International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Derangement of Serum Electrolyte Status in Cerebrovascular Accident - A Hospital Based Observational Study in Shillong, Meghalaya

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Received: 25/08/2016 *Revised: 20/09/2016* *Accepted: 20/09/2016*

ABSTRACT

Background and Aim: The mortality rate of stroke patients with electrolyte imbalance has been found in previous studies to be higher than in patients with normal level. Hence the present study was carried out in a tertiary care hospital in Shillong, Meghalaya to assess the levels of serum electrolytes in patients admitted with Cerebrovascular accident (CVA).
Settings and design: A total of 164 participants (84 cases and 80 controls) were selected after careful screening, considering all relevant inclusion and exclusion criteria for the present hospital based observational case-control study. The serum samples were analyzed for electrolytes (sodium, potassium and chloride) on the same day of collection.
Results: A greater preponderance of CVA was seen in males as compared to females with a male: female ratio of 2.36:1. The levels of serum sodium and chloride in the cases were found to be higher than that in the controls, and the levels of serum potassium were found to be lower. This difference was statistically significant for all three parameters. Analysis by ANOVA between the three groups of cases found no significant difference in the levels of serum sodium and potassium. A significant difference was found in cases with chloride.
Conclusion: Prompt identification of such derangements along with their immediate correction can prove to be of tremendous importance in decreasing mortality as well as in dissipating the long term consequences of stroke. Further studies will be required to elucidate the role of serum electrolytes in CVA.

Keywords: #Cerebrovascular accident, #Dyselectrolytemia, #Sodium, #Potassium, #Chloride, #North-East India.

INTRODUCTION

Stroke is defined by the World Health Organization as "a clinical syndrome typified by rapidly developing signs of focal or global disturbance of cerebral functions, lasting more than 24 hours or leading to death, with no apparent causes other than of vascular origin". [1] Stroke, along with its devastating and long term complications are one of the leading causes of morbidity and mortality in the world as well as in India. Reliable morbidity and mortality estimates for stroke in India are limited due to incomplete death certification, incorrect death classification, and uncertainty of etiology in cases of sudden death or multiple co-morbidities. In India, although a system for recording cause of death was introduced in 1998; only 14% of deaths are ever classified. Despite these hindrances, it

is now known that strokes or Cerebrovascular accidents (CVA) in India have a prevalence of 55.6 per 100,000 all ages, [2] with an estimated 0.63 million deaths. [1]

High mortality in stroke is due to some complications like cerebral edema and brainstem herniation; infection, electrolyte imbalance and associated heart disease and metabolic disorder. In hospitalized sick adults, alterations of sodium levels are among the most common complications reported. Some authors consider sodium imbalance to be of little significance, whereas some others are of the opinion that high morbidity and mortality of patients are related to these electrolyte imbalances.

The role and significance of serum electrolytes in vascular studies has been observed in previous studies. It has been shown that high dietary sodium intake is associated with increased risk of different types of cerebral vascular events. [3,4] High sodium intake may increase the mortality of stroke as well as cardiovascular diseases. [5] It has been previously shown that higher sodium intake is associated with incidence of congestive heart failure in overweight patients. [6] Higher potassium excretion has been associated with a lower risk of CVA, [5,6] and increased potassium intake is inversely related to mortality due to coronary artery disease. [4]

Studies describing these electrolyte disturbances in CVA patients are rare from India and especially from the North-East region of this nation. Prompt identification of such derangements along with their immediate correction can prove to be of tremendous importance in decreasing mortality as well as in dissipating the long term consequences of stroke. In this scenario, it was thus found that there was potential in knowing the extent of the problem to assist in planning prompt corrections in the clinical set-up. We therefore undertook this study to observe the changes in serum electrolytes in stroke and its sub-types.

MATERIALS AND METHODS

Type of study: Hospital based Observational study

Study Design: Case Control study

Study Population: After approval from the Institutional Ethical Committee and informed consent from the patients, as well as all relevant inclusion and exclusion criteria, a total of 84 patients were registered for the study. Patients were selected on the basis of clinical diagnosis and confirmed with brain computed tomography (CT scan). Patients with Diabetes, Hypertension or with serious co morbidities such as Congestive Heart Disease, Kidney or Liver Failure, or conditions with pre-existing electrolyte disturbances were excluded from the study. Furthermore, patients who were using medications with an effect on electrolyte metabolism including diuretics were also excluded. Subsequently patients with hyperglycemia and hyperlipidemia are also excluded to rule out possibilities of misinterpretation of serum sodium level and to exclude pseudo hyponatremia. Patients with T.I.A and S.A.H. were also excluded from study. The control group consisted of 80 age and gender matched healthy controls admitted with some other ailment other than CVA and not suffering from conditions known to produce electrolyte derangements. The study protocol was explained to the participants in the appropriate languages, best understood by them. A full medical history was obtained from these participants and informed consent was signed by each of them.

Sample Collection and Biochemical Analysis

Taking all septic and antiseptic precautions, five (5) ml of venous blood was collected from each patient with cerebrovascular accident as well as from the control group. To minimize fluctuations due to diurnal variations in the electrolyte levels, samples for measurement were collected between 9 and 10 A.M of the post admission day. Apart from routine investigations, the serum samples were analyzed for electrolytes on the same day of

collection by ion selective electrode technology and recorded through standard laboratory methods. Electrolytes analyzed in this study were sodium, potassium and chloride. Sodium level in a range of 135-145 mmol/L was defined as normal. Potassium level in a range of 3.5-5.5 mmol/L was defined as normal. The normal range of chloride was from 98-108 mmol/L. These values were established in our laboratory, and any value beyond this range was considered to be abnormal.

Statistical analysis

Data was at first arranged in Microsoft Excel 2007 worksheet. Data are expressed as mean ±SD for continuously distributed variables, and in absolute numbers and percentages for the discrete variables. Tests of significance were done with unpaired student's t-test/ ANOVA as needed. Significance with p value of less than 0.05 was considered significant.

RESULTS AND OBSERVATIONS

This study was a hospital based case-control observational study carried out in a tertiary care hospital in Shillong, Meghalaya. A total of 164 participants (84 cases and 80 controls) were selected careful screening, considering all relevant inclusion and exclusion criteria. A greater preponderance of CVA was seen in males as compared to females with a male: female ratio of 2.36:1 (Table 1). The highest number of stroke patients was found in the age group of 61-70 years of age. The mean age of the participants with ischemic CVA was 61.29 years, of hemorrhagic CVA was 60.9 years and the mean age of stroke patients with combined lesions was 56.5 years. Analysis by ANOVA revealed no significant differences between the three groups of cases and controls in terms of age. Among the patients with stroke, ischemic stroke was found to be more common, both in males and females (Table 2). 79.76% of the cases were found to be admitted with ischemic stroke, whereas hemorrhagic stroke accounted for 16.67%. Three patients were diagnosed with combined lesions (both infarct and hemorrhagic lesions could be seen on CT scans).

Table 1: Age and sex distribution of patients

Age group (years)	Male	Female	Percentage	Total
< 50	9	4	15.48%	13
51-60	18	7	29.76%	25
61-70	23	11	40.48%	34
>70	9	3	14.28%	12

Table 2: Age and sex distribution in different types of stroke

	Ischemic		Hemorrhagic		Combined lesion		Control	p value
	n	%	n	%	n	%		
Male	45	53.58	12	14.28	2	2.38	54	0.368
Female	22	26.19	2	2.38	1	1.19	26	
Age in years (Mean ± SD)	61.29±11.12		60.9±11.45		56.5±11.5		59.38±8.87	0.546

Table 3: Serum electrolyte levels of the participants

Study group	Sodium (mmol/L) (Mean ± SD)	Potassium (mmol/L) (Mean ± SD)	Chloride (mmol/L) (Mean ± SD)
Cases	139.2 ± 6.213	3.287 ± 1.028	108.2 ± 8.090
Controls	144.8 ± 13.43	4.067 ± 0.7976	105.8 ± 6.896
p value	< 0.0001(****)	< 0.0001(****)	0.0363 (*)

Both the groups were analyzed for serum electrolytes and the following results were found. The levels of serum sodium and chloride in the cases were found to be higher than that in the controls, and the levels of serum potassium were found to be lower (Table 3). This difference was statistically significant for all three parameters. In the present study, it was found that the mean level of serum sodium in controls was 139.2 ± 6.213, and in the cases it was 144.8 ± 13.43. Serum sodium in cases was thus higher than that in controls, and this difference was statistically highly significant (p value < 0.0001). The mean level of serum potassium in controls was found to be 4.067 ± 0.7976 and in cases it was 3.287 ± 1.028. In the participants with CVA the serum potassium levels were thus found to be lower, and this difference was

statistically highly significant (p value < 0.0001). Patients with cerebrovascular accidents also had higher serum chloride levels (108.2 ± 8.090) compared to the controls (105.8 ± 6.896) and this difference was statistically significant (0.0363).

Table 4: Serum electrolyte levels of the patients in ischemic stroke

Serum electrolytes (mEq/L)	Ischaemic	Control	p value
Sodium (Mean ± SD)	144.5 ± 12.58	139.2 ± 6.21	0.0012 (**)
Range	112 - 166	122 - 164	
Potassium (Mean ± SD)	3.26 ± 1.09	4.06 ± 0.8	< 0.0001 (****)
Range	1.45 – 6.2	2.2 – 6.2	
Chloride (Mean ± SD)	107.4 ± 7.79	105.8 ± 6.85	0.2183
Range	94 - 123	94 - 121	

Table 5: Serum electrolyte levels of the patients in hemorrhagic stroke

Serum electrolytes (mEq/L)	Hemorrhagic stroke	Control	p value
Sodium (Mean ± SD)	143.5 ± 16.23	139.2 ± 6.21	0.0806
Range	118 - 179	122 - 164	
Potassium (Mean ± SD)	3.33 ± 0.73	4.06 ± 0.8	0.0018 (**)
Range	2.0 – 5.0	2.2 – 6.2	
Chloride(Mean ± SD)	109.8 ± 8.07	105.8 ± 6.85	0.0657
Range	95 - 122	94 - 121	

Analysis was also done for serum electrolytes in the different subtypes of stroke. In patients with ischemic stroke, statistically significant difference could be seen for serum sodium and potassium, with serum sodium levels being higher and potassium levels being lower as compared with controls (Table 4). Though levels of serum chloride were found to be higher in cases with ischemic stroke as compared with controls, this difference was not statistically significant. In patients with hemorrhagic stroke (Table 5), serum potassium level was lower as compared with controls and this difference was statistically significant. Although levels of both serum sodium and chloride were found to be higher in patients with hemorrhagic stroke, this difference was not statistically significant. When serum electrolytes of patients admitted with combined lesions was analyzed (Table 6), it was found that the levels of both serum sodium and chloride were higher as compared to controls, and this difference was statistically significant. Though levels of serum potassium were found to be lower in cases with combined lesions as compared with controls, this difference was not statistically significant.

Table 6: Serum electrolyte levels of the stroke patients with combined lesions

Serum electrolytes (mEq/L)	Combined lesion	Control	p value
Sodium (Mean ± SD)	162 ± 4.24	139.2 ± 6.21	< 0.0001 (****)
Range	159 - 165	122 - 164	
Potassium (Mean ± SD)	3.7 ± 1.13	4.06 ± 0.8	0.5270
Range	2.9 – 4.5	2.2 – 6.2	
Chloride (Mean ± SD)	120.7 ± 2.3	105.8 ± 6.85	0.0007 (***)
Range	118-122	94 - 121	

Table 7: Serum electrolyte levels of the patients in different sub-types of stroke

Serum electrolytes (mEq/L)	Ischaemic	Hemorrhagic	Combined lesion	p value
Sodium (Mean ± SD)	144.5 ± 12.58	143.5 ± 16.23	162 ± 4.24	0.1802
Range	112 - 166	118 - 179	159 - 165	
Potassium (Mean ± SD)	3.26 ± 1.09	3.33 ± 0.73	3.7 ± 1.13	0.8313
Range	1.45 – 6.2	2.0 – 5.0	2.9 – 4.5	
Chloride (Mean ± SD)	107.4 ± 7.79	109.8 ± 8.07	120.7 ± 2.3	0.0141
Range	94 - 123	95 - 122	118-122	

Analysis by ANOVA between the three groups of cases found no significant difference in the levels of serum sodium and potassium. A significant difference was found in cases with chloride. Post-hoc analysis revealed that this difference was significant when the serum levels of chloride in cases with combined lesions were compared with patients with ischemic stroke (Table 7).

DISCUSSION

The present study was a hospital based case-control observational study carried out in a tertiary care hospital in Shillong, Meghalaya. A greater preponderance of CVA was seen in males as compared to females with a male: female ratio of 2.36:1. This was in accordance with the Mumbai registry [7] and Bangalore study [8] where a greater incidence rate of stroke was seen in males. Among the patients with stroke, ischemic stroke was found to be more common. This was consistent with other studies which had found a higher occurrence of cerebral infarct as compared with hemorrhage. [9]

In the present study, significant hypernatremia and hyperchrloridemia was found in patients with stroke, along with significantly depleted serum potassium levels. Chakraborty *et al* (2013) also reported similar results of serum electrolytes, with increased sodium levels and decreased potassium concentrations in stroke patients compared to controls at p <0.001. [10] Studies analyzing serum chloride levels in stroke are relatively limited. Similar electrolyte disturbances were also found by N. Swetha (2014) in a recent study of stroke patients in Tamil Nadu. [11]

It is found from other studies that mortality rate of stroke patients with electrolyte imbalance was higher than in patients with normal level. This is especially true for hypernatremia because of its contribution on the development of brain edema. Again, it has been previously shown that for an actual increase in brain volume to occur, additional fluid must be added to the brain's extracellular space. During permanent ischemia, blood sodium rapidly enters the extracellular fluid of the brain, leading to consequences of brain edema. [12] Therefore Chakraborty *et al.* (2013) hypothesized that higher serum sodium levels are associated with higher risk and exacerbation of events following brain ischemia. [10] It has been documented that exchangeable sodium is increased in hypertensive patients who is well corroborated with arterial pressure. [13] The same study also hypothesized that in hypertensive subjects increased dietary sodium also increased exchangeable sodium but arterial pressure increased on average more than in normal subjects. Brain edema is an important clinical complication of cerebral ischemia. Numerous studies have shown that, in the first several hours following a stroke, brain edema is principally of the cytotoxic type. The blood-brain barrier (BBB) remains intact, and fluid accumulates in response to an increase in tissue osmoles. While a portion of the increase in tissue osmoles is due to breakdown of cellular constituents there is also a good correlation between ischemic edema and increases in brain sodium. [14] Since the increased sodium content is seen only during incomplete and not during total ischemia, [15] the source of sodium must be the blood. Therefore, some investigators have proposed that during incomplete ischemia, the rate of sodium influx from blood to brain is increased as the result of either diffusion down a concentration gradient [15] or stimulation of specific sodium transport systems in the BBB. [16] A limited number of clinical observations also indicate that blood pressure (BP) is not increased in humans by high dietary sodium intakes in the absence of chloride. In 1929, Berghoff *et al* [17] reported that blood pressure increased in seven hypertensive individuals on a high sodium chloride (NaCl) intake, but not on a high sodium bicarbonate intake. Further suggesting a modulating effect of dietary chloride on blood pressure, in hypertensive and normotensive subjects, substitution of dietary NaCl with equimolar sodium bicarbonate leads to a reduction of blood pressure. [18] Additionally, in hypertensive humans, the reduction of blood pressure by dietary potassium is attenuated by potassium chloride compared with that of potassium citrate. [19]

Besides its role on blood pressure, a high dietary intake of potassium is also

believed to exert other protective effects against CVA. For example, increasing dietary intake of potassium from approximately 60 to 80 mmol/day has been shown to be inversely and significantly related to the incidence of CVA mortality in women. [20] A similar pattern was demonstrated in US men: the multivariate relative risk of CVA of any type for men in the top fifth of potassium intake (median intake, 4.3 g/d) versus those in the bottom fifth (median intake, 2.4 g/d) was 0.62. [21]

Epidemiologic studies further demonstrate that a high potassium intake is related to a lower risk of CVA, and some of this effect may be independent and additive to the effect of potassium on blood pressure. Several observational studies have also found a link between potassium intake and risk reduction for CVA. In a 12-year prospective study by Khaw and Barret-Connor, [22] an increase in potassium intake of 10 mmol/day among 859 men and women resulted in a 40% reduction in stroke mortality. This association was found to be independent of other dietary variables, independent of BP and CVD risk factors. In two additional studies with much larger cohorts, US health professional men (43,738 men) [21] and US nurses (85,764 women) [23] high potassium intake also resulted in a lower risk of CVA.

CONCLUSION

In the present study, we have found significant changes in serum electrolyte levels in stroke patients. If such derangements are promptly identified and corrected, it is our belief that it could be of tremendous help in decreasing mortality due to stroke as well as in prevention of complications that might arise as a result of such derangements. Our study was limited as the causal factors between electrolyte derangements and stroke could not be fully established. Also, all possible causes which might influence the serum concentration of electrolytes could not be excluded. Despite this, our study is a pointer in the direction helping in exploring serum electrolyte thresholds in which interventions for reducing dietary sodium and increasing dietary potassium and chloride intake may benefit the population at risk, as well as to initiate effective therapy to maintain the equilibrium of electrolytes to prevent further recurrence of strokes.

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How to cite this article: Borah M, Bora K, Gogoi DM et al. Derangement of serum electrolyte status in cerebrovascular accident - a hospital based observational study in Shillong, Meghalaya. Int J Health Sci Res. 2016; 6(10):84-90.

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