

# The effects of ANTIEPILEPTIC DRUGS in relation to Dentistry

Janet Mifsud, BPharm (Hons); PhD(QUB)

Vice President (Europe), International Bureau of Epilepsy

Advisor, Caritas Malta Epilepsy Association

Department of Clinical Pharmacology and Therapeutics, University of Malta

## INTRODUCTION: 'THERE IS MORE TO EPILEPSY THAN JUST SEIZURES'

Epilepsy is the most chronic neurological disorder with an incidence of approximately 45/100,000 per year and point prevalence of 0.5-1%. It is important to distinguish between seizures and epilepsy (see Figure 1) and epilepsy is currently defined as a tendency to have recurrent seizures (sometimes called fits). A seizure is caused by a sudden burst of excess electrical activity in the brain, causing a temporary disruption in the normal message passing between brain cells. This disruption results in the brain's messages becoming halted or mixed up<sup>1</sup>.

It is more accurate to refer to epilepsies. The International Bureau for Epilepsy classifies epilepsy in over forty different types and conditions. Epilepsy is classified "generalized" when the discharge affects the entire brain cortex. The main seizures types in this group are tonic-clonic (grand mal) and absence (petit mal). An epilepsy is called "partial" when the electrical discharge causing it occurs in a specific area of the brain.

Simple partial seizures result in no loss of consciousness, while complex partial seizures are characterized by automatisms. Based on the cause, epilepsy can be symptomatic (caused by a developmental mal-formation), idiopathic (when a genetic condition is responsible) or cryptogenic (when the cause is unknown). There are various

possible etiologies of seizures and epilepsy across various ages: prenatal or birth injury, inborn error of metabolism, or congenital malformation, idiopathic/genetic syndrome, CNS infection, or trauma, head trauma, drug intoxication and withdrawal or stroke, brain tumor, and neurodegenerative conditions<sup>2</sup>.

Despite huge medical advances which have resulted in 70% of persons with epilepsy being seizure free due to the availability of pharmacological therapy, epilepsy is surrounded by social stigma, superstition, and rarely discussed in media. In Malta it is colloquially known as "tal-qamar", a term associated with a huge stigma and large efforts are being made to replace it with the term epilepsija. It is a condition which has a significant negative impact on the quality of a patient's life and the treatment goal of epilepsy is to make the patient be completely seizure-free without significant side effects.

## WHY IS EPILEPSY OF INTEREST TO DENTISTS?

Understanding epilepsy and seizures is important in order to raise awareness of the this condition's impact on a patient's general medical and psychological health. In almost all aspects of oral health and dental status, the condition of patients with epilepsy is significantly worse than age-matched groups in the general (nonepileptic) population. Patients with poorly controlled epilepsy and who experience frequent generalized tonic-clonic seizures have worse oral health in comparison with

patients who are better controlled or who only have seizures that do not involve the masticatory apparatus.

The number of decayed and missing teeth, the degree of abrasion and periodontal indexes are also significantly worse in patients with epilepsy. Those with epilepsy also have significantly fewer restored and replaced teeth than the general population<sup>3</sup>.

## ANTIEPILEPTIC DRUGS (AEDS)

Appropriate treatment is often lifelong and usually consists of pharmacological medications with antiepileptic drugs (AEDs). In Malta, persons with epilepsy are entitled to free medication under Schedule V (yellow cards). On first therapeutic choice, 60% of patients become seizure free which increases to 80% with some dose/therapy adjustments. Yet many of these drugs may have severe adverse effects which may impair the quality of life of persons with epilepsy, including dental care. These side effects can be direct ie affecting dental care, or indirect influencing the patient's ability to ensure their dental care.

## ADVERSE EFFECTS WITH AEDS

Phenobarbital, which despite being an older drug is still widely used, can cause CNS depression, resulting in sedation, lethargy, and cognitive impairment. It associated with an increase in falls in the elderly, porphyria, folate deficiency, osteomalacia, and megaloblastic anemia.

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Phenytoin can result in fatigue, lethargy, blurred vision, drowsiness, incoordination, and nystagmus, hirsutism, acne, osteomalacia, folic acid deficiency, coarsening of facial features, Stevens-Johnson syndrome, bone marrow suppression, and hepatitis. Yet the main problem is the high incidence of gingival hyperplasia which is characterized by unusual growth of the gingival subepithelial connective tissue and epithelium, which is reversed once the drug is discontinued. About 50% of patients will develop it within 12–24 months of initiation of treatment.

The use of chlorhexidine, folic acid rinses or both, and good oral hygiene will significantly decrease the severity of the condition. In severe cases, surgical reduction is needed. Carbamazepine will cause diplopia, dizziness, headache, nausea, vomiting, sedation, and lethargy, skin rash, hyponatremia, and, very rarely, bone marrow suppression.

Valproate may result in nausea, vomiting, and dyspepsia, tremor, weight gain, thinning or loss of hair, and menstrual irregularities including amenorrhea, liver toxicity, thrombocytopenia, pancreatitis, polycystic ovary disease and has a high significant risk for teratogenicity<sup>4</sup>.

The newer AEDs, despite various promises, also have adverse effects that may affect dental care. Lamotrigine can lead to vomiting, coordination abnormality, dyspepsia, nausea, dizziness, and rhinitis; ataxia, somnolence, headache, diplopia, and blurred vision. More serious is a hypersensitivity reaction primarily presenting as rash which may progress to Stevens-Johnson syndrome and may result in fatalities.

Topiramate causes ataxia, poor concentration, confusion, dysphagia, dizziness, fatigue, paresthesia, word-finding difficulties, and cognitive slowing. Levetiracetam users have reported psychiatric and behavioral events such as emotional lability, nervousness and hostility. (see Table 1)<sup>5</sup>

## DRUG INTERACTIONS WITH AEDS

In addition, AEDs interact with several drugs which the dentist may prescribe in certain conditions. Antifungal agents and antibiotics may interfere with the metabolism of certain AEDs. The coadministration of fluconazole and phenytoin is associated with a clinically significant increase in phenytoin's plasma concentration, and the dose of the latter may require adjustment to maintain safe therapeutic concentrations. Clarithromycin increases the plasma concentration of carbamazepine, and coadministration of these drugs should be monitored very carefully to avoid carbamazepine toxicity. Valproate may be displaced from plasma proteins and metabolic pathways may be inhibited by high doses of aspirin; this interaction will free serum valproate concentrations resulting in subsequent toxicity<sup>1</sup>.

## PROBLEMS THAT A DENTIST MAY ENCOUNTER

It is important for dentists to ensure prevention of peri-operative seizures. Patients must take their anticonvulsant medication and if necessary dentists should consult with patient's neurologist or family physician. Most persons with epilepsy who are well-controlled on medication, and can undergo surgery without difficulty or complication

Generalized tonic-clonic seizures often cause minor oral injuries, such as tongue biting, but also frequently lead to tooth injuries and in some cases to maxillofacial trauma. Patients with epilepsy can be at increased risk of fracture because enzyme-inducing antiepileptic drugs (e.g., phenytoin, phenobarbital, carbamazepine) alter the metabolism and clearance of vitamin D and have been associated with osteopenia and osteomalacia. It is important to ensure adequate calcium and vitamin D supplementation especially in patients taking phenobarbital, phenytoin or primidone<sup>3</sup>.

A recent analysis of the prosthodontic status of patients with epilepsy, found that compared with age-matched controls, PWE have a tendency to become edentulous earlier.

Prosthodontic treatment is suboptimal, as significantly fewer teeth are replaced, despite the fact that epileptic patients tend to have more missing teeth. Specific guidelines are recommended such as the discouragement of incisal restorations, use of fixed rather than removable prostheses and inclusion of additional abutments if fixed partial dentures are to be used. The use of metal base for complete dentures and telescopic retention with denture bases made of metal or reinforced with metal for nearly edentulous patients was recommended for those having seizures involving the masticatory apparatus, and seizures associated with falls<sup>6</sup>.

## WHAT THE PATIENT SHOULD KNOW ABOUT AEDS AND DENTAL CARE

Children with epilepsy who are prescribed AEDs in syrup form may have problems with their teeth due to the syrup content in the medication, particularly if the dose is taken at night. It is important to use sugar-free liquid preparations. Some drugs e.g. carbamazepine, primidone and phenobarbitone, may cause dryness of the mouth, due to changes in the composition or reduction in the production of saliva which is necessary for digestion of food. Other possible oral side effects of AEDs include glossitis, a smooth and painful tongue and oral ulceration (carbamazepine) and taste disturbances (phenytoin)<sup>4</sup>.

Patients should be advised that in the event of a fall due to seizures tooth fragments, crowns, fillings or even loose dentures may become dislodged or swallowed and if teeth are damaged, appointment with the dentist should be arranged as soon as possible. Sometimes, during a seizure, the inside of the mouth is bitten making it painful to brush the teeth and the use Corsodyl® mouthwash instead of brushing until any soreness or ulcers subside. Swelling can be reduced by holding a cold compress to the cheek or sucking an ice cube. Hot salt water mouthwash (half a teaspoon of salt to one tumbler of water) can help soothe and heal<sup>1</sup>.


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## RECOMMENDATIONS

It is important to dentists to ensure that persons with epilepsy who are medication which may affect dental care are educated about the importance of seeking appropriate dental treatment due to the adverse effects of pharmacological therapy or damage to their teeth due to physical injury subsequent to seizures. Dental surgeons in turn should keep abreast of their clients medical and drug history and if possible liaise with the patient's neurologist if it is necessary to alter the patients treatment plan due to unacceptable adverse effects due to the AEDs (see Table 2). Treatment plan and design restorations should be undertaken in order to minimise the risk of damaging or displacing dental prosthesis due to an epilepsy seizure.<sup>3</sup>

Patients should also be made aware of local and national resources for information and support relative to their condition. The Caritas Malta Epilepsy Association (CMEA) ([www.caritasmalta.org/epilepsy](http://www.caritasmalta.org/epilepsy)) was set up by voluntary workers in 1996 and now lists almost 300 members. In May 2001, the Association was accepted as a Full Member of the International Bureau for Epilepsy (IBE). The Association is for persons with epilepsy and their families. It aims to promote education and local awareness about epilepsy, especially because of the stigma suffered by people with this condition in society particularly in employment and improve health care services, treatment and social acceptance of epilepsy, as a serious yet treatable brain disorder. It has often invited dentists to the meetings to explain the importance of dental care to members. CMEA has also liaised with the Association of Dental Students of Malta in the production of an information leaflets about epilepsy. 

## REFERENCES

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Figure 1: Seizure vs Epilepsy

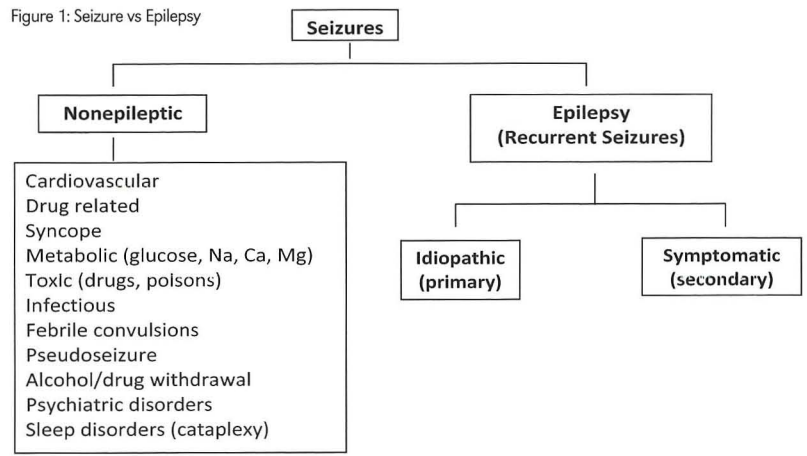


Table 1: Summary of most common oral side effects and dental considerations with ACDs

Medication	Indications (seizure type)	Most common oral side effects and dental considerations
Phenobarbital	Partial and secondarily generalized	Drowsiness/sedation, osteopenia/osteomalacia
Carbamazepine	Partial and secondarily generalized	Xerostomia, stomatitis, gingival bleeding, rash, osteopenia/osteomalacia
Phenytoin	Partial and secondarily generalized	Gingival hyperplasia, gingival bleeding, osteopenia/osteomalacia
Valproate	Partial and generalized	Gingival bleeding, petechiae, decreased platelet aggregation
Primidone	Partial and generalized	Drowsiness/sedation
Lamotrigine	Partial and generalized	Rash
Topiramate	Partial and generalized	Mild cognitive side effects
Clobazam	Partial and generalized	Drowsiness/sedation
Ethosuximide	Generalized	Drowsiness/sedation
Vigabatrin	Partial	Unknown
Diazepam	Generalized	Drowsiness/sedation
Gabapentin	Partial	Drowsiness/sedation
Levetiracetam	Partial and generalized	Unknown

Table 2: Acute, Dose-Related Adverse Effects of AEDs

<p><b>Neurologic/psychiatric: most common</b></p> <ul style="list-style-type: none"> <li>● Sedation, fatigue               <ul style="list-style-type: none"> <li>● More pronounced with traditional AEDs</li> </ul> </li> <li>● Unsteadiness, uncoordination, dizziness               <ul style="list-style-type: none"> <li>● Mainly traditional AEDs</li> <li>● May be sign of toxicity with many AEDs</li> </ul> </li> <li>● Tremor               <ul style="list-style-type: none"> <li>● VPA</li> </ul> </li> <li>● Diplopia, blurred vision, visual distortion               <ul style="list-style-type: none"> <li>● CBZ LTG</li> </ul> </li> <li>● Mental/motor slowing or impairment               <ul style="list-style-type: none"> <li>● TPM</li> </ul> </li> </ul>	<p><b>Mild to moderate laboratory changes</b></p> <ul style="list-style-type: none"> <li>● Hyponatremia               <ul style="list-style-type: none"> <li>● CBZ</li> </ul> </li> <li>● Increases in ALT or AST               <ul style="list-style-type: none"> <li>● VPA</li> </ul> </li> <li>● Leukopenia and thrombocytopenia</li> </ul>
<p><b>Teratogenicity</b></p> <ul style="list-style-type: none"> <li>● increased risk of cleft lip and/or palate in the new born               <ul style="list-style-type: none"> <li>● PHT CBZ VPA</li> </ul> </li> </ul>	<p><b>Endocrine/Metabolic Effects</b></p> <ul style="list-style-type: none"> <li>● Osteomalacia, osteoporosis               <ul style="list-style-type: none"> <li>● CBZ PHB VPA PHT</li> </ul> </li> <li>● Folate (anemia, teratogenesis)               <ul style="list-style-type: none"> <li>● CBZ PIB VPA PIIT</li> </ul> </li> <li>● Altered connective tissue metabolism or growth (facial coarsening)</li> </ul>
	<p><b>Weight gain/appetite changes VPA GPB PGB</b></p> <p><b>Weight loss TPM ZMS FBM</b></p>