Epileptic seizures: An overview of the new 2017 classification and role of the pharmacist

Labuschagne Q, Matsuanga B, Bronkhorst E
School of Pharmacy, Sefako Makgatho Health Sciences University (SMU)
Correspondence to: Elmien Bronkhorst, e-mail: elmien.bronkhorst@smu.ac.za

Keywords: epilepsy, seizure types, antiepilepsy treatment

Abstract
Epilepsy is a chronic neurological disorder that affects people of all ages. Epilepsy is a brain disorder, distinguished by a persisting predisposition to initiate epileptic seizures, with no identifiable cause in up to 50% of clinical cases. It may occur because of a number of conditions, including genetic predisposition, infections and head trauma, as well as a number of other triggers, including stress, lack of sleep, alcohol and drug abuse/withdrawal.

Epilepsy can be classified as focal seizures, or an epileptic seizure where the initial activation of neurons is limited to only one cerebral hemisphere, and generalised seizures involving both cerebral hemispheres.

Treatment options can be divided between those drugs used to terminate an acute seizure and those drugs that are used to prevent seizures. The goal of therapy is to maximise quality of life by eliminating seizures or diminishing seizure frequency, while minimising adverse effects.

© Medpharm

Introduction
The pivotal clinical tool in assessing a patient who presents with seizures is epilepsy classification; the latter has evolved dramatically since its commencement in the 1960s.1 Epilepsy, also known as an epileptic seizure disorder, is a chronic neurological disorder that affects people of all ages.2 It is characterised by an enduring predisposition to generate epileptic seizures. Epileptic seizures may be defined as brief episodes of signs or symptoms due to disturbances of electrical activity in the brain. Signs or symptoms include:
• Seizures or periods of unusual behaviour
• Sensations and sometimes loss of consciousness

According to the World Health Organization (WHO) epilepsy fact sheet updated in February 2016, approximately 10% of the world’s population may have a single unprovoked seizure and about 50 million people around the world have epilepsy, making it one of the most common neurological diseases worldwide.3 Nearly 80% of people with epilepsy live in low- and middle-income countries (LMIC) and in about 70% of cases people with epilepsy respond to treatment.4 In South Africa, epilepsy affects one in every 100 people.4

Epilepsy overview
Both the International League Against Epilepsy (ILAE)5 and the International Bureau for Epilepsy (IBE)6 define epilepsy as a brain disorder distinguished by a persisting predisposition to initiate epileptic seizures.6 Seizures are the evidence of abnormal hypersynchronous or hyperexcitable discharges of cortical neurons. The location, extent and pattern of propagation of the epileptic discharges in the cerebral cortex will determine the clinical signs and symptoms.6 No identifiable cause is present in about 50% of cases. Epilepsy may occur as a result of a number of other conditions, including genetic predisposition, infections, head trauma, stroke, brain tumours, lead poisoning and metabolic insults (e.g. hypoglycaemia). Various triggers can also contribute to epileptic seizures; these include stress, lack of sleep, alcohol and drug abuse/withdrawal and flashing lights.1,6

Classification of seizure types
The largest academic body in the epilepsy community is the ILAE which takes the principal role in the epilepsy community.7 The ILAE consists of a group of experts that routinely review the classification system.7 The first epileptic seizure classification system was adopted in 1981, with modifications in 1989, 2001 and 2010. The 1981 classification system had two major classifications of epilepsy: 1) partial seizures, and 2) generalised seizures. According to Chang, et al (2017),7 a partial seizure is defined as an epileptic seizure where the initial activation of neurons is limited to only one cerebral hemisphere, whereas generalised seizures involve both cerebral hemispheres. Both partial and generalised seizures are further classified into three and six subtypes respectively.
New revised 2017 ILAE classification of seizure types and epilepsy classification

The ILAE introduced a new classification system for both seizures and the epilepsies. The proposed classification groups epilepsy into three categories, namely seizure type, epilepsy type and epileptic syndrome. Seizures are now classified as focal, generalised or of unknown onset. Focal and generalised seizures may be divided into either motor or non-motor onset. The earliest symptoms can differentiate and further categorise seizures. The category, unknown-onset, was added to the classification system to classify undetermined seizures during initial clinical assessment until clinical workup is available. Epileptic syndrome includes features such as clinical presentation, age of onset, natural course, seizure type, electroencephalogram (EEG) and neuroimaging. Epileptic syndrome is of relevance due to its treatment and prognostic implications. See Figure 1 for the ILAE 2017 classification of seizure types. Table I also provides definitions of the different terms used in epilepsy.

Treatment options

Treatment options can be divided between those drugs used to terminate an acute seizure and those drugs used to prevent seizures. The goal of therapy is to maximise quality of life by eliminating seizures or diminishing seizure frequency while minimising adverse effects.

There are three general mechanisms of action of antiepileptic drugs. They either block voltage-gated ion-channels (Na⁺ or Ca²⁺) or they enhance inhibitory gamma-aminobutyric acid (GABA) or they interfere with excitatory glutamate transmission. Antiepileptics suppress seizures and do not cure epilepsy. Table II provides the various options for epilepsy treatment.

Treatment of status epilepticus (SE)

The latest guideline from the American Epilepsy Society recommends that a benzodiazepine should be the initial drug therapy for SE. Any of three benzodiazepines, midazolam, lorazepam, or diazepam, should be given if first-aid stabilisation measures do not stop the seizure within five minutes. If a patient does not respond to the benzodiazepine, three options,
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Pharmacokinetics</th>
<th>Indications</th>
<th>Drug interactions</th>
<th>Major side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>phenytoin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e.g.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barbiturates e.g.</td>
<td>Potentiates the action of GABA leading to increased opening of GABA-channels and enhancing hyperpolarisation.</td>
<td></td>
<td>Use limited because of adverse effects. Status epilepticus (emergency) when other agents have failed.</td>
<td>Powerful inducer of the hepatic microsomal enzymes.</td>
<td>CNS depression. Respiratory depression.</td>
</tr>
<tr>
<td>phenobarbital</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primidone</td>
<td>Mechanism of action may be more like that of phenytoin.</td>
<td></td>
<td>Focal and generalised tonic-clonic seizures.</td>
<td>Decreases serum levels of oral contraceptives.</td>
<td>Hypersensitivity sometimes with rash.</td>
</tr>
<tr>
<td>Benzodiazepines e.g.</td>
<td>Increases opening of GABA-channels and enhances hyperpolarisation.</td>
<td></td>
<td>Adjunctive, short-term therapy.</td>
<td>Increases CNS depression with alcohol consumption.</td>
<td></td>
</tr>
<tr>
<td>lorazepam or diazepam</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproates</td>
<td>Blocks GABA transaminase and sodium channels and also has action on T-type calcium channels.</td>
<td>Well absorbed from gut after oral dose. Food may delay absorption. Metabolises to active metabolites and inactive conjugates. Highly protein bound.</td>
<td>Absence seizures and myoclonic seizures. It can also be used in generalised tonic-clonic seizures. Intravenous formulation for status epilepticus.</td>
<td>Inhibits metabolism of phenobarbital and ethosuximide. Valproate displaces phenytoin from plasma proteins leading to phenytoin toxicity. Valproate also increases level of carbamazepine epoxide.</td>
<td>Nausea, vomiting, abdominal pain, heartburn. Weight gain, increased appetite and hair loss. Warnings: Foetal hepatotoxicity (monitor liver for the first six months). Severe birth defects (spina bifida and lower intelligence quotient). Foetal pancreatitis and suicidal ideation.</td>
</tr>
</tbody>
</table>
Phenytoin, valproic acid, or levetiracetam as a single dose should be administered intravenously. If one of these agents does not work, the guideline recommends trying another one. When this strategy fails, the next step is an aggressive phase that involves continuous electroencephalography monitoring, while repeating second-line therapy, or with anaesthetic doses of thiopental, pentobarbital or propofol.¹²

**Role of the pharmacist**

Various formulations of medications are available and judicious medication choice entails detailed knowledge of the therapeutic response and side-effects associated with the available medications. Decisions on treatment should be based upon informed patient preferences and the treatment responses observed during the titration period.¹³ The clinical pharmacist has a major role to play in relation to performing therapeutic drug monitoring to optimise the dose for each individual patient as well as to prevent adverse drug reactions. Furthermore, they should educate healthcare professionals and patients about drug effects, increasing their level of awareness regarding adverse drug effects. Pharmacy services are essential for minimising adverse drug reactions, which will improve the quality of life of patients.¹³

**Conclusion**

Epilepsy may occur as a result of a number of conditions including genetic predisposition, infections, head trauma, stroke, brain tumours, lead poisoning and metabolic insults (e.g. hypoglycaemia). Various triggers can also contribute to epileptic seizures; these include stress, lack of sleep, alcohol and drug abuse/withdrawal and flashing lights. Treatment options may be divided between drugs used to terminate an acute seizure and drugs used to prevent seizures. The goal of therapy is to maximise quality of life by eliminating seizures or diminishing seizure frequency while minimising adverse effects. The pharmacist has a major role to play in relation to performing therapeutic drug monitoring to optimise the dose for each individual patient as well as to prevent adverse drug reactions.

**References**