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# Autonomic manifestations of epilepsy

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**Abstract:** An epileptic fit does not only manifest as bizarre motor activity but can destabilize autonomic functions. Abnormal electrical discharge originating from the cerebral cortex can spread to involve the autonomic system thus creating a dysfunction of the sympathetic and the parasympathetic which modulate the cardio-respiratory, digestive, genitourinary systems. The autonomic phenomenon can be encountered in simple partial, complex partial, generalised tonic-clonic, absence and generalized tonic seizures. Both the motor and the autonomic components may manifest simultaneously; at times the autonomic symptoms may precede or outlast the motor components. Autonomic features affecting the cardiopulmonary function may be life-threatening and contributes to 8-17% of deaths in individuals with epilepsy. Hypoventilation,

apnoea, atrial fibrillation, sinus arrhythmias, atrial and ventricular premature depolarisations, bundle branch block and asystole are known to manifest in the peri-ictal and also in interictal phases of epilepsy. Poor control, and polytherapy in the management of patients, render some epileptics more vulnerable to excessive excitability of the autonomic nervous system. The aim of this communication, therefore, is to alert and remind healthcare givers on the autonomic phenomena of epileptic fits some of which may result in sudden unexpected death. Clinician should always take a holistic approach in the evaluation of epilepsy patients and watch out especially for cardiorespiratory variability during and in-between attacks.

**Key Words:** Epilepsy, Autonomic dysfunction.

## Introduction

Epilepsy is an established tendency to recurrent unprovoked seizures due to an abnormal discharge from brain cells. The neuronal discharge can manifest as abnormal motor activity, behavioural anomalies, sensory disturbances and impaired consciousness. This electrical activity can also spread to involve central centres for the regulation of autonomic activity in the individual.

During a seizure episode, electrical activity arising from the cortex spreads through the limbic system with involvement of the amygdala, hippocampus, thalamus and hypothalamus. This in turn is propagated to involve the autonomic nervous system (ANS) nuclei in the brain stem from where the sympathetic and parasympathetic efferent discharges are then generated<sup>1</sup>. The cranial nerves involved are III, VII, XI and X.

The autonomic nervous system (ANS) is divided into sympathetic and parasympathetic divisions both of which are important in maintaining homeostatic functions. The cerebral cortex influences these divisions largely through the hypothalamus. Both the sympathetic and the parasympathetic function independently to maintain the blood pressure, heart rate, and blood flow; activate the sweat and salivary glands; regulate body

temperature, the alimentary system and genitourinary functions. Other functions include pupillary changes and lacrimation. The sympathetic division provides more general control over the entire organism, whereas the parasympathetic division regulates local functions more precisely.

The cardiovascular changes during the ictal and postictal phases of seizure attack have been a regular area of research. With the use of polygraphic studies, Van Buren<sup>2</sup> was the first to evaluate the autonomic changes in actively convulsing patients by simultaneously recording EEG, ECG, pulse oximetry and blood pressures. He also recorded respiratory movements, skin temperature and resistance, oesophageal and gastric pressures. Neurophysiology methodology has also been developed to evaluate the regulation of sweating, bladder function, erectile function, gastrointestinal tract motility and pupillary reactions during seizures.

Autonomic symptoms can occur in the ictal, postictal, and even during the interictal phases of epilepsy. In some instances, the autonomic phenomena may constitute the initial seizure manifestation. In a number of cases, the autonomic manifestation such as tachycardia may precede the ictal manifestations, and bradycardia

may linger into the postictal phase<sup>1,2</sup>. The interictal phase in epilepsy is the interval between active seizures. During this seizure-free period, which may last weeks or months, the EEG of more than 80% of epileptics continue to show spikes wave pattern. This indicates an ongoing electrical emission from the cerebral hemisphere which can secondarily excite the autonomic centres thus causing active sympathetic and parasympathetic manifestations without any concomitant motor component. This phenomenon, which may even carry a risk of sudden and unexpected death from cardiorespiratory dysfunction, occurs both in adults and children<sup>3</sup>.

The propagation of the hypersynchronized electrical impulse to autonomic centres can occur in simple partial, complex partial, generalised tonic-clonic, absence and generalized tonic seizures. Autonomic symptoms accompany all generalised tonic-clonic seizures and one third of simple partial seizure<sup>1</sup>. Patients with epilepsy have a mortality rate that is 2-3 times that of the general population which is deaths, largely due to autonomic involvement<sup>4</sup>.

The autonomic aspect of epilepsy appears to be an area of minimal interest and emphasis to clinicians hence the aim of this communication which is to bring to the fore an in-depth knowledge, particularly the dangers related to this subject. With this awareness, clinicians will be expected to holistically evaluate the epileptics under their care and institute appropriate measures.

#### *Cardiovascular manifestation in epilepsy*

With simultaneous EEG and ECG recordings, several observations have been documented on the cardiac manifestations of patients with unprovoked seizures. Palpitations, chest pain, tachycardia, bradycardia, arrhythmia, hypotension, hypertension can be detected. Seizure related bradycardia followed by tachycardia can occur in patient with absence and generalised tonic-clonic attacks. Rhythm and conduction abnormalities have been reported in patients with partial seizures. This cardiovascular phenomena are prevalent when the primary foci is in the mesial temporal region of the brain. Mayer et al<sup>5</sup> recorded tachycardia in 98% of children suffering from complex partial seizures of temporal lobe origin. Rhythm aberrations may include atrial fibrillation, sinus arrhythmias, atrial and ventricular premature depolarisations, bundle branch block and asystole.

#### *Effect on the respiratory system*

Hyperventilation, cough, hypoventilation, apnoea and cyanosis have been documented during epileptic attacks of generalised tonic-clonic type and with fits arising from the temporal lobe. Since the cardiomodulatory centres and the respiratory control centres are closely linked at the brainstem level, the cardiac and respiratory impairment can occur simultaneously. It is pertinent to note that in some patients presenting with recurrent autonomic events, a seizure may be the underlying primary pathology. For example, apnoeic attacks, cyanosis and heart rate variations are well known features of neonatal seizures which may not be apparent otherwise.

#### *Gastrointestinal manifestations*

Abdominal pain is a very common complaint in children, and may be a forerunner of an impending motor manifestation. This could be accompanied with nausea, vomiting and faecal incontinence.

#### *Genitourinary symptoms*

Urinary incontinence is frequent in generalised tonic-clonic fits due to bladder muscle contraction and external sphincter relaxation. Erotic feeling, sexual arousal, erection and orgasm are reported. All these arise as a consequence of involvement of the limbic system and the temporal cortex.

#### *Skin, secretory gland and eye involvement*

During an episode of generalised tonic-clonic seizure, excessive sweating, salivation and lacrimation can occur. Flushing, erythema, blanching, pallor and piloerection can follow complex partial seizure of temporal lobe origin. Pupillary dysfunction can be bilateral or unilateral manifesting as mydriasis or miosis.

#### *Sudden unexpected death in epilepsy (SUDEP)*

SUDEP is defined as sudden, unexpected, witnessed or unwitnessed, nontraumatic and nondrowning death in a patient with epilepsy, with or without evidence of a seizure and excluding status epilepticus<sup>6</sup>. Autopsy in this condition does not reveal an anatomical or toxicological cause of death. This condition is not rare; it contributes 8-17% of deaths in people with epilepsy<sup>6</sup>. The average age for SUDEP is 28- 35 years but has also been reported in children<sup>7,8</sup>. Various pathophysiologic events contribute to SUDEP. These include central apnoea, neurogenic pulmonary oedema and airway obstruction; others are cardiac arrhythmias leading to acute cardiac failure and arrest. Cardiac arrhythmias, during the ictal and interictal periods, leading to acute cardiac failure may contribute significantly to SUDEP. Death is not usually as a direct result of a seizure or status epilepticus but occurs suddenly during normal or benign circumstances. In a majority of cases, patients had had a seizure immediately before death. In all witnessed deaths, seizure had stopped before death, and in many cases, the patient had even regained full consciousness before death<sup>9,10,11</sup>.

Evaluation of autonomic cardiovascular reflexes in patients with epilepsies indicates dysfunction of both the sympathetic and parasympathetic components. Repetitive exposure to catecholamines during fits is known to cause myocardial fibrosis. These fibrotic areas act as foci for cardiac arrhythmias. Autopsies following death from SUDEP have demonstrated fibrosis of the cardiac conducting system in some patients.<sup>12,13</sup> Poor control of epilepsy, and polytherapy in the management of patients render some epileptics vulnerable to SUDEP. Frequent and potentially fatal asystole is an indication for a permanent pacemaker insertion to avoid sudden

unexpected death.

#### *Some differential diagnosis of autonomic phenomena*

The pathophysiology of syncope involves bradycardia, arrhythmia, hypotension and asystole which are also encountered in the autonomic reflexes of epileptic fits. Where a clear distinction cannot be made between convulsion and syncope, ineffective and dangerous therapeutic measures may be applied. Syncope is primarily a cardiovascular event involving a 20% reduction or an abrupt cessation of blood flow to the brain. Contrastingly, a seizure can occur in a patient adopting any posture whereas syncope usually occurs in individuals while in an upright position. Syncope manifests with dizziness, light headedness, dimming vision before unconsciousness; consciousness is regained shortly after resuming a supine position. Very rarely, a patient with a prolonged syncopal attack may exhibit myoclonic jerks, tonic spasms and urinary incontinence during the event<sup>14</sup>.

Some antiepileptic drugs can negatively impact on the autonomic nervous system. Arrhythmias, hypotension and respiratory depression have been recorded with carbamazepine, lorazepam, phenobarbitone and phenytoin medication. Sodium valproate, Ethosuximide and

Felbamate can cause gastrointestinal disturbances. However, studies have shown that patients on antiepileptic drugs tend to have less impaired regulation of the autonomic cardiovascular reflexes compared with patients who are not on treatment<sup>15</sup>.

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#### **Conclusion**

It is pertinent that clinicians should not lack depth in understanding the link between epilepsy and the autonomic reflexes so that the variability in clinical manifestations can be appropriately identified and appropriately managed. When epileptic attacks are well controlled, the autonomic reflexes are less prominent. In the event of cardiorespiratory compromise the administration of oxygen, use of CPAP and vagal stimulation may suffice. With repeated threats of bradycardias and asystoles, a pacemaker introduction becomes inevitable. Whereby a particular antiepileptic medication constitutes autonomic-related cardiovascular or respiratory risk, such an offending drug needs to be replaced. A proper control of seizures with monotherapy is the hallmark in the prevention of SUDEP.

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