INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Paper

Current Approaches to Epilepsy Management: A Compressive Case-Based Evidence Review of Pathophysiology, Diagnosis, Pharmacotherapy and Clinical Outcomes

Harshal Tale[1]*, Kartik Tale[2], Tejas Khote[3], Prachi Shamkuwar[4], Tanishka Thool[5], Kalyani Lad[6], Bhumi Sonone[7]

[1,2] Rajarshi Shahu College of Pharmacy, Buldhana, Dist- Buldana, M.S, India 443001
[3,4,5,6,7] Government College of Pharmacy, Chhatrapati Sambhaji nagar, Dist- Sambhaji nagar, M.S India 431005.

ARTICLE INFO

Published: 25 Sept 2026
Keywords:
epilepsy, drug-resistant epilepsy, antiseizure medications, levetiracetam, topiramate, polytherapy, case study
DOI:
10.5281/zenodo.22953424

ABSTRACT

Background: Epilepsy affects around 65 million people globally and approximately one-third of sufferers continue to have seizures despite treatment. Management is challenged by heterogeneity of etiology, imprecise classification and a diagnosis primarily dependent on clinical history.Objective: To examine the current knowledge of epilepsy categorization, etiology, risk factors and pathophysiology and demonstrate the optimization of antiseizure drug therapy in drug resistant epilepsy using a case.Methods: A narrative review was conducted on the ILAE categorization, etiological categories (idiopathic, symptomatic, provoked, cryptogenic), risk factors (genetic, traumatic, environmental, treatment gap), and the roles of astrocytes, microglia, and oligodendrocytes in seizure genesis. Then a 44-year-old man with medication resistant focal epilepsy was analysed in SOAP style with a pharmacological profile, ADR monitoring plan and counseling points.Case findings: The patient had a right temporal choroid cyst, bilateral hippocampal sclerosis and cerebral atrophy. He was on topiramate 225 mg, phenytoin 400 mg and clobazam 10 mg daily. Levetiracetam (2000 mg/day) was added and reduced his seizures to nearly nothing but he felt drowsy and unsteady. Seizure control was maintained with slow withdrawal of topiramate, as a previous phenytoin withdrawal had resulted in increasing seizure frequency.

INTRODUCTION

According to the International League against Epilepsy (ILAE), an epileptic seizure is defined as "a transient neurological event caused by abnormal synchronous neuronal activity". Epilepsy is conceptually defined as "an enduring

***Corresponding Author:** Harshal Tale
Address: *Rajarshi Shahu College of Pharmacy, Buldhana, Dist- Buldana, M.S, India 443001.*
Email ✉: taleharshal3@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

predisposition of the brain to generate epileptic seizures and to thereby lead to neurobiological, cognitive, psychological and social consequences." [1]. Epilepsy is the most frequent, chronic, dangerous neurological condition, affecting 65 million people throughout the world [2]. Following the major achievements in developing drug treatments for epilepsy in the mid-20th century, later efforts to find more effective therapies have produced only gradual improvements and have not addressed the issue of medically refractory epilepsy. In fact, about one-third of epilepsy patients still experience uncontrolled seizures [3]. Epilepsy is not a single disease entity, but rather a spectrum of underlying neurologic illnesses [4]. There are several elements that determine whether a person will have an epileptic seizure or an epileptic condition and when the epileptic seizure may happen. Currently, epileptic diseases are believed to be genetically transmitted ailments (idiopathic or primary epilepsies) or results of specific brain irregularities (symptomatic or secondary epilepsies) [5].

Epileptic seizures are defined as paroxysmal events (behavioural expressions) often associated with a transient alteration in the level of consciousness and with signs and symptoms that are due to abnormal, excessive or synchronized neuronal discharges of the brain that may be widespread or localized [6].

Non-epileptic seizures, however, are not caused by aberrant neural discharges. They can be split into two big kinds. Organic non-epileptic seizures (Atypical syncope and parasomnias) and Psychogenic non-epileptic seizures-NEPS (Conversion symptoms, and dissociative states). Prolonged strong eye closure may be observed during a NEPS paroxysmal event, but any type of ocular closure is uncommon in epileptic seizures [7]. People are often just labelled with epilepsy but the diagnosis should be as specific and precise as possible. Classification is at three levels: seizure type, epilepsy type and syndrome. At each stage, the cause and comorbidities should be addressed as they may have substantial therapy consequences. The causes are divided into six categories: genetic, structural, metabolic, infectious, immunological and unknown. Seizures are characterized by onset as focal, generalized, or unknown. Focal seizures are classified by level of awareness into those with retained awareness and those with impaired awareness. The focal seizures are further characterized according to the earliest and most pronounced motor or non-motor manifestation [9, 10, 11]. The diagnosis of epilepsy mainly rests on a description of events given by the person having the events, sometimes augmented by information gained from an observer. Every trial lawyer knows that the observations of witnesses might be incomplete and deceptive. Diagnosis of epilepsy might be difficult without a clear account of events, including their prodromes and aftermaths. There is no substitute for a poor description of a probable seizure [8].

In clinical practice, most seizures are discrete events with consistent electrical and behavioral patterns, but there is no universally agreed classification of the various behavioral, sensory and perceptual symptoms of seizures. Arbitrary criteria have been used to describe experimental seizures, including specific motor phenomena (e.g. clonic or tonic-clonic activity), a defined duration of a seizure, or the presence of a postictal state. None of these are employed in the diagnosis of human epilepsy. There are distinctive ictal behaviors for which electrographic discharges cannot be observed or confirmed, but subclinical seizures may also occur with electrographic alterations on the EEG without any visible behavioral indications. Sometimes, stereotyped behavioral occurrences of short duration such as tics and other indications of movement disorders, in humans can be seen but are not associated with

electrographic alterations as they are not seizures. Even EEG, which is more reliable than behavioral observation, is not often adequate by itself to prove epilepsy. A recent study shown that clinicians who were blinded to all other clinical data when analyzing video EEG monitoring data were able to draw different findings as to whether seizures are of an epileptic origin [12].

Causes:

Idiopathic epilepsy: epilepsy of primarily genetic origin, with no gross neuroanatomical or neuropathological abnormalities. Some rare epilepsies are caused by a single gene. More common are epilepsies with suspected polygenic or complex inheritance. But the nature of the genetic pathways has remained obscure. Most of the 'idiopathic generalized epilepsies' and most of the 'benign epilepsies of children' are in this category. The word idiopathic is preferred as the genesis of the epilepsy is a complicated mixture of probable hereditary and non-genetic causes and also involves epigenetic and epistatic mechanisms with chance and environmental effects acting over time as the brain grows. Symptomatic epilepsy: epilepsy due to an acquired or hereditary disorder, with neuroanatomical or neuropathological abnormalities symptomatic of an underlying disease or condition. This category encompasses (a) acquired problems and (b) developmental and congenital illnesses where these are connected with brain pathological changes whether hereditary or acquired (or perhaps cryptogenic) in origin.

Provoked epilepsy: epilepsy in which a specific systemic or environmental factor is the major cause of the seizures and in which there are no substantial causal neuroanatomical or neuropathological alterations. Some 'provoked epilepsies will have a hereditary basis and some will have an acquired base. This category includes the reflex epilepsies (which are frequently hereditary) as well as the epilepsies with a noticeable seizure precipitant. Cryptogenic epilepsy – epilepsy of assumed symptomatic nature for which the cause has not yet been established. The frequency of such instances is decreasing, although this is still an important category at present, accounting for at least 40% of adult-onset cases of epilepsy [30].

Types of epilepsy:

1) Partial epilepsy

Partial epilepsies usually originate from neural tissue in the vicinity of a lesion. Experimental lesions provide evidence that the structure, function and connections of neurons are altered and this ultimately leads to anomalies in the function of neuronal groups. If of sufficient intensity the disruption of function produces disturbance of behavior which we witness clinically as a focal seizure. The electroencephalogram (EEG) shows electrical disruption from the area sometimes for several seconds or minutes before the onset of more powerful or more broad discharges which follow the seizure. One practical means of gaining a knowledge of the pathophysiology of partial epilepsy is to study the electrical recordings from an intracellular micro-electrode in a neuron at an epileptic focus in conjunction with the electrical potentials in the EEG. The ideal experiment would be to have simultaneous intracellular, regional and surface electrical recordings coupled with concurrent behavioral recordings. Some of the links have been investigated and they are informative but this has yet to be done [31]. Focal motor seizures can be defined more precisely. Motor-onset manifestations include automatisms, epileptic spasms, and atonic, clonic, hyperkinetic, myoclonic or tonic seizures. Automatisms are purposeful, coordinated, repetitive motor movements which under other circumstances may

look normal. Focal atonic seizures cause loss of tone in a portion of the body. Clonic seizures are defined by repetitive, evenly spaced, stereotyped jerking movements. Epileptic spasms were previously considered as solely generalized seizures. These include autonomic, behavior arrest, cognitive, emotional or sensory seizures, when the first prominent feature is a nonmotor symptom. Autonomic seizures present with changes in heart rate, blood pressure, perspiration, skin colour, piloerection or abdominal feelings. Behavioral arrest seizures are characterized by a cessation of movement, which should be the primary feature throughout the entire seizure, not just a brief episode, and clinical indicators include a blank look and halting of speech or activity. Nonmotor cognitive seizures can manifest as alterations in language, thought, or other higher brain functions such as déjà vu, jamais vu (a feeling of unfamiliarity), or hallucinations. Emotional seizures are dramatic emotional shifts, such as dread, terror, worry or pleasure. Focal sensory seizures are classified according to the altered sensory perception of taste, smell, hearing, vision, pain, numbness or tingling [32].

2) Generalized epilepsy

Generalized seizures are also classified according to whether their manifestations are motor or nonmotor as in the focal seizures. Motor seizures are often classified into two types: tonic-clonic seizures and other motor seizures. Absence seizures are frequently included in generalized nonmotor seizures. The motor onset includes more specific types: tonic-clonic, clonic, tonic, myoclonic, myoclonic-tonic-clonic, myoclonic-atonic, atonic or epileptic spasms. Generalized tonic-clonic seizures involve sudden loss of awareness or consciousness, which usually lasts 1 to 3 minutes. The first phase is the tonic phase, in which all the limbs stiffen. At first the sufferer may groan or cry out when air is forced past the vocal cords. In this period, the tongue may also be bitten. The tonic phase is followed by the clonic phase. In the clonic phase, the limbs jerk rhythmically and continuously. If the person is not breathing well, they may look dusky or bluish. Relaxation of the body may be followed by incontinence of bladder or bowel. A generalized clonic seizure is defined by continuous, bilateral, rhythmic jerking. The patient will suffer rigidity of all limbs in generalized tonic seizures. Generalized myoclonic seizures, compared to generalized clonic seizures, feature an irregular jerking that does not have to occur on both sides at the same time and may affect the limbs, face, eyes, or eyelids. Myoclonic-tonic-clonic seizures are a recently described seizure type that starts with irregular jerking on both sides and subsequently progresses into a tonic-clonic seizure [32].

3) Absence epilepsy

Clinically, absence seizures are classically defined by a sudden loss of consciousness, which starts and ends abruptly and is accompanied by a bilateral synchronous 3-Hz spike and wave discharge (SWD) on the electroencephalogram (EEG). Absence epilepsy has not been reported to exhibit auras whereas other kinds of epilepsy have. Subjects with absence epilepsy in fact have no memory of events that occur during the seizure which normally lasts ,3–10 seconds. These episodes are commonly confused with day-dreaming, as they are characterized by a fixed, vacant stare and, in particular, the condition is met with largely in children. In typical absence epilepsy, individuals suffer from orofacial twitches. Atypical absence seizures exhibit more complicated automatisms. Such abnormal episodes are more frequent and longer lasting and are frequently linked with cognitive deficits. The start and end of seizures on EEG are more gradual and there is less association between EEG and behavior abnormalities. For example, children

may be able to walk or talk during seizure episodes [33].

Risk factors:

Epilepsy is a curable disease with a high percentage of therapeutic response. The control of epilepsy with antiepileptic medicines is about 70% of patients [34]. Epilepsy is the second most debilitating condition among neurological disorders [35]. Neurological illnesses are a huge burden on society, impacting millions of people globally and having substantial social and economic consequences. Known contributions include genetic and lifestyle variables, but environmental exposures have also been implicated in the onset and progression of many illnesses in recent decades [36]. Modern agricultural systems usually rely on pesticides to protect crops from pests and illnesses, enabling the bulk production of food. But its widespread use has led to concerns about possible health dangers, especially neurological problems. In recent years the relation between pesticide exposure and epilepsy has been considered [37]. The therapy Gap is the proportion of patients with a particular ailment that require therapy but do not receive it. In a prevalence research, the TG can be calculated as the number of patients not receiving any treatment. Untreated persons with epilepsy are subject to various psychosocial and medical consequences. Although epilepsy is a very treatable disorder, a large proportion of people in underprivileged countries of the world do not obtain treatment. This is the basis of the “paradox of epilepsy” [38]. The causes of TG in epilepsy are population-specific and may differ depending to the cultural beliefs and the socioeconomic environment [39]. Those with penetrating brain injury are at significant risk of developing epilepsy [40].

Following injury there are several processes that may contribute to the circuit changes that lead to later epilepsy including necrosis, microhaemorrhage, axonal injury, apoptosis, demyelination, microgliosis, inflammation and oxidative stress and later phases of neurodegeneration, regeneration, revascularization and remodelling [41].

Pathophysiology:

Seizures are caused by abnormal synchronous neuronal firing in part or all of the brain due to irregularly established networks or networks damaged by structural, viral or metabolic problems. Genetic factors, impairment from prenatal traumas, and anomalies of cortical development are the primary causes of seizures in young patients [13]. In individuals without a hereditary predisposition for epilepsy, typical causes of seizures include encephalitis/meningitis, traumatic brain damage and brain tumors [14]. The causes of epilepsy in the elderly are most often primary neurodegenerative illnesses, head trauma and brain tumors [15, 16]. Differences in etiology of epilepsy between age groups result in a bimodal prevalence of epilepsy - with genetic/developmental causes peaking in childhood and accumulated harm to the brain (e.g. trauma, tumors) peaking in the elderly [17]. Seizures and epilepsy are sometimes used interchangeably; however, they are not the same. Focal. The start of a seizure is called Generalized Unknown Unclassifiable. Having one seizure does not prove a person has epilepsy; the seizure may have been induced and not repeated. The word “epileptogenesis” describes the development leading to status epilepticus. This idea describes the sequence of events that transforms the brain from a normal state to one that is vulnerable to seizures. This alteration assumes that clusters of neurons become hyperexcitable and tend to discharge inappropriately (18). In general, all types of epilepsy are characterized by high amounts of extracellular Ca2+ ions and glutamate,

which lead to hyperpolarization and hyperexcitability of motor neurons [19]. 1 Severe epilepsy is nowadays very much connected to genetics. Genetic epilepsy is present in around 0.4% of the human population, and comprises about 30% of all known epilepsies. More than 50 genes related to this illness have been found recently. Mutations in ion channel neurotransmitters that cause neuronal hyperexcitability or depletion of inhibitory mechanisms eventually resulting in seizures are known to be the key genetic basis of severe epileptic disorders. But other genes that cause mutations in transcription factors, intracellular signalling molecules, chromatin remodels, metabolic enzymes and even mitochondrial complex genes have been discovered in persons with hereditary epilepsy [20].

Astrocytes are a diverse cell population. They actively participate in the regulation of neuronal homeostasis and excitability, play a major role in the formation and maintenance of the BBB and are an important downstream component of the neuroinflammatory response. Disruption of any of these roles results in aberrant neural activity that predisposes to seizures. A hallmark of the epileptic focus is reactive astrogliosis, defined as astrocyte hypertrophy and altered gene expression. Altered astrocyte functions and release of gliotransmitters, pro-inflammatory cytokines and chemokines exert both seizure-promoting and seizure-protective effects on the brain microenvironment. The participation of astrocytes in epilepsy and their key functions in the modulation of neuronal excitability were originally discussed within the framework of convulsive epilepsies, as comprehensively described by our group and others [21]. Microglia are macrophage-like cells that are located in the brain and constantly interact with neurons and other glial cells to modulate neuronal activity, under normal and pathological situations [22]. Recent studies have further defined the complicated involvement of microglia in epilepsy and provided new insights into the particular molecular processes and pathways through which microglial activation promotes seizure onset and neuroinflammation [24]. Although there is growing understanding regarding microglial properties under normal conditions, it is mostly unknown whether and how microglia affect the construction and function of neuronal circuits in diseased conditions. Microglia are rapid responders to infections and primary injuries such as traumatic brain injury or stroke, contributing to neuroinflammation and/or imbalance in neurotransmission control, and also synthesis and release neurosteroids as an anti-epileptogenic target [23]. Oligodendrocytes are specialized glial cells in the CNS that nourish and sustain neurons. The functionally integrated neuron–glia network is now known to be involved in the etiology of seizures and epilepsy. Oligodendrocytes that communicate with other glial cells via GJs have a major function of forming the myelin sheath that surrounds and insulates axons, providing rapid and efficient neurotransmission [21].

Oligodendrocytes wrap a multi-layered lipid rich membrane, myelin, around the axons of neurons. This is necessary for quick and effective propagation of action potentials in the CNS. It acts as a natural electrical insulator for axons, decreases membrane capacitance and is an important structural factor in governing precise synaptic connections between neurons [26]. Oligodendrocytes are responsible not only for producing the myelin sheath that envelopes axons and controls the pace of action potential conduction, but also for metabolically supporting axons and finely adjusting the dynamics of neuronal circuits [25]. Myelination is not simply the wrapping of the axon; neuronal axons undergo many alterations before and during the myelination process. Such changes include the

organization and localization of major voltage-gated ion channels and seem to be crucial in epilepsy. Myelin abnormalities have been already described in patients with epilepsy and seizures are common in demyelinating disorders such as multiple sclerosis, suggesting that myelination may be involved in the facilitation of seizure activity [27]. Genetic background contributes to the genesis of epilepsy in about 40% of persons with epilepsy. Most familial epilepsies, such as juvenile myoclonic epilepsy, children absence epilepsy and benign childhood epilepsy with centrotemporal spikes, have a complex pattern of inheritance, with the interaction of several loci and environmental variables [28, 29].

Case

Mr OB is a 44-year-old man who suffers from partial epilepsy. An MRI scan shows a choroid cyst on the right temporal lobe, bilateral hippocampal sclerosis and cerebral atrophy. Seizures take the form of complex partial attacks and at night secondary generalisations occur. He has had trials of treatment with every single drug in the book and almost every combination. Six months ago, he was taking 225mg of topiramate (could not tolerate more), 400mg of phenytoin and 10mg of clobazam each day. At this point levetiracetam was added and titrated up to 2000mg a day. This led to a significant improvement in seizure control. Indeed, seizures have almost completely been abolished and he is only having occasional nocturnal events. He is, however, complaining of drowsiness and periods of unsteadiness.

Question

What treatment is appropriate for this patient?

Answer

Mr OB needs his drug regimen optimising. The decision should be made to reduce either the dose of topiramate or that of phenytoin. The consensus view is that phenytoin should probably be reduced first. However, this patient had a bad experience in the past when an attempt was made to discontinue phenytoin, at which time he had a significant increase in seizure frequency. It would, therefore, be more appropriate to discontinue topiramate in Mr OB. This was done and his improvement has been maintained [42].

Mr. OB is a 44-year-old male patient with drug-resistant (pharmacoresistant) focal epilepsy, meaning seizures that originate in a specific area of the brain but have not responded well to previous attempts with antiseizure drugs, with secondary generalization, or the spread of the seizure activity from its focal onset to both sides of the brain. The clinical issue here is rationalizing his antiseizure polytherapy* (ie, reviewing and adjusting his combination of antiseizure medications). He responded very well to levetiracetam, an antiseizure drug.

S- Subjective Assessment

Chief Complaints:
Name of patient- Mr OB
Age- 44 years old
Gender- Male
Medical history- longstanding partial epilepsy characterized by complex partial seizures, with secondary generalization occurring predominantly during the night. Neuroimaging revealed a right temporal choroid cyst, bilateral hippocampal sclerosis, and cerebral atrophy, indicating significant structural abnormalities associated with his refractory epilepsy
Medication history- Six months earlier, his treatment consisted of topiramate 225 mg/day, phenytoin 400 mg/day, and clobazam 10 mg/day. Higher dose of topiramate could not tolerate because it shows adverse effects. Levetiracetam

was subsequently introduced and gradually increased to 2000 mg/day. This addition resulted in a marked improvement in seizure control, with the seizures becoming almost completely controlled and only occasional nocturnal episodes persisting.

Social history- The patient experienced drowsiness or somnolence, with increased sleepiness and reduced alertness that could affect daily activities. The patient experienced episodes of instability and unsteady movements, sometimes failing to maintain an upright posture. There was also improvement in the general condition; however, isolated night seizures were still present, which means that the patient's condition is not fully controlled yet. These residual night time seizure episodes suggest that, although the treatment was effective in substantially reducing the overall seizure burden, some breakthrough events continued to occur.

O- Objective Assessment

Parameter	Finding
Age/Sex	44-year-old male
Diagnosis	Focal epilepsy with secondary generalization; difficult-to-control history
MRI	Right temporal choroid cyst; bilateral hippocampal sclerosis; cerebral atrophy
Topiramate	225 mg/day; higher doses not tolerated
Phenytoin	400 mg/day
Clobazam	10 mg/day
Levetiracetam	2000 mg/day; substantial improvement in seizure control
Current adverse effects	Drowsiness and unsteadiness
Previous phenytoin withdrawal	Significant increase in seizure frequency

A- Assessment

Primary assessment:

The patient has drug resistant focal epilepsy that is manifested by seizures limited to one area of the brain which then can spread to involve both sides of the brain causing secondary generalized seizures. Addition of levetiracetam has resulted in substantial reduction in seizure frequency implying that the patient's epilepsy is well controlled despite being drug resistant.

Drug related problems:

Excessive CNS adverse effects – The patient is experiencing adverse effect of the central nervous system which may hinder his daily activities. This includes sleepiness, dizziness, imbalance and coordination problems.

Polypharmacy – Concurrent use of four antiseizure medicines poses as a great challenge especially since the addition of levetiracetam has improved the situation tremendously.

Risk of increase in seizures – Discontinuation of one of the antiseizure medicines that is effective poses a great risk of aggravation of seizures. This is evident by the fact that discontinuation of

phenytoin resulted in increased number of seizures.

Need to sustain seizure control while reducing treatment burden – the main issue in this case is the need to maintain the impressive seizure control while reducing the treatment burden and adverse effect on the CNS.

Clinical decision

I would advocate for discontinuation of topiramate rather than phenytoin due to the fact that although the addition of levetiracetam resulted in substantial improvement, discontinuation of phenytoin resulted in increased number of seizures. The fact that phenytoin contributed to increased number of seizures when withdrawn implies that it was effective in maintenance of seizure control hence the need to continue with it. It is therefore recommended to taper the dose of topiramate under the specialist's supervision to reduce adverse effects associated with polypharmacy and excessive CNS depression.

P- Plan

Goal of plan

Ensure near-complete seizure control: The major goal is to prevent a recurrence of focal or nocturnal generalized seizures after the addition of levetiracetam. Reduce the quantity of drug taken with extra precaution to ensure that there is no effect of seizures

Decrease drowsiness and unsteadiness: The patient presents with CNS-related adverse effects, such as drowsiness, dizziness, coordination and unsteadiness. The drugs that shows a adverse effects that drugs should be avoid

Decrease the number of coexisting antiseizure medication: Multiple antiseizure medications can have a large number of negative interactions and also cause adverse effects. It would be best to reduce the number of drugs to the lowest effective number.

Avoid the development of withdrawal-type seizures: Stopping an antiseizure drug suddenly or reducing it in an unwise manner might result in a worsening of the condition as the body does not get used to the abrupt change in drug levels in the system. Any drug that will be stopped should be slowly tapered down to a point where it is no longer needed.

Enhance the patient's quality of life, degree of consciousness, and functional capabilities: By decreasing adverse effects, the patient will become more conscious and active, which is essential to their overall safety and well-being.

Prevent injuries caused by seizures and their effect on the patient and his family: Seizure episodes frequently cause injuries that can vary from small scrapes to more severe head injuries. Night time generalized seizures were also worrying because they could lead to serious problems. Keeping seizures well controlled greatly helps reduce the chance of these dangers.

Pharmacological treatment

Slow and gradual withdrawal of topiramate: The topiramate discontinuation must be performed slowly in order to minimize the risk of developing seizures which might occur if the drug is reduced too quickly. During this process, the patient should continue taking levetiracetam in a dosage of 2000 mg/day, as well as phenytoin and clobazam in 400 mg/day and 10 mg/day, respectively. The decision to stops the medication is taken by the neurologist it depends upon the patient tolerate the medication and seizure control.

Rationale for choosing topiramate for withdrawal: Topiramate was the preferred drug to be discontinued because the patient already had a significant increase in the number of seizures after the last withdrawal of phenytoin. This suggests that topiramate may not be a major contributor to the development of seizures. However, since this was not the case for phenytoin, it would be best to first withdraw any drug except for this one.

The rationale behind continuing levetiracetam is that it had a significant positive effect on the patient, as it helped to control the seizures almost completely after being added to the treatment regimen. It is important to continue using this drug to keep the protective effect, especially during the period of withdrawal of another medication. After topiramate has been successfully withdrawn and the patient has stabilized, the remaining drugs will be considered for discontinuation on an individual basis.

Drug profile [43- 46]

Drug	MOA	ADRs	Drug Interaction
Levetiracetam	Bind to synaptic vesicle proteins SV2A	Tremor, dizziness, behavioural disturbances	Bamazepine, methotrexate or phenytoin due to toxicity in some patients
Phenytoin	Blockade of neuronal voltage dependent sodium channels	Ataxia, cognitive dysfunction, dyskinesia	Phenytoin is an enzyme inducer and may reduce the serum levels and clinical effects of many other drugs
Clobazam	1,5-benzodiazepine; enhances GABA-A	Unsteadiness, risk of falls, weakness	___
Topiramate	Enhance GABA receptor, block sodium channel	Somnolence and fatigue	Plasma concentration of digoxin decreased by 12%

Non-pharmacological treatment

Therefore, strict adherence to a normal sleep-wake pattern is part of 'lifestyle hygiene' essential for these patients, and should be addressed as part of their treatment regimen [47]. Another well-known non-specific factor that increases seizure vulnerability is excessive alcohol intake [48]. The ketogenic diet is a treatment for epilepsy that is resistant to antiepileptic medicines and is mainly used in young individuals with difficult-to-control episodes. The ketogenic diet is a particular diet that is high in fat and low in carbohydrates, commonly with a ratio of 4:1 or 3:1. It is converted into ketone bodies (beta-hydroxy butyrate or aceto acetate) and it also potentiates the activity of GABA in the brain [49]. Yoga practice is geared toward relaxation, which reduces stress, a major cause for seizures [50]. Biofeedback is a non-invasive behavioral therapy based on the principles of operant training. Subjects acquire self-regulation by receiving direct feedback information on covert physiological signals, leading to a better volitional control of physiological processes of which they were not even aware before [51]. Music therapy is one of the complementary treatments for patients with DRE. The processes by which music stimuli may operate to improve epilepsy control are currently poorly understood [52]. Aromatherapy is an alternative/complementary treatment of stress symptoms associated with epilepsy. Some essential oils are known to have a calming and relaxing impact, which may be involved in people with epilepsy provoked by stress. The technique is

based on massages using essential oils diluted in a light oil for external massage. The oils are absorbed by the skin and their ingredients swiftly move to the CNS. Probably a part is absorbed through the olfactory system as well [53].

Points to Patient

Explain the problem Patient's seizure control has improved significantly since the addition of levetiracetam. The ongoing issue is excessive drowsiness and unsteadiness, which may be related to the overall CNS effects of several antiseizure medicines. Do not suddenly stop antiseizure medicines as withdrawal may precipitate seizures. Medication Counselling Take medicines as prescribed. Do not alter or stop any antiseizure medicine independently. Avoid alcohol and other CNS depressants as they may intensify sedation/unsteadiness. Maintain good hydration especially while taking topiramate the reference recommends enhanced fluid intake to reduce risk of kidney stones. Report worsening drowsiness, severe imbalance, abnormal eye movements, confusion, rash or increased seizures.

Safety

Due to his unsteadiness, counsel regarding precautions taking driving, working at heights, operating machinery and other activities where impaired coordination could result in injury. Maintain a good sleep pattern. Avoid known seizure precipitants. Maintain a seizure diary including date, time, type, duration and possible triggers.

Points for Physician

Main therapeutic problem Drug related problem: adverse effects of combination treatment, particularly drowsiness and unsteadiness, despite impressive improvement in seizure control. The clinical-pharmacy approach emphasizes recognition of medication-related problems and selection of an appropriate regimen that achieves therapeutic goals without causing toxicity. Recommended Intervention Primary recommendation: discontinue/topiramate reduction instead of phenytoin.

Reason

Levetiracetam has led to significant improvement in seizure control. The patient is experiencing clinically significant CNS adverse effects.
Phenytoin is usually thought about for lowering because it has side effects and a small safe dose range. But this patient had a big increase in seizures before when phenytoin was stopped. So, the case clearly says to stop topiramate instead. The published case reports that seizure improvement was maintained following topiramate withdrawal. Important Caution Topiramate should not just be stopped abruptly without specialist supervision. Antiseizure medicines should generally be tapered to reduce the risk of withdrawal seizures; the reference warns specifically against the abrupt withdrawal of AEDs.

Drug ADR Monitoring Plan

Mr OB – Partial Epilepsy

Drug & Dose	Why Monitoring Is Important	Relevant ADRs	Monitoring Parameters	Action / Clinical Recommendation
Phenytoin – 400 mg/day	Phenytoin has nonlinear pharmacokinetics and a	• Nystagmus • Ataxia/unsteadine	• Serum phenytoin concentration • Seizure frequency	Continue initially. Previous phenytoin withdrawal caused

Drug & Dose	Why Monitoring Is Important	Relevant ADRs	Monitoring Parameters	Action / Clinical Recommendation
	narrow therapeutic range. Small dose adjustments can cause substantial changes in serum concentration. Approximate therapeutic range: 10–20 mg/L.	ss • Lethargy • Gingival hypertrophy • Skin rash	• Nystagmus • Ataxia/unsteadiness • Lethargy • Gingival status • Skin rash • Drug interactions • CBC/LFTs when clinically indicated	increased seizure frequency. Because of current unsteadiness, assess phenytoin exposure carefully.
Topiramate – 225 mg/day	Topiramate may cause CNS adverse effects including drowsiness, dizziness, impaired concentration and fatigue.	• Drowsiness • Dizziness • Impaired concentration • Fatigue • Paraesthesia • Nephrolithiasis/kidney stones	• Drowsiness • Cognitive function • Dizziness/coordination • Seizure frequency during taper • Renal function/clinical renal status • Symptoms of kidney stones • Hydration	Gradual withdrawal/discontinuation under neurologist supervision. This is the preferred drug to withdraw in Mr OB because of his previous worsening after phenytoin withdrawal.
Clobazam – 10 mg/day	Clobazam is a benzodiazepine and may contribute to CNS depression. Withdrawal may be difficult.	• Sedation/drowsiness • Dizziness • Behavioural effects • Dry mouth • Withdrawal symptoms	• Sedation/drowsiness • Dizziness • Cognitive impairment • Behavioural changes • Dependence • Withdrawal symptoms • Seizure recurrence	Continue initially. Do not discontinue abruptly. If withdrawal is later required, taper gradually with close seizure monitoring.
Levetiracetam – 2000 mg/day	Levetiracetam produced significant improvement in seizure control, with seizures almost completely abolished. It should therefore initially be retained while the regimen is optimized.	• Drowsiness/somnolence • Mood/behavioural changes	• Seizure frequency and severity • Drowsiness/somnolence • Alertness and functional status • Mood/behavioural changes • Adherence • Renal function when clinically appropriate	Continue initially because it produced the major improvement in seizure control. Reassess drowsiness after topiramate withdrawal.

Overall Clinical Goal: Maintain seizure control, minimize adverse effects and polypharmacy.

Suggestions to Physician

Immediate Plan

Step 1 – Assess current adverse effects Assess severity of drowsiness and unsteadiness. Neurological examination including gait/coordination and nystagmus. Review medication adherence/timing. Review alcohol/other sedatives. Check if there is any medication changes.

Step 2 – Review phenytoin exposure Check serum phenytoin concentration when clinically indicated, especially due to ataxia/unsteadiness. Review interacting medicines. Avoid unnecessary dose changes since phenytoin has nonlinear pharmacokinetics.

Step 3 – Deprescribe topiramate Reduce topiramate gradually according to treating neurologist's individualized taper. Do not abruptly stop it. Continue levetiracetam, phenytoin and clobazam initially while assessing response.

Step 4 – Evaluate response Determine if drowsiness and unsteadiness improve. Ensure seizure control remains satisfactory.

Step 5 – Reassess polytherapy If symptoms persist despite topiramate withdrawal, reassess remaining regimen. when last time phenytoin withdrawal led to enhanced seizure frequency, phenytoin should not be withdrawn casually.

Follow-up Plan

Follow-up period What to assess 1-2 weeks-Drowsiness, gait/unsteadiness, adherence, seizure diary, adverse effects 2-4 weeks-Response to topiramate dose reduction, seizure recurrence, phenytoin toxicity 4-8 weeks-Stability of seizure control and functional improvement ~3 months-Full medication review, seizure frequency, adverse effects, need for further optimization of the seizure regimen Long Term-Periodic neurologist/epilepsy-clinic review, seizure diary, medication adherence and safety.

REFERENCES

1. Fisher RS, Boas WV, Blume W, Elger C, Genton P, Lee P, Engel Jr J. Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia. 2005 Apr;46(4):470-2.
2. Thurman DJ, Beghi E, Begley CE, Berg AT, Buchhalter JR, Ding D, Hesdorffer DC, Hauser WA, Kazis L, Kobau R, Kroner B. Standards for epidemiologic studies and surveillance of epilepsy. Epilepsia. 2011 Sep;52:2-6.
3. Duncan JS, Sander JW, Sisodiya SM, Walker MC. Adult epilepsy. The Lancet. 2006 Apr 1;367(9516):1087-100.
4. Engel Jr J. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. Epilepsia. 2001 Jun;42(6):796-803.
5. Lee BI. Classification of epileptic seizures and epilepsy syndromes. Neurology Asia. 2013 Mar 2;18(1):1-4.
6. Krumholz A, Wiebe S, Gronseth G, Shinnar S, Levisohn P, Ting T, Hopp J, Shafer P, Morris H, Seiden L, Barkley G. Practice Parameter: evaluating an apparent unprovoked first seizure in adults (an evidence-based review):[RETIRED] report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2007 Nov 20;69(21):1996-2007.
7. DeToledo JC, Ramsay RE. Patterns of involvement of facial muscles during epileptic and nonepileptic events: review of 654 events. Neurology. 1996 Sep;47(3):621-5.
8. Beghi E, Balzarini C, Bogliun G, Logroscino G, Manfredi L, Mazzini L, Micheli A, Millul A, Poloni M, Riva R, Salmoiraghi F. Reliability of the El Escorial diagnostic criteria for amyotrophic lateral sclerosis. Neuroepidemiology. 2002 Nov 1;21(6):265-70.
9. Fisher RS, Cross JH, D'souza C, French JA, Haut SR, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshé SL, Peltola J. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia. 2017 Apr;58(4):531-42.
10. Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshé SL, Peltola J, Roulet Perez E, Scheffer IE. Operational classification of seizure types by

the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017 Apr;58(4):522-30.
11. Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, Hirsch E, Jain S, Mathern GW, Moshé SL, Nordli DR. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017 Apr;58(4):512-21.
12. Benbadis SR, LaFrance Jr WC, Papandonatos GD, Korabathina K, Lin K, Kraemer HC. Interrater reliability of EEG-video monitoring. Neurology. 2009 Sep 15;73(11):843-6.
13. Aaberg KM, Surén P, Søraas CL, Bakken IJ, Lossius MI, Stoltenberg C, Chin R. Seizures, syndromes, and etiologies in childhood epilepsy: the international league against epilepsy 1981, 1989, and 2017 classifications used in a population-based cohort. Epilepsia. 2017 Nov;58(11):1880-91.
14. Bosak M, Słowik A, Kacorzyk R, Turaj W. Implementation of the new ILAE classification of epilepsies into clinical practice—A cohort study. Epilepsy & Behavior. 2019 Jul 1;96:28-32.
15. Liu S, Yu W, Lü Y. The causes of new-onset epilepsy and seizures in the elderly. Neuropsychiatric disease and treatment. 2016 Jun 17:1425-34.
16. Cloyd J, Hauser W, Towne A, Ramsay R, Mattson R, Gilliam F, Walczak T. Epidemiological and medical aspects of epilepsy in the elderly. Epilepsy research. 2006 Jan 1;68:39-48.
17. Tanaka A, Akamatsu N, Shouzaki T, Toyota T, Yamano M, Nakagawa M, Tsuji S. Clinical characteristics and treatment responses in new-onset epilepsy in the elderly. Seizure. 2013 Nov 1;22(9):772-5.
18. Scharfman HE. The neurobiology of epilepsy. Current neurology and neuroscience reports. 2007 Jul;7(4):348-54.
19. Boleti AP, Frihling BE, e Silva PS, Cardoso PH, de Moraes LF, Rodrigues TA, Biembengute ME, Koolen HH, Migliolo L. Biochemical aspects and therapeutic mechanisms of cannabidiol in epilepsy. Neuroscience & Biobehavioral Reviews. 2022 Jan 1;132:1214-28.
20. Hebbar M, Mefford HC. Recent advances in epilepsy genomics and genetic testing. F1000Research. 2020 Mar 12;9:F1000-aculty.
21. Onat F, Andersson M, Çarçak N. The role of glial cells in the pathophysiology of epilepsy. Cells. 2025 Jan 10;14(2):94.
22. Paolicelli RC, Sierra A, Stevens B, Tremblay ME, Aguzzi A, Ajami B, Amit I, Audinat E, Bechmann I, Bennett M, Bennett F. Microglia states and nomenclature: A field at its crossroads. Neuron. 2022 Nov 2;110(21):3458-83.
23. Kinoshita S, Koyama R. Pro-and anti-epileptic roles of microglia. Neural regeneration research. 2020 Dec 12;16(7):1369.
24. Pinto MJ, Ragozzino D, Bessis A, Audinat E. Microglial modulation of synaptic maturation, activity, and plasticity. Microglia: Physiology, Pathophysiology and Therapeutic Potential. 2024 Aug 30:209-19.
25. Knowles JK, Batra A, Xu H, Monje M. Adaptive and maladaptive myelination in health and disease. Nature Reviews Neurology. 2022 Dec;18(12):735-46.
26. Bradl M, Lassmann H. Oligodendrocytes: biology and pathology. Acta neuropathologica. 2010 Jan;119(1):37-53.
27. de Curtis M, Garbelli R, Uva L. A hypothesis for the role of axon demyelination in seizure

generation. Epilepsia. 2021 Mar;62(3):583-95.
28. Gardiner RM. Impact of our understanding of the genetic aetiology of epilepsy. Journal of neurology. 2000 May;247(5):327-34.
29. McNamara JO. Emerging insights into the genesis of epilepsy. Nature. 1999 Jun 24;399(6738):A15-22.
30. Shorvon S, Guerrini R, Cook M, Lhatoo S, editors. Oxford textbook of epilepsy and epileptic seizures. OUP Oxford; 2012 Dec 20.
31. Ayala GF, Dichter M, Gumnit RJ, Matsumoto H, Spencer WA. Genesis of epileptic interictal spikes. New knowledge of cortical feedback systems suggests a neurophysiological explanation of brief paroxysms. Brain research. 1973 Mar 30;52:1-7.
32. Pack AM. Epilepsy overview and revised classification of seizures and epilepsies. Continuum. 2019 Apr;25(2):306-21.
33. Manning JP, Richards DA, Bowery NG. Pharmacology of absence epilepsy. Trends in pharmacological sciences. 2003 Oct 1;24(10):542-9.
34. Brodie MJ, Barry SJ, Bamagous GA, Norrie JD, Kwan YP. Patterns of treatment response in newly diagnosed epilepsy. Neurology. 2012 May 15;78(20):1548-54.
35. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V, Abraham J. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. The lancet. 2012 Dec 15;380(9859):2163-96.
36. Fu C, Kuang D, Zhang H, Ren J, Chen J. Different components of air pollutants and neurological disorders. Frontiers in public health. 2022 Nov 28;10:959921.
37. Requena Mullor MD, Parrón Carreño T, Navarro A, García González J, Ventura Miranda MI, Hernández AF, Alarcón Rodríguez R. Association between environmental exposure to pesticides and epilepsy.
38. Kale R. The treatment gap. Epilepsia. 2002 Jul;43:31-3.
39. Mbuba CK, Ngugi AK, Fegan G, Ibinda F, Muchohi SN, Nyundo C, Odhiambo R, Edwards T, Odermatt P, Carter JA, Newton CR. Risk factors associated with the epilepsy treatment gap in Kilifi, Kenya: a cross-sectional study. The Lancet Neurology. 2012 Aug 1;11(8):688-96.
40. Raymont V, Salazar AM, Lipsky R, Goldman D, Tasick G, Grafman J. Correlates of posttraumatic epilepsy 35 years following combat brain injury. Neurology. 2010 Jul 20;75(3):224-9.
41. Pitkänen A, Ndode-Ekane XE, Lapinlampi N, Puhakka N. Epilepsy biomarkers–toward etiology and pathology specificity. Neurobiology of disease. 2019 Mar 1;123:42-58.
42. Walker R. Clinical pharmacy and therapeutics E-Book. Elsevier Health Sciences; 2011 Oct 24.
43. Howard P, Remi J, Remi C, Charlesworth S, Whalley H, Bhatia R, Hitchens M, Mihalyo M, Wilcock A. Levetiracetam. Journal of pain and symptom management. 2018 Oct 1;56(4):645-9.
44. Shorvon S, Perucca E, Engel Jr J, editors. The treatment of epilepsy. John Wiley & Sons; 2015 Sep 15.
45. Tolbert D, Larsen F. A comprehensive overview of the clinical pharmacokinetics of clobazam. The Journal of Clinical Pharmacology. 2019 Jan;59(1):7-19.
46. Rosenfeld WE. Topiramate: a review of preclinical, pharmacokinetic, and clinical data. Clinical therapeutics. 1997 Nov 1;19(6):1294-308.

47. Janz D. Pitfalls in the diagnosis of grand mal on awakening. Epileptic seizures and syndromes. 1994:213-20.
48. Bourgeois BF. Behavioural and social therapy. Epilepsy in children. London: Chapman & Hall. 1996:557-9.
49. Bough KJ, Schwartzkroin PA, Rho JM. Calorie restriction and ketogenic diet diminish neuronal excitability in rat dentate gyrus in vivo. Epilepsia. 2003 Jun;44(6):752-60.
50. Shawahna R, Hattab S, Al-Shafei R, Tab'ouni M. Prevalence and factors associated with depressive and anxiety symptoms among Palestinian medical students. BMC psychiatry. 2020 May 19;20(1):244.
51. Alqahtani F, Imran I, Pervaiz H, Ashraf W, Perveen N, Rasool MF, Alasmari AF, Alharbi M, Samad N, Alqarni SA, Al-Rejaie SS. Non-pharmacological interventions for intractable epilepsy. Saudi Pharmaceutical Journal. 2020 Aug;28(8):951-62.
52. Haut SR, Gursky JM, Privitera M. Behavioral interventions in epilepsy. Current Opinion in Neurology. 2019 Apr 1;32(2):227-36.
53. Betts TI. Use of aromatherapy (with or without hypnosis) in the treatment of intractable epilepsy—a two-year follow-up study. Seizure. 2003 Dec 1;12(8):534-8.

HOW TO CITE: Harshal Tale, Kartik Tale, Tejas Khote, Prachi Shamkuwar, Tanishka Thool, Kalyani Lad, Bhumi Sonone, Current Approaches to Epilepsy Management: A Compressive Case-Based Evidence Review of Pathophysiology, Diagnosis, Pharmacotherapy and Clinical Outcomes, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 9, 3206-3221, https://doi.org/10.5281/zenodo.22953424