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Original Article

Evaluating the Serum Levels of Calcium, Chloride, Potassium and Sodium in the Stroke Patients

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A B S T R A C T

Backgrounds and Aims: Stroke incidence rate has increased during the past 2 decades. The question of whether calcium, chloride, potassium, sodium levels are associated with stroke has remained controversial. The present study aimed to evaluate the serum levels of potassium, sodium, calcium, and chloride within stroke patients.

Materials and Methods: The study participants consisted of 53 cconsecutive stroke patients as well as 53 healthy subjects.The stroke was defined by focal neurological signs. After collection of blood samples, serum levels of calcium, chloride, potassium and sodium concentration were measured by standard laboratory method.

Results: Serum calcium level in the patient group was significantly increased as compared to the control group [11.0±1.3) vs. 9.4±0.7, mg/dl], whereas serum potassium level in the patient group was decreased as compared to the control group [3.5±0.6 vs. 3.9±0.4, mmol/L]. Serum sodium level in the patient group was slightly low as compared to the control group [136.3 ±0.6 vs. 136.7 ±5.5, mmol/L]. Moreover, serum chloride level in the patient group was slightly high as compared to the control group [102.4±7.9 vs. 100.7±6.2, mmol/L].

Conclusions: The study results demonstrated that a statistically significant positive correlation was observed between serum electrolytes or ionic levels and stroke status. Changes in calcium, chloride, potassium and sodium levels during stroke may be a good biochemical marker of diagnosis for this disease. Therefore, these biochemical factors could play a useful role in the stroke. However, further studies are demanded to confirm the validity of study.

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Introduction

Some pieces of evidence suggest that stroke is one of the most common neurological disorders within old people. Obviously, most of the survived cases of stroke have severe disability and have high costs for their families. Its incidence is well recognized to increase with increasing numbers of risk factors, such as age, hypertension, diabetes mellitus, hyperlipidemia, cardiovascular diseases. In addition, several other factors have an impact on stroke, including environment and gene. Stroke is regarded as the second cause of death among elderly people [1]. According to findings of several studies conducted on the relation between high salt intake and stroke, people with a high intake of salt, have high blood pressure and risk factors for cardiovascular diseases. The effect of sodium on blood pressure seem to be clearly well known [2, 3]. Moreover, high potassium intake were demonstrated to have inhibitory effects on the cardiovascular diseases. High levels of serum potassium lowers blood pressure due to decreased sodium level. Trace elements are essential components of biological structures, that changes in the concentration of essential trace elements may affect acute hemorrhagic stroke. As a matter of fact, increased Cd, Pb, and Fe levels; and decreased Cu, Zn, Mg, and Mn levels were observed in patients with acute hemorrhagic stroke [4]. Different studies have revealed a relatively little correlation between the level of serum calcium and stroke. On the other hand, calcium can play an important role in the body's cell necrosis. In this regard, parathyroid hormone and vitamin D are known to regulate the calcium level. Aaccumulation of intracellular calcium helps the activation of enzymes involved in the cell death. In addition, increasing its concentration in the cell also increases the area of cerebral infarction. It has been shown calcium to play an important role in the pathogenesis of stroke. Calcium increased infarct size and clinical symptoms of stroke [5, 7]. In another study, the age was introduced as the most important risk factor for stroke. Elderly patients were demonstrated to be the first victims of stroke [8]. Based on above mentioned issues, electrolytes or ionic concentrations in stroke may be regarded as an attractive issue to further improve the accuracy of predicting the individual patient's functional outcome. Thus, the present study aimed to access the potential diagnostic utility of serum calcium, chloride, potassium, and sodium levels in predicting the stroke.

Materials and Methods

Between August 1, 2012 and May 30, 2015, patients from the Ayatollah Rouhhani Hospital were invited to participate in the study. This study was conducted based on the guidelines in the declaration of Helsinki, and all procedures involving human patients were approved by our University Committee (No. 49). Written informed consent was obtained from all subjects after a full explanation of the purpose and nature of all procedures was provided. In this cross-sectional study, 53 consecutive patients (30 males and 23 female)

were enrolled with a diagnosis of stroke who were admitted to the neurology department at the Ayatollah Rouhhani Hospital, Babol. Inclusion criteria entailed patients with stroke. In fact, stroke was defined by focal neurological signs. In addition, 53 healthy subjects (30 males and 23 females) without signs of stroke or other systemic diseases were enrolled as a healthy control group. Clinical evaluation involved complete medical history and physical examination was performed by one neurologist. Exclusion criteria included in the controls were: having vascular diseases or any risk factors for stroke and taking drugs can interfere with the concentration of elements, diabetes, kidney and myocardial infarction disease, getting damage of corticosteroids hormone. The drug can interfere with the element concentration. The study sample was collected in the section of the nerves of brain disease within 2012-2015. No blood samples were drawn for the purpose of the study unless an informed consent form was signed. Blood samples were obtained at the time of admission. After collection of blood samples, electrolyte levels were measured via a commercially available standard method. On the other hand, concentrations of serum calcium and chloride were measured using spectrophotometer model 2100 made in Spain. Serum potassium and sodium were determined by flame photometer, made in the USA, according to the manufacturer's manual.

Statistical analysis

The study data were analyzed applying SPSS for windows (version 21), according to which the results were expressed as mean value ± SD and P-value <0.05 was considered significant. Moreover, independent samples T-test, 2 - independent sample chi-square were utilized.

Results

General characteristics of patients and healthy controls enrolled in the study are reported in table 1. In addition, the mean serum calcium, chloride, potassium and sodium levels were shown in table 2. The frequency of risk factors (vascular diseases, hyperlipidemia, high blood pressure, and diabetic diseases) were examined, as well (Table 3). The mean level of serum calcium, chloride, potassium and sodium were demonstrated based on gender (Table 4). The number and frequency of each risk factor in both groups of patients and controls were studied, between which a significant association was observed in regard with risk factors (Table 5).

Table 1. General characteristics of patients and healthy controls

Variable		Total	Patient	Control	P-value
Age		64.37±8.35	63.45±8.68	65.28±8.00	0.234
Gender N (%)	Men	60(56.6%)	30(56.6%)	30(56.6%)	>0.99
	Women	46(43.4%)	23(43.4%)	23(43.4%)	>0.99
Hyperlipidemia N (%)		58(54.7%)	40(75.5%)	18(34%)	<0.001
Diabetes Mellitus N (%)		14(13.2%)	11(20.8%)	3(5.7%)	0.022
Hypertension N (%)		54(50.9%)	42(79.2%)	12(22.6%)	<0.001
Ischemic Heart Disease N (%)		38(35.5%)	33(62.3%)	5(9.4%)	<0.001

Table 2. The mean levels of serum calcium, chloride, potassium and sodium

Groups	Calcium (mg/dl)		Potassium (mmol/L)		Sodium (mmol/L)		Chloride (mmol/L)	
	Mean±SD	Medium (Min-Max)	Mean±SD	Medium (Min-Max)	Mean±SD	Medium (Min-Max)	Mean±SD	Medium (Min-Max)
Patient	11.0±1.3	10.8 (8.1-14)	3.5±0.6	3.6 (2.1-6.5)	136.3±0.6	137 (123-150)	102.4±7.9	102 (80-120)
Control	9.4±0.7	9.3 (7.8-11.2)	3.9±0.4	4 (3-4.6)	136.7±5.5	138 (121-150)	100.7±6.2	101 (78-115)
P-value	< 0.001		0.455		0.455		0.208	

Table 3. The frequency of risk factors (vascular diseases, hyperlipidemia, high blood pressure, and diabetic disease)

Risk Factors		Stroke N (%)	Control N (%)	Total N (%)	P-value
Hyperlipidemia	Positive	40 (75.5%)	18 (34%)	53 (100%)	< 0.001
	Negative	13 (24.5%)	34 (66%)		
Diabetes Mellitus	Positive	11 (20.8%)	3 (5.7%)	53 (100%)	0.022
	Negative	42 (79.2%)	50 (94%)		
Ischemic Heart Disease	Positive	33 (62.3%)	5 (9.4%)	53 (100%)	< 0.001
	Negative	20 (37.7%)	48 (90.6%)		
Hypertension	Positive	42 (79.2%)	12 (22.6%)	53 (100%)	< 0.001
	Negative	11 (20.8%)	41 (77.4%)		

Table 4. The mean levels of calcium, chloride, potassium and sodium serum based on gender.

Groups	Calcium (mg/dl)	Potassium (mmol/L)	Sodium (mmol/L)	Chloride (mmol/L)
Patient with HLP	10.32±1.25	3.75±0.62	135.62±5.82	102.13±6.82
Patient Without HLP	10.10±1.42	3.76±0.51	137.67±4.93	100.92±7.58
P-value	0.395	0.968	0.023	0.393
Patient with HTN	10.63±1.44	3.67±0.65	136.89±6.12	136.89±6.12
Patient Without HTN	9.79±1.04	3.84±0.48	136.19±4.81	102.21±7.07
P-value	0.001	0.125	0.277	0.378
Patient with DM	10.75±1.40	3.62±0.44	136.93±4.34	99.34±6.91
Patient Without DM	10.14±1.30	3.78±0.59	136.49±5.68	101.92±7.18
P-value	0.108	0.343	0.811	0.210
Patient with IHD	1082±1.30	3.58±0.51	135.82±6.69	102.17±6.52
Patient Without IHD	9.88±1.23	3.85±0.59	136.96±4.72	101.25±7.53
P-value	<0.001	0.024	0.277	0.531

HLP=Hyperlipidemia, HTN=hypertensions, DM=diabetes Mellitus, IHD=Ischemic Heart Disease
Data are presented as Mean±SD

Table 5. The number and frequency of each risk factor in both groups of patients and controls

Gender	Element	Patient	Control	Total	P-value
Male	Calcium	11.44±1.39	9.46±0.64	10.43±1.45	<0.001
	Chloride	101.42±6.89	101.80±5.24	101.61±6.07	0.813
	Potassium	3.42±0.77	3.92±0.39	3.67±0.65	0.002
	Sodium	137.37±	137.07±5.50	137.22±4.99	0.899
Female	Calcium	10.53±1.05	9.37±0.82	9.95±1.10	<0.001
	Chloride	103.82±9.15	99.28±7.18	101.55±8.45	0.068
	Potassium	3.79±0.33	3.93±0.52	3.86±0.43	0.288
	Sodium	135±6.48	136.35±5.65	135.67±6.05	0.310

Data are presented as Mean±SD

Discussion

In the present study, the possible predictive power of a series of serum electrolytes or ionic levels, involved in the stroke, were examined. Indeed, mean serum levels of calcium in the stroke group significantly increased compared to the control group, which has been confirmed in the findings of other scholars [5, 6]. Appeal et al. showed a relationship between serum calcium and acute stroke [5]. Many studies have demonstrated a relationship between reduced infarct size and serum calcium in the stroke. Other investigators reported that there was no correlation between serum calcium levels and mortality. In another study, subjects with high serum calcium levels were reported to be at increased risk of death [5, 6]. In the present study, serum potassium levels compared to the control group showed a slight decrease, which is in line with the findings of other studies [11-13]. One study indicated that serum potassium levels were associated with stroke. Hypokalemia in patients with stroke were demonstrated to be more common than in the control group, and the serum potassium levels in the patient group were reported to be lower compared to the control group. In addition, a relationship was observed between trace element status, and brain damage biomarkers in transient ischemic attack patients. The study results revealed a significant association between trace elements concentration and the studied parameters [12, 13].

In the present study, no significant difference was observed between groups of stroke patients and controls with respect to serum sodium concentration. In a study conducted on rats, the channels of Na, K and Cl could be expressed in vascular endothelial cells after stroke. This channel causes sodium and water excretion from the blood to brain cells in the brain, which inflammation starts with entry of water and sodium. In a cohort study conducted on 42,000 subjects, the relationship between

diastolic blood pressure, heart disease and stroke were examined. In this study, 843 patients suffered from stroke. In fact, subjects with low blood pressure were demonstrated to have lower chance of stroke [14]. In the present study, no significant difference was observed in the serum chloride levels between control and patient groups. The relationship between admission serum calcium and phosphate levels with short- and long-term outcomes were assessed in patients with acute intracerebral hemorrhage. The study results showed that elevated admission serum calcium level, but not phosphate level, was positively associated with excellent outcome at discharge or 3 months in acute intra-cerebral hemorrhage patients [15].

Electrolyte imbalance is well recognized to be one fundamental mechanism leading to cell death during brain injury. Dietary modifications are regarded as an important means of preventing stroke. Dietary factors influencing electrolyte or ionic level may affect the risk of stroke. Electrolyte is believed to contribute to the deteioration of the brain. According to results of this study, a relationship was detected between serum ionic level and stroke. However, the question of whether electrolyte or ionic level is associated with risk of stroke remains controversialand , thus it should be noted that further work is needed to illuminate this association. Hence, chose to continue research to evaluate the electrolyte status with more number of patients. In future studies, more number of stroke patients are recommended to be applied in order to evaluate the role of serum electrolytes. Lack of access to more patients, as well as failure to cooperate with the staff sampler can be mentioned as the limitations of this study.

Conclusion

The current study results revealed that serum electrolyte levels changes may reflect stroke occurrence which may be regarded as a potential therapeutic target for diagnosis of stroke. Moreover, the findings of the current study encourage the use of serum electrolytes as a reliable biomarker for diagnosis of stroke.

Conflict of Interest

The authors declare no conflict of interest in this study.

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References

[1]. Afshari L, Amani R, Soltani F, Haghighizadeh MH, Afsharmanesh MR. The relation between serum Vitamin D levels and body antioxidant status in ischemic strokepatients: A case-control study. Adv Biomed Res. 2015; 28; 4:213.

[2]. Appel LJ, Frohlich ED, Hall JE, Pearson TA, Sacco RL, Seals DR, et al. The importance of population-wide sodium reduction as a means to prevent cardiovascular disease and stroke a call to action from the American heart association. Circulation 2011; 123(10): 1138-143.

[3]. Cappuccino F.P, C Ji. Less Salt and Less Risk of Stroke, Further Support to Action. Stroke 2012; 43(5): 1195-196.

[4]. Karadas S, Sayın R, Aslan M, Gonullu H, Katı C, Dursun R, et al. Serum levels of trace elements and heavy metals in patients with acute hemorrhagic stroke. J Membr Biol. 2014; 247(2): 175-80.

[5]. Appel SA, Molshatzki N, Schwammenthal Y, Merzeliak O, Toashi M, Sela BA, et al. Serum calcium levels and long-term mortality in patients with acute stroke. Cerebrovascular Diseases 2010; 31(1): 93-9.

[6]. Buck BH, Liebeskind DS, Saver JL, Bang OY, Starkman S, Ali LK, et al. Association of higher serum calcium levels with smaller infarct volumes in acute ischemic stroke. Archiv Neurology 2007; 64(9): 1287-291.

[7]. Guven H, Cilliler AE, Koker C, Sarikaya SA, Comoglu SS. Association of serum calcium levels with clinical severity of acute ischemic stroke. Acta Neurologica Belgica 2011; 111(1): 45.

[8]. Liu F, Akella P, Benashski SE, Xu Y, McCullough LD. Expression of Na-K-Cl cotransporter and edema formation are age dependent after ischemic stroke. Experimental Neurology 2010; 224 (2): 356-61.

[9]. Pignataro G, Gala R, Cuomo O, Tortiglione A, Giaccio L, Castaldo P, et al. Two sodium/calcium exchanger gene products, NCX1 and NCX3, play a major role in the development of permanent focal cerebral ischemia. Stroke 2004; 35(11): 2566-570.

[10]. Poole KE, Loveridge N, Barker PJ, Halsall DJ, Rose C, Reeve J, et al. Reduced vitamin D in acute stroke. Stroke 2006; 37(1): 243-45.

[11]. Landmark, K. Hypokalemia can accelerate the development of cerebrovascular and cardiovascular disease. Tidsskr Nor Laegeforen 2002; 122(5): 499-501.

[12]. Larsson SC, Virtanen MJ, Mars M, Männistö S, Pietinen P, Albanes D, et al. Magnesium, calcium, potassium, and sodium intakes and risk of stroke in male smokers. Archiv Int Med. 2008; 168(5): 459-65.

[13]. Klimenko LL, Skalny AV, Turna AA, Tinkov AA, Budanova MN, Baskakov IS, et al. Serum Trace Element Profiles, Prolactin, and Cortisol in Transient Ischemic Attack Patients. Biol Trace Elem Res. 2016; 172(1): 93-100.

[14]. MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, et al. Blood pressure, stroke, and coronary heart disease: part 1, prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. The Lancet 1990; 335(8692): 765-74.

[15]. You S, Han Q, Xu J, Zhong C, Zhang Y, Liu H, et al. Serum Calcium and Phosphate Levels and Short- and Long-Term Outcomes in Acute Intra-cerebral Hemorrhage Patients. J Stroke Cerebrovasc Dis. 2016; 25(4): 914-20.