ejpmr, 2025, 12(7), 586-589

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN (O): 2394-3211

ISSN (P): 3051-2573

REVIEW STUDY ON GELASTIC SEIZURES

[1]Yalamanchili Roshini, [1]Macharla Eswar Subhash, [1]Thiruveedula Kumari, [1]Anasuri Kusuma Sri, [1]Yogendar Yaswanth Babu Pamula, [2]Sreenu Thalla, [3]Puttagunta Srinivasa Babu and [*1]Pusuluri Siva Krishna

[*1]Department of Pharmaceutical Analysis, Vignan Pharmacy College (Autonomous), Vadlamudi, Guntur, Andhra Pradesh, India.

[2]Department of Pharmacology, Vignan Pharmacy College (Autonomous), Vadlamudi, Guntur, Andhra Pradesh, India.

[3]Department of Pharmaceutics, Vignan Pharmacy College (Autonomous), Vadlamudi, Guntur, Andhra Pradesh, India.

***Corresponding Author: Pusuluri Siva Krishna**

Department of Pharmaceutical Analysis, Vignan Pharmacy College (Autonomous), Vadlamudi, Guntur, Andhra Pradesh, India.

Article Received on 22/05/2025 **Article Revised on 12/06/2025** **Article Accepted on 02/07/2025**

ABSTRACT

Gelastic seizures, characterized by sudden bursts of laughter or giggling, represent a unique and often misdiagnosed form of epilepsy. This review aims to synthesize current understanding of gelastic seizures, including their clinical presentation, etiology, pathophysiology, and management strategies. We explore the diverse causes, ranging from hypothalamic tumors to genetic factors, and highlight the challenges in diagnosis due to their atypical presentation. Furthermore, we examine the neurophysiological mechanisms underlying these seizures, emphasizing the role of the hypothalamus and limbic structures. Treatment modalities, including antiepileptic drugs and surgical options, are discussed in detail, alongside their efficacy and associated outcomes. This comprehensive review underscores the need for heightened awareness among clinicians to facilitate timely diagnosis and improve patient management, ultimately enhancing the quality of life for individuals affected by gelastic seizures.

KEYWORDS: Gelastic seizures, epilepsy, hypothalamus, limbic structures.

INTRODUCTION

Gelastic seizures are a rare and distinctive form of focal epilepsy, primarily characterized by episodes of involuntary laughter or giggling. The term "gelastic" is derived from the Greek word ‘gelos’, meaning laughter. Unlike laughter that is triggered by external stimuli or emotions, the laughter seen in gelastic seizures is inappropriate, unprovoked, and often devoid of emotional content. These seizures are most commonly associated with hypothalamic hamartomas—benign masses in the hypothalamus—although they can originate from other brain regions such as the temporal and frontal lobes.[1] Typically emerging during infancy or childhood, gelastic seizures can be challenging to diagnose due to their atypical presentation and subtle onset. They are frequently accompanied by other seizure types as the condition progresses, which can lead to developmental delays, cognitive impairment, and behavioral changes in patients. Despite their unusual presentation, early recognition and intervention are essential, as timely treatment can significantly improve neurological outcomes and overall quality of life. This review aims to provide an in-depth analysis of the clinical presentation, underlying pathophysiology, diagnostic approaches, and current therapeutic strategies for managing gelastic seizures. Understanding these aspects is critical for developing effective management plans and improving prognoses for affected individuals.

Gelastic seizures are rare, accounting for less than 1% of all epileptic seizures. They most commonly begin in childhood, often presenting before the age of 3 to 4 years, but can occur at any age. The exact incidence and prevalence are difficult to determine due to their rarity and the challenges in recognizing their distinctive presentation. Males appear to be slightly more affected than females, but the gender difference is not significant. The majority of gelastic seizures are associated with hypothalamic hamartomas (HH), a benign, non-cancerous tumor in the hypothalamus. Approximately 70-80% of patients with hypothalamic hamartomas experience gelastic seizures as a primary symptom. However, in a smaller subset of patients, these seizures may originate from other brain regions, such as the temporal or frontal lobes, making diagnosis more challenging. The onset of gelastic seizures in patients with hypothalamic hamartomas is typically early, often manifesting in infancy or early childhood. These seizures are usually resistant to conventional anti-epileptic drugs (AEDs), contributing to a prolonged course and often leading to additional seizure types and developmental delays over time. Although they are rare, awareness and understanding of their epidemiological characteristics are

critical for early diagnosis, which can improve management outcomes for affected individuals.

Causes

Gelastic seizures are primarily caused by abnormal electrical activity in specific brain regions, most notably the hypothalamus. The most common underlying cause is the presence of a hypothalamic hamartoma (HH) — a benign, non-cancerous tumor or malformation in the hypothalamus. Hypothalamic hamartomas are believed to generate abnormal discharges that lead to the characteristic episodes of laughter or giggling without a corresponding emotional trigger. This is the most frequently observed cause, with up to 70-80% of gelastic seizures being associated with hypothalamic hamartomas. In addition to hypothalamic hamartomas, gelastic seizures can also originate from other areas of the brain. These include the temporal lobe, frontal lobe, and, less commonly, the parietal lobe. In such cases, the underlying causes may include structural abnormalities such as cortical dysplasia, gliomas, or other focal brain lesions that disrupt normal brain function.

Genetic factors may also play a role in some cases, especially in syndromic conditions that can include gelastic seizures as a symptom, though such cases are rare. Some individuals with specific genetic mutations, such as those involving the KCNQ2 or DEPDC5 genes, may present with gelastic seizures as part of a broader epilepsy phenotype. However, most cases are sporadic rather than inherited. The causes of gelastic seizures are often complex and multifactorial, with the exact mechanisms varying between individuals. The presence of a structural brain abnormality like a hypothalamic hamartoma is the most recognized and well-documented cause, but other focal brain lesions and potential genetic factors also contribute to their development. Accurate identification of the underlying cause is essential for tailoring appropriate treatment strategies, such as surgical intervention or targeted medication.

Risk Factors

The risk factors for gelastic seizures are primarily related to underlying brain abnormalities and, in some cases, genetic predispositions. Understanding these risk factors is important for early detection and effective management.

- **Hypothalamic Hamartomas (HH) –** The most significant risk factor for developing gelastic seizures is the presence of a hypothalamic hamartoma. These benign growths in the hypothalamus are present from birth, and their abnormal electrical discharges can trigger the characteristic episodes of inappropriate laughter. Nearly 70-80% of patients with hypothalamic hamartomas experience gelastic seizures as a primary symptom.
- **Structural Brain Abnormalities –** In addition to hypothalamic hamartomas, other structural abnormalities in the brain can increase the risk of gelastic seizures. These include lesions in the temporal, frontal, or parietal lobes, such as cortical dysplasia, gliomas, or other focal brain lesions. Abnormalities in these regions can alter normal brain function and trigger seizures.
- **Genetic Factors –** Although most cases of gelastic seizures are sporadic, some genetic conditions can predispose individuals to develop them. Mutations in certain genes, such as KCNQ2 or DEPDC5, may be associated with epilepsy syndromes that include gelastic seizures as a symptom. Additionally, genetic conditions that cause brain malformations or developmental abnormalities can also increase the likelihood of these seizures.
- **Early Childhood Onset of Seizures** – Gelastic seizures frequently manifest in early childhood, often before the age of 3 or 4 years. A history of early-onset epilepsy, particularly if associated with developmental delays or behavioral changes, may suggest a higher risk of gelastic seizures.
- **Family History of Epilepsy –** While gelastic seizures themselves are not typically inherited, a family history of epilepsy or seizure disorders can indicate a genetic predisposition to abnormal brain activity, which may increase the risk of various seizure types, including gelastic seizures.

Identifying these risk factors can help guide appropriate diagnostic and therapeutic approaches, potentially improving the long-term outcomes for those affected.

Symptoms

- **Involuntary Laughter –** The hallmark symptom is sudden, uncontrollable laughter or giggling, which may sound hollow or unnatural. This laughter is not usually related to external stimuli like jokes or a funny situation.
- **Laughter without Joy** – While the person is laughing, they do not experience a sense of joy or happiness. The laughter is typically not associated with an emotion.
- **Facial and Behavioral Changes** – The person may have facial expressions that don't match their mood or the situation. For example, their face might remain neutral or appear distressed while they are laughing.
- **Altered Awareness** – Some individuals may experience confusion or a change in their level of awareness during the seizure, and they may not remember the event afterward.
- **Aura or Preceding Sensation** – Some individuals report experiencing an aura (a strange sensation) before the laughter begins, which can manifest as a feeling of fear, discomfort, or a sensation rising through the body.
- **Possible Physical Signs –** In some cases, the person may have other physical manifestations during the seizure, like lip-smacking, fidgeting, or other involuntary movements.

These seizures are often associated with abnormalities in the hypothalamus but can also be linked to other areas of the brain. They can occur at any age but are most commonly seen in childhood.

Diagnosis

- **Detailed Symptom Description** – The physician will ask about the nature, frequency, and duration of the laughter episodes, including any preceding sensations (auras), changes in behavior, or altered awareness.
- **History of other Seizures** – A thorough history of any other types of seizures or neurological issues in the patient or their family may also be relevant.
- **Developmental History** – For children, a history of developmental milestones can be important to determine if there are any associated developmental delays or behavioral abnormalities.
- **Neurological Examination –** The physician conducts a neurological exam to assess the patient's overall brain function, checking reflexes, muscle strength, coordination, and sensory responses. This helps rule out other neurological conditions that might cause similar symptoms.

Electroencephalogram (EEG)

- **Standard EEG –** An EEG measures electrical activity in the brain and is essential for diagnosing gelastic seizures. During the test, electrodes are placed on the scalp to record brain waves.
- **Video EEG Monitoring** – Often, a longer-term video EEG is used to capture the seizure events on video while simultaneously recording brain activity. This helps correlate the episodes of laughter with electrical changes in the brain.
- **Interictal Spikes** – In gelastic seizures, the EEG may show abnormal electrical discharges (interictal spikes) even between seizures, but in some cases, changes may only be detected during the seizure itself.

Brain Imaging

- **Magnetic Resonance Imaging (MRI)** – An MRI is often recommended to look for structural abnormalities in the brain that may be causing the seizures. For gelastic seizures, the focus is often on the hypothalamus, as these seizures are frequently associated with hypothalamic hamartomas (benign tumors or malformations in the hypothalamus).
- **Positron Emission Tomography (PET) or Single-Photon Emission Computed Tomography (SPECT)** – These scans may be used if the MRI results are unclear, as they can provide information about areas of abnormal metabolic activity in the brain.
- **Neuropsychological Testing –** If there are concerns about cognitive or developmental issues, especially in children, a neuropsychologist might perform tests to assess the impact of seizures on memory, learning, and behavior.
- **Consultation with Epileptologists** – For complex cases, a referral to a specialist in epilepsy (epileptologist) is often necessary. This can help confirm the diagnosis and determine the best treatment approach, particularly if surgery might be considered. This comprehensive approach helps to confirm that the episodes are indeed gelastic seizures, determine their origin, and rule out other possible causes of the symptoms.

Management

Managing gelastic seizures involves a combination of medication, possible surgical intervention, and supportive care. The goal is to control the seizures, minimize their impact on daily life, and address any underlying causes, such as hypothalamic hamartomas.

Medication

- **Antiepileptic Drugs (AEDs) –** These are typically the first line of treatment. Medications like carbamazepine, valproate, lamotrigine, and levetiracetam may be used to control seizure activity. However, gelastic seizures can be resistant to medication, especially when associated with hypothalamic hamartomas.
- **Medication Adjustment –** It often takes time to find the right medication or combination that is effective for a specific individual. The response to AEDs can vary widely, and some patients may experience partial relief from seizures.
- **Surgical Interventions –** Surgery may be considered if medications do not adequately control the seizures or if there is a structural abnormality like a hypothalamic hamartoma that can be addressed surgically. Surgical options include:
- **Resection of the Hamartoma –** If the seizures are due to a hypothalamic hamartoma, surgical removal or resection may be considered. This can often lead to significant improvement or even cessation of seizures.
- **Laser Interstitial Thermal Therapy (LITT) –** This minimally invasive technique uses a laser to target and ablate the hamartoma. It is less invasive than traditional surgery and may have a faster recovery time.
- **Gamma Knife Radiosurgery** – A type of non-invasive radiation therapy that focuses high doses of radiation on the hamartoma. It is another option for cases where traditional surgery is not possible.
- **Vagal Nerve Stimulation (VNS)** – In cases where surgery is not an option or is not fully effective, VNS can be considered. A small device is implanted in the chest, sending electrical impulses to the brain via the vagus nerve, which can help reduce seizure frequency.

Supportive Care

- **Psychological Support and Counseling –** Gelastic seizures can impact social interactions and self-esteem, especially in children and adolescents.

Psychological support or counseling can help patients and their families cope with the social and emotional challenges.

- **Educational Support –** Children with gelastic seizures may benefit from individualized educational plans (IEPs) or other forms of support in school, particularly if cognitive or learning difficulties are present.

Lifestyle Modifications

- **Regular Sleep and Stress Management –** Ensuring adequate sleep and reducing stress can help in managing seizure activity. While these measures are not a substitute for medical treatment, they can complement it.
- **Avoiding Triggers –** Though gelastic seizures often do not have specific triggers, maintaining a healthy lifestyle with proper sleep and a balanced diet can be beneficial.
- **Regular Follow-Up and Monitoring** – Continuous follow-up with a neurologist or epileptologist is crucial to monitor the effectiveness of treatment and make adjustments as needed. Regular brain imaging and EEGs may be used to track changes in seizure activity and evaluate the impact of treatments.
- **Research and Clinical Trials –** In some cases, patients may be eligible for clinical trials involving new medications or treatment methods for epilepsy that are under investigation. This can be a consideration if other treatments have not been effective.

The management of gelastic seizures requires a personalized approach, as responses to medication and other therapies can vary. A multidisciplinary team, including neurologists, neurosurgeons, psychologists, and educators, can help provide comprehensive care for those affected. While medication can be effective for some, surgery is often the most definitive treatment for cases related to hypothalamic hamartomas.

Gelastic seizures, though rare, present significant challenges due to their atypical presentation, often involving unprovoked episodes of laughter. These seizures are most commonly linked to hypothalamic hamartomas but can also arise from other brain regions, complicating the diagnostic process. Accurate diagnosis requires a combination of clinical observation, EEG, and brain imaging to identify the seizure's origin and underlying causes. Management typically begins with antiepileptic medications, though surgical interventions, such as resection, laser ablation, or neuromodulation techniques, are often necessary for cases resistant to medication. When appropriate, these surgical options can dramatically improve seizure control and overall quality of life. However, the impact of gelastic seizures extends beyond the physical, affecting social interactions, emotional well-being, and development, especially in children. Thus, a holistic treatment approach that includes psychological support and educational accommodations is vital. Ongoing research and advancements in treatment methods hold promise for better outcomes, providing hope for those affected by this challenging condition. A multidisciplinary, patient-centered approach remains essential to optimize care and support long-term well-being.

CONCLUSION

Gelastic seizures, with their unique presentation and potential underlying causes, require careful diagnosis and tailored management strategies. While treatment can be challenging, advances in surgical techniques and a better understanding of the condition offer promising avenues for improving patient outcomes. Addressing the social and psychological impacts of these seizures is equally important, ensuring that patients receive not only medical but also emotional and social support throughout their journey.

REFERENCES

1. Fawcett J, Davis S, Manford M. Further advances in epilepsy. J Neurol., 2023; 270(11): 5655-5670.
2. Rana M, Steenari M, Shrey D. Hyperventilation and Seizures: Not a New Sense: A Literature Review. Neuropediatrics., 2023; 54(6): 359-364.
3. François L, Romagnolo A, Luinenburg MJ, Anink JJ, Godard P, Rajman M, van Eyll J, Mühlebner A, Skelton A, Mills JD, Dedeurwaerdere S, Aronica E. Identification of gene regulatory networks affected across drug-resistant epilepsies. Nat Commun., 2024; 11; 15(1): 2180.
4. Hamza A, Sureshbabu S, Nc K, Narayanan P, Pillai DP. Gyratory Seizures in Hypothalamic Hamartoma. J Epilepsy Res., 2024; 30; 14(1): 47-49.
5. Liao YS, Gao LL, Lin M, Wu CH. Temporal lobe malacia as a rare cause of gelastic seizure: A case report. World J Clin Cases., 2024 Jul 16; 12(20): 4440-4445.
6. Mackenzie, C. A., & O'Brien, T. J.. Gelastic seizures: A review of the literature and a case report. Seizure, 2020; 78: 99-104.
7. Hasegawa, Y., et al.. Gelastic seizures due to hypothalamic hamartomas: Clinical features and surgical treatment. Neurosurgical Review, 2017; 40(2): 245-251.
8. Vadera, S., & Kuo, A. Vagal nerve stimulation for the treatment of gelastic seizures: A case report. Epileptic Disorders, 2020; 22(1): 100-104. 4.
9. S Thalla, K. Venkata, Ramana, K. S, Kumar, V. L, Reddy, Y.A, Kumar. Anticonvulsant activity of hydroalcoholic extract of Ocimum gratissimum leaves. World Journal of Pharmaceutical ReseaRch., 2014; 3(3): 4106-4112.
10. Chalifoux, J. R., & Doss, R. C. Surgical treatment of epilepsy. Journal of Neurosurgery, 2018; 129(4): 1197-1210.