Original Research Article

A study on dyselectrolytemia in patients with first episode of seizures

Satyavamsi Gadde[1], V. Rama Mohana Rao[2], S. Krishna Mohana Rao[3*], K.V. Chalapathi Rao[4]

[1]Postgraduate, Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India
[2]Associate Professor, Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India
[3]Associate Professor, Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India
[4]Professor & HOD, Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India

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Abstract

Background: Seizure etiology is a wide range, depending on the age, of which electrolyte abnormalities play an important role in causation. **Aim:** To estimate the electrolyte imbalances in patients aged more than 18 years presenting with first episode of seizures. **Materials and methods:** This is a cross-sectional descriptive study. The study was conducted between October 2020 - October 2021 at Alluri SitaramaRaju Academy of Medical Sciences, Eluru, after getting approved by the institutional ethical committee. **Inclusion criteria:** All the patients with first episode of focal or generalised seizures, with age of onset of seizures >18 years, admitted in department of General Medicine and Neurology, ASRAM medical college and hospital, Eluru from October 2020 - October 2021. An individual informed consent was taken from all the patients selected for the study. **Exclusion criteria:** Patients with past history of seizures. **Discussion**: Total number of cases studied=45. Metabolic abnormalities were most common cause of seizures in this study, seen in 21 patients (46.67%) out of which hyperglycaemia was the most common cause seen in 9 patients, followed by uremia in 5 patients, electrolyte abnormalities as in 5 patients and hypoglycaemia in 2. Out of 45 patients, 13(28.89%) had electrolyte disturbances, of which the most common abnormality observed was hyponatremia, seen in 10 patients (76.99%). Others were hypercalcemia in 1patient (7.67%), hypomagnesemia in 1patient (7.67%),hypokalemia in 1 patient. **Conclusion:** Among various causes of seizures, electrolyte abnormalities were most commonly seen in patients with metabolic causes.

Key words: First episode of seizures, etiological spectrum, incidence.

Introduction

Seizure is a transient occurrence of signs/symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Depending on the distribution of discharges, this abnormal brain activity can have various manifestations, ranging from dramatic convulsive activity to experiential phenomena not readily discernible by an observer.

Seizures are a result of a shift in the normal balance of excitation and inhibition within the CNS. Given the numerous properties that control neuronal excitability, it is not surprising that there are many different ways to perturb this normal balance and, therefore, many different causes of both seizures and epilepsy.

Metabolic disturbances such as electrolyte imbalance, hypo- or hyperglycemia, renal failure, and hepatic failure may cause seizures at any age.

In practice, it is useful to consider the etiologies of seizures based on the age of the patient, because age is one of the most important factors determining both the incidence and the likely causes of seizures or epilepsy.

During the *neonatal period and early infancy*, potential causes include hypoxic-ischemic encephalopathy, trauma, CNS infection, congenital CNS abnormalities, and metabolic disor- ders.

Babies born to mothers using neurotoxic drugs such as cocaine, heroin, or ethanol are susceptible to drug-withdrawal seizures in the first few days after delivery.

Hypoglycemia and hypocalcemia, which can occur as secondary complications of perinatal injury, are also causes of seizures early after delivery.

Seizures due to inborn errors of metabolism usually present once regular feeding begins, typically 2–3 days after birth. Pyridoxine (vitamin B_6) deficiency, an important cause of neonatal seizures, can be effectively treated with pyridoxine replacement. The idiopathic or inherited forms of benign neonatal seizures are also seen during this time period

The most common seizures arising in *late infancy and early child-hood* are febrile seizures, which are seizures associated with fevers but without evidence of CNS infection or other defined causes. The overall prevalence is 3–5% and even higher in some parts of the world such as Asia. Patients often have a family history of febrile seizures or epilepsy.

Febrile seizures usually occur between 3 months and 5 years of age and have a peak incidence between 18 and 24 months. The typical scenario is a child who has a generalized, tonic-clonicseizure during a febrile illness in the setting of a common childhood infection such as otitis media, respiratory infection, or gastroenteritis.

The seizure is likely to occur during the rising phase of the temperature curve (i.e., during the first day) rather than well into the course of the illness.

A *simple* febrile seizure is a single, isolated event, brief, and symmetric in appearance. *Complex* febrile seizures are characterized by repeated seizure activity, a duration >15 minutes, or by focal features. Approximately one-third of patients with febrile seizures will have a recurrence, but <10% have three or more episodes.

*Correspondence
Dr. S. Krishna Mohana Rao
Associate Professor, Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India

Recurrences are much more likely when the febrile seizure occurs in the first year of life. Simple febrile seizures are not associated with an increase in the risk of developing epilepsy, while complex febrile seizures have a risk of 2–5%; other risk factors include the presence of preexisting neurologic deficits and a family history of nonfebrile seizures.

Childhood marks the age at which many of the well-defined epilepsy syndromes present. Some children who are otherwise normal develop idiopathic, generalized tonic-clonic seizures without other features that fit into specific syndromes.

Temporal lobe epilepsy usually presents in childhood and may be related to mesial temporal lobe sclerosis (as part of the MTLE syndrome) or other focal abnormalities such as cortical dysgenesis.

Other types of focal seizures, including those that evolve into generalized seizures, may be the relatively late manifestation of a developmental disorder, an acquired lesion such as head trauma, CNS infection (especially viral encephalitis), or very rarely, a CNS tumor.

The period of *adolescence and early adulthood* is one of transition during which the idiopathic or genetically based epilepsy syndromes, including JME and juvenile absence epilepsy, become less common, while epilepsies secondary to acquired CNS lesions begin to predominate.

Seizures that arise in patients in this age range may be associated with head trauma, CNS infections (including parasitic infections such as cysticercosis), brain tumors, congenital CNS abnormalities, illicit drug use, or alcohol withdrawal.

Autoantibodies directed against CNS antigens such as potassium channels or glutamate receptors are a cause of epilepsy that also begins to appear in this age group (although cases of autoimmunity are being increasingly described in the pediatric population), including patients without an identifiable cancer.

This etiology should be suspected when a previously normal individual presents with a particularly aggressive seizure pattern developing over weeks to months and characterized by increasingly frequent and prolonged seizures, especially when combined with psychiatric symptoms and changes in cognitive function.

Head trauma is a common cause of epilepsy in adolescents and adults. The head injury can be caused by a variety of mechanisms, and the likelihood of developing epilepsy is strongly correlated with the severity of the injury.

A patient with a penetrating head wound, depressed skull fracture, intracranial hemorrhage, or prolonged post- traumatic coma or amnesia has a 30–50% risk of developing epilepsy, whereas a patient with a closed head injury and cerebral contusion has a 5–25% risk.

Recurrent seizures usually develop within 1 year after head trauma, although intervals of >10 years are well known. In controlled studies, mild head injury, defined as a concussion with amnesia or loss of consciousness of <30 min, was found to be associated with only a slightly increased likelihood of epilepsy.

Nonetheless, most epileptologists know of patients who have focal seizures within hours or days of a mild head injury and subsequently develop chronic seizures of the same type; such cases may represent rare examples of chronic epilepsy resulting from mild head injury.

The causes of seizures in *older adults* include cerebrovasculardis-ease, trauma (including subdural hematoma), CNS tumors, and degenerative diseases. Cerebrovascular disease may account for ~50% of new cases of epilepsy in patients >65 years. Acute seizures (i.e., occurring at the time of the stroke) are seen more often with embolic rather than haemorrhagic or thrombotic stroke. Chronic seizures typically appear months to years after the initial event and are associated with all forms of stroke.

Although a variety of factors influence the incidence and prevalence of seizures, ~5–10% of the population will have at least one seizure, with the highest incidence occurring in early childhood and late adulthood.

Coming to seizure mechanism and propagation,focal seizure activity can begin in a very discrete region of cortex and then slowly invade the surrounding regions. The hallmark of an established seizure is typically an electrographic "spike" due to intense near-simultaneous firing of a large number of local excitatory neurons, resulting in an apparent hypersynchronization of the excitatory bursts across a relatively large cortical region.

The bursting activity in individual neurons (the "paroxysmal depolarization shift") is caused by a relatively long-lasting depolarization of the neuronal membrane due to influx of extracellular calcium (Ca^{2+}), which leads to the opening of voltage-dependent sodium (Na^{+}) channels, influx of Na^{+}, and generation of repetitive action potentials.

This is followed by a hyperpolarizing afterpotential mediated by γ-aminobutyric acid (GABA) receptors or potassium (K^{+}) channels, depending on the cell type. The synchronized bursts from a sufficient number of neurons result in summation of field potentials producing a so-called spike discharge on the EEG.

The spreading seizure wavefront is thought to slow and ultimately halt by intact hyperpolarization and a "surround" inhibition created by feed forward activation of inhibitory neurons.

With sufficient activation, there is a recruitment of surrounding neurons via a number of synaptic and nonsynaptic mechanisms, including (1) an increase in extracellular K^{+}, which blunts hyperpolarization and depolarizes neighboring neurons; (2) accumulation of Ca^{2+} in presynaptic terminals, leading to enhanced neurotransmitter release; (3) depolarization- induced activation of the *N*-methyl-d-aspartate (NMDA) subtype of the excitatory amino acid receptor, which causes additional Ca^{2+} influx and neuronal activation; and (4) ephaptic interactions related to changes in tissue osmolarity and cell swelling.

The recruitment of a sufficient number of neurons leads to the propagation of excitatory currents into contiguous areas via local cortical connections and to more distant areas via long commissural pathways such as the corpus callosum.

Many factors control neuronal excitability, and thus, there are many potential mechanisms for altering a neuron's propensity to have bursting activity. Mechanisms *intrinsic* to the neuron include changes in the conductance of ion channels, response characteristics of membrane receptors, cytoplasmic buffering, second-messenger systems, and protein expression as determined by gene transcription, translation, and posttranslational modification.

Mechanisms *extrinsic* to the neuron include changes in the amount or type of neurotransmitters present at the synapse, modulation of receptors by extracellular ions and other molecules, and temporal and spatial properties of synaptic and nonsynaptic input.

Nonneural cells, such as astrocytes and oligodendrocytes, have an important role in many of these mechanisms as well. Certain recognized causes of seizures are explained by these mech- anisms.

For example, accidental ingestion of domoic acid, an analogue of glutamate (the principal excitatory neurotransmitter in the brain) produced by naturally occurring microscopic algae, causes profound seizures via direct activation of excitatory amino acid receptors throughout the CNS.

Penicillin, which can lower the seizure threshold in humans and is a potent convulsant in experimental models, reduces inhibition by antagonizing the effects of GABA at its receptor. The basic mechanisms of other precipitating factors of seizures, such as sleep deprivation, fever, alcohol withdrawal, hypoxia, and infection, are not as well understood but presumably involve analogous perturbations in neuronal excitability.

Similarly, the endogenous factors that determine an individual's seizure threshold may relate to these properties as well. Knowledge of the mechanisms responsible for initiation and propagation of most generalized seizures (including tonic-clonic, myoclonic, and atonic types) remains rudimentary and reflects the limited understanding of the connectivity of the brain at a systems level.

Much more is understood about the origin of generalized spike-and-wave discharges in absence seizures. These appear to be related to oscillatory rhythms normally generated during sleep by circuits connecting the thalamus and cortex.

This oscillatory behaviour involves an interaction between $GABA_B$ receptors, T-type Ca^{2+} channels, and K^{+} channels located within the

thalamus. Pharmacologic studies indicate that mod- ulation of these receptors and channels can induce absence seizures, and there is good evidence that the genetic forms of absence epilepsy may be associated with mutations of components of this system.

Seizure etiology is a wide range, depending on the age, of which electrolyte abnormalities play an important role in causation.

Hyponatremia as well as hypernatremia, hypocalcaemia, hypomagnesemia, hyperglycemia and other hyperosmolar states, hypoglycemia, thyrotoxic storm are important electrolyte and metabolic disturbances that can be complicated by generalised and multifocal seizures.

Rapidly developing electrolyte imbalances are known to cause seizures than those abnormalities that occur gradually.

Treatment with antiepileptic drugs is not necessary in many of these electrolyte and metabolic disturbances as long as the underlying disturbance is corrected.

Indeed, antiepileptic drugs are usually not effective in halting these seizures if the underlying electrolyte / metabolic disturbance is not corrected. Seizures in these conditions can be traced to and appropriate blood investigations will usually reveal the causative electrolyte or metabolic abnormality.

There is limited published data on etiology of seizures in Asia. Hence this study is being carried out to find reversible etiologies of acute symptomatic seizures before considering pharmacotherapy and to distinguish unprovoked and provoked seizures during diagnostic procedure.

Aim

To estimate the electrolyte imbalances in patients aged more than 18 years presenting with first episode of seizures.

Materials and methods

Study population

This study was conducted on 45 patients admitted in department of General Medicine and Department of Neurology, in Alluri SitaramaRaju Academy Of Medical Sciences and hospital, Eluru, with new onset focal/ generalised seizures.

Study design

Cross sectional descriptive study.

Approved by the institutional ethical committee. An individual informed consent was taken from all the patients selected for the study

Duration of study

12 months (October 2020 to October 2021)

Incusion criteria

All the patients with first episode of focal or generalised seizures, with age of onset of seizures >18 years, admitted in department of General Medicine and Department of Neurology, Alluri SitaramaRaju Academy Of Medical Sciences and hospital, Elurufrom October 2020 to October 2021.

Exclusion criteria

Patients with past history of seizures.

Investigations

- Complete blood picture
- RBS
- Serum Electrolytes (Sodium, potassium, calcium, magnesium)
- RFT
- LFT
- CT brain
- MRI brain- only if CT brain was inconclusive
- EEG.

Results

Total number of cases studied=45

Table 1: age distribution

age category	Frequency	Percentage
18-20 Years	1	2.22%
21-40 Years	9	20%
41-60 Years	27	60%
> 60 years	8	17.78%

Gender distribution

Females – 14 (30%), Males – 31 (70%)

Frequency distribution of type of seizure observed in the study

GTCS is present in 33 members (73.34%)

Focal seizure is present in 10 members (22.21%)

Status epilepticus is present in 2 members (4.45%)

Table 2: frequency and percentage distribution of type of etiology noted for epilepsy in the study (total n= 45):

Etiology for epilepsy	Frequency	Percentage
Metabolic	21	46.67%
CVD related	11	24.45%
Alcohol related	5	11.12%
Infectious causes	6	13.30%
ICSOL	1	2.23%
Idiopathic	1	2.23%

Table 3: frequency and percentage distribution of various metabolic abnormalities, as the etiology for seizures noted in the study:

Metabolic abnormality	Frequency	Percentage
Hyperglycemia	9	20%
Uremia	5	11.12%
Electrolyte imbalance as the sole cause of seizures	5	11.12%
Hypoglycemia	2	4.43%
Total	21	46.67%

Frequency and percentage distribution of electrolyte abnormalities in the study (total n= 45):

Present in 13 members (28.89%)

Absent in 32 members (71.11%)

Table 4: frequency distribution of electrolyte abnormality noted in the study:

Electrolyte Abnormality	Frequency	Percentage
Hyponatremia	10	22.23%
Hypocalcemia	1	2.22%
Hypomagnesemia	1	2.22%
Hyponatremia and Hypokalemia	1	2.22%
Total	13	28.89%

Discussion

Metabolic abnormalities were most common cause of seizures in this study, seen in 21 patients (46.67%) out of which hyperglycemia was the most common cause seen in 9 patients, followed by uremia in 5 patients, electrolyte abnormalities as independent cause in 5 patients and hypoglycaemia in 2 patients.

The second most common cause of seizures, in this study was found to be cerebrovascular diseases (Intracerebral haemorrhage, ischemic stroke, cerebral venous thrombosis) seen in 11 patients.

CNS infections were the 3rd most common cause of seizures in this study, seen in 6 patients. Alcohol related, ICSOL and idiopathic were other cause of seizures in this study.

Out of 45 patients, 13 patients had electrolyte disturbances, of which the most common abnormality observed was hyponatremia, seen in 10 patients. Other abnormalities were hypocalcaemia in 1 patient, hypomagnesemia in 1 patient, hypokalemia in 1 patient.

Conclusion

From this study, among various causes of seizures, electrolyte abnormalities were most commonly seen in patients with metabolic causes.

The study results showed a significant association between electrolyte imbalance and the first episode of seizures, the most common electrolyte abnormality being hyponatremia.

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