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A REVIEW OF ANTIEPILEPTIC DRUGS AND THEIR ASSOCIATED ADVERSE EVENTS

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ABSTRACT

Epilepsy is such a chronic neurological disorder that has recurrent unprovoked seizures and affects millions of people worldwide. Antiepileptic drugs are central in managing the disease to lessen or eradicate seizure episodes and improve patients' quality of life. Despite their therapeutic potential, AEDs are often associated with various unwanted events that can significantly adversely affect treatment adherence, tolerability, and long-term outcomes. This overall review elaborates on the pharmacological classifications, mechanisms of action, and clinical applications of first-generation and second-generation AEDs. More importantly, common drug reactions, which may range from mild side effects such as dizziness and gastrointestinal discomfort to more severe events including hepatotoxicity, dermatological reactions, psychiatric disturbances, and hematological abnormalities. Genetic and patient-specific factors in adverse drug reactions, therapeutic drug monitoring, and individualized approaches are discussed in this review. Safety profile evaluation is essential for treatment optimization to prevent risks and improve patient outcomes.

KEYWORDS: Epilepsy, Antiepileptic drugs (AEDs), Adverse drug reactions, Mechanism of action, Individualized treatment.

INTRDOUCTION

Seizures are episodes that recur, having no provocation and being resultant from abnormal electrical activities in the brain. Epilepsy is a chronic neurological disorder wherein the seizures are differentiated according to their types, number, and intensity, which may amount from a few minute lapses of attention or limited muscle contraction to serious, much longer periods of violent spasms.

All ages can be affected by epilepsy, which additionally is important in social, psychological, and economic terms. Although considered as one of the more common neurological disorders, there is considerable stigma and misunderstanding associated with it, especially in low- and middle-income countries (LMICs).[1,2] Epilepsy is a chronic neurological disorder with recurrent unprovoked seizures due to abnormal electrical activity in the brain. It affects individuals of all ages, with a global estimate of It counts around 50 million persons worldwide making one of the most common diseases in neurologies.

The higher incidence of this condition has been attributed to low-and-middle-income countries because of the inadequacy of health available to them, increasing the threat of infections that mostly affect the brain, and factors that have genetic predisposition. In high-income countries, a prevalence of 5-10 cases of epilepsy is estimated per 1,000; however, in low and middle-income countries, the estimate can rise as high as 10-20 cases in concerned ratios.

Stigma associated with epilepsy and its related unawareness is a major public health challenge, especially within underserved areas. Timely diagnosis and apt treatment including antiepileptic medicine and surgical intervention become important measures for improving the quality of life for people concerned with epilepsy.[3,4,5]

TYPES OF EPIELPSY/SEIZURES[6,7,8]

Table 1: Types of Epilepsy/Seizures.

Type	Subtype	Description
Focal Seizures	Focal Aware Seizures	Seizures limited to one area of the brain with preserved awareness; may involve motor or sensory symptoms.
	Focal Impaired Awareness	Seizures start in one area, with impaired awareness; may involve automatisms (e.g., lip-smacking).
Generalized Seizures	Absence Seizures	Brief episodes of staring or loss of awareness; commonly seen in children.
	Tonic-Clonic Seizures	Involves loss of consciousness, stiffening of muscles (tonic), followed by rhythmic jerking (clonic).
	Myoclonic Seizures	Sudden, brief muscle jerks involving part or all of the body.
	Tonic Seizures	Sudden stiffening of muscles, often affecting the back, arms, and legs.
	Atonic Seizures	Sudden loss of muscle tone, leading to falls ("drop attacks").
	Clonic Seizures	Repetitive, rhythmic muscle jerking, typically bilateral.
Unknown Onset	Seizures of Unclear Origin	Seizures whose onset is unclear or not witnessed.
Epilepsy Syndromes	Lennox-Gastaut Syndrome	Severe epilepsy with multiple seizure types and intellectual disability.
	Juvenile Myoclonic Epilepsy	Characterized by myoclonic seizures, often after waking up, in teens or young adults.
	Dravet Syndrome	Rare genetic epilepsy beginning in infancy, resistant to treatment, with various seizure types.

PATHOGENESIS OF EPILEPSY

Disruption in the normal activity balance between excitation and inhibition at appropriate places in the brain is a complex process that leads to aberrant synchronized electric discharges in epilepsy and seizures.

The pathogenesis of epilepsy and seizures includes multifactored involvement of various circuitry in the brain which is inwardly attributed to imbalance in excitatory and inhibitory signals. Neuronal activities in the brain are relayed mainly through electrical impulses. Epilepsy is that kind of electrical abnormality that results in seizures.

The imbalances can be caused by genetic mutations, structural brain abnormalities, or environmental factors like head trauma or infections. Excitatory neurotransmitters (for instance, glutamate) become hyperactive but inhibitory neurotransmitters (for instance, gamma-aminobutyric acid, or GABA) do not curtail hyperactivity.

For this reason communications fail and it results in the phenomenon called abnormal synchronous firing of neurons hence seizures. Structural changes contribute at some times like scar tissue, neuroinflammation, or failed neuronal connections, as well play a major role in epilepsy's inception and detriment.

Sometimes damage to the brain can be insult or injury. This is a condition of excitogenesis that transforms normal brain into epileptic brain, thus predisposing it towards having recurrent seizures.[9,10,11]

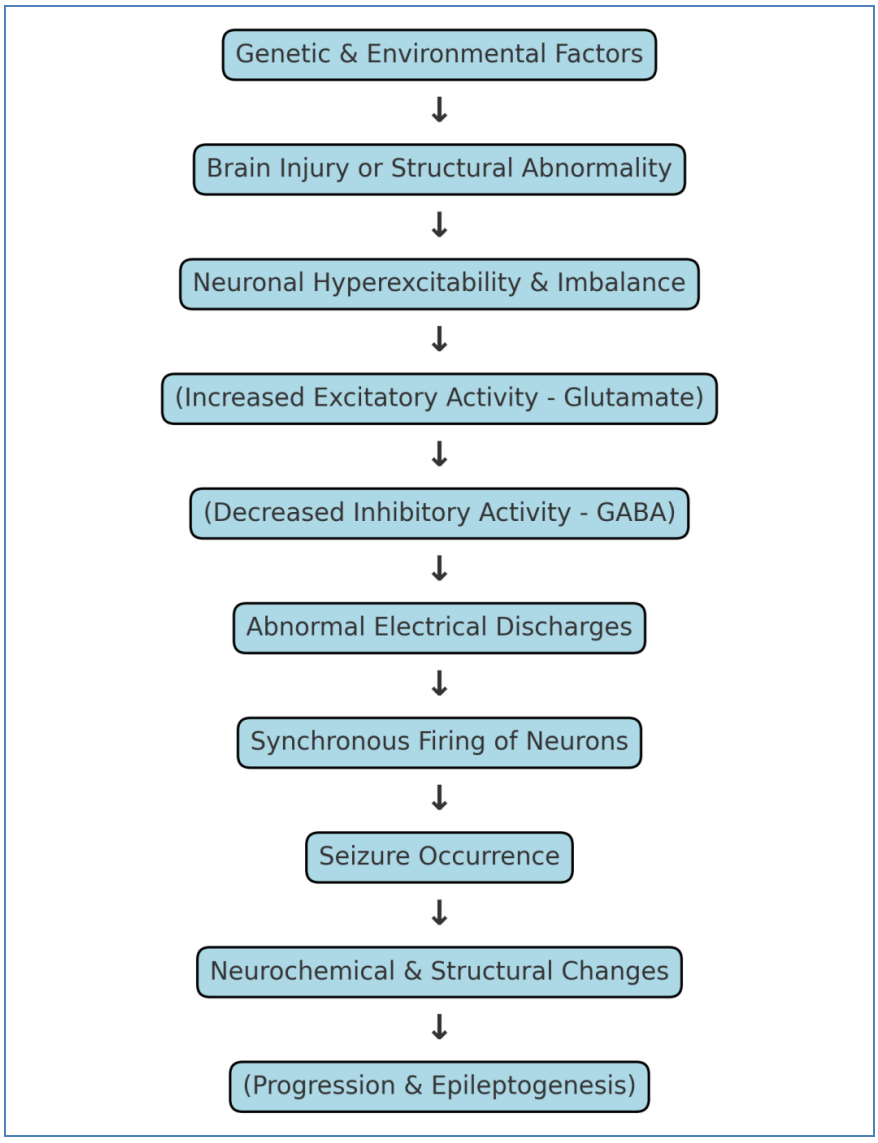

Figure 1: Pathogenesis of Epilepsy.

Risk Factors/Etiological Factors[12,13,14]

Table 2: Risk factors of Epilepsy.

Category	Specific Factors
Genetic Factors	- Mutations in genes affecting ion channels, neurotransmitter systems, or synaptic function.
	- Genetic syndromes such as Dravet syndrome, Lennox-Gastaut syndrome, and juvenile myoclonic epilepsy.
Structural Causes	- Congenital brain malformations (e.g., cortical dysplasia, heterotopia).
	- Brain tumors, stroke, traumatic brain injury, or neurodegenerative diseases (e.g., Alzheimer's disease).
Infections	- Central nervous system (CNS) infections like meningitis, encephalitis, neurocysticercosis, and brain abscess.
Immune-Mediated Causes	- Autoimmune encephalitis (e.g., anti-NMDA receptor encephalitis).
	- Inflammatory conditions like multiple sclerosis.
Metabolic Disorders	- Hypoglycemia, hyperglycemia, hyponatremia, hypernatremia, hypocalcemia, or uremia.
Perinatal/Neonatal Factors	- Hypoxic-ischemic encephalopathy, birth trauma, or neonatal infections.
	- Maternal substance abuse or malnutrition.
Toxic or Drug-Induced	- Drug withdrawal (e.g., alcohol, benzodiazepines).
	- Toxic exposures (e.g., heavy metals, carbon monoxide).
Idiopathic	- Cases where no identifiable cause is found, often presumed to be genetic or functional.

DIAGNOSIS

The diagnosis of epilepsy is comprehensive, including a careful medical history, physical examination, and a variety of tests, to confirm and to try to understand the possible cause of epilepsy. The initial step is to obtain a very comprehensive medical history. The physician, who is here, carefully scales the symptoms as well as seizure characteristics (beginning, duration, type, triggers, etc), and the presence of a family history of epilepsy or other conditions of the nervous system. In patients who have had a seizure episode, a comprehensive physical and neurological examination can be performed looking for possible neurological deficits that could explain abnormality in the brain.[15,16]

The next step would be to perform an electroencephalography (EEG) recording test, which is vital for diagnosis because it shows electrical activity in the brain. EEG can also show abnormal patterns of an activity between seizures or in seizure-like forms and help in estimating the types of epilepsy. Neuroimaging, such as magnetic resonance imaging (MRI) or tomodensitometry, is performed to detect an organic cause of seizures such as a tumor, malformation, lesion, etc. Then, for a metabolic or genetic cause, blood tests and genetic screening may be done to check for abnormalities in electrolytes and glucose and genetic mutations involving epilepsy.

Some other tests such as Video EEG monitoring or functional MRI may be required to perform a more in-depth evaluation. Moreover, neuropsychological tests should be employed to evaluate cognitive function, particularly when the seizures impact the mental capabilities of the patient. Diagnosis is thereby made after eliminated the potential other possible causes for the seizures plus confirming that there are recurrent unguided seizures which are in accordance with epilepsy. Diagnosis is particularly important since it will inform the history and most effective approach to treating that person, be it through antiepileptic medication or surgery.[17,18]

TREATMENT

To treat the symptoms of epilepsy, one tends to focus on helping control seizures, enhancing the life quality of individuals dealing with the disease, and alleviating any other conditions associated with it. Choosing an individualized treatment for managing epilepsy requires taking into account several essentials such as form of epilepsy, seizure frequency, patient's age, presence of co-morbidities, and previous treatment responses. The following serves as the major approaches for treating epilepsy:

1. Antiepileptic Drugs (AEDs)

- **First-Line Therapy:** Antiepileptic drugs (AEDs) are the mainstay treatment in drug therapy for seizures. They control seizures through attenuation of neuronal excitability. The commonly used AEDs include: phenytoin; carbamazepine; valproate; lamotrigine; levetiracetam; and topiramate. AED choice depends on many patient factors (including side effects and potential drug interactions) as well as seizure type.
- **Drug Monitoring:** Certain AEDs require drug levels in blood to be regularly monitored to ensure therapeutic efficacy and avoid toxicity (e.g., phenytoin, valproate).[19,20,21]

2. Surgical Treatment

- **Resective Surgery:** Where seizures are not controlled with antiepileptic medications and are clearly defined arising from a localised cortical area (e.g. hippocampus), surgery is considered. The operation may entail excising the epileptogenic focus and perhaps, causing an extensive reduction or complete remission of seizures.
- **Vagus Nerve Stimulation (VNS):** VNS treats patients with drug-resistant epilepsy who are not viable candidates for surgery by implanting a device that delivers electrical signals to the brain through the vagus nerve.
- **Responsive Neurostimulation (RNS):** Newer still, this therapy places a device in the brain in order to detect abnormal activity and stimulate delivery of electrical impulses to inhibit seizure occurrence.[22,23,24,25]

3. Dietary Therapy

- **Ketogenic Diet:** The A high-fat, low-carbohydrate diet has proven successful in lessening the occurrence of seizures in cases of hard-to-treat childhood epilepsy. The application of ketogenic nutrition generates ketones, which in turn control seizures.
- **Modified Atkins Diet:** It is just a lighter version of the ketogenic meal plan that may help some patients.

4. Behavioral and Psychological Interventions

- **Cognitive Behavioral Therapy (CBT):** CBT may help the patient cope with his psychological problems arising from epilepsy; for example, anxiety, depression, or stress that sometimes leads to increased attacks.
- **Biofeedback and Relaxation Techniques:** These approaches help reduce stress and improve seizure control in some individuals.[26,27,28]

5. Addressing Underlying Causes

- Treatment may include surgery, chemotherapy, or management of the infection if seizures are due to an underlying condition (e.g., brain tumor, infection, metabolic disorder).

6. Emergency Management

- For example, in seizure emergencies such as status epilepticus (recurrent or long-lasting seizures without recovery), the person needs to get emergency management with benzodiazepines (lorazepam, diazepam) to stop the seizures and prevent brain damage as quickly as possible.

7. Lifestyle Modifications

- Patients are instructed to keep a consistent schedule for sleeping, try to stay away from seizure triggers (for instance flashing lights, stress), and abstain from alcohol or recreational drug use. Wearing a medical alert bracelet and informing family and friends about seizure first aid are also important for safety.[29,30]

Table 3: Antiepileptic Drugs.

S. No.	Class Name	Drug Names
1	Sodium Channel Blockers	Phenytoin, Carbamazepine, Oxcarbazepine, Lamotrigine, Lacosamide, Zonisamide
2	Calcium Channel Blockers (T-type)	Ethosuximide, Zonisamide
3	GABA-A Receptor Agonists (GABA Enhancers)	Phenobarbital, Diazepam, Clonazepam, Lorazepam, Midazolam, Clobazam
4	GABA Transaminase Inhibitors	Vigabatrin
5	GABA Reuptake Inhibitors	Tiagabine
6	SV2A Modulators (Synaptic Vesicle Protein Modulators)	Levetiracetam, Brivaracetam
7	Glutamate Inhibitors (AMPA/NMDA Antagonists)	Perampanel (AMPA), Felbamate (NMDA), Topiramate (weak AMPA inhibition)
8	Multiple Mechanism Drugs	Valproic Acid, Topiramate, Lamotrigine, Zonisamide, Rufinamide
9	Carbonic Anhydrase Inhibitors	Acetazolamide, Topiramate, Zonisamide
10	Potassium Channel Openers	Retigabine (Ezogabine)
11	CRMP-2 Modulators (Sodium Channel Slow Inactivation)	Lacosamide
12	Neurosteroid Analogs	Ganaxolone (under development/approved in specific regions)
13	Hormonal Modulators (Catamenial Epilepsy)	Acetazolamide
14	NMDA Receptor Antagonists	Felbamate
15	Alpha-2 Delta Ligands (Calcium Channel Modulators)	Gabapentin, Pregabalin

SAFETY OF ANTICONVULSANTS

The safety of anticonvulsants is an important aspect in the management of epileptic and neurological disorders, as these medications are usually needed for prolonged periods. Anticonvulsants can control seizures effectively; however, their adverse drug reactions (ADRs) can considerably harm the health of the patient, and thus his ability to adhere to treatment programs and his overall quality of life. Safety profiles differ for each drug; certain anticonvulsants are at higher risks for various adverse effects, with neurological, psychiatric, hepatic, hematological, and dermatological being the most common complications.[31,32]

For example, Levetiracetam and Brivaracetam have behavioral and mood-related adverse drug reactions, whereas Valproic Acid and Phenytoin can be hepatotoxic and impair cognitive functioning. Carbamazepine and Lamotrigine may cause severe hypersensitivity reactions such as Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Careful drug selection to reduce risk is thus warranted in special populations such as pregnant women, elderly patients, and those with comorbidities.

It is potentially beyond a doubt the most significant route to improving the safety of anticonvulsant therapy, especially with therapeutic drug monitoring and genetic and clinical screening. Understanding and avoiding these hurdles allow clinicians to consider optimizing seizure treatment strategies towards effective seizure control with an accompanying reduction in adverse effects, in turn improving overall clinical outcomes.[33]

Table 3: Common ADR's of Anti-Convulsant Drugs.

ADR System Organ Class	ADR Name	Drugs Associated
Neurological	Dizziness, sedation, ataxia	Phenytoin, Carbamazepine, Valproic Acid
	Cognitive impairment, memory loss	Phenytoin, Valproic Acid, Carbamazepine
	Tremors	Valproic Acid, Lamotrigine
Psychiatric	Mood changes, aggression, depression	Levetiracetam, Brivaracetam, Lamotrigine
	Anxiety, irritability	Levetiracetam, Phenytoin
	Psychosis-like symptoms	Phenytoin, Carbamazepine
Dermatological	Skin rash	Lamotrigine, Carbamazepine, Phenytoin
	Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN)	Lamotrigine, Carbamazepine, Phenytoin
Hepatic	Hepatotoxicity, elevated liver enzymes	Valproic Acid, Phenytoin, Carbamazepine
Hematological	Aplastic anemia, agranulocytosis	Carbamazepine, Phenytoin
	Thrombocytopenia	Valproic Acid
Metabolic & Endocrine	Weight gain	Valproic Acid, Carbamazepine
	Osteoporosis, vitamin D deficiency	Phenytoin, Carbamazepine, Valproic Acid
	Hyperammonemia	Valproic Acid
Gastrointestinal	Nausea, vomiting, diarrhea	Valproic Acid, Lamotrigine, Carbamazepine
Renal & Electrolyte	Hyponatremia (SIADH)	Carbamazepine, Oxcarbazepine
Cardiovascular	Arrhythmias, hypotension	Phenytoin (IV use), Carbamazepine
Ophthalmic	Blurred vision, diplopia	Phenytoin, Carbamazepine, Lamotrigine[34,35,36]

Overview on few anti-epileptic drugs

Table 4: Overview of Drugs.

Drug	Mechanism of Action	Pharmacokinetics	Clinical Uses
Levetiracetam	This molecule binds to the SV2A protein and modulates neurotransmitter release, as well as inhibits calcium channels.	100% oral bioavailability, minimal hepatic metabolism, renal excretion, half-life ~6–8 hrs.	Focal seizures, generalized tonic-clonic seizures (GTCS), juvenile myoclonic epilepsy (JME).
Brivaracetam	Like Levetiracetam, this binds to SV2A but is 20 times more efficient than Levetiracetam	High bioavailability (~97%), hepatic metabolism (CYP2C19), renal excretion, half-life ~8–10 hrs.	Focal seizures (monotherapy or adjunct).
Lamotrigine	It inhibits the voltage-dependent sodium channels and so reduces the release of neurotransmitter glutamate.	98% bioavailability, hepatic metabolism (glucuronidation), renal excretion, half-life ~24–30 hrs.	Focal and generalized epilepsy, bipolar disorder.
Valproic Acid	It enhances GABA activity, inhibits sodium channels, and reduces glutamate release.	Extensive hepatic metabolism (CYP2C9, UGT), 95% renal excretion, half-life ~9–16 hrs.	Generalized epilepsy (GTCS, absence, myoclonic seizures), bipolar disorder, migraine prophylaxis.
Phenytoin	It prevents the repetitive firing of neurons because voltage-gated sodium channels are blocked.	Hepatic metabolism (CYP2C9, CYP2C19), non-linear kinetics, renal excretion, half-life ~12–36 hrs.	Focal and generalized seizures, status epilepticus (IV use).
Carbamazepine	It inhibits sodium channels,	Hepatic metabolism (CYP3A4	Focal seizures,

	stabilizes neuronal membranes, and modulates serotonin pathways.	inducer, autoinduction), renal and fecal excretion, half-life ~12–17 hrs.	generalized epilepsy, trigeminal neuralgia, bipolar disorder.[37,38,39]

ADVERSE DRUG REACTION (ADR)

According to using common terminology for adverse drug reactions (ADRs), these can be harmful or unintended responses to a medication at normal therapeutic doses required to diagnose, treat, or prevent a disease. The World Health Organization defines an ADR as a "noxious, unintended response to a drug that occurs at doses typically administered to humans for prophylaxis, diagnosis, or therapy." Unlike side effects, which can sometimes be predicted, adverse drug reactions can be very unpredictable and manifest symptoms of anything from mild discomfort to life-threatening conditions. They hamper treatment adherence and compromise patient safety and healthcare costs. Thus, the identification and management of ADRs are particularly important in clinical practice.[40]

TYPES OF ADVERSE DRUG REACTIONS

ADRs can be further differentiated on the mechanism acting, their severity, or whether they can be considered predictable or unpredictable.

1. **Type A (Augmented)** – susceptibility dose-dependent or predictable-for example, sedation related to benzodiazepines.
2. **Type B (Bizarre)** – unpredictable, dose not relate to the drug or to therapy; ex, stevens-johnson syndrom from carbamazepine.
3. **Type C (Chronic)** – Chronic- continuing with treatment, e.g. osteoporosis due to phenytoin.
4. **Type D (Delayed)** – Delayed- reaction that develops after therapy stops, e.g. valproic acid teratogeny.
5. **Type E (End of Use)** – emerges after stopping taking a drug, e.g. seizures after benzodiazepines cessation.
6. **Type F (Failure of Therapy)** – The drug does not produce the desired effect; for example, antibiotic resistance.[41,42]

ADVERSE DRUG REACTION (ADR) SEVERITY ASSESSMENT

The Adverse Drug Reaction (ADR) severity assessment process determines the clinical dimension of an ADR on the basis of its intensity, medical intervention required, and patient outcome. As such, ADRs are classified into mild, moderate or severe according to scales like Hartwig and Siegel severity scale, thereby constituting a management guide for treatment alteration and patient intervention.[43,44]

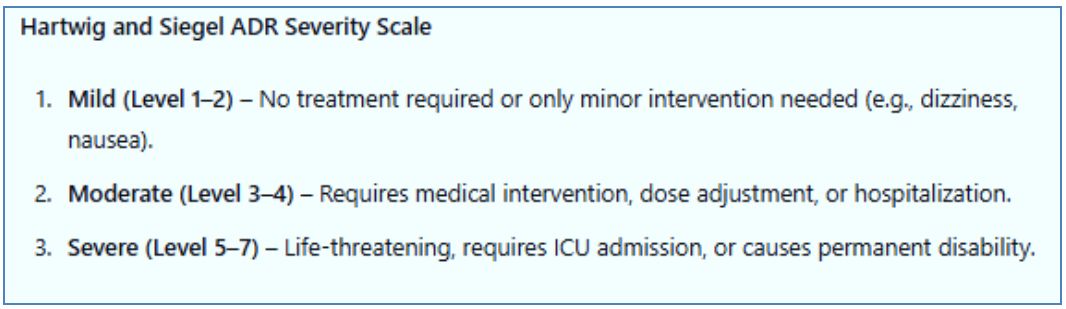

Figure 3: Hartwig and Siegel ADR Severity Scale.

ADVERSE DRUG REACTION (ADR) CAUSALITY ASSESSMENT

Adverse Drug Reaction (ADR) Causality Assessment is the procedure followed to ascertain the likelihood of a drug being implicated in an adverse reaction. Depending on standardized tools such as the WHO-UMC Scale and Naranjo's Algorithm, ADRs will be classified as certain, probable, possible, or unlikely; the results thereof will feed back into clinical decision-making and pharmacovigilance.[45,46]

WHO-UMC Causality Categories

1. **Certain** – A clear temporal relationship with the drug, no other explanation, and ADR disappears after stopping the drug.
2. **Probable** – Strong association with drug intake, reasonable explanation, but not confirmed by rechallenge.
3. **Possible** – ADR occurs after drug intake, but other factors could also explain the reaction.
4. **Unlikely** – ADR occurs but has little or no relation to drug administration.

Figure 4: WHO-UMC Causality Scale.

ADVERSE DRUG REACTION (ADR) PROBABILITY ASSESSMENT

ADR Probability Assessment is the probability that a specific annoying effect has been caused by taking that particular drug rather than some other factors, such as an underlying disease or interactions with other drugs. It is usually determined using an ADR algorithm called Naranjo's algorithm, which will assign an ADR probability score on the aspects of temporal relationship, dose-response, dechallenge/rechallenge, and absence of other alternatives.[47,48]

Naranjo's ADR Probability Scale

Score Range	Probability Category	Interpretation
≥9	Definite	Strong evidence that the ADR is drug-related.
5–8	Probable	Likely caused by the drug, but other explanations are possible.
1–4	Possible	ADR could be related to the drug, but other factors may contribute.
0	Doubtful	ADR is unlikely to be due to the drug.

Figure 5: Naranjo's ADR Probability Scale.

IMPACT OF ADRS ON TREATMENT ADHERENCE (MMAS-8)

Anticonvulsant-related adverse drug reactions (ADRs) become prominent on-treatment adherence issues that necessitate modification of doses, skipping doses, or even complete discontinuation of drugs. Neuropsychiatric ADRs (mood changes, aggression) like Levetiracetam and Brivaracetam, sedation, dizziness, and cognitive impairment with Phenytoin and Valproic Acid usually lead to nonadherence. Life-threatening adverse reactions such as Lamotrigine-induced Stevens-Johnson syndrome or Valproic Acid-induced hepatotoxicity increase treatment discontinuation rates. Poor scores on the MMAS-8 for patients with intolerable adverse effects suggest poor adherence levels. Addressing the ADRs by modifying doses and treating symptomatically improves adherence, thus providing effective seizure control and reducing relapse rates during epilepsy management.

The Morisky Medication Adherence Scale (MMAS-8) is an 8-item validated questionnaire designed to evaluate the level of adherence in relation to the medication-taking behavior of patients.[49,50]

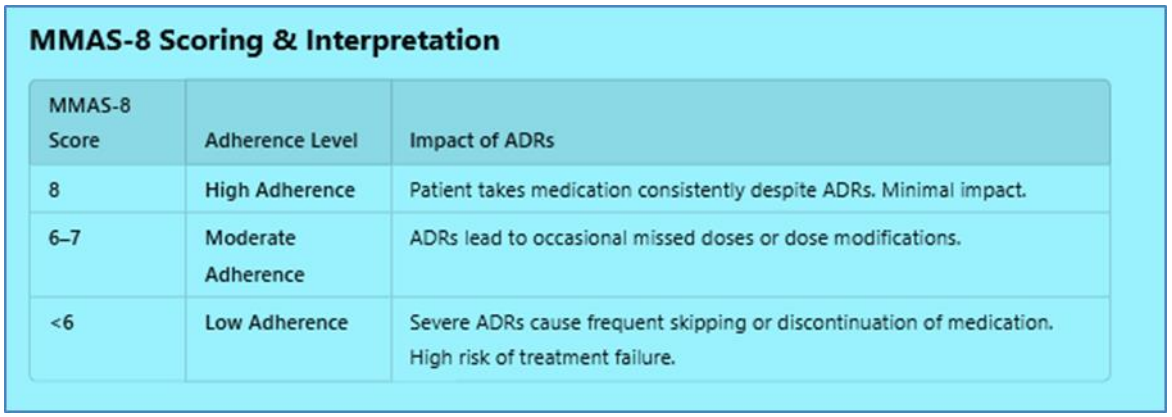

Figure 6: Morisky Medication Adherence Scale (MMAS-8).

ADR MANAGEMENT STRATEGIES USED

Timely management of ADRs is necessary to uphold patient safety and guarantee compliance with anticonvulsant treatment. The selection of the managing plan would, however, vary depending on the degree of severity, nature, and interference, as the ADR could be causing the treatment outcome.

Table 5: ADR Management Strategies.

Management Strategy	Description	When Used
Dose Adjustment	Reducing or modifying drug dosing so as not to decrease adverse drug reaction profile while maintaining efficacy.	For instance, sedation would be considered a dose-dependent adverse reaction with Levetiracetam and Phenytoin.
Drug Substitution	Replacement of the offending drug by a safer drug.	Used for severe adverse reactions, e.g., SJS from Lamotrigine, hepatotoxicity from Valproic Acid.
Symptomatic Treatment	Use of supportive medications for the symptoms of ADR.	Used for nausea, dizziness, mood disturbances, weight gain.
Monitoring & Patient Education	Regular follow-ups, laboratory assays, and counseling will improve adherence to calling processes.	Monitoring for long-term safety will include hepatotoxicity and other blood dyscrasias
Discontinuation of Therapy	Withdrawal of the drug totally on life-threatening adverse reactions	Used for anaphylaxis, SJS/TEN, severe hepatotoxicity.[51,52]

QUALITY OF LIFE IN EPILEPSY

Seizure frequency, treatment burden, side effects of medication, and social stigma are significant impediments to the quality of life (QoL) for patients suffering from epilepsy. Cognitive dysfunction, emotional distress, restricted daily functioning, and adverse events (including adverse drug reactions) caused by the anticonvulsants further compromise well-being. Neuropsychiatric adverse effects, such as mood swings, aggression, or depression from Levetiracetam and Brivaracetam, as well as cognitive decline blackmarked by Phenytoin and Valproic Acid, produce marked reductions in QoL scores. By and large, the QOLIE-31 scale is applied for rating emotional, cognitive, and social factors affecting well-being. Improving seizure control to limit the adverse drug effects will contribute in greater measure to the enhancement of QoL and the outlook for better long-term outcomes.

Serious adverse drug reactions (ADRs), poorly controlled seizures, and low self-esteem are often associated with higher incidences of anxiety and depression. These symptoms result in social isolation and poor compliance to treatment among this group of patients. The cognitive effects of drugs, especially those associated with Phenytoin, Valproic Acid, and Carbamazepine, will be felt in areas of memory, learning, and working productivity. In addition, there are challenges that women with epilepsy face that are specific to them, for instance, pregnancy-related concerns owing to teratogenic affects of anticonvulsants such as Valproic Acid. Different treatment plans, regular assessments of adverse drug reactions, psychological support, and education for patients should improve quality of life in epilepsy. Changes in lifestyle, adherence support, and reduction in trigger seizure may further improve daily functioning and social participation. By optimizing seizure control with minimal side effects, clinicians can help make epilepsy patients live much more independently and, in that way, make more effort for having a fulfilling life.[53,54,55]

FACTORS ASSOCIATED WITH ADVERSE EVENTS OF ANTIEPILEPTIC DRUGS (AEDS)

Type and Generation of AED

The risk of adverse effects is highly heterogeneous with regard to generation and class of antiepileptic drug used. For example, phenytoin, carbamazepine, and valproate are classified as first-generation AEDs. Their pattern of use is extensive, but the drugs are associated with a higher incidence of severe side effects that include hepatotoxicity, hematological abnormalities, and teratogenic effects. Their newer generations, such as lamotrigine, levetiracetam, and topiramate, are said to be having significantly improved safety profiles. Yet, they are still not free from adverse events, such as cognitive dysfunction, mood changes, and dermatological reactions. The pharmacokinetic and pharmacodynamic differences between these drugs are major factors in tolerability.[53,54]

Patient-Specific Factors

Individual patient characteristics are significant in determining whether one has the propensity to develop an adverse drug reaction from AEDs. Age is one important factor. Side effects in children and adults may differ according to the age-related maturity of organ systems. In contrast, altered pharmacokinetics may predispose the elderly to sedation and cognitive impairment. Gender may also influence susceptibility, as certain drug rashes and idiosyncratic reactions appear to affect women more than men. Weight and BMI may also influence the distribution volume of a drug in the human body, thereby contributing to side effects. The presence of liver or renal impairment will also disturb metabolism and excretion of the drug, thus increasing the chances of developing toxicity.

Genetic Predisposition

Genetics play an important role in susceptibility to AED-associated adverse events. Polymorphisms in genes coding for drug metabolizing enzymes (for example, CYP450 family) or specific HLA alleles have been implicated in increased risk of hypersensitivity reactions: for instance, the HLA-B*1502 allele has been reported to be associated with Stevens-Johnson syndrome among carbamazepine-treated individuals, particularly in specific Asian populations. Recognizing these genetic markers can facilitate individualized treatments with AEDs while averting catastrophic reactions.

Polytherapy and Drug Interactions

The involvement of numerous concurrent AEDs or medications creates an increasing propensity for drug-drug interactions, which aggravate unwanted effects. AEDs that induce enzymes, like phenytoin and carbamazepine, could act on the metabolism of other drugs causing toxicity or reduced efficacy. Polytherapy may also add up to the total

burden of adverse effects, such as dizziness, ataxia, and cognitive dysfunction. Thus, usually, monotherapy is preferred if at all possible to minimize this risk.[55,56]

Duration and Dosage of Therapy

The length of time a patient is on AEDs and the dose given are important factors in determining the risk of adverse events. Side effects like gastrointestinal discomfort, dizziness, or behavioral changes might be more common at high doses or with rapid titration schedules. Chronic complications resulting from the prolonged use of some AEDs (e.g. valproate or phenytoin) include osteoporosis, peripheral neuropathy, or hepatotoxicity. By titrating the dosage slowly and through careful monitoring, these risks may be reduced.

Comorbid Conditions

Patients suffering from other comorbidities like psychiatric disorders, cardiovascular disease, or autoimmune conditions may have a higher risk of developing adverse effects caused by AED use. For example, depressed individuals may worsen mood symptoms when taking levetiracetam or topiramate. Similarly, other AEDs, such as valproate, can further compromise metabolic parameters in those with existing metabolic syndrome. An appropriate clinical evaluation is necessary to select the most appropriate and safer AED for each patient, according to patient's overall health status.

Non-Adherence and Self-Medication

The irrational use of AEDs or self-titration of dose may lead to subtherapeutic levels, withdrawal seizures, or further toxicity if overdosed. Patients tend to stop drugs when mild side effects are associated with them. This can jeopardize seizure control and increase the risk for rebound effects. Counseling patients about compliance and careful observation of adverse effects are mandatory to ensure safety and therapeutic effectiveness.[57,58]

CONCLUSION

Adverse drug events of antiepileptic drugs arise due to numerous factors like drug type and generation of the drug, individual patient variables, genetic vulnerability, duration of treatment, comorbid conditions, and polytherapy. Although newer AEDs have a better safety profile, they cannot be completely divorced from risk. An opportunity to lessen the incidence of serious adverse effects significantly exists for those patients identified clinically, through genetic screening, and therapeutic drug monitoring as being at greater risk. The optimization of seizure control against the liability of undesirable effects lends itself to a more personalized and patient-centered approach, taking into account clinical and pharmacogenetic factors. Education of the patient and adherence on both parts, as well as regular follow-up, are essential to making the AEDs safe and effective.

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