

Electrolyte Profile Of Epileptic Patients On Carbamazepine Monotherapy

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Abstract

Epileptic seizures result from disruption in electrical activity among neurons. Adequate amount of electrolytes is essential for a healthy nervous system. The existing knowledge on the impact of antiepileptic drugs on serum electrolyte is still controversial.

This study was designed to determine the effects of long term use of carbamazepine on serum concentrations of calcium, magnesium, inorganic phosphate and alkaline phosphatase in complex partial and generalized tonic-clonic seizure patients at University of Ilorin Teaching Hospital, Ilorin, Nigeria. It was a cross-sectional study involving 23 seizure disorder adult patients on carbamazepine monotherapy. Serum was analyzed for calcium, magnesium, inorganic phosphate, alkaline phosphatase and albumin using complexometric and colorimetric methods.

Serum concentration of calcium (albumin adjusted calcium 3.47 ± 0.09) and alkaline phosphatase (261.87 ± 14.53) were significantly ($P < 0.05$) higher in subjects on carbamazepine compared to the control group (2.64 ± 0.04 and 146.67 ± 4.11) respectively. In addition serum concentration of magnesium (1.35 ± 0.04) was significantly higher in the subjects compared to the control group (1.04 ± 0.02) but within the normal range. Inorganic phosphate though significantly lower in the subjects was also within the normal range. In the control group, serum concentration of calcium was strongly correlated with concentration of magnesium, alkaline phosphatase and inorganic phosphate. This linearity was lost completely in epileptic patients on carbamazepine.

In this study, an increase in serum calcium, alkaline phosphatase, magnesium and a decrease in inorganic phosphate were found in epileptic patients on carbamazepine monotherapy. Monitoring serum concentration of these electrolytes may be of benefit to the patients' management.

Keywords: Epilepsy, serum calcium, magnesium, alkaline phosphatase, inorganic phosphate

Introduction

Epilepsy is a neurological disorder that affects people in every country throughout the world. It is characterized by a tendency to recurrent seizures and defined by two or more unprovoked seizures. Epilepsy affects at least 50 million people in the world¹ and about 3 percent of the general population will experience an epileptic seizure by age seventy-five². Studies in developing countries reveal a prevalence of more than 10 per 1,000³. In both developed and developing countries up to 70 % of newly diagnosed children and adults with epilepsy are successfully treated with anti-epileptic drugs¹. The use of these drugs is often limited by side-effects, but therapy of epilepsy needs to be maintained to avoid recurrent seizures with all its potential personal and social problems⁴. The existing knowledge on the impact of epilepsy and antiepileptic drugs (AEDs) on serum electrolyte is still controversial. Serum levels of magnesium and calcium have been found to play a vital role for seizure condition to develop⁵. Hypomagnesaemia and hypocalcaemia cause hyper-excitability of neurons and have been associated strongly with seizures in adults and children⁶. The calcium/magnesium ratio has also been found to be closely associated with initiation and continuation of seizures⁷. The most common laboratory findings reported with respect to AED use are hypocalcaemia, hypophosphatemia and elevated levels of alkaline phosphatase⁸. This study aims to determine the effect of long term use of carbamazepine (CBZ) on electrolyte profile in epileptic patients attending neurology clinic at the University of Ilorin Teaching Hospital, Ilorin Nigeria.

Materials and Methods

The study was prospective, case-controlled involving 23 adult patients with complex partial or generalized tonic-clonic seizure disorder on CBZ monotherapy for more than one year. The control group consisted of 23 non-epileptic patients matched for age and sex.

This study was carried out in the Departments of Neurology and Chemical pathology of the University of Ilorin Teaching Hospital, Ilorin, Nigeria.

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Patients on antiepileptic drugs other than carbamazepine, protein energy malnutrition and history of hepatic or renal failure were excluded from the study. None of the patients were on folate, vitamin D or calcium supplements. This protocol was approved by the Ethical Review Committee of the University of Ilorin Teaching Hospital, Ilorin and informed consent was obtained from all participants.

Blood collection

A total of 5 mls of venous blood was collected from each subject at the neurology clinic of the hospital. Immediately after collection, the sample was centrifuged at 3000 rpm for five minutes. The serum was stored at 4 °C, until analysis was done. The serum was analyzed in the Department of Chemical Pathology, University of Ilorin, for calcium and magnesium using complexometric method⁹, inorganic phosphate and alkaline phosphatase (colorimetric method)^{10,11} and albumin (bromocresol green method)¹².

Table 1: Age and Sex distribution in subjects on carbamazepine therapy

Age (years)	Frequency (%)
20 - 29	15 (65.21)
30 - 39	3 (13.04)
40 - 49	3 (13.04)
50 - 59	2 (8.69)
Sex	
Male	12 (52%)
Female	11 (48%)

List of Abbreviations

Calcium	Ca
Magnesium	Mg
Alkaline phosphatase	ALP
Inorganic phosphate	IP
Albumin	Alb

Statistical Analysis

Data are expressed as mean $\pm$ standard deviation. Comparison between the test and control groups was performed using the Student's t-test. Pearson's correlation was determined for the different electrolytes. Statistical significance was taken at $P < 0.05$.

Results

A total of twenty-three epileptic patients on CBZ therapy participated in the study. They were comprised of 12 (52%) males and 11 (48%) females of which 15 (65.21%) were between the age of 20-29 (Table 1). Serum calcium (albumin adjusted calcium) and alkaline phosphatase were significantly ($P < 0.05$) higher in subjects on carbamazepine compared to the control group. These values were found to be higher than the normal range. Serum magnesium and albumin were also significantly ($P < 0.05$) higher in the subjects but within the normal range. Inorganic phosphate though

Table 2: Electrolyte profile in subjects on carbamazepine therapy

Electrolyte	Concentration	Control	Subjects	P-value
Calcium (mmol/l)	Normal value	2.64 $\pm$ 0.04	3.47 $\pm$ 0.09	$P < 0.05^*$
Magnesium (mmol/l)	2.25-2.65	1.04 $\pm$ 0.02	1.35 $\pm$ 0.04	$P < 0.05^*$
Phosphate (mmol/l)	0.65-1.7	1.59 $\pm$ 0.03	1.14 $\pm$ 0.06	$P < 0.05^*$
Alkaline phosphatase (iu/l)	0.87-1.45	146.67 $\pm$ 4.11	261.87 $\pm$ 14.53	$P < 0.05^*$
Albumin (g/l)	20 - 140	35.07 $\pm$ 0.68	39.57 $\pm$ 0.75	$P < 0.05^*$
	35 - 50			

* $P < 0.05$, Students t-test, $n = 23$

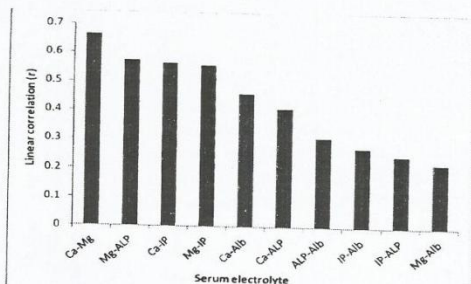


Figure 1: Linear correlation (r) between serum electrolytes in the control group. Ca and Mg concentrations strongly correlated with an absolute value greater than 0.6

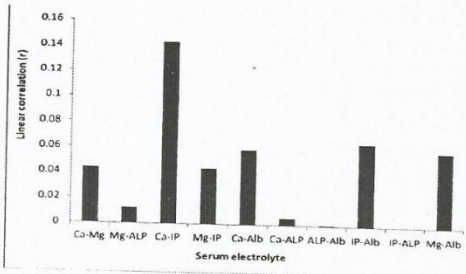


Figure 2: Linear correlation (r) between serum electrolytes in subjects on carbamazepine. Ca and Mg concentrations not correlated with a value of 0.04.

significantly ($P < 0.05$) lower in the subjects was within the normal range (Table 2).

In the control group, the serum concentration of calcium was strongly correlated to that of magnesium, organic phosphate and alkaline phosphatase. The correlation between calcium and magnesium was stronger than that between organic phosphate and alkaline phosphatase with an absolute value greater than 0.6 (Figure 1).

The correlation between calcium and magnesium and that between calcium and alkaline phosphatase was lost completely in subjects on CBZ therapy with a value of 0.04 and 0.005 respectively. (Figure 2).

Discussion

In the present study, epileptic patients on long term CBZ therapy had increased serum calcium, magnesium, alkaline phosphatase, albumin with decreased serum phosphate concentration. Increased serum calcium and magnesium concentration have been reported to be beneficial to seizure control and used as a marker for seizure control⁶. Our findings is similar to that of Hamed et al.,¹³ who found an increase in serum calcium concentration in CBZ- treated groups of patients¹³. The neurochemical basis of the abnormal discharge in epilepsy is not well understood and maybe associated with enhanced excitatory amino acid transmission, impaired inhibitory transmission, or abnormal electrical properties of the affected cells¹⁴. CBZ is one of the most widely used antiepileptic drug and affects membrane excitability by inhibiting voltage-dependent sodium channels¹⁴. This study further revealed that serum concentration of calcium was strongly correlated with that of magnesium and phosphate in the control group, but this correlation was lost in subjects on carbamazepine therapy. This shows that serum concentration of electrolytes is altered in epileptic patients on carbamazepine therapy, with calcium and alkaline phosphatase above normal range while magnesium was within the normal range. Magnesium modulates seizure activity by antagonizing the excitatory calcium influx through the N-methyl-D-aspartate (NMDA) receptor¹⁵. Increased mean alkaline phosphatase with decreased organic phosphorus seen in this study has also been reported in both children and adults receiving AEDs¹⁶. In a study, isoenzymes of alkaline phosphatase in epileptic patients receiving carbamazepine monotherapy was determined and increase in total alkaline phosphatase was reported to be due to the bone fraction¹⁷. Elevated plasma alkaline phosphatase concentration is often associated with drugs that induce hepatic microsomal enzyme including; CBZ, phenobarbitone, primidone and phenytoin¹⁸. Induction of hepatic microsomal enzymes by CBZ accelerates the metabolism of

antiepileptic drugs and other drugs resulting in decreased plasma concentration¹⁴. For this reason, combination of CBZ with other antiepileptic drugs is inadvisable except in situations where the therapeutic benefit outweighs the risk of a potential drug interaction.

Conclusion

This study revealed an increase in serum calcium, alkaline phosphatase, magnesium, albumin concentrations and a decrease in inorganic phosphate in epileptic patients on long term carbamazepine monotherapy. More research with larger sample size will be required before we can conclude on the use of these findings in the management of epileptic patients.

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