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Lower Total Serum Protein, Albumin and Zinc in Depression in an Iranian Population

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We studied associations between lowered serum zinc, total protein and albumin with depression and their correlations. In the present study serum zinc, albumin and total protein were determined in 144 depressed patients and 161 age-sex-matched healthy controls. The serum zinc concentration was significantly lower in depressive patients (64.94±13.9 μg dL^{-1}) than in normal controls (69.67±11.29 μg dL^{-1}) ($p = 0.001$). Albumin and total serum protein were significantly lower in depressed patients than in normal controls too. The significant correlation between serum zinc and albumin was observed in depressed patients while serum zinc, albumin and total protein concentrations were significantly decreased in depressed patients than normal controls also.

Key words: Depression, zinc deficiency, albumin, total serum protein

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INTRODUCTION

Depression is a psychiatric disorder with high morbidity and mortality. It is estimated that depression is the cause of 50-70% suicides (Lecomte and Fornes, 1998). The World Health Organization (WHO) predicts that depression will be the second most important cause of human disability-adjusted life years by the year 2020 (Murray and Lopez, 1997). There are some evidences that depression is accompanied by activation of the Inflammatory Response System (IRS). Increased numbers of leukocytes, monocytes, neutrophils, activated T-lymphocytes and increased secretion of neopterin and prostaglandins (Song *et al*., 1998; Bonaccorso *et al*., 1998). An Acute Phase (AP) response indicated by changes in serum acute phase proteins (Maes *et al*., 1997) and increased secretion of proinflammatory cytokines, such as IL-1b, IL-6 and interferon-g (IFNg). Since these proinflammatory cytokines induce IRS activation, the above changes in depression may be caused by increased production of IL-1b, IL-6 and IFNg (Maes *et al*., 1997).

IRS activation is also accompanied by decreasing in serum zinc. Zinc is, in the plasma, tightly bound to a macroglobulin (40%), while the remaining zinc is loosely bound to albumin (55%) or amino acids (5%). The loosely bound zinc fraction provides the zinc delivery to the tissues (Black, 2001). Lowered serum zinc during IRS activation may be secondary to sequestration of the intracellular heavy metal binding protein metallothionein in the liver, which, in turn, may be related to an increased production of the pro inflammatory cytokines, IL-1 and IL-6 (Van Miert *et al*., 1990). There is now evidence that depression is accompanied by lower serum zinc (Maes *et al*., 1997). IRS activation results in decreased serum albumin concentration and availability of less Zinc binding protein (Kushner, 1993). However, it is not known whether the decrease in serum zinc in depression is attributable to lower serum albumin. Maes *et al.* (1997) found that sub chronic treatment with antidepressants did not significantly alter serum zinc.

During the last several years, many articles have been presented indicating important role of zinc in the psychopathology and therapy of depression (Kushner, 1993).

Zinc is one of the trace elements necessary for health and growth. It is present in biological fluid as Zn^{++}. This cation has many biological functions, which is related to its main function as a co-factor in more than 300 enzymes (Nowak *et al*., 2005). Zinc also participates in the distribution of proteins and gene expression. It also stabilizes the structure of protein and nucleic acids. Zinc also preserves the intracellular organelles situation, plays a role in transfusion and is a important modulator of mammalian immune and nerves system (Burits and Ashwood, 1994).

In 1991, a report was published which emphasized the importance of zinc and also indicated that in countries such as Iran, Egypt, Turkey, China, Yugoslavia and Canada due to low consumption of red meat and high consumption of fiber, zinc deficiency was seen quiet often. Zinc deficiency in humans was reported for the first time in Iran and Egypt in 1963 (Prasad *et al*., 1963).

According to high zinc deficiency prevalence in Iran, in the present study we investigated the association between the occurrence of depression and zinc deficiency in Iranian patients.

MATERIALS AND METHODS

Study subjects: Clinically identified depressive patients (n = 144; 60 males and 84 females) by Psychologist from Zahedan Psychiatry Hospital were studied between Feb and Nov 2006. The control group consist of 161 individuals (68 males and 93 females), within the same range as patients who had no history of depression, nerves diseases and general illness. Healthy volunteers were free of any medication for at least 1 month prior to blood sampling. No one had ever been taking psychotropic drugs. Normal volunteers were excluded for past, present and family history of psychiatric disorders.

Blood samples were obtained from all subjects after 12 h fasting and placed in EDTA tubes and stored at -20°C until the time of assay. The study protocol was approved by Ethics Committee of Zahedan University of Medical Sciences.

Biochemical analysis: The serum zinc was determined by atomic absorption spectrophotometer (PU9100X-Philps). Those samples having zinc less concentration than 70 μg dL^{-1} marked as zinc deficient (12). Total Serum Protein (TSP) was determined by Biuret Method (ZiestChem Diagnostics) and albumin was determined by colorimetric method (ZiestChem Diagnostics)

Statistical analysis: All statistical analysis was performed with SPSS (version11.5). Numeric data are presented as Mean±SD. The differences between groups were examined by Chi-square test or independent Student t-test when appropriate.

RESULTS

The clinical characteristics of clinically depressed and normal population of different age, sex and marital status was studied and is shown in Table 1.

Table 1: Clinical characteristics of the study population

Variables	Depressive patients	Controls	p-value
No. of subjects	161	144	
Male/Female	68/93	60/84	0.51
Age (years)	35.37±10.13	38.53±10.4	0.061
Married (%)	78.3	73	0.16

Control subjects were matched to the case patients for gender and age

Table 2: Comparison of mean serum zinc, total serum protein and albumin concentrations in depressed patients and in normal controls

Groups	No.	Zinc (μg dL^{-1})	TSP (μg dL^{-1})	Albumin (μg dL^{-1})
Patients	144	64.94±13.9	66.1+7.2	39.1+7.5
Controls	161	69.67±11.29	69.6+8.9	42.6+9.2
p-value		0.001	0.000	0.000

Table 3: Frequency distribution of serum zinc deficiency in depressed patients and in normal controls

Groups	Zinc<70 (μg dL^{-1}) (%)	No.	TSP>70 (μg dL^{-1}) (%)	No.	Total
Patients	65	93	35	51	144
Controls	50	81	50	80	161
	$\chi^2 = 6.32$	p = 0.005			

Married condition showed no significant differences between the patients and the control subjects too.

The serum zinc concentration was 64.94±13.9 μg dL^{-1} in depressive patients and 69.67±11.29 μg dL^{-1} in controls. We found that serum zinc concentration was significantly lower in depressive patients than in normal controls (p = 0.001). In total study, there was no significant difference in serum zinc between men and woman (p = 0.15) (Table 2).

Total serum protein concentration was significantly lower in depressive patients (66.1±7.2 mg dL^{-1}) than in normal controls (69.6±8.9 mg dL^{-1}) (p = 0.0001). Serum albumin concentration was 39.1±7.5 mg dL^{-1} in depressive patients and 42.6±9.2 mg dL^{-1} in controls and there were significant differences between two groups too (p = 0.0001). In depressed patients but no normal controls there were significant and positive correlations between zinc and TSP (r = 0.261, p = 0.002). Also there were significant and positive correlations between zinc and albumin in depressed patients (r = 0.264, p = 0.001) (Table 2). Zinc deficiency frequencies were 65 and 50% in depressive patients and normal controls, respectively and differed significantly between two groups ($\chi^2 = 6.3$ p = 0.005, Odds ratio = 1.8, CI = 1.14-2.85) (Table 3).

DISCUSSION

The first major finding of this study is that serum zinc is decreased in depression.

Present finding on lower serum zinc in depression is consistent with many other studies (McLoughlin *et al*., 1990; Maes *et al*., 1994, 1999a). Ciubotariu and Nechifor (2007) revealed that plasma zinc concentration is decreased in major depression and it significantly increases following sertraline or amitriptyline treatment.

The second major finding of this study were significant positive relationships between serum zinc and serum albumin and total serum protein as previously reports (Maes, 1999). These findings on lowered serum albumin and total serum protein in depression are in agreement with some other reports (Van Hunsel *et al*., 1996; Maes *et al*., 1997). Since albumin is the most important zinc binding protein, less albumin concentration is available and thus, serum zinc is less in consequent of lower serum albumin (Goldblum *et al*., 1987). Maes *et al*. (1994, 1999) suggested several possible causes for decreased serum zinc and albumin concentrations in depression. Their first hypothesis was that, decreased serum zinc and albumin are related to the anorexia and subsequent malnutrition. But they were unable to find significant relationships between serum zinc and anorexia or weight loss and since no nutritional deficiencies, either of the marasmic or kwashiorkor like type, can be detected in depression (Maes *et al*., 1997). In second hypothesis they said: lower serum zinc could be the consequence of Hypothalamic-Pituitary-Adrenal (HPA) hyperfunction which frequently occurs in depression (Maes *et al*., 1997).

In the most acceptable hypothesis they believed that lower serum zinc and albumin are related to IRS activation. Previously, Maes *et al*. (1997) found significant inverse relationships between lower serum zinc and markers of IRS activation in depression e.g., increased serum IL-6. Also they report a significant inverse relationship between serum zinc and haptoglobin values >150 mg dL^{-1}. The relationships between serum zinc and IL-6 or positive AP proteins in depression, strongly suggests that lower serum zinc is caused by increased production of IL-6 (Maes *et al*., 1997).

Nowak *et al*. (2005) believed that zinc is an antagonist of the glutamate/N-methyl-D-aspartate (NMDA) receptor and exhibits antidepressant-like activity in rodent tests/models of depression. Their preliminary clinical study demonstrated the benefit of zinc supplementation in antidepressant therapy. All the data indicate the important role of zinc homeostasis in psychopathology and therapy of depression and potential clinical antidepressant activity of this ion.

CONCLUSION

The present study may suggest that, lower serum zinc is a marker of depression and there were significant and positive correlations between zinc, total serum protein and albumin.

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