Original Article

LOCAL EXPERIENCE OF MANAGEMENT OF INFANTILE SPASMS AND ITS TREATMENT: A RETROSPECTIVE STUDY OF TEN CASES

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ABSTRACT

Objective: To evaluate and assess the efficacy of ACTH and Vigabatrin in Symptomatic variety of Infantile Spasm in Pakistani patients to document local experience.

Methodology: This is a retrospective study carried out at Neuro Diagnostic Centre, Hamdard University Hospital (Taj Medical Complex), Karachi, from January 2006 to December 2008. Patients registered with Infantile Spasm to the Neuro Diagnostic Centre, Karachi, Pakistan between January 2006 to December 2008 were included in the study. The total number of patients was ten; six male and four female. Age ranged from four months to three and a half years. All patients demonstrated electroencephalographic evidence of hypsarrhythmia and a variety of jerks representing Infantile Spasm.

Results: ACTH was administered in nine out of ten patients but always in combination. Six out of ten patients had Vigabatrin used in tandem with ACTH initially and later Vigabatrin alone (was continued in five of these patients). In one patient Vigabatrin was continued with ACTH and Valproate. ACTH was combined with Valproate in three of the patients while Valproate alone was tried in one patient. All patients on ACTH in whatever combination responded adequately and some of them dramatically becoming seizure-free. The patient on Valproate alone did not respond early and took almost 20 days from start of treatment to become seizure-free.

Conclusion: ACTH was highly effective especially in patients with symptomatic form of Infantile Spasm. Although prednisolone (oral) has not been tried in this study but in affording patients ACTH should remain the first-line treatment for Infantile Spasm especially the symptomatic variety.

KEY WORDS: Infantile Spasms, Hypsarrhythmia, Epilepsy, Fits, Jerks, Pakistan.

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INTRODUCTION

Infantile spasm is a rare seizure disorder of infancy and early childhood. The onset is predominantly in the first six months of life. Characteristic features of infantile spam also known as West syndrome, include myoclonic seizures, hypsarrhythmia (abnormal, chaotic electroencephalogram), and mental retardation. The spasms are sudden, brief contractions of one or more muscle groups, and may be followed by a longer (less than 10 seconds) tonic phase.

Most often the spasms occur in clusters during which the intensity or the frequency of the spasms may increase progressively to a peak, decline, or cease. The clusters tend to occur soon after arousal from sleep. They are not a feature of falling asleep.

The spasms usually involve the muscles of the neck, trunk, and extremities. The intensity of the contraction and the number of muscle groups involved varies in different attacks and from infant to infant. Neurological abnormalities other than seizures and retardation—such as cerebral atrophy, congenital abnormalities and hydrocephalus—are commonly reported among patients with infantile spasm.

Some patients may be treated successfully with either ACTH (adrenocorticotrophic hormone) or prednisone. The effectiveness of benzodiazepines or of antiepileptic drugs is doubtful. Infantile spasm is one of the most devastating seizure disorders affecting infants. Spontaneous cessation of spasms occurs in most patients with increasing age and in some cases within the first month after onset. Overall, however, the prognosis for patients with infantile spasm is generally poor because a large number of these individuals have neurological impairment prior to the onset of spasms.

To-date many diverse treatment options have been tried in infantile spasms and very few have shown efficacy not only in controlling the often unremitting seizures but also improving on the mental backwardness of these unfortunate children. Since the combination of ACTH in tandem with the anti-epileptic drugs improved most of the children especially those with symptomatic infantile spasm; these observations need to be highlighted. The purpose of this study was to show the efficacy of certain therapies which were found to be more effective in this rare but debilitating infantile disorder. In spite of multiple studies, research and changing treatment options, there are still a lot to be desired in some patients with infantile spasms where diagnosis remains ambiguous.[1]

Although other options like ketogenic diet have been advocated in resistant forms of infantile spasms, incidentally the highly effective combination especially of ACTH and Vigabatrin was instrumental in treating these children without its help.[2]

ACTH is an established treatment for infantile spasm. The objective of this study was to evaluate and assess the efficacy of ACTH and Vigabatrin in Symptomatic variety of Infantile Spasm to document experience in local population.

METHODOLOGY

Patients registered with Infantile Spasm / West Syndrome reporting to the Neuro Diagnostic Centre, Karachi, Pakistan between January 2006 to December 2008 were included in the study. The total number of patients were ten; six males and four females. Age ranged from four months to three and a half years.

The diagnostic criteria used to confirm the presence of infantile spasms was the typical occurrence of infantile jerks with an onset between four to eight months of age, EEG pattern of hypsarrhythmia and mental retardation. One of the patients did not have mental retardation, he was still labelled as infantile spasm since it is known that even in the absence of mental retardation, the patient can still be suffering from this disorder. The term infantile spasm was used to describe the seizure type epilepsy syndrome or both.

RESULTS

Moderate to severe mental retardation was evident in eight patients while one patient had mild mental decline. One patient in the study showed normal mental development with timely attainment of milestones.

Details regarding urinary chromatography, metabolic profile of patients, CSF studies and treatment options are given in Table I, II and III respectively. Urinary chromatography were found to be negative for amino-acid ureas in all the patients. About 80% of the patients demonstrated some degree of mental retardation. Other metabolic parameters like serum calcium, blood glucose, serum potassium, serum sodium and serum magnesium levels were also ascertained to exclude any metabolic derangement. The calcium profile demonstrated some degree of hypocalcemia in three patients, while the

Table-I: Types, Etiology & Pathology

Patient	*Types of Seizures*	*Pathology*	*Etiology*
1	Flexors, Tonic (arching), Runs	Dandy-Walker	Symptomatic
2	Jack Knife / Flexors	Hypoxic Insult	Symptomatic
3	Flexors	Hypoxic Insult	Symptomatic
4	Flexors, Extensors (arching)	Hypoxic Insult	Symptomatic
5	Flexors, Extensors (arching)	Normal Imaging	Cryptogenic
6	Flexors	Hypoxic Insult	Symptomatic
7	Runs of Spasms and Singles	Hypoxic Insult	Symptomatic
8	Flexors, Extensors	Tuberous Sclerosis	Symptomatic
9	Flexors + GTCs (Nocturnal)	Hypoxic Insult	Symptomatic
10	Focal (arm), Jack-Knife	Not Identified	Symptomatic

blood glucose levels were normal in eight patients, serum potassium was normal in all patients, the sodium levels were low only in two patients and magnesium levels were found normal in all patients. Therefore involvement of metabolic derangement alone as an etiological factor in infantile spasm is highly doubtful. Incidentally, CSF Cytology and bio-chemistry, which was possible in five out of ten were found to be normal.

ACTH and Vigabatrin combination played very significant role in patients who showed the maximum improvement. About 60% of the children had this combination and faired best while 30% were without vigabatrin and did not fair as well. However, the substantial cost of ACTH over other drugs prevented a long term continuation of this drug. Even after the withdrawal most patients continued to recuperate.

Jerks were noticeable in practically every patient although the variety was different. From single jerks to succession of jerks, jack knife spasms, extensors flexors spasms; practically every variety of jerks were all seen in the patients (Table-I).

During the clinical assessment of these affected children, pupillary reflexes, ocular fundi and the possible visual evaluation were done. Various pupillary abnormalities were seen in majority of the patients (Table-II).

Patients who were treated with ACTH responded adequately, some even dramatically. All patients had become seizure-free starting from 1st week of treatment. Treatment was continued with ACTH for the first six weeks and later the patients were continued on Vigabatrin either alone or in combination with Valproate (Table-III). Recurrence of jerks was seen in one patient and nine of the patients had favourable outcome with improvement in mental milestones. Children three to six months post onset of treatment had showed improved awareness and attainment of motor milestones even in the symptomatic group of infants. Since only one patient was exposed to Valproate alone, it was difficult to make any comments on the role of Valproate monotherapy in this study.

Changes in electroencephalogram of children treated with ACTH and other adjuncts showed definite improvement in the intensity of the hysarrhythmic activity. The classical hypsarrhythmia in many of the patients at onset transformed into more mild abnormality with spikes, polyspikes and slow waves.

Table-II: Clinical signs

Patient	*Pupillary Reflexes*	*Ocular Fundi*	*Perception of Light*
1	Small, Normal	Disc Pale	Response to threat
2	Small, Normal	Normal Disc	No response to threat
3	Small, Sluggish	Normal Disc	Blinks to threat
4	Small & Sluggish	Disc Pale	Does not blink on threat
5	Equal, Dilated, Reactive	Normal Disc	Can see whole objects in hand
6	Anisochorea, left pupil dilated, sluggish, right small; Startle reflex positive	Pale Disc	Poor, Blink good
7	Small & Sluggish	Pale, Disc & Retina	No blinking to threat
8	Large, Sluggish, Equal	Normal Disc	Normal
9	Small, Circular, Equal	Normal Disc	Normal
10	Sluggish	Normal Disc	Blinks to threat

Table-III: Treatment options and response

Patient	*Treatment*	*Response to treatment*
1	ACTH, Vigabatrin / Vigabatrin Alone	Fit-free after first week
2	ACTH, Valproate	Fit-free after second week
3	ACTH, Vigabatrin / Vigabatrin Alone	Fit-free after first week
4	Valproate	Fit-free after twenty days
5	Vigabatrin, Valproaic Acid, ACTH	Fit-free on second day
6	ACTH, Vigabatrin / Vigabatrin Alone	Fit-free after first week
7	ACTH, Vigabatrin / Vigabatrin Alone	Fit-free after first week, relapse sixth week
8	ACTH, Vigabatrin / Vigabatrin Alone	Fit-free after two weeks and improvement in mentation and awareness in six weeks
9	ACTH, Valproate	Fit-free soon after start of treatment
10	ACTH, Epival	Fit-free after second week

DISCUSSION

This study and similar other studies have inspired the use of ACTH in infantile spasm.[3] A local study however used both Prednisolone and ACTH in two groups of patients; they did not find much difference in response in the two.[4] Another local study found ACTH to be the most effective treatment option in patients with infantile spasm.[5] However, ACTH was found to be less effective than Vigabatrin in another study.[6]

This study also shows that CSF abnormality is not an important factor. Amino-Acid Ureas did not show any evidence of involvement. Hypomagnesemia which is now gaining more momentum in metabolic derangement of epileptic syndromes may not be an important factor in infantile spasm and its aetiology. However it can be concluded that ACTH has been by far the most effective treatment in infantile spasms[7,8] and its combination with Vigabatrin makes it even more beneficial.

The above treatment also improves the mental impairment in patients with symptomatic variety of salaam attacks especially the ones with hypoxic insult only. The study also shows evidence that amongst the varieties of infantile spasms the symptomatic variety dominates the picture.[9] Since ACTH is an expensive treatment especially in under developed country like Pakistan, it is suggested that this treatment option should be addressed so that NGOs and other such agencies help supply this wonderful drug to the suffering population of children with salaam attacks.

Limitation of the Study: The number of patients enrolled in this study is small but since infantile spasms or salaam attacks is a rare disease; we could enlist just ten patients in three years. Further studies with a large sample size are needed to confirm our observations. Similar other studies have also highlighted the rare occurrence of infantile spasms.[10]

CONCLUSION

ACTH was found to be the most effective treatment in this study. However, in view of the cost of ACTH, it is worth trying oral prednisolone either alone or as a follow-up after termination of ACTH therapy, especially in view of some inspiring results from international studies.

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