Study of Serum Magnesium and Calcium Levels in Patients with new onset Seizures

Authors
Dr Shiva Kumar Mohanta, Dr Manoranjan Naik, Dr Malati Murmu
ViMSAR, Burla

Abstract
Background: The electrolyte imbalances cause various neurological dysfunction & these electrolyte abnormalities frequently cause seizures AS these ions are important in the normal functioning of nervous system. Seizures are especially common with hypomagnesemia and hypocalcemia.

Objective: To study the serum magnesium and calcium levels in patients with new onset seizures.

Methods: The study was carried out from November 2016 to October 2018 at VSS institute of medical science & research, Burla Sambalpur. The study included 120 cases presented with seizures & 120 controls matched with the cases.

Results: Serum magnesium and calcium levels were low in patients with new onset seizures when compared to controls.

Conclusion: Serum magnesium and calcium level may be used for evaluation of seizures as rapid and timely identification and correction can help to reduce morbidity and mortality associated with seizures due to electrolyte disturbances.

Keywords: Serum, Magnesium, Calcium, Hypomagnesemia, Hypocalcemia, Seizure.

Introduction
Epilepsy describes a condition in which a person has recurrent seizures due to a chronic, underlying process. This definition implies that a person with a single seizure or recurrent seizures due to correctable or avoidable circumstances, does not necessarily have epilepsy.1 Using the definition, Epilepsy is defined as two or more than two unprovoked seizures.2

The incidence of epilepsy is ~0.3–0.5% in different populations throughout the world and the prevalence of epilepsy has been estimated at 5–30 persons per 1000.1

A seizure (from the latin SACIRE, “to take possession of”) is a paroxysmal event due to abnormal, excessive or synchronous discharges from an aggregate of CNS neurons. Seizures can vary from the briefest lapses of attention or muscle jerks to severe and prolonged convulsions.2

Basically seizures can be classified as generalised or focal. It is very important to collect the information from the person who has observed the ‘fit’ for the classification of the seizure.

Focal seizures originate within networks limited to one brain region. Generalized seizures arise within and rapidly engage networks distributed across both cerebral hemisphere.
Causes of epilepsy are multiple. Seizure itself is a symptom of an underlying disorder of brain, which may be structural, chemical, physiological or a combination of all three. Seizures are accompanied by profound changes in the cerebral metabolism and conversely metabolic changes in the brain can give rise to seizure. Disturbances in mineral and electrolyte homeostasis clinically manifest commonly as convulsions and can be accompanied by reversible neurological dysfunction. Minerals such as magnesium and Calcium play active role in various metabolic processes. The disturbances in homeostasis of these elements cause various neurological dysfunction & these electrolyte abnormalities are important in the pathophysiology of seizures.

Magnesium is well known for its diverse actions within the human body. From neurological standpoint, magnesium plays an essential role in nerve transmission and neuromuscular conduction. Magnesium results in state of neuronal hyper excitability and marked irritability and results in epileptic seizures. Mg deficiency should be considered a possible contributing factor in many seizure disorders because it is responsible for maintaining homeostasis of other electrolytes such as potassium and calcium and for regulating action potentials within the nervous system.

For example, extracellular Mg ions affect the voltage dependent activation of the N-methyl-d-aspartate (NMDA) receptor Chronic magnesium deprivation lowers NMDA receptor-related seizure threshold and severe magnesium deficiency has been shown to cause seizure. One of the main neurological functions of magnesium is due to magnesium’s interaction with the N-methyl-D-aspartate (NMDA) receptor. Magnesium serves as a blockade to the calcium channel in the NMDA receptor and must be removed for glutamatergic excitatory signaling to occur. Glutamate is a major excitatory neurotransmitter in the brain acting as an agonist at NMDA receptors. Extracellular Mg2+ normally blocks NMDA receptors. Thus hypomagnesemia may release the inhibition of NMDA receptor. This leads to glutamate-mediated depolarization of the postsynaptic membrane and enhancement of epileptiform electrical activity.

Low magnesium levels may theoretically potentiate glutamatergic neurotransmission, leading to a supportive environment for excitotoxicity, leading to seizure.

Hypocalcemia and hypomagnesemia cause mainly CNS neuronal irritability with seizures. When the extracellular concentration of calcium ions falls below normal, the nervous system becomes progressively more excitable, because this causes neuronal membrane permeability to sodium ions, allowing easy initiation of action potentials. At plasma calcium ion concentrations about 50 percent below normal, the peripheral nerve fibers become so excitable that they begin to discharge spontaneously, initiating trains of nerve impulses that passes to the peripheral skeletal muscles to elicit tetanic muscle contraction.

As mechanics of calcium at cellular level are dependent on serum magnesium levels, hypomagnesemia via causing hypocalcemia causes the same. Mechanism of calcium regulation on neurons is coherent with magnesium levels and hypomagnesaemia in itself interferes with the action of calcium at cellular level causing seizures.

**Materials and Methods**

The study was carried out in Department of General Medicine, VSSIMSAR, Burla, Sambalpur. From November 2016 to October 2018. 120 cases with new onset seizures were selected based on clinical characteristics supplemented by circumstantial evidence and objective imaging or electrophysiological correlation. The control group comprised of 120 normal healthy individuals matched with age & sex without h/o convulsion. The study was approved by ethical committee. Routine laboratory investigations were done in all cases at admission included complete blood count, ESR,
serum electrolytes (sodium, potassium, magnesium, calcium), liver function tests, random blood sugar, serum albumin. Corrected calcium was calculated for those with hypoalbuminemia. EEG was done in all patients within 24 hr of admission. Brain imaging CT scan was done in all cases and MRI was done in selected cases. For Data analysis, MS Office Excel was used.

Results

Table – 1 Sex Wise Distribution of Cases (n=120)

| SEX    | NO OF CASES | PERCENTAGE(%) |
|--------|-------------|---------------|
| MALE   | 83          | 69            |
| FEMALE | 37          | 31            |
| TOTAL  | 120         | 100           |

Out of 120 cases, 83 (69%) were males & 37 (31%) were females. Above table shows male preponderance with Male : Female ratio of 2.24 : 1

Figure - 1 Sex Wise Distribution of Cases (n=120)

Table-2 Age & Sex Wise Distribution of study Subjects (n= 120)

| AGE GROUP | MALE | FEMALE | TOTAL |
|-----------|------|--------|-------|
| 15-25     | 8(66.7)% | 4(33.3)% | 12(100)% |
| 26-35     | 22(71%) | 9(29%)  | 31(26%) |
| 36-45     | 30(72%) | 12(28%) | 42(35%) |
| 46-55     | 19(68%) | 9(32%)  | 28(23%) |
| 56-65     | 2(50%)  | 2(50%)  | 4(3%) |
| >65       | 2(66.7%) | 1(33.3%) | 3(3%) |
| TOTAL     | 83(69%) | 37(31%) | 120(100%) |

In this study, mean age of males, females, & total cases are 39.7, 41 & 40.1 respectively. Maximum no of cases 42 (35%) were in the age group 36-45 years & minimum cases 7(6%) were in age group of >55 years

Figure-2 Age & Sex Wise Distribution of study Subjects (n= 120)

Table-3 Sex Wise Distribution of Seizure Types (n=120)

| TYPE OF SEIZURE       | MALE | FEMALE | TOTAL |
|-----------------------|------|--------|-------|
| GENERALISED TONIC CLONIC SEIZURE | 55   | 29     | 84    |
| FOCAL SEIZURE         | 28   | 8      | 36    |
| TOTAL                 | 83   | 37     | 120   |

This study accounts for 84 (70%) cases of generalised tonic clonic seizure, 36 (30%) cases of focal seizure.

Table-4 Age wise Distribution of Seizure Types

| AGE GROUP | GTCS | FS | TOTAL |
|-----------|------|----|-------|
| 15-25     | 8    | 4  | 12    |
| 26-35     | 19   | 12 | 31    |
| 36-45     | 30   | 12 | 42    |
| 46-55     | 21   | 7  | 28    |
| 56-65     | 3    | 1  | 4     |
| >65       | 3    | 0  | 3     |
| TOTAL     | 84   | 36 | 120   |

Present study shows most cases of GTCS were in age group of 36-45 yr followed by 46-55 yr and most cases of FS were in age group of 36-45 and 26-35.
Table No 5: Serum Electrolyte Level in Cases (n=120)

| ELECTROLYTE | SERUM VALUE | NO OF CASES |
|-------------|-------------|-------------|
| MAGNESIUM   | LOW         | 49          |
|             | NORMAL      | 71          |
| CALCIUM     | LOW         | 29          |
|             | NORMAL      | 91          |

Study group showed 49 patients having hypomagnesemia and 29 patients having hypocalcemia.

Figure-3: Serum Electrolyte Level in Cases (n=120)

Table - 7: Serum Calcium in Study Subjects (n=240)

| CALCIUM LEVEL | CASES(n=120) | CONTROLS(n=120) |
|---------------|-------------|-----------------|
|               | MALE | FEMALE | TOTAL | MALE | FEMALE | TOTAL |
| NORMAL LEVEL  | 8.5-10.5 mg/dl | 65 | 26 | 91 | 80 | 40 | 120 |
| LOW LEVELS    | <8.5 mg/dl  | 18 | 11 | 29 | 0 | 0 | 0 |

Study group showed 29 patients having serum calcium level less than 8.5 mg/dl. compared to 120 controls where serum calcium level was normal. Hypocalcemia was seen in 18 male patients and 11 female patients.

Table 8: Mean Electrolyte Level in Study Subjects

| ELECTROLYTE | STUDY SUBJECTS | NUMBER | MEAN | STANDARD DEVIATION |
|-------------|----------------|--------|------|-------------------|
| MAGNESIUM   | CASES 120      | 1.37   | 0.29 |
|             | CONTROLS 120   | 1.92   | 0.19 |
| CALCIUM     | CASES 120      | 7.92   | 0.17 |
|             | CONTROLS 120   | 9.12   | 0.27 |

The mean serum magnesium in cases and controls was 1.37±0.29 & 1.92 ±0.19 respectively. The mean value of serum calcium in cases and controls were 7.92±0.17 & 9.12±0.27 respectively.

Table 9: Mean Electrolyte Level in Seizure Types

| ELECTROLYTE | SEIZURE TYPES | NUMBER | MEAN | STANDARD DEVIATION |
|-------------|---------------|--------|------|-------------------|
| HYPMAGNESIEMIA | GTCS | 34 | 1.39 | 0.52 |
|             | FS            | 15     | 1.42 | 0.34 |
| HYPOCALCEMIA | GTCS | 21 | 7.85 | 0.18 |
|             | FS            | 8      | 8.14 | 0.47 |

The mean serum magnesium in GTCS and FS was 1.39±0.52 & 1.42 ±0.34 respectively. The mean value of serum calcium in GTCS and FS were 7.85±0.18 & 8.14±0.47 respectively.
Table -10: Mean Magnesium Level in Seizure Types

| SEIZURE TYPES | MAGNESIUM LEVEL | NUMBER | MEAN  | STANDARD DEVIATION |
|---------------|-----------------|--------|-------|--------------------|
| GTCS          | NORMAL Mg       | 50     | 1.94  | 0.52               |
|               | LOW Mg          | 34     | 1.39  | 0.52               |
| FS            | NORMAL Mg       | 21     | 2.12  | 0.18               |
|               | LOW Mg          | 15     | 1.42  | 0.34               |

Out of GTCS cases, serum magnesium was low in 34 cases & 50 cases. Out of FS cases, serum magnesium was low in 15 cases & normal in 21 cases.

Figure- 4: Serum Magnesium Level in Seizure Types

Table -11: Mean Calcium Level In Seizure Types

| SEIZURE TYPES | CALCIUM LEVEL | NUMBER | MEAN  | STANDARD DEVIATION |
|---------------|---------------|--------|-------|--------------------|
| GTCS          | NORMAL Ca     | 63     | 9.42  | 0.22               |
|               | LOW Ca        | 21     | 7.85  | 0.18               |
| FS            | NORMAL Ca     | 24     | 9.28  | 0.18               |
|               | LOW Ca        | 8      | 8.14  | 0.47               |

Out of GTCS cases, serum calcium was low in 21 cases & 63 cases. Out of FS cases, serum calcium was low in 8 cases & normal in 28 cases.

Discussion

The present study entitled ‘Study of Serum magnesium and calcium level in patients with new onset seizures’ included 120 patients presented with new onset seizures, admitted to Department of General medicine, VSS Institute of Medical Science and Research, Burla during the period from November 2016 to October 2018. Out of 120 cases , 83 cases were males & 37 cases were females with male preponderance with male to female ratio of 2.24 :1 The mean age of presentation of cases was 40.1 .The mean age of females having marginally higher was 41 and of males was 39.7.

The study population was divided in to 6 age groups with highest no of cases 42 cases were in age group 36-45, 31 cases were in age group 26-35, 28 cases were in age group 46-55, 12 cases were in age group15-25, 4 cases were in age group 56-65, 3 cases were in age group >65 yr. Significant hypomagnesemia and hypocalcemia was observed in different age groups of cases as compare with controls. Observation was same with Jassim M et al13

Hypomagnesemia was seen in 49 cases & serum magnesium was found in the normal range in controls. The value of Mean serum magnesium &Standard deviation of cases were 1.37±0.29 compared to controls were 1.92±0.19. The difference in serum magnesium level was found statistically highly significant by perfoming unpaired t test analysis (p<0.01).
Other studies by Ramakrishna C et al, Chavan V D et al, Oladipo OO et al, Canclas H et al, Djokic G et al, Jassim M et al had more or less similar results. According to study, hypocalcemia was seen in 29 cases. The mean value of serum calcium in cases and controls were 7.92±0.17 & 9.12±0.27 respectively. The mean value of serum calcium is low in cases compared to the controls found to be statistically significant (p <0.01). Other studies by Ramakrishna C et al, Jassim M et al, Parihar P et al had more or less similar results. Present study showed Generalised tonic clonic seizure as most common type of presentations accounting for 84 cases and Focal seizures 36 cases. Out of GTCS cases, serum magnesium was low in 34 cases & normal in 50 cases. Out of FS cases, serum magnesium was low in 15 cases & normal in 21 cases. Out of GTCS cases, serum calcium was low in 21 cases & normal in 63 cases. Out of FS cases, serum calcium was low in 8 cases & normal in 28 cases. The hypomagnesaemia and hypocalcemia in GTCS & FS cases was observed statistically highly significant when compared with healthy controls. (p <0.01). This goes in accordance with the study by Parihar P et al. The mean serum magnesium in GTCS and FS was 1.39±0.52 & 1.42 ±0.34 respectively. The mean value of serum calcium in GTCS and FS were 7.85±0.18 & 8.14±0.47 respectively.

**Conclusion**

Serum magnesium and calcium levels decreased significantly in patients with new onset seizures when compared to the controls. Seizures manifest an important clinical manifestations of electrolyte disturbances. Hence measurements of these electrolytes should be part of the initial diagnostic work up in adult patients with new onset Seizures. The study also found a statistically significant association with hypomagnesemia and hypocalcemia with seizure. Considering the role of magnesium and calcium in the pathophysiology of seizures and by evaluating the results from the present study, magnesium and calcium levels in patients with seizures could be a useful strategy for managing severity of new onset seizures.

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