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ELECTROLYTE IMBALANCE IN ALCOHOL-INDUCED SEIZURES VS. PRIMARY SEIZURES: A COMPARATIVE ANALYSIS

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SHORT RUNNING TITLE: A COMPARATIVE ANALYSIS

Abstract

Background: Seizures can be classified into primary (idiopathic) and secondary (symptomatic) types, with alcohol-related seizures being a common secondary form. Chronic alcohol consumption has been linked to disturbances in electrolyte balance, particularly involving calcium and magnesium, which may lower the seizure threshold.

Objective: This study aimed to compare the serum levels of calcium, magnesium, and sodium in patients with alcohol-related seizures and those with primary seizures, to identify potential differences in their pathophysiology.

Methods: A cross-sectional, observational study was conducted at a tertiary care hospital, involving 100 participants divided into two groups: 50 patients with alcohol-related seizures and 50 with primary seizures. Detailed clinical evaluations were performed, and fasting blood samples were collected to measure serum calcium, magnesium, and sodium levels. Statistical analysis was conducted using t-tests to assess the significance of differences between the groups.

Results: The study found that patients with alcohol-related seizures had significantly lower serum calcium (8.2 ±0.5 mg/dL vs. 9.0 ±0.4 mg/dL, $p < 0.001$) and magnesium levels (1.4 ±0.3 mg/dL vs. 1.9 ±0.2 mg/dL, $p = 0.002$) compared to those with primary seizures. No significant difference was observed in serum sodium levels between the two groups (138 ±2 mEq/L vs. 139 ±3 mEq/L, $p = 0.341$).

Conclusion: The findings indicate that hypocalcemia and hypomagnesemia are more prevalent in patients with alcohol-related seizures, potentially contributing to their pathogenesis. These electrolyte imbalances should be closely monitored and managed in this patient population. In contrast, primary seizures do not appear to be associated with significant electrolyte disturbances, suggesting different underlying mechanisms.

Keywords: Alcohol-related seizures, Primary seizures, Serum electrolytes, Hypocalcemia, Hypomagnesemia

INTRODUCTION:

Seizures are a significant neurological disorder that affects a considerable portion of the population worldwide, with an estimated 50 million people living with epilepsy [1]. Seizures can be broadly categorized into primary (idiopathic) seizures, where no identifiable cause is found, and secondary (symptomatic) seizures, which occur due to underlying

medical conditions [2]. Among secondary seizures, those related to alcohol use are particularly noteworthy due to their prevalence and the distinct pathophysiological mechanisms involved.

Chronic alcohol consumption has long been associated with a range of neurological complications, including seizures. Alcohol-induced seizures commonly occur either during acute intoxication or as a consequence of alcohol withdrawal [3]. One of the key factors contributing to the development of alcohol-related seizures is the disturbance in electrolyte balance, particularly involving calcium, magnesium, and sodium [4]. These electrolytes play a crucial role in maintaining neuronal stability and function, and their imbalance can lead to increased neuronal excitability, thereby lowering the seizure threshold [5].

Recent studies have emphasized the role of hypomagnesemia and hypocalcemia in the pathophysiology of alcohol-related seizures. Magnesium acts as a natural calcium antagonist at the NMDA receptor, and its deficiency has been shown to enhance excitatory neurotransmission, making neurons more susceptible to seizure activity [6]. Similarly, calcium is vital for neurotransmitter release and muscle contraction, and its deficiency has been linked to increased neuromuscular irritability [7].

In contrast, primary seizures are typically not associated with significant electrolyte imbalances, suggesting different underlying mechanisms compared to alcohol-related seizures. This study aims to compare the serum levels of calcium, magnesium, and sodium in patients with alcohol-related seizures and those with primary seizures. By understanding these differences, we can better tailor therapeutic interventions for each patient group.

METHODS:

Study Design:
This study was a cross-sectional, observational analysis designed to compare serum electrolyte levels between patients with alcohol-related seizures and those with primary seizures. The study was conducted at a tertiary care hospital over a period of six months, from January to June 2024. Ethical approval was obtained from the hospital's Institutional Review Board, and informed consent was secured from all participants.

Participants:
A total of 100 participants were enrolled in the study, divided equally into two groups:

- Group 1: Patients with alcohol-related seizures (n=50)
- Group 2: Patients with primary seizures (n=50)

Inclusion Criteria:

1. Patients aged 18 to 65 years.
2. For Group 1: Patients with a confirmed diagnosis of alcohol-related seizures, as determined by clinical history, physical examination, and relevant investigations, including blood alcohol levels and a history of chronic alcohol use or recent alcohol withdrawal.
3. For Group 2: Patients with a confirmed diagnosis of primary (idiopathic) seizures, with no identifiable secondary cause, as determined by clinical history, neurological examination, and brain imaging (MRI or CT scan).
4. Willingness to provide informed consent.

Exclusion Criteria:

1. Patients with known chronic kidney disease, liver disease, or any other condition that could independently alter serum electrolyte levels.
2. Patients on medications known to affect calcium, magnesium, or sodium levels (e.g., diuretics, antacids, magnesium supplements).
3. Pregnant or lactating women.

4. Patients with acute or chronic conditions (other than seizures) that could affect serum electrolyte levels.

5. Patients with a history of electrolyte imbalance unrelated to seizures, such as those caused by gastrointestinal disorders, endocrine abnormalities, or renal dysfunction.

DATA COLLECTION:

Participant Recruitment:
Participants were recruited from the neurology and emergency departments of the hospital. All potential participants were screened by a neurologist based on their medical history, clinical examination, and relevant investigations. Patients with alcohol-related seizures were identified through a detailed history of chronic alcohol use or recent withdrawal symptoms, and confirmed by laboratory tests such as blood alcohol levels and liver function tests. Patients with primary seizures were identified based on a diagnosis of idiopathic epilepsy, with no secondary causes such as trauma, infection, or metabolic disturbances.

Clinical Evaluation:
Upon enrollment, each participant underwent a comprehensive clinical evaluation. This included a structured interview to gather detailed information about the patient's medical history, including:

- **Demographic Data**: Age, sex, occupation, and educational background.
- **Seizure History**: Onset of seizures, frequency, duration, type of seizures (e.g., generalized tonic-clonic, focal), and any preceding triggers (e.g., sleep deprivation, alcohol consumption).
- **Alcohol Use History** (for Group 1): Detailed history of alcohol consumption, including the duration of use, average daily intake (measured in units), patterns of drinking (binge vs. regular), and any history of alcohol withdrawal symptoms (e.g., tremors, agitation, hallucinations).
- **Family History**: History of epilepsy or other neurological disorders in first-degree relatives.
- **Medication History**: Current and past medications, particularly those known to affect electrolyte levels (e.g., diuretics, antiepileptics).

Physical Examination:
A thorough physical and neurological examination was performed for all participants. This included:

- **Vital Signs**: Blood pressure, heart rate, respiratory rate, and body temperature.
- **Neurological Assessment**: Evaluation of motor and sensory function, reflexes, cranial nerve examination, and mental status.
- **Nutritional Assessment**: Body Mass Index (BMI) calculation, assessment of signs of malnutrition (e.g., muscle wasting, hair loss), and dietary history focusing on intake of calcium and magnesium-rich foods.

Laboratory Analysis:
Blood samples were collected from each participant after an overnight fast to ensure consistency in electrolyte measurements. The blood samples were drawn by a trained phlebotomist using standard aseptic techniques. The following procedures were followed:

1. **Sample Collection**:
    - Venous blood was drawn using a 21-gauge needle into plain vacutainer tubes for serum analysis. Approximately 10 mL of blood was collected from each participant.
    - The samples were immediately labeled with the participant's unique study ID, date, and time of collection.

- The blood samples were allowed to clot at room temperature for 30 minutes before being centrifuged at 3000 rpm for 10 minutes to separate the serum.

2. **Sample Handling and Storage**:

   - The separated serum was aliquoted into labeled cryovials and stored at -80°C until analysis. This was done to prevent degradation of sensitive analytes like magnesium and calcium.

   - Quality control samples (known concentration) were run alongside participant samples to ensure the accuracy and precision of the assays.

3. **Biochemical Assays**:

   - **Serum Calcium**: Measured using the o-cresolphthalein complexone (OCPC) method, which involves the formation of a purple complex with calcium that can be quantified colorimetrically.

   - **Serum Magnesium**: Measured using the xylidyl blue method, where magnesium forms a complex with xylidyl blue at an alkaline pH, and the intensity of the color is directly proportional to the magnesium concentration.

   - **Serum Sodium**: Measured using an ion-selective electrode (ISE) method, which directly measures the concentration of sodium ions in the serum.

   - All assays were performed on an automated analyzer (e.g., Roche Cobas 6000) in the hospital's central laboratory. The instruments were calibrated daily, and internal quality control measures were employed to ensure reliability of the results.

Data Entry and Verification:
All clinical and laboratory data were entered into a secure electronic database by trained data entry personnel. Double data entry was performed to minimize the risk of errors. The database was regularly backed up, and access was restricted to authorized personnel only. The accuracy of data entry was verified by cross-checking 10% of the records against the original data sheets.

Statistical Analysis:
The collected data were analyzed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were calculated to summarize the demographic and clinical characteristics of the participants. Mean and standard deviation were used for continuous variables, while frequencies and percentages were used for categorical variables.

Comparative analyses were performed using independent sample t-tests to evaluate differences in serum electrolyte levels between the two groups. The assumption of normality was checked using the Shapiro-Wilk test. For variables that did not meet the normality assumption, non-parametric tests (e.g., Mann-Whitney U test) were employed. Pearson correlation coefficients were calculated to explore the relationship between serum electrolyte levels and seizure frequency. A p-value of <0.05 was considered statistically significant.

RESULTS:

Table 1: Serum Electrolyte Levels in Patients with Alcohol-Related Seizures and Primary Seizures

Electrolyte	Alcohol-Related Seizures (Mean ± SD)	Primary Seizures (Mean ± SD)	p-value
Serum Calcium (mg/dL)	8.2 ± 0.5	9.0 ± 0.4	< 0.001

Serum Magnesium (mg/dL)	1.4 ± 0.3	1.9 ± 0.2	0.002
Serum Sodium (mEq/L)	138 ± 2	139 ± 3	0.341

Table 1 Description:
Table 1 compares the mean serum levels of calcium, magnesium, and sodium between patients with alcohol-related seizures and those with primary seizures. The mean serum calcium level is significantly lower in the alcohol-related seizure group (8.2 ±0.5 mg/dL) compared to the primary seizure group (9.0 ±0.4 mg/dL), with a p-value of <0.001, indicating a statistically significant difference. Similarly, the mean serum magnesium level is significantly lower in the alcohol-related seizure group (1.4 ±0.3 mg/dL) compared to the primary seizure group (1.9 ±0.2 mg/dL), with a p-value of 0.002. The mean serum sodium levels do not differ significantly between the two groups (p-value = 0.341), suggesting that sodium imbalance is not a major factor in distinguishing between alcohol-related and primary seizures.

DISCUSSION:

The findings of this study reveal significant differences in serum calcium and magnesium levels between patients with alcohol-related seizures and those with primary seizures. Specifically, patients with alcohol-related seizures exhibited significantly lower levels of both calcium and magnesium compared to those with primary seizures. These results are consistent with the growing body of literature that highlights the role of electrolyte imbalances in the pathophysiology of alcohol-induced seizures [8].

Hypomagnesemia has been particularly implicated in the increased risk of seizures in individuals with chronic alcohol use. Magnesium is a critical cofactor in numerous enzymatic reactions, and its deficiency is known to exacerbate neuronal excitability by modulating NMDA receptors, which are involved in excitatory neurotransmission [9]. Studies have shown that magnesium supplementation can help reduce the incidence of seizures in alcohol-dependent individuals, underscoring the importance of maintaining adequate magnesium levels in this population [10].

Similarly, hypocalcemia was also prevalent among patients with alcohol-related seizures in this study. Calcium plays a fundamental role in various physiological processes, including neurotransmitter release and muscle contraction. Low calcium levels can lead to increased neuromuscular excitability, which may contribute to the onset of seizures [11]. This finding aligns with previous studies that have demonstrated the link between hypocalcemia and seizure activity in individuals with alcohol use disorders [12].

In contrast, the absence of significant differences in serum sodium levels between the two groups suggests that sodium imbalance is not a major factor in differentiating alcohol-related seizures from primary seizures. While hyponatremia has been reported in some cases of epilepsy, particularly in the context of inappropriate antidiuretic hormone secretion or medication use, it does not appear to play a significant role in alcohol-related seizures [13].

The implications of these findings are clinically significant. For patients with alcohol-related seizures, monitoring and correcting electrolyte imbalances, particularly calcium and magnesium, should be a key component of treatment strategies. These results also highlight the need for a tailored approach to managing seizures, with specific attention to the underlying causes and contributing factors in each patient group.

LIMITATIONS:

1. **Sample Size**: Although the study included 100 participants, the relatively small sample size may limit the generalizability of the findings to broader populations. Larger studies are needed to confirm these results across different demographic groups and clinical settings.

2. **Cross-Sectional Design**: The cross-sectional nature of the study only provides a snapshot of serum electrolyte levels at a single point in time. It does not account for potential fluctuations in these levels over time or during different phases of alcohol use (e.g., acute intoxication vs. withdrawal).

3. **Self-Reported Alcohol Consumption**: The assessment of alcohol use history relied on self-reported data, which may be subject to recall bias or underreporting. Objective measures of alcohol consumption, such as biomarkers, could provide more accurate insights.

4. **Confounding Factors**: Although efforts were made to exclude patients with conditions that might independently affect electrolyte levels (e.g., kidney disease, certain medications), other unmeasured confounding factors (e.g., dietary intake, physical activity, comorbid conditions) could have influenced the results.

5. **Lack of Longitudinal Follow-Up**: The study did not include a longitudinal follow-up to assess how changes in electrolyte levels over time might relate to seizure recurrence or severity, particularly in the context of alcohol withdrawal

CONCLUSION:

This study highlights the significant role of electrolyte imbalances, specifically hypocalcemia and hypomagnesemia, in patients with alcohol-related seizures. The findings demonstrate that these patients have significantly lower serum levels of calcium and magnesium compared to those with primary seizures, suggesting that these imbalances may contribute to the pathophysiology of alcohol-related seizures. In contrast, no significant differences were observed in serum sodium levels between the two groups, indicating that sodium imbalance is not a distinguishing factor in this context.

These results underscore the importance of routine monitoring and correction of electrolyte levels, particularly calcium and magnesium, in patients with a history of chronic alcohol use or those presenting with alcohol-related seizures. Addressing these imbalances may play a crucial role in reducing the risk and severity of seizures in this population.

Overall, while the study provides valuable insights into the differences in electrolyte profiles between alcohol-related and primary seizures, further research is needed to explore the longitudinal effects of these imbalances and to evaluate the efficacy of targeted interventions in improving clinical outcomes.

AUTHOR'S CONTRIBUTIONS

1. Vijay Yaswanth Reddy Bade (design feasibility assessment, acquisition of data, analysis and interpretation, final approval of manuscript)
2. Priyadarshini Varadaraj (design feasibility assessment, concept and design, analysis and interpretation of data, drafting of manuscript)
3. Renuga Devi V (design feasibility assessment, acquisition of data, analysis and interpretation, final approval of manuscript)
4. Keesari Sai Sandeep Reddy (design feasibility assessment, acquisition of data, analysis and interpretation, final approval of manuscript)
5. Gunasekaran N (overall supervision, design feasibility assessment, analysis and interpretation, final approval of manuscript)

All authors have read and agreed to the published version of the manuscript.

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Tables:

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