International Journal of Scientific Research and Engineering Development-– Volume 3 Issue 3, May – June 2020

Available at www.ijsred.com

RESEARCH ARTICLE OPEN ACCESS

Lennox- Gastaut syndrome (LGS) cognitive impairment and seizure onset in children and adolescent

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Abstract:

Lennox- Gastaut syndrome (LGS) or Late Lennox- Gastaut syndrome (LLGS) is a developmental encephalopathy, which is a severe form of epileptic disorder with higher mortality and morbidity rate. It is characterized by electroencephalographic feature abnormalities, multiple seizure types and intellectual disability. However associated with behavioral problems and intellectual disability are characteristic of LGS, they are not found as a part of diagnosis as it is not seen in the early stages of the seizure onset. Children with Lennox- Gastaut syndrome (LGS) have seizures of different types which originate from different part of the brain. Lennox- Gastaut syndrome (LGS) is treated with a combination of pharmacological drugs and supportive therapies which helps the patient for reasonable prognosis. The Lennox- Gastaut syndrome (LGS) treatments and managements decisions are challenging, because of the multiple seizure types and comorbidities conditions with an early onset in children. Patients with Lennox-Gastaut syndrome LGS are recommended to undergo review by a neurologist on annual basis which includes required assessments for diagnosis and treatment plans. The Clinicians should be aware of the possibility of treatable etiologies and also possibility that a patient's diagnosis might vary, depending upon the seizure types and electroencephalographic features that evolves over time in Lennox- Gastaut syndrome (LGS). Although till date the available treatments do not likely lead to seizure remission in most cases of LGS. Many Anti-epileptic Drugs (AED) are available as for control of the various types of seizures which are present in Lennox- Gastaut syndrome (LGS).Many physicians although focus on secondary treatments in LGS which to an extent helps the patient with improving learning, behavioral ,cognitive management to live a quality life.

Keywords **—Lennox- Gastaut syndrome (LGS), intellectual disability, supportive therapies,behavioral and cognitive management.**

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I. INTRODUCTION

Lennox–Gastaut syndrome is a severe epileptic disorder and developmental encephalopathy, with onset between the ages of 3 and 8 years (most commonly 2–5 years). The syndrome persists throughout adolescence into adulthood, or also have late onset (10).Many cases are due to brain abnormality which was caused due to brain damage during birth or other birth injuries, encephalitis, congenital infection, brain malformation and hereditary metabolic diseases. Although accurate diagnosis of LGS is nearly difficult due to non-pathognomonic EEG features and also the type of seizures evolve over along with the children. Electroencephalogram (EEG) is used as one of the diagnosis feature in Lennox- Gastaut syndrome (LGS).Early diagnosis of the Lennox- Gastaut

syndrome (LGS) can play effective management of treatment of the patient assuring safety, appropriate treatment and following secondary therapies. Although a precise diagnosis of LGS needs to be made clear .there are few criteria that is considered in diagnosing the Lennox- Gastaut syndrome (LGS) are as follows (a) multiple types of seizures (tonic, atonic, and atypical absence seizures) (b) abnormal interictal EEG patterns with slow spike wave at <2.5Hz under normal conditions (c) profuse seizures under non rapid eye movement with tonic-clonic epilepsy. In addition intellectual disability and behavioural problems are commonly described in all patients with Lennox- Gastaut syndrome (LGS) (8), they are not present at its early onset and thereby the presence or absence are not considered in the diagnostic criteria.

II. Brain physiology

There are many postulates which shows evidences of involvement sub cortical structures such as thalamus and pons, which are suspected to have increased neuronal activity in Lennox-Gastaut syndrome (LGS).EEG recordings during generalized epileptic discharges of LGS patients confirms thalamus excitation [16, 17].Although EEG and functional magnetic resonance imaging (fMRI) shows involvement of thalamus in Slow spike wave and generalized spike wave in patients with LGS. The pons are involved in tonic seizures. During a tonic seizure there is seen an increased blood flow in the pons, that indicates high neuronal activity. Hence there are proven involvement of thalamus and pons in seizure, but they are not the main initiators of the epileptic episode or the seizure.

A. Other causes and clinical outcomes

There are many pathophysiology which underlies in the Lennox- Gastaut syndrome (LGS) although there are age dependency on the brain which contributes to the development of the LGS phenotypes. Lennox- Gastaut syndrome (LGS) patients have notable focal, multifocal and structural abnormalities in their brain. In addition encephalitis, ischemic stroke, perinatal anoxia, cortical dysplasia and intracranial haemorrhages are predominate in Lennox- Gastaut syndrome (LGS) patients. Electro clinical features of ictal discharge and tonic seizures are identical in Lennox- Gastaut syndrome (LGS) with no evidences of structural abnormality.

III. Subject and Method

The case study included kids from the age of 2-8, our sample size includes 4 male and 6 female children, their identities are kept unknown based on the concern forms issued. The kids had normal premorbid development was brought for evaluation of seizure. Initially all of them had generalized tonic clonic convulsion with several episodes in a day. Over a period of time 3 to 5 years they have developed other types of seizures such as myoclonic jerks, tonic –clonic attacks and absence seizures. Detailed cases studies of the children revealed that most of them was born full term at hospital. Antenatal, perinatal and postnatal history is insignificant, with no dysmorphism. During the examination most of the children (3 males and 4 females) had absences seizures. Most children had stooping gait with instability. Their vision and hearing were normal. The EEG was recorded for 4 male and 6 female children, with clinical findings characterized by slow spike-wave pattern (< 2.5 Hz) [fig1].The children was diagnosed with LGS as they fulfil three most important criterions for diagnosis which included multiple types of generalized seizures, with less prognosis with intellectual disabilities.

B. Network disorders

The electro clinical and cognitive features of LGS reveals that there are common cerebral networks that are involved. Epilepsy is being accepted as a disorder of cerebral networks with increasing clinical evidences. The electro clinical features of an epilepsy syndrome reflects the specific cerebral networks which are involved. A neural network is said to comprise anatomical and functional connections of cortical and subcortical brain structures, where activity in one part can interfere with activity at another part. Network-based clinically relevance of epilepsy can help understand

the seizure semiology and also suggest dysfunctionality in cerebral networks in interictal state can help in treatment.

C. Cognitive Impairment

Lennox- Gastaut syndrome (LGS) is an epileptic encephalopathy as it likely seems to inhibit cognition and cognitive developments of the patients. LGS patients predominantly show slow cognition or developmental delay around the time of diagnosis of the disease, it can't be refuted that Lennox- Gastaut syndrome (LGS) causes moderate to severe cognitive impairment. Majority of the patient's shows intellectual disability during diagnosis. The impairment increases steadily over the individual's life time. Children and adolescents with Lennox- Gastaut syndrome (LGS) Show low IQ levels, behavioural and psychiatric disturbances, poor cognitive and motor functioning with low response to stimulus which is found throughout their life expectancy. There are also other clinical symptoms like aggression, hyperactivity and autism which is found common among children with LGS. Cognitive impairments are common in LGS but are also age of onset and seizure persistent dependent. The onset of the seizure below the age of 5 years have severe intellectual disability while cases with onset after the age of 9 are said to have moderate and are able to cope up to the condition with a fair cognitive development. If there is a poor control of the seizures, there is a declination in the cognitive coping over time. Long-term outcomes of the children are typically poor, with majority of Lennox- Gastaut syndrome (LGS) patients remain under home-care or special supervision, while some have the need to wear a helmet to prevent head and face injuries.

D. Etiology

In about majority of the affected children cause were not able to be identified. The cases are called to as cryptogenic LGS2 [3]. On the other hand, it is noted that children who developed LGS had a pre-existing brain injury or disorder. Few of the cause's identified include brain damage during birth or other birth injuries, encephalitis, congenital infection, brain malformation and hereditary metabolic diseases.

Typical Clinical features, of LGS is hard to conclude as they are multiple seizure types. Of which, more frequent occurrences is tonic seizures and are often at sleep stages. Also there can be atonic, myoclonic, partial, tonic-clinic or absence seizures. Whilst most children with the Lennox-Gastaut syndrome have learning disability and intellectual impairment which ranges from mild to severe. In addition behavioural problems and depression are also common, which are due to the brain injury, frequent epilepsy and the lack of normal social behaviour or also some of the side effects of Antiepileptic Drugs (AEDs) [5,7].While other conditions which children with LGS have progressive decline in IQ, gait disturbances, cerebral palsy .In some cases they look more irritated, tired or bored. Many children also fail in school and require special care. Many at times the seizures can cause imbalance and fall its always advised for the patients to wear proper personal protective equipment's.

The diagnosis of LGS depends on the clinical findings along with a typical EEG graph characterized by an interictal EEG with disturbance of slow spike-wave pattern (< 2.5 Hz).

E. Results

The long term Prognosis outcome is poor with seizure control and intellectual development. All the children had multiple generalized seizures with spike waves (< 2.5 Hz) found in both the hemispheres of the brain [Fig.1]. Most of the children with Lennox-Gastaut syndrome (LGS) have seizures throughout their childhood and adult life.

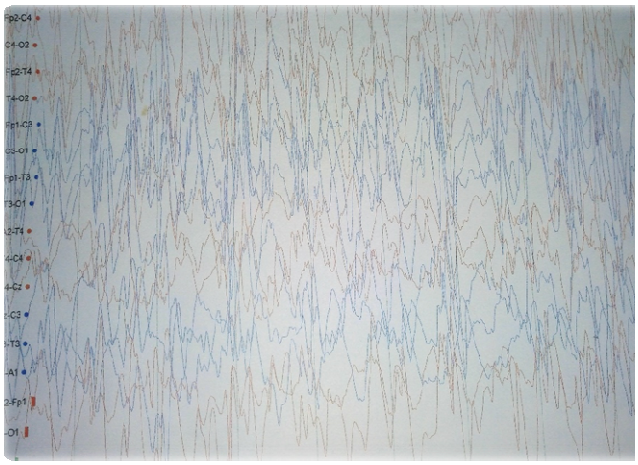

Fig. 1Generalized spike /spike and wave discharges at both hemispheres

F. Discussions

Lennox- Gastaut syndrome (LGS) is one of the severe childhood epileptic disorders. It has triad of symptoms which encompasses of multiple types of generalized seizures, which have varied onset and evolves being difficult to control , slower intellectual abilities often with mental retardation and behavioural issues and electroencephalogram (EEG) pattern which show a slow spike and wave pattern (<2.5Hz),which is present higher when the child is awake [1-4].William Lennox first described the clinical symptoms of the syndrome in 1930s, later he presented triad of symptoms for the syndrome. Lennox Gastaut explained his original observations of Lennox- Gastaut syndrome (LGS) [5-6] In addition, to the Commission on Classification and Terminology of the International League Against Epilepsy published and described the criteria of Lennox- Gastaut syndrome (LGS) and the frequency of occurrences which are: (a) Diffusion of continuous slow spike waves in the EEG in most cases, (b) Status epilepsy,(c) Atonic seizures,(d) Tonic seizures, (e) Runs of rapid spikes in NREM sleep in sleep studies,(f) Atypical absences. It is also observed that resistance to therapy and persistent of epilepsy continuing over a long period of time are the most frequent features. Mental retardation is a leading comorbid condition which is occurring in majority of the cases [7].

IV. CONCLUSIONS

The complete awareness of the epileptic disorder is important for the parents or caregivers of the patients which must include the understanding of the disease and the importance of the treatment. Children with Lennox- Gastaut syndrome (LGS) experiences seizure for over a long period of time and the aim is to have in control the number of seizures episodes and maintain alertness. The primary therapeutic target of Lennox- Gastaut syndrome (LGS) focus on atypical seizures that can exacerbate encephalopathy in children which leads to sudden imbalances and fall causing injury .Anti-epileptic drugs controls the exacerbation to a limited extend does not necessarily reduces the side effect, especially in cases of Lennox- Gastaut syndrome (LGS) with comorbid developmental disorders need to be given special attention. The primary therapy involves treatments with drugs and the secondary supportive therapies need to be given more emphasis which can help the patient achieve a better quality of life .These discussions on primary and secondary therapy are under serious consideration as they require expert reviews depending upon the seizure type and frequency.

ACKNOWLEDGMENT

I would like to thank my all research guides, project fellows of the department of neurology Institute of child health and hospital for children for helping mecomplete my case study.

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