Topic Brief: Seizure Treatment in Lennox-Gastaut Syndrome

Date: 2/10/2023

Nomination Number: 0988

Purpose: This brief summarizes the information addressing a nomination submitted on May 27, 2022, through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program's decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most appropriate.

Issue: Lennox-Gastaut Syndrome (LGS) is a severe chronic epilepsy syndrome caused by a wide range of etiologies that presents in early childhood and commonly persists throughout life. People with LGS often experience difficult-to-manage drug-resistant seizures and develop significant comorbidities, including cognitive, behavioral, and motor impairments. Presently there is no standardized clinical guidance on the treatment of seizures in LGS which results in a wide variability in clinical practice. The American Epilepsy Society (AES) is interested in an evidence review comparing the effectiveness of different modalities for seizure treatment in patients with LGS.

Findings: We identified a 2021 systematic review that addresses part of the nomination and the nominators are aware of an in-progress systematic review that is expected to cover the full scope of the nomination. When the in-progress review is complete, the nominator will assess the review and follow-up if it does not address their needs.

Background

Lennox-Gastaut syndrome (LGS) is a severe form of epilepsy. Seizures usually begin before age four and are varied in type, including tonic seizures, atypical absences, atonic seizures, myoclonic seizures, and generalized tonic-clonic seizures. Accompanying symptoms may include impaired intellectual functioning or information processing, along with developmental delays and behavioral disturbances. There are a variety of cause, which may include brain malformations, tuberous sclerosis, perinatal asphyxia, severe head injury, central nervous system infection, and inherited genetic and degenerative or metabolic conditions.[1]

The condition is estimated to affect 1 to 2 million people, and is more common in males than females.[2] Average total health care costs from 2010 to 2015 for LGS patients were significantly higher ($65,026) vs. those without LGS ($3,849), and the biggest cost contributors were inpatient care among commercially insured patients, and home health services in the Medicaid-insured patients.[3] There is currently no formal clinical guidance on treatment of the condition, resulting in practice variation.

Nomination Summary

The nominator requested a systematic review that would be used to develop guidelines for LGS treatment. During discussion, the nominator communicated that they were aware of another group developing a review that might meet their needs. They will assess the review when complete and determine if a new review is needed from AHRQ.

Scope

1. What are the effectiveness and harms of different modalities for the treatment of seizures in children with LGS?
2. What are the effectiveness and harms of different modalities for the treatment of seizures in adults with LGS?

Table 1. Questions and PICOS (population, intervention, comparator, outcome, and setting)

Questions	1. Effectiveness and harms of seizure treatments in children with LGS	2. Effectiveness and harms of seizure treatments in adults with LGS
Population	Children (aged 1.5 to 18 years) with a diagnosis of LGS	Adults (older than 18) with a diagnosis of LGS
Interventions	a) Pharmacologic treatment, including monotherapy or combination therapy of one or more of the following antiepileptic medications: • Fenfluramine • Cannabidiol • Stiripentol • Clobazam • Rufinamide • Valproic Acid • Sulfamate • Lamotrigine • Other antiepileptic medications b) Surgical treatment, including vagus nerve stimulation, deep brain stimulation, corpus callosotomy and others. c) Dietary modifications, including ketogenic diet, etc.	a) Pharmacologic treatment, including monotherapy or combination therapy of one or more of the following antiepileptic medications: • Fenfluramine • Cannabidiol • Stiripentol • Clobazam • Rufinamide • Valproic Acid • Sulfamate • Lamotrigine • Other antiepileptic medications b) Surgical treatment, including vagus nerve stimulation, deep brain stimulation, corpus callosotomy and others. c) Dietary modifications, including ketogenic diet, etc.
Comparators	Placebo or one of the above treatment modalities, used alone or in combination, compared to one another	Placebo or one of the above treatment modalities, used alone or in combination, compared to one another
Outcomes	• Morbidity • Mortality • Cessation of all seizure types (including absence seizures, tonic seizures, drop seizures, etc.) • 50% reduction in all seizure types • Proportion of patients experiencing a reduction in seizure frequency • Proportion of patients experiencing a reduction in seizure related injuries • Proportion of patients experiencing improvement in cognitive outcomes	• Morbidity • Mortality • Cessation of all seizure types (including absence seizures, tonic seizures, drop seizures, etc.) • 50% reduction in all seizure types • Proportion of patients experiencing a reduction in seizure frequency • Proportion of patients experiencing a reduction in seizure related injuries • Proportion of patients experiencing improvement in cognitive outcomes

	• Reduction in the use of rescue antiseizure medications • Reduction in the use of emergency care • Patient quality of life • Patient satisfaction with treatment • Caregiver quality-of-life • Adverse events leading to treatment discontinuation • Any adverse events	• Reduction in the use of rescue antiseizure medications • Reduction in the use of emergency care • Patient quality of life • Patient satisfaction with treatment • Caregiver quality-of-life • Adverse events leading to treatment discontinuation • Any adverse events
Setting	Any (i.e., outpatient, inpatient, emergency department)	Any (i.e., outpatient, inpatient, emergency department)

Abbreviations: LGS=Lennox-Gastaut Syndrome.

Assessment Methods

We assessed nomination for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
4. Assess the *potential impact* a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

Summary of literature findings: We identified a completed 2021 Cochrane systematic review on pharmacological interventions for Lennox Gastaut, which covers part of the scope of the nomination.[4] Additionally, the nominators are aware of an in-progress systematic review that is expected to cover the entire scope of the nomination.

Summary of Selection Criteria Assessment: Lennox-Gastaut Syndrome (LGS) is a severe chronic epilepsy syndrome caused by a wide range of etiologies that presents in early childhood and commonly persists throughout life. Presently there is no standardized clinical guidance on the treatment of seizures in LGS which results in a wide variability in clinical practice. The American Epilepsy Society (AES) is interested in an evidence review comparing the effectiveness of different modalities for seizure treatment in patients with LGS. We found a recent high-quality review that covers part of the scope of the nomination (pharmacological interventions) and the nominators are waiting to review the completed version of an in-progress review that is expected to address the entire scope of the nomination.

References

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