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LETTER TO THE EDITOR

UNIPOLAR DEPRESSION AND SERUM ELECTROLYTES

Sir,

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Following *in vitro* demonstration of dependence of synaptosomal preparation on divalent cations for neurotransmitter precursor uptake particularly of tyrosine and tryptophan and evolution of biogenic theory of causation and therapeutic response to monoamine oxidase (MAO) inhibitors in affective disorders, blood electrolytes have gained considerable attention in pathogenesis of depressive illnesses.

Fewer studies have been done on Na+ and K^+ in such patients and hence no consensus has evolved on the levels of these electrolytes in blood or other body fluids. Increased (1) and normal (2) plasma levels of Sodium and low levels of K^+ (2, 3) have been reported in depressed patients. Changes in extracellular Ca^{++} and Mg^{++} have also been noted in depression. Moreover, divalent cations acquire significance in view of their relationship with severity of symptoms (4) and the Ca^{++} and Mg^{++} ratio to the response of lithium therapy (5). Mg^{++} alone has been reported to enhance the efficacy of antidepressant drugs in refractory depression patients (6).

While divalent cations have been associated with severity and efficacy of antidepressant in bipolar depressions such associations which might possibly exist between electrolytes and severity and or efficacy of antidepressant have not been studied in unipolar depression cases. Therefore we planned to study any possible association between electrolyte levels and severity in unipolar depression.

Fifty eight unmedicated patients of unipolar depression (Age: 16–69yrs) reporting to the J. N. Medical College Psychiatry Out Patients Department were included in this study. The diagnosis of major depression was based on DSM-IV criterion assessed by two Psychiatrists independently. The gradation of severity of depression into mild (4–12), moderate (13–18), and severe (>18) was based on Hamilton Depression Rating Scale (HAMD) score. Twenty five healthy hospital staff member (Age: 19–50 yrs.) served as controls.

Bloods samples were collected by venepuncture, serum was separated and stored at –20°C until estimations were done. Na^+ were estimated by flame photometry, Ca^{++} and Mg^{++} by Cresolphalein complex (CPC) and Calmagite method respectively on a spectrophotometer.

Statistical analysis of data for significance was done by student 't' test and correlation coefficient between HAMD score and serum electolyte levels were calculated.

TABLE I: Serum sodium, potassium, magnesium and calcium levels in control subjects and patients of different grades of severity of depression.

Electrolyte	*Control*	*Patients*			
	(M±SD)	*All*	*Mild*	*Moderate*	*Severe*
n	25	58	20	13	25
Mg++ (Meq/L)	2.09±0.28	1.40±0.52***	1.69±0.49**	1.55±0.49***	1.08±0.43***
Ca++ (Mg/dL)	9.09±1.43	10.10±2.96***	9.68±1.0***	10.72±1.0***	10.12±1.45**
Na+ (Meq/L)	128.68±11.75	125.11±15.29	124.	43±18.46	126.36±14.6
K+ (Meq/L)	3.87±0.44	4.06±0.64	3.9±0.74	4.00±0.69	4.23±0.52**

**P<.01; ***P<.001

Serum Mg^{++} indicates significant lower levels in depression patients compared to control subjects (Table I). The fall in each grade of severity of depression was significant as against the control serum Mg^{++} levels. On the contrary there was significant increase in serum. Ca^{++} levels in patients particularly in moderate and severe grade of disease. Potassium levels were significantly increased only in patients with severe grade of depression as against the control subjects.

When HAMD score was correlated with levels of mono and divalent cations of the patients, Mg^{++} showed significant negative correlation with HAMD score ($r = -0.4695$, $P>.01$) while none of the other electrolytes correlated significantly with HAMD score.

Increase in plasma or serum Ca^{++} as observed in our study were reported by other workers as well (7, 8, 9), though, Bothwell and coworkers (10) were unable to find any remarked alteration in serum Ca^{++} levels which could possibly be due to inclusion of large number of patients of milder severity, as it is evident from our study also in which mildly depressed patients did not show significant alteration of serum Ca^{++}.

Mg^{++} levels in all grades of severity were significantly lower than that of the healthy control subjects which is similar to earlier reports on Mg^{++} levels in depressed patients (9, 11). On the contrary other workers have reported increase in serum Mg^{++} levels (2, 3, 8, 12). However, many of these studies which showed increase in serum Mg^{++} levels were conducted on patients already on antidepressants for long time in contrast to our patients group who had not received any antidepressant at any point of time during the course of their illness. The negative correlation between severity of depression and Mg^{++} levels as it is evident from our data, suggests that antidepressant therapy by reducing the severity could influence the Mg^{++} levels.

In the present study we have found an increase in K^+ levels in patients with severe depression which is similar to earlier reports (3, 13). This has been attributed to disordered function of Na^+-K^+ pump which in turn was associated to hypothyroidism (14). We too in our previous study (15) have found hypothyroidism in unipolar depression patients.

Mg^{++} ions are associated in a number of

enzymatic reactions like it is a co-factor in glycolytic pathway (16) and a modulator of Ca^{++} and Na+ channels in various organs (17). Further it has shown that Mg^{++} is responsible for increase uptake of L-tryptophan (serotonin precursor) in *in-vitro* preparation of synaptosomes (18). Hence, it is plausible to speculate that lower levels of Mg^{++} could influence the synthesis of monoamines particularly serotonin and could be a crucial factor in pathogenesis of depression.

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