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Early Diagnosis and Treatment of Lennox-Gastaut Syndrome

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Abstract

Lennox-Gastaut syndrome (LGS) is a severe form of childhood-onset epilepsy associated with high morbidity and mortality. The peak period for manifestations of Lennox-Gastaut syndrome is between ages 3 and 5 years, a time of critical brain development and corresponding vulnerability to the electroclinical dysfunction arising from Lennox-Gastaut syndrome. Diagnosis is based on a triad of symptoms: multiple seizure types, cognitive impairment, and slow spike-and-wave pattern on electroencephalography. In practice, Lennox-Gastaut syndrome presentation is diverse, and there may be a delay between initial symptoms and emergence of the full triad of clinical features. Additionally, differential diagnosis is complicated by the resemblance of Lennox-Gastaut syndrome to other forms of epilepsy and by the need for varied diagnostic techniques requiring specific clinical skills. Because diagnosis is complex and early intervention may lead to improved outcomes, clinicians should consider treatment when Lennox-Gastaut syndrome symptoms are present, even in the absence of a formal diagnosis.

Keywords

Lennox-Gastaut syndrome, LGS, diagnosis, early treatment, treatment-resistant, refractory

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Lennox-Gastaut syndrome (LGS) describes a severe form of childhood-onset epilepsy associated with a variety of different seizure types, most commonly tonic, atypical absence, and atonic seizures, but also myoclonic, generalized tonic-clonic, and partial seizures.[1-3] "Drop attacks," which are common in Lennox-Gastaut syndrome, can be caused by multiple seizure types, including tonic and atonic seizures, and may involve the head only or the whole body, resulting in falls.[4,5] Lennox-Gastaut syndrome is generally associated with a triad of features that are frequently, but not always, present. The classic Lennox-Gastaut syndrome triad consists of (1) numerous seizure types, including tonic seizures; (2) cognitive impairment/regression; and (3) a slow spike-and-wave pattern on electroencephalography (EEG) (Figure 1).[1-3,6,7] Lennox-Gastaut syndrome onset is normally first observed in children under the age of 8 years, usually between the ages of 3 and 5 years. A minority of cases of Lennox-Gastaut syndrome emerge in early adulthood. Features of childhood-onset Lennox-Gastaut syndrome often persist into adulthood.[2(pp82,83)]

Because of the variable presentation and timing of the Lennox-Gastaut syndrome triad of symptoms, early diagnosis can be difficult and misdiagnosis is common, a pitfall that is important to avoid, because the potential efficacy of treatment to alter the clinical course of Lennox-Gastaut syndrome may be greatest early in the development of the syndrome.[6] Indeed, Lennox-Gastaut syndrome is frequently confused with other forms of childhood epilepsy that are also severe and associated with multiple seizure types. This may add to treatment challenges, because certain diagnostic features are often absent at Lennox-Gastaut syndrome onset and because the resemblance to other early-onset childhood epilepsy syndromes may confound Lennox-Gastaut syndrome diagnosis.[1,6] The purpose of the present article is to review how early diagnosis of Lennox-Gastaut syndrome can be helpful in facilitating the initiation of appropriate treatment more quickly and thereby prevent poorer clinical outcomes.

Evolution and Prognosis of Lennox-Gastaut Syndrome

Lennox-Gastaut syndrome is a relatively rare condition, more common in males, with a reported annual prevalence of 0.26 per 1000 at age 10 years, according to a population-based study

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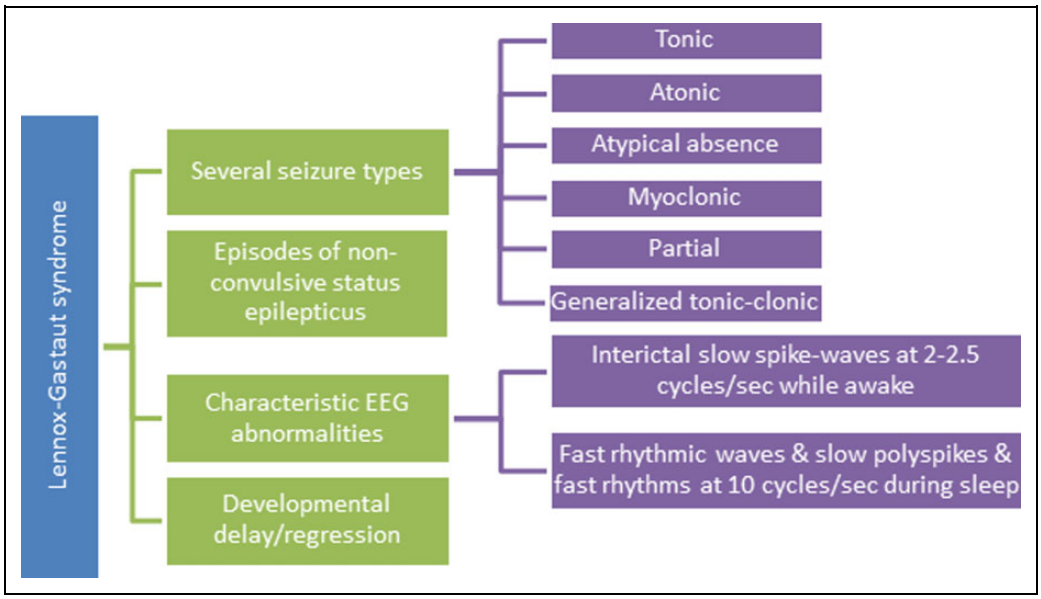

Figure 1. Hierarchy of symptoms characteristic of Lennox-Gastaut Syndrome.[6,7] EEG, electroencephalogram.

of Lennox-Gastaut syndrome conducted in Atlanta, Georgia.[8] Lennox-Gastaut syndrome comprises approximately 4% of all cases of childhood epilepsy, whereas approximately 10% of children who experience epilepsy before the age of 5 years will be diagnosed with Lennox-Gastaut syndrome.[8,9] Mortality rates among patients with Lennox-Gastaut syndrome are high, with deaths often related to accidents or status epilepticus; limited data suggest that 20 years after diagnosis, approximately one-quarter of Lennox-Gastaut syndrome patients are likely to have died.[10,11] A follow-up study to the Atlanta epidemiologic study of 10-year-old children observed a mortality rate—adjusted for age, gender, and race—that was nearly 14-fold higher than in the general population.[12] Patients with Lennox-Gastaut syndrome are at a higher risk for sudden unexpected death in epilepsy (SUDEP) than patients with epilepsy overall, and SUDEP is the most frequent cause of death among patients with Lennox-Gastaut syndrome.[13] Given the high mortality risk associated with Lennox-Gastaut syndrome, it is critical that clinicians be aware of the evolution of the syndrome when treating these patients (Figure 2).

In cases of childhood onset of Lennox-Gastaut syndrome, the effects of electroclinical dysfunction during a child's critical period of brain development may cause irreversible structural modifications and damage.[14] Children with early-onset Lennox-Gastaut syndrome often experience an evolution through several related conditions or syndromes.[15] Newborns with significant damage or malformations of the brain may experience Ohtahara syndrome, which is characterized by numerous brief tonic seizures, burst-suppression EEG patterns, and severe delays in development. At around age 3 months to 10 months, Ohtahara syndrome can evolve into West syndrome, which is associated with a continuation of developmental delay in addition to highly irregular EEG patterns (hypsarrhythmia) and infantile spasms. Approximately 30% of children with West syndrome will go on to develop Lennox-Gastaut syndrome.[15] As patients with Lennox-Gastaut syndrome reach adolescence and adulthood, seizure patterns may shift, with substantially fewer daytime seizures being observed, and only tonic seizures occurring during sleep. EEG patterns can also shift over time, and with these changes, patients may no longer fulfill all of the diagnostic criteria for Lennox-Gastaut syndrome.[14]

Patients whose Lennox-Gastaut syndrome develops later in life are likely to have better outcomes, as structural effects on the developing brain are partially or entirely avoided.[16] Patients expected to have a worse prognosis include those with symptomatic Lennox-Gastaut syndrome (whose prognosis is even worse if Lennox-Gastaut syndrome presentation is preceded by West syndrome); cognitive impairment before onset of Lennox-Gastaut syndrome; early onset of Lennox-Gastaut syndrome (ie, younger than 3 years); high frequency of status epilepticus; and consistent diffuse slowing of the EEG background combined with a generalized, slow spike-and-wave pattern.[5] Thus, the rationale for early diagnosis and treatment of Lennox-Gastaut syndrome derives from the goal of limiting permanent neurologic damage from a condition that emerges, in most cases, very early in life.[4,17] At the same time, an improved understanding of the pattern and evolution of Lennox-Gastaut syndrome symptoms can facilitate diagnosis and treatment of a syndrome that is complicated by the diversity of its manifestations, and by the unfortunate fact that a universally agreed-upon definition of Lennox-Gastaut syndrome does not, at present, exist.[18,19]

Early Recognition of Lennox-Gastaut Syndrome Patterns and Evolution of Symptoms

Early diagnosis and treatment are vitally important in the Lennox-Gastaut syndrome patient population, particularly

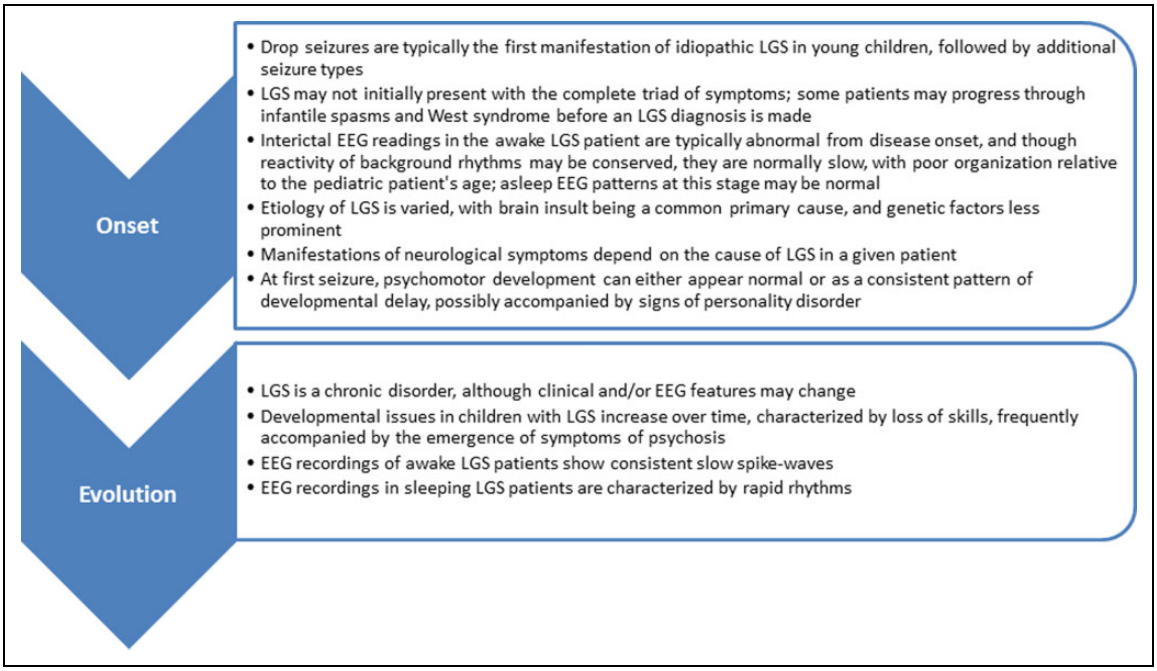

Figure 2. Onset and evolution of LGS features.[2] EEG, electroencephalogram; LGS, Lennox-Gastaut syndrome.

considering the degree of damage occurring in brain structures of infants and children in the early stages of the syndrome.[4,6] However, the difficulties of early diagnosis can often cause delays in treatment that result in poorer overall outcomes. The complexity and heterogeneity of Lennox-Gastaut syndrome presentation, and cases with no evident cause, can delay diagnosis, usually requiring a more complex diagnostic approach. Early diagnosis may also be confounded by the absence of an established definition of the syndrome, and the lack of a clear consensus on the ideal methods for achieving differential diagnosis.[4,6,20] Early diagnosis of Lennox-Gastaut syndrome is yet more challenging because of the typical gap of 1-2 years between a patient's initial seizure and the emergence of the Lennox-Gastaut syndrome diagnostic triad.[3] Therefore, it is important for physicians to be mindful of the individual symptoms associated with Lennox-Gastaut syndrome and to consider the possibility of an Lennox-Gastaut syndrome diagnosis early, before the full triad of symptoms have appeared (Figure 3).

In addition to being able to recognize patterns of Lennox-Gastaut syndrome symptoms, physicians must employ and integrate several techniques for diagnosing Lennox-Gastaut syndrome, including the use of neuroimaging and EEG, as well as assessment of a patient's developmental, neuropsychological, and genetic/metabolic status. Patient assessment should include, to the extent possible, an understanding of the patient's family history and birth history to determine whether injuries, hypoxic/ischemic insults, infection, or infantile spasms played a role in Lennox-Gastaut syndrome etiology. High-resolution magnetic resonance imaging (MRI) can be useful in the early identification of Lennox-Gastaut syndrome etiologies relating to focal brain lesions and should be considered for all patients in whom an Lennox-Gastaut syndrome diagnosis is being considered.[20] MRI should include a T_1-weighted gradient-recalled-echo sequence, an axial and coronal T_2-weighted sequence, a fluid-attenuated inversion recovery (FLAIR) sequence, and high-resolution scanning of the hippocampus (coronal oblique T_2-weighted fast or turbo spin echo sequence). In children under the age of 2, MRI should also include sagittal, axial, and coronal T_1-weighted sequences. Incomplete myelination in children younger than 1 year may allow for the identification of cortical and subcortical dysplasia on T_2-weighted high-resolution images, but also causes T_1-weighted volumetric sequences to be less useful. If imaging findings are normal in a child younger than 2 years with persistent seizures, MRI should be repeated at 6-month intervals through age 24-30 months, as incomplete myelination during infancy may make it difficult to identify some lesions. Not all Lennox-Gastaut syndrome patients will present with abnormal MRI findings, and additional diagnostic tools may be employed to identify alternate etiologies. For example, nuclear magnetic spectroscopy (MRS) and positron emission tomography (PET) may be useful in identifying underlying metabolic disorders in patients with clinical features of Lennox-Gastaut syndrome but normal MRI.[21(pp2,4,5),22(p762),23] Psychological testing should also be conducted at baseline and repeated intermittently throughout the patient's life to track developmental changes.[20]

The slow spike-and-wave EEG findings that represent one of the three components of the classic triad may not be present at seizure onset. Abnormal awake EEG findings may be observed, while sleep EEGs may be normal, only evolving into abnormal patterns with the emergence of additional features of the syndrome. Only about one-eighth of patients who are initially diagnosed with Lennox-Gastaut syndrome actually

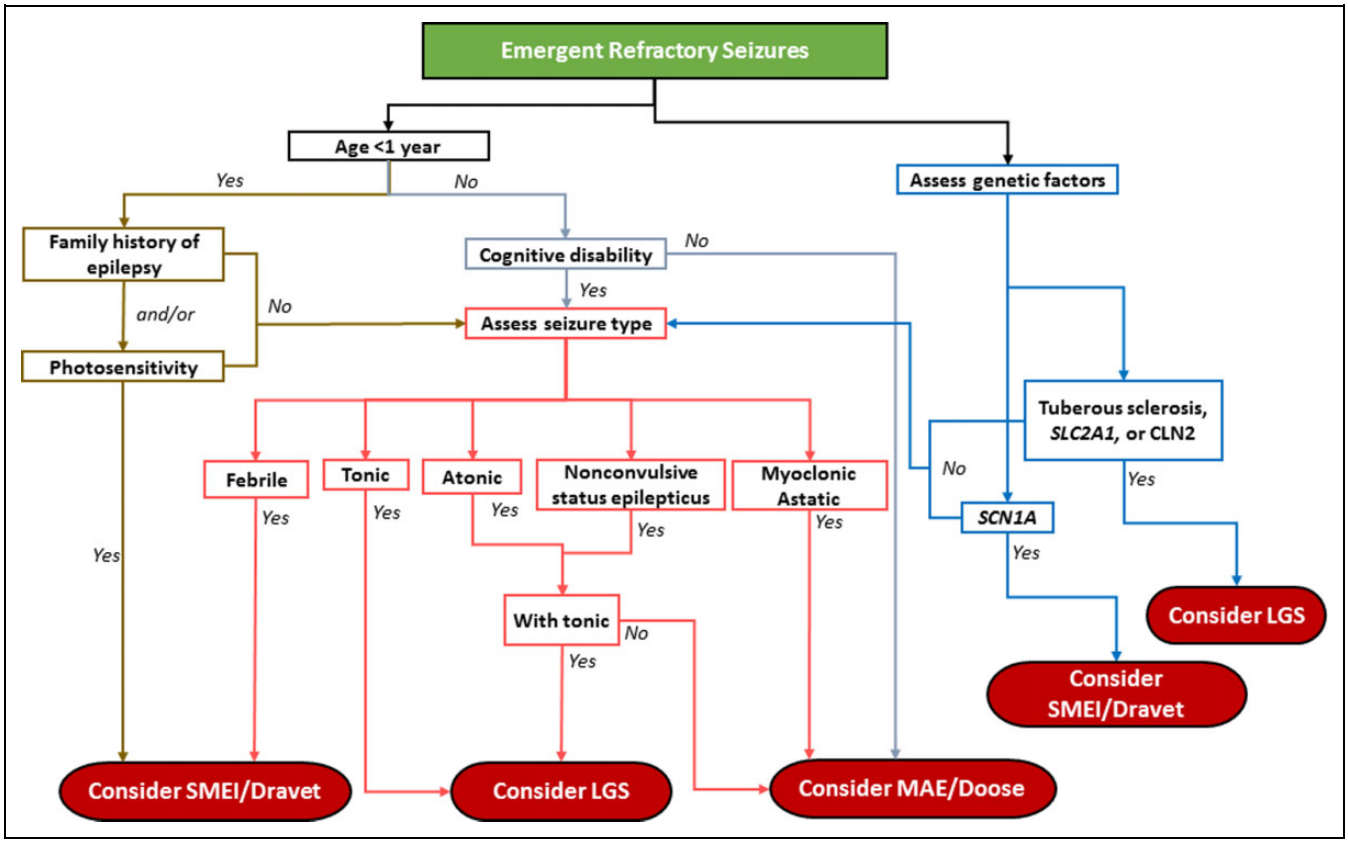

Figure 3. LGS diagnostic flow chart.[6,7,20] LGS, Lennox-Gastaut syndrome; MAE, myoclonic-astatic epilepsy; SMEI, severe myoclonic epilepsy of infancy.

display a slow spike-and-wave EEG. Slow spike-and-wave EEG patterns are also a feature of focal epilepsy with secondary bilateral synchrony.[3,24] Cognitive dysfunction and behavioral disorders associated with Lennox-Gastaut syndrome are also variable at seizure onset. Approximately 30% of patients exhibit psychomotor delay preceding Lennox-Gastaut syndrome onset, although the true rate of psychomotor delay in these patients is likely to be higher due to underdiagnosis of Lennox-Gastaut syndrome in infants.[3,24]

Differential diagnosis represents a significant part of the challenge of Lennox-Gastaut syndrome treatment, because other conditions, such as Dravet (also known as severe myoclonic epilepsy of infancy [SMEI]) and Doose (also known as myoclonic-astatic epilepsy [MAE]) syndromes, can resemble Lennox-Gastaut syndrome, and without biological markers, distinctions in disease features can be difficult to recognize, especially in cases of unknown cause. Nevertheless, differences in presentation, such as patterns of EEG abnormalities, as well as disease course, make differentiation feasible among clinicians familiar with these distinctions.[2,6] Atypical benign partial epilepsy, sometimes called pseudo-Lennox syndrome, is difficult to distinguish from Lennox-Gastaut syndrome, although particular spike-and-wave patterns can help differentiate the 2 conditions. The presence of tonic seizures can be used to rule out atypical benign partial epilepsy.[2] Accurate diagnosis of Lennox-Gastaut syndrome ultimately depends on a nuanced understanding of the particular pattern of symptoms and on the ability to distinguish patterns of EEG abnormalities characteristic of Lennox-Gastaut syndrome that are recognizably distinct from other conditions with similar presentations (Table 1). It is important to note that Lennox-Gastaut syndrome symptoms not only are heterogeneous but also vary and evolve with age. Overall, the features of the syndrome are not significantly different between adult and pediatric patients.[2,19]

Treatment of Lennox-Gastaut Syndrome: Focus on Early Diagnosis and Treatment

The goal of Lennox-Gastaut syndrome treatment is to lower the frequency and severity of seizures to the greatest extent possible to improve quality of life, recognizing that freedom from seizures is unlikely to be achieved for most Lennox-Gastaut syndrome patients.[3,25] The successful treatment of Lennox-Gastaut syndrome is confounded, however, by multiple factors.

Pharmacologic Treatment

Although it is widely accepted that the use of antiepileptic drugs (AEDs) represents the primary treatment modality for Lennox-Gastaut syndrome, no single antiepileptic drug has proved consistently effective among patients with Lennox-Gastaut syndrome, and multiple agents are often used

Table 1. Features of Several Epileptic Syndromes.

Syndrome	Age of Onset	EEG	Tonic Seizure	Atonic Seizure	Intellect Impaired	Other Seizure Types
LGS	1-8 y	<3 Hz spike wave and 10 Hz in sleep	80%-90% in sleep	Some	Yes	All
Doose (MAE)	1-5 y	4 Hz theta and GPSW	++	++	Rarely	M
Dravet (SMEI)	Febrile seizures at <1 y; other seizures at 2-3 y	Slow with irregular spike wave	Rare	Rare	Yes	M, AA, GTC, focal
West	Usually <1 y	Hypsarrhythmia	Yes	Yes	Usually impaired	
Pseudo- Lennox (ABPE)	2-5 y	Central spikes and GSW	No	Yes	26%-56%	M, AA, focal

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Abbreviations: AA, atypical absence; ABPE, atypical benign partial epilepsy; EEG, electroencephalogram; GPSW, generalized polyspike and wave; GSW, generalized spike wave; GTC, generalized tonic-clonic; LGS, Lennox-Gastaut syndrome; M, myoclonus; MAE, myoclonic-astatic epilepsy; PSW, polyspike and wave; SMEI, severe myoclonic epilepsy of infancy.

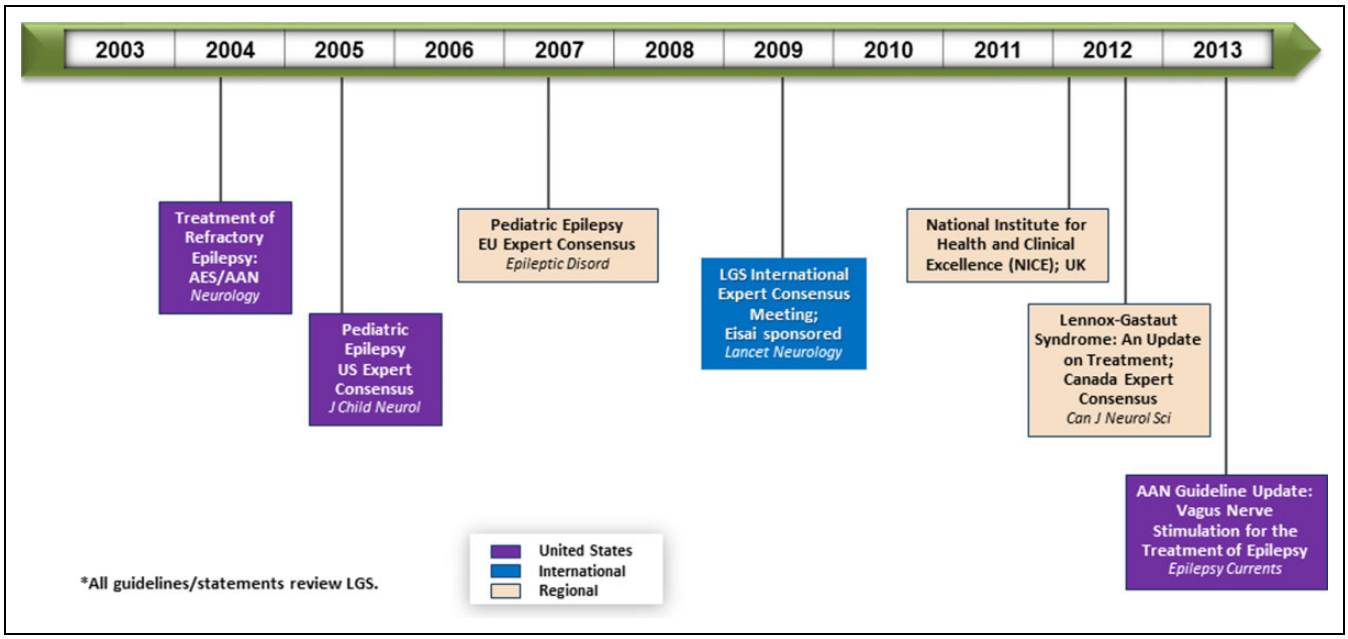

Figure 4. Epilepsy treatment guidelines with discussion of LGS or LGS-specific treatment.[2,3,26-30] AAN, American Academy of Neurology; AES, American Epilepsy Society; LGS, Lennox-Gastaut syndrome.

concurrently.[3] Several specific antiepileptic drugs are often used to treat Lennox-Gastaut syndrome, including valproic acid, lamotrigine, topiramate, rufinamide, and clobazam, in addition to other antiepileptic drugs such as cinromide, felbamate, levetiracetam, zonisamide, and benzodiazepines.[20] Clinical treatment guidelines that offer recommendations for the use of antiepileptic drugs for Lennox-Gastaut syndrome have been published (Figure 4).[2,3,26-29] The guidelines are limited, however, by the difficulties of guiding treatment for such a heterogeneous disease, by the uncertainties surrounding Lennox-Gastaut syndrome treatment efficacy in general, and by the fact that selection of appropriate treatment is highly dependent on the individual patient presentation, which cannot be easily conveyed by published guidelines. Treatment is additionally challenged by the use of combination antiepileptic drug treatments, which may improve one type of seizure while exacerbating another, and complicated to an even greater extent by the fact that the use of multiple antiepileptic drugs increases the risk of adverse events.[2] Moreover, reliance on clinical guidelines and summaries of expert opinion on the treatment of Lennox-Gastaut syndrome is limited, as only the most recent of these publications reflect the availability of newer antiepileptic drugs.[3,26]

Independent of the uncertainty of antiepileptic drug efficacy data and the limitations of treatment guidelines, the risk of exacerbating seizures is a constant concern in the treatment of Lennox-Gastaut syndrome with antiepileptic drugs.[10,31] In fact, the potential for paradoxical effects of antiepileptic drugs among patients with various forms of epilepsy is a well-known phenomenon, and one that is more likely to occur

in Lennox-Gastaut syndrome patients, whose seizures are typically varied and whose disease is unpredictable.[31,32] Loss of efficacy of antiepileptic drugs in the treatment of epilepsy is another common complication. It may occur as a result of metabolic tolerance arising from the induction of antiepileptic drug–metabolizing enzymes, normally an issue with first-generation antiepileptic drugs (which may be overcome by increased dosing), or due to functional tolerance arising from adaptations to treatment targets, as with a loss of receptor sensitivity.[33]

Among antiepileptic drugs, valproic acid is generally considered first-line therapy, and has demonstrated efficacy in the treatment of myoclonic, atypical absence, and atonic seizures. Its use is limited, however, by the rare but serious risk of liver toxicity, and by its potential to interact with other antiepileptic drugs.[3] Valproic acid–induced liver toxicity is associated with the neurometabolic disorder Alpers-Huttenlocher syndrome, which is caused by rare mutations in the gene for mitochondrial DNA polymerase γ (*POLG*). Genetic screening for *POLG* variants should be employed to identify patients at risk for potentially fatal valproic acid–induced hepatotoxicity.[34(p7)] A 2013 Cochrane review of clinical trials in Lennox-Gastaut syndrome observed that the optimal treatment is uncertain, but that rufinamide, lamotrigine, topiramate, and felbamate offer potential efficacy as add-on therapy, whereas clobazam may be effective for drop seizures.[35] Various benzodiazepines (diazepam, clonazepam, and nitrazepam, in addition to clobazam) have also been used in the treatment of Lennox-Gastaut syndrome; however, association with sedation, drooling, and exacerbation of the frequency of seizures in children with Lennox-Gastaut syndrome, in particular tonic seizures, make them less desirable as first-line therapy.[3,20] The United Kingdom's National Institute for Health and Clinical Excellence (NICE), which produced a clinical guideline for the pharmacologic treatment of epilepsies in 2012, recommends sodium valproate as first-line treatment for children with Lennox-Gastaut syndrome, acknowledging the lack of supporting evidence from head-to-head trials against other antiepileptic drugs, while also noting the risk of teratogenicity in women and girls of current or future childbearing potential.[26] NICE also recommends lamotrigine as adjunctive therapy in children, young people, and adults for whom sodium valproate is ineffective or not tolerated, while rufinamide and topiramate are also recommended if adjunctive therapy with lamotrigine is ineffective or not tolerated.[26]

Psychiatric and behavioral considerations. Psychiatric and behavioral comorbidities such as attention-deficit hyperactivity disorder (ADHD), depression, anxiety, aggression, and psychosis are frequently seen in pediatric patients with Lennox-Gastaut syndrome. Drug treatment of Lennox-Gastaut syndrome can have a direct exacerbating impact on these comorbidities, and also an indirect impact via drug-drug interactions. Thus, selection of drug therapy for patients with Lennox-Gastaut syndrome should take into consideration the risk of psychiatric and behavioral comorbidities. Moreover, neuropsychological and psychiatric assessments should be conducted at diagnosis in children with Lennox-Gastaut syndrome, and periodically thereafter, in order to identify specific features of psychiatric and behavioral problems experienced by a given patient and to guide treatment selection.[13]

Nonpharmacologic Treatment

For many patients with Lennox-Gastaut syndrome, nonpharmacologic treatments play a central role in managing the disease.[3,26,36]

Ketogenic diet. A ketogenic diet is a high-fat, moderate protein, and low-carbohydrate diet that has long been in use for seizure treatment, and emerged from the observed reduction in seizures among patients with epilepsy during fasting periods when ketone levels are elevated.[37] A Johns Hopkins study of 71 pediatric patients with Lennox-Gastaut syndrome given a ketogenic diet found that after 1 year, 44% of patients had a >50% reduction in seizures, and 18% had a 90% to 99% seizure reduction. Notably, the rate of seizure reduction diminished over the 1-year period, with better efficacy being seen at 3 months and 6 months compared to 1 year.[38] For patients in whom a ketogenic diet is being trialed, a minimum of 3 months is required to assess efficacy, and ideally, a risk-to-benefit evaluation should be based on 1 to 2 years of incorporating a ketogenic diet into daily life.[37]

Surgery. Results from a study presented at the American Epilepsy Society meeting in 2014 described the outcomes of epilepsy surgery in 36 Lennox-Gastaut syndrome patients under age 18 years (median age at time of surgery, 7 years; range 0.25-18 years). Surgery consisted of focal, lobar, or multilobar resection (n=15) and hemispherectomy (n=21) conducted at a single center (Cleveland Clinic) from 2002 to 2012. After follow-up ranging from 6 months to 6.6 years (median, 34 months), 19 patients (53%) were seizure-free and an additional 10 patients (28%) had a seizure reduction of 50% to 90%.[39] An earlier study in 27 pediatric patients with intractable epilepsy syndromes, including 9 with Lennox-Gastaut syndrome, observed improvements in both seizure frequency and in IQ. After follow-up, which took place 9 to 23 months after surgery (average, 14.2 months), IQ levels rose from a mean of 61.4 ± 12.2 presurgery to 75.0 ± 11.0 after surgery.[36]

Vagus nerve stimulation. Vagus nerve stimulation is used in cases of refractory epilepsy and involves the implantation in the chest of a generator of intermittent electrical stimuli to an electrode wrapped around the left vagus nerve in the neck.[37] In the overall Lennox-Gastaut syndrome patient population, more than half experience a >50% reduction in seizures after initiation of vagus nerve stimulation.[37] With regard to specific Lennox-Gastaut syndrome subtypes, vagus nerve stimulation has been found to be effective for children who experience myoclonic seizures, but has shown limited efficacy in tonic seizures, and has been less effective than corpus callosotomy for atonic seizures.[40,41]

Corpus callosotomy. Corpus callosotomy is usually employed in refractory epilepsy, when all other options have failed. Vagus nerve stimulation is typically tried first in these patients, because it is reversible and is not associated with the risks inherent with craniotomy.[41] Corpus callosotomy has been shown to reduce seizure frequency among patients with Lennox-Gastaut syndrome, particularly in those with atonic seizures, although in other types of seizures associated with Lennox-Gastaut syndrome, the efficacy of corpus callosotomy is approximately equivalent to that of vagus nerve stimulation.[40,41]

Early Diagnosis and Treatment of Lennox-Gastaut Syndrome: Influencing Patient Outcomes

At present, the overall limitations of available data on Lennox-Gastaut syndrome make drawing clear conclusions about early treatment difficult. Until recently, no high-quality clinical trials have studied Lennox-Gastaut syndrome at onset or very early in the disease course, and therefore treatment recommendations have been based on clinical experience and surveys of experts in Lennox-Gastaut syndrome.[2,42] In certain less-severe forms of epilepsy than Lennox-Gastaut syndrome, an argument against early treatment can be made, based on clinical data showing that postponement of antiepileptic drug treatment may not have a significant impact on patients who exhibit brief periods of clustered seizures surrounded by long seizure-free periods, patients who have benign partial epilepsy, and patients who experience sporadic generalized tonic-clonic seizures.[43] By contrast, as previously noted, to limit seizure frequency, severity, and long-term effects, patients with treatment-resistant epilepsies such as Lennox-Gastaut syndrome should be treated early and aggressively. When there is failure to suppress seizures, particularly in patients with intractable frequent daily seizures, the likelihood of a variety of serious risks associated with seizures, such as anoxia, status epilepticus, falls and accidents, and death, is high.[43]

The notion that early antiepileptic drug use may not only reduce seizures but may also limit cognitive dysfunction and improve quality of life in Lennox-Gastaut syndrome patients is a compelling one, and is based in part on findings that early use of antiepileptic drugs in Dravet syndrome appears to result in better outcomes. It also points to the possibility that early treatment of Lennox-Gastaut syndrome could potentially alter the course of the disease, as a result of slowing or limiting structural changes, reducing cognitive decline, and reducing drop attack–associated injuries.[4] It is important to note that early treatment should not be confined to antiepileptic drug use, but should also include consideration of a ketogenic diet, vagus nerve stimulation, and epilepsy surgery, as well as various combinations of these therapies to both optimize seizure control and improve quality of life in patients with Lennox-Gastaut syndrome.

Conclusions

Lennox-Gastaut syndrome is a disease that evolves, and therefore the challenges of diagnosis can cause delays in treatment, resulting in poorer overall outcomes. It is not necessary to wait for a formal diagnosis of Lennox-Gastaut syndrome before initiating treatment for presumed Lennox-Gastaut syndrome. Physicians treating patients with suspected Lennox-Gastaut syndrome should carefully consider early symptoms associated with Lennox-Gastaut syndrome when they are observed, and not let the lack of a definitive diagnosis hinder planning and treatment. Prescribing information for current antiepileptic drugs is often directed at the treatment of seizures associated with Lennox-Gastaut syndrome, thus permitting treatment of features of the syndrome without having all the diagnostic criteria fulfilled. Based on clinical experience and outcomes from clinical studies, broad-spectrum antiepileptic drugs are recommended for the treatment of early-stage Lennox-Gastaut syndrome, during which time drop attacks represent a large proportion of the seizure types, and may also offer efficacy for the treatment of atypical absence seizures. Among the available broad-spectrum antiepileptic drugs used in Lennox-Gastaut syndrome are valproic acid, benzodiazepines, topiramate, lamotrigine, and rufinamide.[3,44] Nonpharmacologic treatments—including a ketogenic diet, vagus nerve stimulation, and surgical intervention, if appropriate—should also be initiated as soon as possible after diagnosis.[17,35,43] Ultimately, because of the resistance of seizures to pharmacologic treatment, multiple therapeutic approaches are often considered for Lennox-Gastaut syndrome patients. Further research is needed to fully assess the impact of early diagnosis and treatment of Lennox-Gastaut syndrome.

Declaration of Conflicting Interests

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