



A Tale of Two Bivalent Cations in Major Depressive disorder

Soma Gupta^{1*}, Saswati Nath², Harendra Nath Das³

¹Prof. & Head, Department of Biochemistry, N.R.S. Medical College
(Formerly attached to College of Medicine & Sagore Dutta Hospital)

²Associate Prof. Department of Psychiatry, R. G. Kar Medical College

³Prof & Ex Head, Department of Biochemistry, R. G. Kar Medical College

*Corresponding author: guptasomarus@yahoo.com

Abstract

The level of calcium and magnesium was estimated in 150 cases of Major Depressive Disorder (MDD) along with age and sex matched 150 control subjects. The level of magnesium was found to be decreased statistically. This finding was also consistent when the cases were graded according to the severity. This simple test can easily be used in diagnosis of MDD cases and supplementation in necessary cases may be helpful for the patients.

Keywords: Major Depressive Disorder, Calcium, Magnesium

Introduction

Numerous factors are known to contribute in pathogenesis of Major Depressive Disorder (MDD), among which nutritional status of vitamins and minerals were found to play important role as they are involved in different metabolic regulations. A study on adult men reported that supplement of oral multivitamins in combination with calcium, magnesium, and zinc had an effect on relieving anxiety and perceived stress (1). Neuronal deficits of Magnesium ion were also found to be induced by stress hormones, excessive dietary calcium as well as dietary deficiencies of magnesium. Cernak et al. (2) showed that chronic stress decreases both free and total plasma ionized magnesium and simultaneously increased oxidative stress in humans. The mechanism can be understood by the fact that Magnesium ions regulate calcium ion

flow in neuronal calcium channels, helping to regulate neuronal nitric oxide production. In magnesium deficiency, neuronal requirements for magnesium may not be met, causing neuronal damage, which could manifest as depression. Magnesium treatment is hypothesized to be effective in treating major depression resulting from intraneuronal deficits. Eby & Eby suggested magnesium deficiency as cause of Major Depressive Disorders and recommended immediate, wide-spread further study on it. Considering the facts that there is an increasing trend of prevalence of depression, throughout the world including India and there is no known biochemical parameter to diagnose the condition, this simple test may have an enormous importance to public health (3).

Aims & Objectives

1. To estimate serum level of Calcium and magnesium in patients suffering from MDD.
2. To find out whether these parameters have any significant difference when the disease is classified according to grade.

Materials and Methods

This Case control study was undertaken in Department of Biochemistry, College of Medicine & Sagore Dutta Hospital in collaboration with Department of Psychiatry of same Institute. The study period was from July, 2013 to Feb, 2016. The study was approved by Institutional Ethics Committee.

I. Selection of study subjects

All patients who were suspected to suffer from Major depressive disorder (MDD) were selected from the Psychiatry outdoor of College of Medicine & Sagore Dutta Hospital. These patients were first evaluated by detailed history taking and clinical examination through a structured proforma designed for this study. Then they were screened with WHO Five well being index (4). The raw score was calculated. When raw score was below 13 or if the patient had answered 0 to 1 to any of the 5 items, they were further tested. Patients were diagnosed as having major depressive disorder according to the Structured Clinical Interview for DSM-IV, and who scored at least 14 points on Major Depression Inventory (MDI)⁵. This inventory was also used to classify the patients according to *ICD 10 criteria for depression*.

The exclusion criteria were significant psychiatric co-morbidity, organic mental disorder, mental retardation, bipolar disorder, intake of any psychotropic drugs during and at least 1 week before the study, substance abuse, history of endocrine disorders, pregnancy, postpartum depression and lactation.

Apparently healthy age and sex matched individuals were assessed using General Health

Questionnaire (GHQ 12). A score of less than or equal to 15 were considered as not to suffer from major psychiatric illness (6). Such individuals were selected as control group.

Informed consents were taken from the patients or legal guardians and from the control subjects.

II. Gradation of MDD cases

MDI score of 20 – 24 was considered as mild grade, 25 – 29 as moderate grade and ≥ 30 was considered as severe grade.

III. Sample Collection, Separation & analysis of serum

An amount of 5 ml of fasting blood samples was drawn from each of the study subjects (Both cases & controls). Serum was separated and was analysed using metal complexing dye cresophthalein for calcium (7) and calmagite for magnesium (8).

IV. Statistical Analysis

The concentration of Calcium and magnesium were expressed in mean \pm SD in both the study groups. The mean values were compared for significance by student's t test. A p value of <0.05 was considered to be significant.

The patients were further subdivided in mild, moderate and severe grade. One-way analysis of variance (ANOVA) with post hoc test is used to test the difference between the means of several subgroups.

The analysis was done using Analyse it Standard edition software version 4_80_9.

Results

A total of 300 subjects (150 cases of MDD, along with 150 age and gender matched control) were included in the study. All cases were further classified according to the severity into mild, moderate and severe grade. Age and gender distribution of each grade is shown in Table 1.

Table 1: Grade wise Age & Gender distribution of cases with Major Depressive Disorder

Grade	Female	Male	Mean age
Mild (n =36)	28	08	23.2 yrs
Moderate (n=55)	39	16	28.9 yrs
Severe (n =59)	45	14	49.7 yrs
Total (n = 150)	112	38	38.6 yrs

The mean age of patients of each grade is also calculated. The distribution table clearly shows a female preponderance.

parameters were found to be decreased in cases with MDD but difference was found to be statistically significant only in case of Magnesium.

Table 2 shows serum level of calcium and Magnesium in both the study groups. Both the

Table 2: Level of Calcium & Magnesium in Study Groups

Biochemical Parameter	Statistical Parameter	Case (n = 150)	Control (n = 150)
Calcium ¹	Arithmetic mean (mg%)	9.1027	9.2751
	Standard deviation	0.9669	0.5625
	Standard error of the mean	0.0789	0.0459
Magnesium ²	Arithmetic mean (mg%)	1.6967	2.1263
	Standard deviation	0.5600	0.8771
	Standard error of the mean	0.0457	0.0716

Test statistic t: 1.8876, Two-tailed probability: P = 0.0601 ¹

Test statistic t: 5.0561, Two-tailed probability: P <0.0001 ²

Moreover, the decreasing trend of blood magnesium level was found to be consistent, when the level was analysed in each grade.

However, In case of calcium the decreasing trend was found to be present in mild and moderate grade only (Table 3).

Table 3: ANOVA test of the study group

Grade of MDD (n = 150)	Biochemical Parameter			
	Calcium		Magnesium	
	Mean (mg%) ± SD	F Ratio (significance)	Mean (mg%) ± SD	F Ratio (significance)
Mild (n = 36)	8.12±0.95	0.85 (P = 0.42)	1.56±0.64	3.02 (P = 0.05)
Moderate (n = 55)	9.16±1.02		1.64±0.53	
Severe (n = 59)	9.16±0.93		1.82±0.50	

Discussion

The finding of low serum magnesium level is in accordance with the findings of Zieba A et al (9) and Kirov GK et al (10). Magnesium remains in the synapse between two neurons where calcium and glutamate also reside. Calcium and glutamate are excitatory, and in excess, toxic. They activate the N-Methyl-D-aspartate (NMDA) receptors, whereas magnesium is a non-competitive inhibitor of the NMDA receptors. Hence Magnesium deficiency results into Neuromuscular hyper excitability, depression and behavior disturbances (11). A study was done among 16 patients with depression and 12 normal subjects. They found that total plasma magnesium levels were lower among patients, but no difference in levels of ionized magnesium (12). Jung et al assessed serum magnesium levels in 112 healthy adult women without psychiatric disorders and observed that women in the lowest tertile of serum magnesium levels had a higher risk of developing depressive mood disorder (13).

Though depletion of magnesium ions is known to impair control of calcium ions in neuronal channels, change in magnesium ion is supposed to be associated with a change in calcium level. Moreover, studies have reported association of low dietary calcium with depression (14) the normal level of calcium can be explained by the fact that serum calcium homeostasis is dynamic, it appears that the subjects were able to keep their serum calcium concentration level in the normal range with the help of vitamin D and Parathyroid hormone. This mechanism is supported by other study group also (15).

Conclusion

The burden of MDD is showing an increasing trend not only in India but throughout the world.

Magnesium deficiency has been found to be a strong component of the disease. Change in dietary habits, water treatment system, increased use of bottled beverage; all might have been contributed to inadequate intake of magnesium. A simple laboratory test is enough to identify the condition of hypomagnesaemia. Necessary

precaution and timely supplementation of magnesium may decrease the incidence of depression. Thus magnesium deficiency as cause of MDD is enormously important and need further study.

Acknowledgements

The authors acknowledge the help of Late Dr. Swati Bera, Associate Professor, Department of Biochemistry, R.G. Kar Medical College. The support from West Bengal University of Health Sciences is duly acknowledged.

Declaration

Funding: None

Conflict of interest: None declared

Ethical approval: Approved by Institutional Ethics Committee

References

1. Carroll D, Ring C, Suter M, and Willemsen G. 2000. The effects of an oral multivitamin combination with calcium, magnesium, and zinc on psychological well-being in healthy young male volunteers: a double-blind placebo-controlled trial. *Psychopharmacology (Berl)*; 150: 220-5.
2. Cernak I, Savic V, Kotur J, Prokic V, Kuljic B, and Grbovic D. 2000. Alterations in magnesium and oxidative status during chronic emotional stress. *Magnes. Res*; 13: 29-36.
3. George A. Eby, Karen L. Eby. 2006. Rapid recovery from major depression using magnesium treatment. *Medical Hypotheses*; 67 (92): 362 – 370.
4. Primack B. A. 2003. The WHO 5 Well Being Index performed the best in screening for depression in primary care. *Evid. Based Med*; 8: 155.
5. Bech P, Rasmussen NA, Olsen R, Noerholm V, and Abildgaard W. 2001. The sensitivity and specificity of the Major Depression Inventory, using the Present State

- Examination as the index of diagnostic validity. *J. Affect. Dis*; 66:159-164.
6. Goldberg D. 1985. Identifying psychiatric illnesses among general medical patients. *British Medical Journal*; 291: 161-162.
 7. Stern J, Lewis W.H.P. 1957. The colorimetric estimation of calcium in serum with O cresophthalein complexone. *Clin Chim Acta*; 2: 576 – 580.
 8. Regulatio Liedtke R.J., and Croon G. 1984. Automated calmagite measurement of magnesium in serum. *Clin Chem*; 30: 1801 – 1804.
 9. Zieba A, Kata R, Dudek D, Schlegel-Zawadzka M, and Nowak G. 2000. Serum trace elements in animal models and human depression: Part III. Magnesium. Relationship with copper. *Hum Psychopharm Clin*; 15: 631–5.
 10. Kirov G.K., Tsachev K.N. Magnesium, schizophrenia and manic depressive disease. *Neuropsychobiology*; 23:79–81.
 11. Sapolsky RM. 1990. Stress the aging brain and the mechanisms of neuron death. Cambridge, MA: A Bradford Book, The MIT Press; page 192.
 12. Frizel D, Coppen A, and Marks V. 1969. Plasma magnesium and calcium in depression. *Br. J. Psychiatry*; 115: 1375–77.
 13. Jung K.I., Ock S.M., Chung J.H., and Song C.H. 2010. Associations of Serum Ca and Mg Levels with Mental Health in Adult Women Without Psychiatric Disorders. *Biol. Trace Elem. Res*; 133: 153–61.
 14. Yun-Jung Bae and Soon-Kyung Kim. 2012. Low dietary calcium is associated with self-rated depression in middle-aged Korean women. *Nutrition Research and Practice*; 6: 527-533.
 15. Roman S.A., Sosa J.A., Pietrzak R.H., Snyder P.J., Thomas D.C., Udelsman R, and Mayes L. 2011. The effects of serum calcium and parathyroid hormone changes on psychological and cognitive function in patients undergoing parathyroidectomy for primary hyperparathyroidism. *Ann Surg*; 253:131-7.

Access this Article in Online	
	Website: www.ijcrims.com
	Subject: Medical Biochemistry
Quick Response Code	

How to cite this article:

Soma Gupta, Saswati Nath, Harendra Nath Das. (2017). A Tale of Two Bivalent Cations in Major Depressive disorder. *Int. J. Curr. Res. Med. Sci.* 3(5): 1-5.

DOI: <http://dx.doi.org/10.22192/ijcrms.2017.03.05.001>