objectives: - *To assess the cumulative response of very high dose steroids and sequentially added Vigabatrin in patients of infantile West Syndrome.*
Methods: - *This was an observational study conducted at a tertiary care hospital from August-2014 to August-2015. Children aged 2-23 months presenting with infantile spasms with hypsarrhythmia on EEG were enrolled. The study participants were started on high dose Prednisolone (8 mg/kg/day maximum 60mg/day). Patients who did not respond to this treatment were started on Vigabatrin (50-150mg/kg/day) in sequentially increasing doses and prednisolone treatment was tapered off. The primary outcome measure was cessation of spasms and clearance of hypsarrhythmia on EEG after initiating Vigabatrin in a cohort of non-responders to steroid therapy. The study was approved by the ethical committee of the college.*
Results: - *The response of high dose steroid alone was nearly 55.55% (20/36) after 2 weeks therapy which was significantly higher as compared with studies done earlier using similar or lower dose regimes. Out of the non-responders to very high dose steroid therapy 68.75% (11/16) responded to sequentially added Vigabatrin therapy. Thus at the end of the study cumulative response was 86.11% (31/36) with this combination regime.*
Conclusion: - *Using a higher dose steroid therapy there was an increase in response rate. But cumulative response of high dose steroid and sequentially added Vigabatrin was as good as or better than that reported with combination of both therapies in earlier studies.*
Keywords: - *hypsarrhythmia, responder, cumulative, non-responder, sequential.*

I. Introduction

West syndrome is a rare but age specific epileptic encephalopathy. Usually provoked by many genetic/structural/metabolic or cryptogenic etiologies. It consists of infantile spasms accompanied with characteristic EEG appearance hypsarrhythmia and its variants plus frequent neurodevelopmental delay or regression. Unsuccessful treatment as well as delay in definitive treatment results in poor neurodevelopmental outcome [5]. Because of the poor response rate, a wide variety of drugs are used to treat Infantile Spasms the world over. However hormonal therapies such as intramuscular adrenocorticotropic hormone (ACTH) [1, 2, 7] oral steroid (Prednisolone) [4, 6] and Vigabatrin [10, 11, 12] are commonly used form. There is no consensus on the role of oral steroid as the first line treatment of infantile spasms [8]. The limitations like high cost, pain associated with intramuscular injections and non availability of skilled personnel to administer injections to young children precludes the use of ACTH in children from resource limited settings. In the present study we assessed the efficacy and safety of cumulative therapy of high dose steroid and Vigabatrin patients of infantile West Syndrome.

II. Methods

Many children with poorly controlled seizures are referred to the pediatric OPD of Subharti Medical College Meerut; U.P. Patients identified as West syndrome without history of prior hormonal therapy were recruited for the study. This observational study was conducted between August 2014 and August 2015. The ethical clearance was obtained from institutional ethical committee. A written informed consent was obtained from the parents.

Study Participants

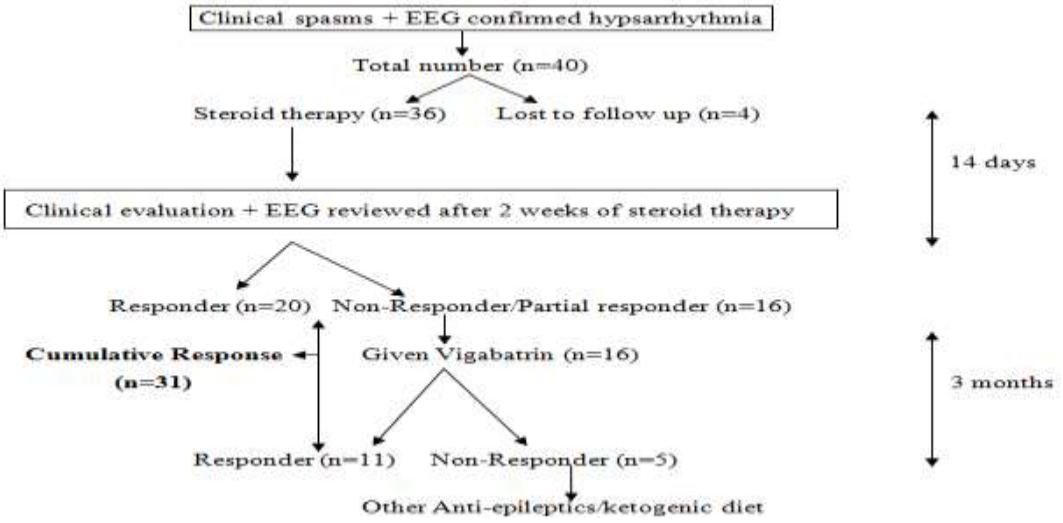
Children aged 2 months to 23 months presenting with clinical spasms with EEG evidence of hypsarrhythmia or its variants (so-called modified and atypical variants)[1] without history of prior hormonal treatment were enrolled. Children with active/chronic systemic infections or severe acute malnutrition as defined by WHO criteria (presence of pedal edema, weight for height <-3SD (WHO child growth charts), visible wasting, mid upper arm circumference <11.5cm) were excluded from the study.

Treatment Procedure

Each child underwent detailed history and examinations. The age at onset, birth history, family history, and the development status were noted. The results of investigations such as neuroimaging, EEG and metabolic testing were documented. MRI scan of brain was performed in all the patients along with EEG as initial investigation. Children with clinical suspicion of a metabolic disorder (a history of parental consanguinity, prior affected siblings, unexplained vomiting, intermittent worsening of symptoms, recurrent episodes of lethargy, altered sensorium, or ataxia or hepato-splenomegaly on examination) or no obvious etiology on clinical evaluation and neuroimaging underwent screening tests for inherited metabolic disorders. These included arterial blood gas, blood lactate, blood ammonia, urinary ketones, and blood tandem mass spectrometry.

Based on the etiology and examination, West syndrome was classified as known etiology or symptomatic and no identified etiology or cryptogenic. On the day of diagnostic confirmation, treatment with oral prednisolone was initiated at 8 mg/kg/day with a maximum of 60 mg/day. After 2 weeks, all patients with clinical response to prednisolone based on parental report and clinical examination underwent repeat EEG to confirm clearance of hypsarrhythmia. Patients who did not respond to high dose steroid treatment were started on Vigabatrin which was increased sequentially from (50-150 mg/kg/day). Patients who failed to achieve response to Vigabatrin were given other antiepileptic/ketogenic diet as illustrated in Figure 1.

Figure 1:- Flow Chart of the patients in study protocol. Response requires EEG confirmation of freedom from hypsarrhythmia and cessation of clinical spasms.



III. Results

The study cohorts of 40 patients with infantile spasms were evaluated at Subharti medical college during the study period. Of these only 36 completed the study protocol.

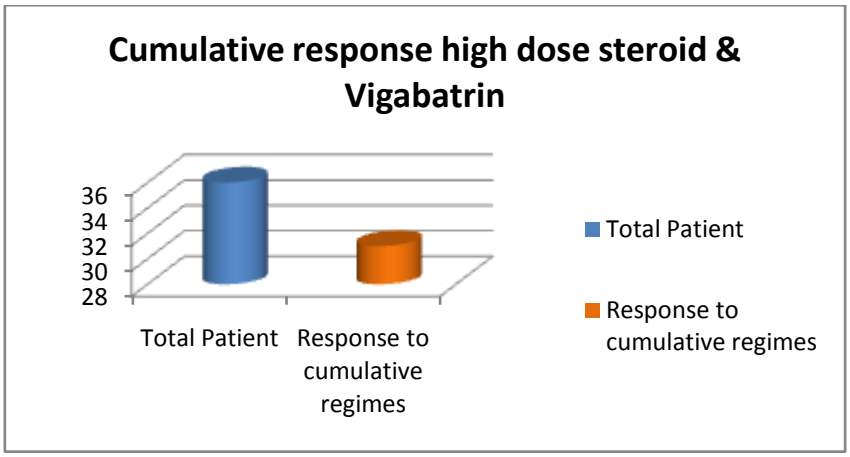
Characteristics of the study population:-

Demographic &clinical characteristics		
a)	Total Patients (n)	36
b)	Sex,	
	i. male, (n)%	28(77.7)
	ii. female, (n)%	8(22.3)
c)	Age of onset of spasms, months, median(IQR)*	7(4-22)
d)	Age at entry to protocol, months, median(IQR)	10(4-23)
e)	Duration of follow up, months, median(IQR)	8(1-22)
f)	Etiological classification& response	
	i. Structural West Syndrome	30(83.3)
	ii. Cryptogenic West Syndrome	6(16.6)
g)	Improvement in development assessment, (n)%	29(80.55)
h)	Response of high dose steroid, (n)%	20(55.55)
i)	Response of Vigabatrin in non-responder, (n)%	11(73.33)
j)	**Cumulative Response of steroid & Vigabatrin, (n)%**	**31(86.11)**
	*IQR(inter quartile range)	

Thirty six patients received steroid therapy for infantile spasms according to the protocol outlined earlier. Twenty20/36(55.55%) patients responded completely to prednisolone after 2 weeks, 16 patients who did not respond to hormonal therapy were started on Vigabatrin and steroid treatment was tapered off. This resulted in 11/15(73.33%) reduction in infantile spasms.

Figure 3:- Cumulative response of high dose steroid &Vigabatrin regimes.

Patient	Response n (%)
36	31(86.11)



IV. Discussion

In this study cumulative response of high dose steroid followed by sequentially added Vigabatrin was assessed using both EEG clearance of hypsarrhythmia and clinical cessation of spasms. Response of very high dose steroid was nearly 20/36 (55.55%) which is significantly higher than in studies done before [4].

The response of sequentially added Vigabatrin was 11/16 (68.75%). The response of Vigabatrin therapy was significantly higher than the 18/61(30%) response shown by Jones k et al [11] and the101/180 (56.9%) response shown by Djuric M et al [10] in controlling spasms. The overall response of both therapy was 31/36 (86.11%) which is better than that reported with a combination of Vigabatrin along with steroid in a study conducted by The International Collaborative Infantile Spasms Study ICISS[12] 133/185 (71.9%). Combined use of Vigabatrin and steroid was not feasible in our resource limited study as Vigabatrin was expensive as compared to steroid.

Because of the low frequency of this clinical entity historical comparators were considered. There could be demographic and etiological variations amongst different study population reported in literature. A large-scale, multicenter, trial is required to conclusively determine whether the response rate of Vigabatrin as add on medication after failure to hormonal therapy with good control of spasms and acceptable side effects.

References

[1]. Hrachovy RA, Frost Jr. JD, Kellaway P. Hypsarrhythmia variations on The theme. Epilepsia.1984; 25:317–325.
[2]. Baram TZ, Mitchell WG, TournayA et al. High-dose corticotrophin (ACTH) versus prednisone for infantile spasms: a prospective, randomized, blinded study. Pediatrics 1996;97:375-379.
[3]. Chellamuthu P, Sharma S, Jain P, Kaushik JS, and Seth A, Aneja S. High dose (4mg/kg /day) versus usual dose (2mg/kg /day) oral prednisolone for treatment of infantile spasms: An open- label, randomized controlled trial. Epilepsy Research. 2014; 108:1378-84.
[4]. Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, Newton RW et al. The United Kingdom Infantile Spasms Study comparing vigabatrin with prednisolone or tetracosactide at 14 days: a multicentre, randomised controlledtrial.Lancet. 2004;364:1773–1778.
[5]. O'Callaghan FJ, Lux AL, Darke K, et al. The effect of lead time to treatment and of age of onset on developmental outcome at 4 years in infantile spasms: evidence from the United Kingdom Infantile Spasms Study. Epilepsia 2011;52:1359-64.
[6]. Kossoff EH, Hartman AL, Rubenstein JE, Vining EPG. High-dose oral prednisolone for infantile spasms: an effective and less expensive alternative to ACTH. Epilepsy Behav. 2009;14:674–676.
[7]. Snead OC, Benton JW, Hosey LC, Swann JW, Spink D, Martin D et al. Treatment of infantile spasms with high-dose ACTH: efficacy and plasma levels of ACTH and cortisol. Neurology. 1989;39:1027–1031.
[8]. Pellock JM, Hrachovy R, Shinnar S, Baram TZ, Bettis D, Dlugos DJ et al. Infantile spasms: a U.S. consensusreport.Epilepsia. 2010;51:2175–2189.
[9]. Go CY, Mackay MT,Weiss SK, StephensD, Adams-Webber T, Ashwal S et al.Evidence-based guideline update: medical treatment of infantile spasms: report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2012;78:1974–1980.
[10]. Djuric M, Kravljanac R, Tadic B, Mrljes-Popovic N, Appleton REet al. Long-term outcome in children with infantile spasms treated with vigabatrin: a cohort of 180 patients. Epilepsia. 2014;55:1918-25.
[11]. Jones K, Boyd A, Ochi A, Go C, Puka K, Snead OC et al. Vigabatrin as First-Line Treatment for Infantile Spasms Not Related to Tuberous Sclerosis Complex. Pediatr Neurol. 2015;53:141-5.
[12]. O'Callaghan FJ, 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 randomized, multicenter, open-label trial. The Lancet Neurology.2017; 16:33-42