

Changes in Serum Electrolytes in Childhood Epilepsy: A Hospital Based Prospective

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ABSTRACT

A study was conducted to compare the blood sodium, potassium, magnesium, calcium, iron, copper, and zinc levels of epileptic children and to determine the ratios of the levels such as: Na/K, Ca/Mg, and Cu/Zn. The children, whose age ranged between 4 months to 14 years (male = 154, female = 73) were admitted to Pediatric Neurology Division of Riyadh Medical Complex (Saudi Arabia). A group of 22 healthy volunteer children (male = 12, female = 10) was taken as normal control. The patients mainly belonged to three seizure groups: Partial seizures (PSZ), Generalized seizures (GSZ), and Un-classified seizures (UNC SZ). In GSZ and UNC SZ groups, potassium levels were found significantly reduced $P < 0.001$ and $P < 0.05$ respectively as compared to the control. A highly significant reduction ($P < 0.001$) in the levels of magnesium and iron was found in all seizure groups as compared with the control subjects. Zinc was found significantly reduced ($P < 0.05$) only in PSZ group. However, sodium, calcium and copper levels did not show any significant change in all the study groups.

The ratios obtained for the levels of different electrolytes revealed a significant increase ($P < 0.05$, $P < 0.001$) in Na/K ratio in GSZ and UNC SZ groups as compared to the control. Similarly a significant elevation ($P < 0.05$) was observed in Ca/Mg ratio in all the seizure groups. However, Cu/Zn ratios were found un-altered in all the study groups as compared to the control. These findings suggest that use of Na/K and Ca/Mg ratios in epileptic children may lead to assist in early diagnosis of epileptic seizures.

(Key Words: childhood epilepsy, seizures, blood serum electrolytes, sodium, potassium, magnesium, calcium, iron, copper, zinc, electrolyte ratios)

INTRODUCTION

Epilepsy is one of the most common neurological conditions, in which seizures recur, usually spontaneously. The phenomenon of epilepsy has been known for at-least 3,000 years (Eadie 1994). However, Jackson correctly defined this disease as follows: Epilepsy is the name for occasional, sudden, excessive, rapid and local discharges of gray matter. Actually this phenomenon occurs in a group of diseases for which recurrent seizures either convulsive or

non-convulsive are caused by partial or generalized epileptogenic discharges in the cerebrum (Menkes 1990).

Epilepsy is a big challenge for scientists and many workers have been exploring different aspects of this disease. Among other reasons, several reports suggested that the body electrolytes and the level of some trace elements play a vital role in seizure conditions to prevail (Rude 1989, lihan et al, 1999). In some cases the altered levels of trace elements in epileptic patients were attributed to anticonvulsant drugs therapy or due to other reasons (Akram et al. 1989).

A careful literature review reveals that a comprehensive record of electrolytes, trace elements and their ratios in epileptic patients is missing for the population in Saudi Arabia. Keeping in view the significance of serum sodium, potassium, calcium, magnesium, copper, iron and zinc levels in epileptic patients, the current study was designed to estimate these levels in children suffering from seizures. Furthermore, an attempt has been made to find out ratios between the levels of some selected electrolytes: Na/k, Ca/Mg, Cu/Zn and to correlate these with epilepsy in a way that such ratios may be used as markers for the future diagnosis of seizure state.

MATERIAL AND METHODS

The present study included investigations on 227 children (male =154, female = 73) suffering from different types of epileptic seizures. The quantitative estimation of some serum electrolytes and trace elements was undertaken. All subjects were registered patients and admitted to Riyadh Medical Complex (RMC), Riyadh (Saudi Arabia) and their relatives were informed about the study. The study comprised of the following groups: (i) Normal Control consisted 22 healthy volunteers (M = 12, F= 10), (ii) Partial Seizures (PSZ) included a total of 112 patients (M =74, F = 38), (iii) Generalized Seizures (GSZ) had 73 patients (M = 51, F = 22), and (iv) Unclassified Seizures (UNC SZ) included a total number of 42 patients (M = 29, F =13).

In each case about 7 ml blood was collected in a plain test tube. The sample was centrifuged at 5,000 rpm and serum was separated. The serum sample was divided into two parts: one part was used for the estimation of copper (Cu) and zinc (Zn) on atomic absorption spectrophotometer while the second part was used to determine different biochemical parameters such as: sodium (Na), Potassium (K), Calcium (Ca), magnesium (Mg), and iron (Fe) by using Dimension® Clinical Chemistry System 1988. The levels of Cu and Zn were determined on Atomic Absorption Spectrometer GBC 906 AA using flame mode at λ 324.7 nm and 213.9 nm respectively. Keeping in view the normal reported ranges of Cu (0.7-1.4 μ g/ml) and Zn (0.7-1.2 μ g/ml) in human serum samples, calibration solutions were prepared covering appropriate range (0.5 ppm - 2 ppm). All calibration samples parameters were found within the internationally accepted ranges (Shah 2000).

The data obtained was statistically analyzed by using the SAS system, (SAS Institute Inc. U.S.A). For the comparison of different groups Student's t-test was used. The minimum level of significance was proposed to be $P < 0.05$.

RESULTS

The levels of different electrolytes found in the control and patient groups are summarized in Table 1 while the ratios obtained for different electrolytes and trace elements in different groups are presented in Table 2.

Table 1: The changes observed in different electrolytes (Mean \pm SE).

Parameters	Control (N=22)	PSZ (N= 112)	GSZ (N= 73)	UNC SZ (N= 42)
Na mmol/L	140.77 \pm 0.90	140.21 \pm 0.45	140.51 \pm 0.45	139.64 \pm 0.49
K mmol/L	4.68 \pm 0.10	4.45 \pm 0.06	4.30 \pm 0.06** \downarrow	4.32 \pm 0.05* \downarrow
Ca mmol/L	2.41 \pm 0.04	2.37 \pm 0.02	2.39 \pm 0.02	2.41 \pm 0.06
Mg mmol/L	0.89 \pm 0.01	0.81 \pm 0.007** \downarrow	0.82 \pm 0.009** \downarrow	0.82 \pm 0.01** \downarrow
Cu μ g/L	0.99 \pm 0.05	0.94 \pm 0.03	1.03 \pm 0.03	0.88 \pm 0.05
Fe μ mol/L	22.08 \pm 1.07	13.62 \pm 0.37*** \downarrow	13.29 \pm 0.35** \downarrow	13.91 \pm 0.61** \downarrow
Zn μ g/L	1.06 \pm 0.02	0.97 \pm 0.03* \downarrow	0.99 \pm 0.029	0.97 \pm 0.04

*P < 0.05, **P < 0.001, ***P < 0.0001 (Students *t*-test).

SE = Standard Error = Increased level \downarrow = Decreased level

The internationally accepted values in children for the parameters under study are as follows:

[Na =133 - 152, K = 3.5 - 5.6 mmol/L]; [Ca = 2.0 - 2.6, Mg = 0.8 - 1.1 mmol/L]; [Cu = 0.7 - 1.4, Zn = 0.7 - 1.2 μ g/L].

In all seizure groups a highly significant decrease (P < 0.001) in Mg and Fe was observed as compared with the control. There was a significant decrease (P < 0.001, P < 0.05) of K levels in the patients of GSZ and UNC-SZ groups as compared with the control. Zinc levels were found significantly low (P < 0.05) only in PSZ patients. However, there were no significant changes in Na, Ca, and Cu serum levels as compared to the control.

Table 2: The ratios obtained for different electrolytes and trace elements in different groups (Mean \pm SD).

SN	RATIOS	Control (N=22)	PSZ (N=112)	GSZ (N= 73)	UNC SZ (N= 42)
1	Na/K	30.36 \pm 0.71	31.96 \pm 0.37	33.09 \pm 0.45*	32.47 \pm 0.41**
2	Ca/Mg	2.71 \pm 0.070	2.94 \pm 0.041*	2.93 \pm 0.040*	2.94 \pm 0.060*

3	Cu/Zn	0.95 ± 0.060	1.118 ± 0.066	1.09 ± 0.046	0.97 ± 0.070
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*P < 0.05, **P < 0.001, ***P < 0.0001 (Student's t-test).

SD = Standard Deviation.

The Na/K ratios in GSZ and UNC SZ groups were found significantly elevated $P < 0.05$, $P < 0.001$ respectively as compared to the control (Table 2). A significant increase ($P < 0.05$) in Ca/Mg ratios as compared to the control was observed in all the study groups. However, the results of Cu/Zn ratio in different groups showed no significant change as compared to the control.

DISCUSSION

The results of our present study demonstrated that serum sodium levels in PSZ, GSZ, and UNC SZ seizure groups were not significantly changed (Table 1). Our findings are in agreement with the results of Natelson et al. (1979) reporting unaffected serum sodium during and after the seizure activity. In general no abnormality was noticed in serum sodium levels of epileptic children. The observed hyponatraemia leading to grand mal seizures in some cases of epileptic children treated with carbamazepine was associated to water intoxication which is a rare side effect of carbamazepine (Koivikko and Valikangas 1983).

During our study potassium levels were found significantly reduced in GSZ and UNC SZ groups ($P < 0.001$). Our results are in agreement with earlier reports where potassium levels ranged between normal to low during attacks of seizure (Natelson et al. 1979). White et al. (1992) reported elevation of potassium (regulated with in extra-cellular compartment of brain) during period of intense seizure activity. Hypokalemia observed in the present study may be expressed as an increase in the ratio of intracellular to extra-cellular potassium concentration, which may result into serious neurological symptoms. Based on the fact that Magnesium-deficiency is linked with K^+ activity (Rude 1989), the possible role of low magnesium levels observed in our patients may also not be ruled out in causing hypokalemia.

It is well documented that alterations in the levels of serum electrolytes and low levels of calcium are responsible for initiation of convulsions (Musiolino et al. 1992, Nzeh et al. 1994, Kiviranta et al. 1996). Neonatal hypocalcaemia and hypomagnesaemia have also been reported to be the cause of convulsions (Lynch et al. 1994 and Sheth 1997). However, in the present study serum calcium levels in all the seizure groups remained comparable to the control. Our observations are supported by the reports of Rutter et al. (1976) where Ca-levels remained normal in children with febrile convulsions.

A significant decrease in serum magnesium level was observed in all seizure groups included in the present study as compared to the control. The deficiency in magnesium levels in general, is correlated to hypokalemia, hypocalcaemia and other disturbances of electrolyte homeostasis. Our results are in agreement with the study of Papierkowski et al. (1999) where serum magnesium concentrations were also found significantly reduced in children with febrile convulsions. Rude (1993) also held magnesium-deficiency responsible for hyper-excitability, hypocalcaemia and hypokalemia in hospitalized patients.

The serum copper levels in different groups included in the present study did not show any significant change. Our results are in agreement with the earlier reports where no appreciable changes in copper levels could be demonstrated in epileptic patients (Kurekci et al. 1995; Liu et al. 1998).

In our present study zinc levels were found significantly reduced in PSZ group. Earlier hypozincemia was associated with seizures (Izumi et al. 1990). Our results are further supported by the findings of different researchers who found hypozincemia to be associated with febrile convulsions in children (Palm et al. 1982; Palm et al. 1986; Suzuki et al. 1992; Burhanoglu et al. 1996; Gunduz et al. 1996; Papierkowski et al. 1999). Hypozincemia during pyrexial state is known to activate the NMDA receptor, which may play an important role in the induction of epileptic discharges. Wallwork (1987) reported perinatal brain damage produced by early zinc deficiency. However, during our present study the changes of zinc levels in the GSZ and UNC SZ groups as compared to the control were statistically non-significant.

The serum Iron levels of patients in different seizure groups included in the present study were found significantly reduced as compared to the control. Iron-deficiency anemia was earlier recorded as a common feature in epileptic patients (Kobrinisky et al. 1995, Takeuchi 1996). Current studies in Saudi children suffering from epilepsy also revealed that in general the patients had low hemoglobin levels due to iron deficiency (Jamil 2000).

Based on the results of our present study the ratios of some selected electrolytes and elements were calculated. It was interesting to note that the mean Na/K ratios in GSZ and UNC SZ groups were significantly higher as compared to the control group. Earlier Natelson et al. (1979) reported unaffected sodium and low potassium levels during seizures. The results of the present study also showed unaltered Na level and hypokalemia in patients leading to high Na/K ratio. On the other hand, Biochonski (1976) reported hypernatremia and hypokalemia in epileptic children. Based on the results of our present study it was concluded that in epileptic patients a rise in Na/K ratio as compared to the control mean values might lead to increase the frequency of seizures.

It was observed that Ca/Mg ratios were significantly elevated in all the seizure groups as compared to the ratios obtained for the control group. It is worth-mentioning that in our study groups' serum Ca levels remained unaltered while Mg levels were significantly lower which led to a coorespondigly higher Ca/Mg ratio as compared to the control. The elevated Ca/Mg ratio was found to be closely associated with initiation and continuance of seizures (Jamil 2000). Leaver et al. (1987) found decline both in calcium and magnesium concentrations resulting in frequent convulsions. Based on the results of their study the calculated Ca/Mg ratio was also found to be high. Our observation on the possible use of Ca/Mg ratio is a new concept and may help to judge enhancement of neuronal excitability.

The results of present study revealed no significant changes in Cu/Zn ratio in all the seizure groups as compared to the control mean value. Our findings were in agreement with the ratios calculated for the observations of earlier workers (Kuzuya et al. 1993).

Keeping in view the results of present study, it is concluded that routine laboratory estimation of serum sodium, potassium, magnesium, calcium, copper and zinc are essential for the rational understanding and management of childhood epileptic seizures. It is emphasized that Na/k and Ca/Mg ratios may be included as diagnostic markers in future cases of seizure disorders. However, it is suggested to conduct a study with greater sample size to evaluate the role of other elements and their ratios in childhood epileptic disorders.

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Cite As: Shah, Q.A., A.A. Jamil, V.P. Gupta, M.M. Kabiraj, and A.H. Shah. 2001. Changes in Serum Elctrolytes in Childhood Epilepsy: A Hospital Based Prospective. *Greenwich Journal of Science and Technology*. 2(1):18-27.

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