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Research article

Evaluation of Plasma Electrolytes in Patients Suffering From Depressive Illness

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ABSTRACT: There are speculations that electrolyte concentrations may play a role in depressive illness but despite a number of studies, no agreement has been reached about blood electrolyte status in depression. One hundred subjects made up of sixty (60) depressed patients with mean age (40.3 ± 12.3) and forty (40) normal controls with mean age (40.1 ± 10.1) were recruited for this study. All patients were free from medication for a period of one month prior to the start of the study. Anthropometric indices of all subjects were also determined. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria and Hamilton Depression Rating Scale were used for diagnosis and measurement of severity of depression respectively. The mean plasma sodium ($p < 0.05$) and potassium ($p < 0.01$) were significantly decreased in depressed patients when compared with corresponding normal controls while the mean plasma calcium ($p < 0.05$) and urea ($p < 0.01$) were significantly increased in depressed subjects in comparison to normal controls. There were no significant differences in blood parameters determined between male and female patients. Similarly, the mean plasma concentrations of biochemical parameters did not significantly change from mild through to severe depression ($p > 0.05$). The results from this study suggest that plasma electrolyte levels could be altered in Nigerian Africans suffering from depressive illness and this may not be gender specific.

Keyword: Depressive illness, electrolytes, urea, calcium.

INTRODUCTION

Sodium and potassium are essential for life and are the main extracellular and intracellular cations respectively (Mayne, 2001). The proper gradient of their concentrations across cell membranes is necessary for the normal functions of the organism. Sodium and potassium are electrolytes involved in polarization and depolarization of the cell membrane. There are

speculations therefore that changes in their concentration may result in behavioral abnormalities (Pelteret, 1990). However, most studies did not arrive at any consensus on the blood electrolyte status in depressed patients. This has been attributed differences in confounding factors like patients' sex and about the severity of their illnesses (Widmer et al, 1992) which were not taken into consideration.

Some studies (Takayanaji et al, 2005) have associated alteration in mood with abnormalities in electrolyte metabolism. Electrolytes are fundamental to the general metabolism of monoamines involved in the pathophysiology of affective disorders (Takayanaji et al, 2005). However, Widmer et al (Widmer et al, 1997) reported that plasma sodium, potassium and calcium levels did not show any significant correlation with the intensity of symptoms in hospitalized patients with major depression. Similarly Kamei et al (1998) did not report significant differences in erythrocyte sodium and potassium concentrations in depressed patients when

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compared with the corresponding values in healthy controls.

Calcium ion is a major component of bones and the cellular structures and it also participates in many biochemical reactions. It functions as one of the major intracellular messengers. Changes in calcium concentration may be important in excitability of neural tissues involved in the regulation of mood (Cheung, 1980). Increased serum calcium concentration have been associated with psychiatric disorder (Jimmerson et al, 1979, Hagforsen et al, 2005). Using experimental animals, Li et al (2000) observed that altering tissue excitability by changing the ionic environment to a high Ca^{2+} /Low Mg^{2+} medium mimics electrical stimulation in the long-term depression.

Depressive illness is a major cause of morbidity and mortality especially in the elderly (Baldwin, 2000). Among Africans, earlier studies suggested that depression was rare (Carothers, 1947, 1951) but later studies have revealed an increasing prevalence in many African communities (Leighton, 1963, Wintrob, 1967). In Black Africans, very little research into the biology of depression, more especially on electrolyte and calcium has been carried out.

The objectives of this study are therefore to; Evaluate electrolyte profiles in adult Nigerians suffering from varying degrees of depression, to ascertain any possible relationship between severity of depression and electrolyte levels and to investigate the confounding effects of gender on the association between electrolyte levels and depression in Nigerians.

SUBJECTS AND METHODS

One hundred (100) subjects were selected for this study. The study group consisted of sixty (60) depressed patients (mean age 40.3 ± 12.3 yrs) and forty (40) normal controls (mean age 40.1 ± 10.1 yrs). Patients were recruited from General Out-patient Department of the University College Hospital, Ibadan who were picked on screening with the Centre for Epidemiological Studies on Depression Scale. All patients were free from medication for at least a month prior to the start of the experiment. All were normotensive, non-diabetic, without renal or liver dysfunction and with a body mass of index (BMI) of less than 30 kg/m^2 . None of the patients had received lithium therapy. Further exclusion criteria were diagnosis of any other disease apart from mood disorder.

Diagnosis of depression was made using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria at the Psychiatry Department of the

University College Hospital, Ibadan. Severity of depression was rated using the Hamilton Depression Rating Scale (HDRS).

Patients were divided into clinical subgroups as follows; those with mild depression (HDRS range 16-25), those with moderate depression (HDRS range 26-34) and those with severe depression (HDRS range >34). The categorization of these patients into these subgroups was done according to the practice and the experience of the psychiatrists.

Normal control subjects were required to score below 16 on application of the Centre for Epidemiological Studies on Depression Scale. They were free from medication, one month prior to the study and none of them had used psychotropic drugs or consumed alcohol regularly. None of the control subjects also reported any past history or family history of psychiatric disorders. Ethical committee approval was obtained from the University of Ibadan/ University College Hospital Ethical Committee and informed consent was obtained from each subject or the caregiver after the objectives of the study was carefully explained to them.

Blood samples were obtained from each of the patients and controls and plasma sodium and potassium estimated using the flame photometer method (Dvorak et al, 1971). Plasma calcium was estimated by the method of Gitelman (1967) and plasma urea and creatinine were determined by applying the methods of Coulomber and Farreau (1963) and Tausky (1956) respectively. Plasma albumin was determined using the bromocresol green method of Doumas and Watson (1971).

Statistical Analysis

Data was analyzed using the SPSS version 11.0 (SPSS Inc. USA). All reported values in this study were expressed as mean \pm standard deviation (SD). Biochemical parameters in the different study groups were compared using the student t-test. Group comparisons were carried out using one way analysis of variance while Pearson's correlation coefficient (r) was used to determine the relationship between variables with $p < 0.05$ regarded as significant.

RESULTS

As shown in Table 1, plasma sodium and potassium were significantly lowered in depressed patients when compared with controls. Mean plasma calcium and urea were however significantly higher in depressed subjects while the mean plasma albumin and creatinine did not significantly change between both groups.

TABLE 1:
Plasma Sodium, Potassium, Calcium, Urea, Creatinine and Albumin Concentrations in Depression (Mean±SD)

Parameters	Depression n=60	Controls n=40	t- value	P
Na ⁺ (mmol/L)	137 ± 5.0	139 ± 4.0	2.431	P<0.05
K ⁺ (mmol/L)	4.3 ± 0.5	4.6 ± 0.6	2.690	P<0.01
Ca ²⁺ (mg/dl)	8.4 ± 1.3	7.9 ± 0.9	2.189	P<0.05
Urea (mg/dl)	36 ± 7.0	31 ± 7.0	3.363	P<0.01
Creatinine (mg/dl)	1.6 ± 0.2	1.6 ± 0.15	0.147	N.S
Albumin (g/dl)	4.2 ± 0.5	4.3 ± 0.4	0.939	N.S

TABLE 2:
Plasma Sodium, Potassium, Calcium, Urea, Creatinine And Albumin Concentrations In Male And Female Patients (Mean ± SD)

Parameter s	DEPRESSIO N	CONTROL	D Vs C
Na ⁺ (mmol/L)	F 136 ± 4.5 (n=38)	F 138 ± 3.8 (n=21)	M vs M NS
	M 138 ± 4.5 (n=22)	M 141 ± 4.5 (n=19)	F vs F NS
	F vs M, NS		
K ⁺ (mmol/L)	F 4.2 ± 0.5 (n=38)	F 4.6 ± 0.4 (n=21)	M vs M NS
	M 4.5 ± 0.4 (n=22)	M 4.6 ± 0.7 (n=19)	F vs F p < 0.01
	F vs M, NS		
Calcium (mg/dl)	F 8.3 ± 1.3 (n=38)	F 7.8 ± 1.0 (n=21)	M vs M NS
	M 8.6 ± 1.4 (n=22)	M 8.1 ± 0.7 (n=19)	F vs F NS
	F vs M, NS		
Urea (mg/dl)	F 36 ± 6.5 (n=38)	F 31 ± 5.2 (n=21)	M vs M p < 0.05
	M 36 ± 8.8 (n=22)	M 30 ± 9.4 (n=19)	F vs F P < 0.05
	F vs M, NS		
Creatinine (mg/dl)	F 1.6 ± 0.2 (n=38)	F 1.6 ± 0.1 (n=21)	M vs M NS
	M 1.6 ± .2 (n=22)	M 1.6 ± .2 (n=19)	F vs F NS
	F vs M, NS		
Albumin (g/dl)	F 4.2 ± 0.6 (n=38)	F 4.2 ± 0.2 (n=21)	M vs M NS
	M 4.3 ± 0.4 (n=22)	M 4.4 ± 0.5 (n=19)	F vs F NS
	F vs M, NS		

There were no significant differences in mean plasma concentrations of biochemical parameters determined between male and female patients (Table 2) Plasma urea levels were however increased in male and female patients compared to their corresponding controls while the mean plasma potassium was significantly decreased in female patients compared to female controls. Similarly, there was no significant association between blood electrolytes and depression rating scores (Table 4) and the blood parameters did not significantly change between those who were mildly depressed, moderately depressed and severely depressed. (Table3).

DISCUSSION

This study revealed significant changes in plasma electrolyte and urea levels. There were significant increases in plasma calcium and urea levels accompanied by significant decreases in plasma sodium and potassium levels in patients compared to control subjects. However, these changes did not significantly correlate with severity of depression. Similar to the findings of an earlier study (Widmer et al, 1997), there was no significant association between plasma sodium and potassium concentrations and gender in depression. It is possible that the significant decreases observed in both potassium and sodium in depressed subjects could be caused by altered activity of Na⁺K⁺-ATPase, a sulphydryl-dependent biocatalyst requiring calcium and intimately involved in the function of the sodium pump (Kobayashi et al, 1974). However, the mean plasma calcium was significantly increased in the patients compared to controls suggesting that any defect in the enzyme system is unrelated to nonavailability of adequate calcium in these patients. Genetic factors may be important in the overall changes. Mendel and Frazer (1974) had previously proposed that some depressed patients have abnormal cell membrane systems which may be genetically determined.

The significant increase in mean calcium level in depression when compared to controls is unlikely to be a consequence of protein alteration since albumin levels were similar in both depressed patients and controls (p>0.05). Serum proteins, especially albumin bind about 45% of total calcium while about 50% are in the ionized form.. However, an intracellular protein, calmodulin regulates the intracellular calcium levels for various reactions by pumping accumulated excess calcium out of the cell (Tolohen, 1990).

Table 3:
Plasma Sodium, Potassium, Calcium, Urea, Creatinine And Albumin Concentrations In Mild, Moderate And Severe Depression (Mean \pm Sd)

Parameters	Mild M1 (N = 25)	Moderate M2 (N = 25)	Severe M3 (N = 10)	F	P
Na ⁺ (Mmol/L)	136 \pm 5	137 \pm 5	139 \pm 3	1.521	Ns
K ⁺ (Mmol/L)	4.3 \pm .5	4.2 \pm .2	4.5 \pm .4	1.36	Ns
Calcium (Mg/Dl)	8.6 \pm 1.4	8.3 \pm 1.3	8.2 \pm 1.2	.466	Ns
Urea (Mg/Dl)	30 \pm 14	30 \pm 10	31 \pm 5	.077	Ns
Creatinine (Mg/Dl)	1.5 \pm .2	1.6 \pm .2	1.6 \pm .3	.757	Ns
Albumin (G/Dl)	4.2 \pm .6	4.2 \pm .5	4.3 \pm .3	.399	Ns

Table 4:
 Correlation Coefficients for Plasma Electrolytes and Depression Rating Scores in Depression

	Na ⁺	K ⁺	Ca	HDRS
Na ⁺	1.00	-.090	-.367 ^b	.135
K ⁺	.089	1.000	.089	.067
Ca	-.367 ^b	.089	1.00	.126
HDRS	.136	.067	.126	1.00

b = p<0.01

This calmodulin regulatory mechanism may be stimulated by depression. Although, plasma urea was significantly increased in both male and female depressed subjects in comparison to corresponding controls, the concentration of plasma creatinine did not show any significant increase probably suggesting that renal dysfunction is not present in depressed patients but the importance of urea in depression should not be overlooked. Leonard and Morris (2002) had reported that urea cycle disorders can cause mild depression of the central nervous system leading to clinical conditions like drowsiness, slow reflexes, slurred speech and general neurological damage.

In conclusion, this study suggests that plasma electrolyte levels could be altered in Nigerian Africans suffering from depressive illness, irrespective of gender.

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