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Original Article

Comparison of Serum Zinc Levels between Patients with Schizophrenia and Healthy Individuals

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Abstract

Background and objectives: Schizophrenia is a debilitating mental disorder characterized by disruptions in thought processes, perceptions, emotional responsiveness, and social interactions. Zinc is a neuroactive element released in synapses during neuronal activity and is required for proper functioning of the nervous system, particularly the brain. Serum and tissue concentrations of zinc may reflect various physiological and pathophysiological conditions. Evidence suggests a link between zinc level and development of schizophrenia. The aim of this study was to compare serum zinc levels between patients with schizophrenia and healthy individuals.

Methods: This case-control study was performed on 55 patients (37 men and 18 women) with schizophrenia who were hospitalized in 5 Azar Hospital in Gorgan (Iran) and 55 healthy individuals. The case subjects were selected based on convenience sampling method using the Positive and Negative Syndrome Scale (PANSS), while the control subjects were enrolled based on the General Health Questionnaire-28 (GHQ-28). The groups were matched in terms of age and gender. Serum concentration of zinc was measured using a commercial colorimetric assay kit (5-Br-PAPS method).

Results: Serum zinc concentration did not differ significantly between the patients and the controls (P=0.93). In schizophrenic patients, there was a significant, negative correlation between age and serum zinc concentration (r=-0.298, P=0.027). In both patients and controls, serum zinc level was significantly higher in men than in women (P<0.05).

Conclusion: Based on the results, it is recommended to pay more attention to the diet of patients with schizophrenia.

Keywords: Zinc; Schizophrenia; Trace elements; Mental disorder

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INTRODUCTION

Schizophrenia is a debilitating, long-term mental disorder that leads to misconceptions, inappropriate actions and deviations from reality due to disturbed connections between thoughts, feelings and behaviors (1). The etiology of schizophrenia is multifactorial, involving the interaction of genetic and environmental factors (2). Recently, a gene called ZNF804A has been implicated in schizophrenia. Strong body of evidence suggests that this gene is functionally linked to schizophrenia and may be considered a new target for therapeutic intervention (3). The age of disease onset is between 18 and 25 years in men and between 25 and 35 years in women. It affects both genders to the same extent, but men show symptoms of the disease at a younger age than women do (4-6).

Cerebral atrophy has been implicated in established schizophrenia, which is associated with cognitive dysfunction (7). In animal models of schizophrenia, hippocampal lesions are expanded, leading to frontal lobe aneurysm rupture (9). Zinc is a neuroactive element released at synapses during neuronal activity. Serum and tissue concentrations of zinc may reflect various physiological and pathological conditions. The recommended daily intake of zinc varies from person to person but is usually 15 mg in men and 12 mg in women (10). This trace element is essential for the proper functioning of the human body, especially the brain. The highest concentrations of zinc are found in the hippocampus and amygdala (11).

Although a link between zinc level and schizophrenia has been suggested (1), research findings on the status of trace elements in patients with schizophrenia have been controversial. A study reported a significant increase in serum copper and hair copper concentrations and a significant decrease in zinc level in schizophrenics compared to healthy controls (12). Cells in the salivary glands, prostate, immune system and intestines utilize zinc signals to communicate with other cells. In the brain, zinc is stored in specific synaptic vesicles by glutamatric neurons and can modulate brain excitability, affecting synaptic plasticity and cognition. Zinc homeostasis also plays an important role in the normal functioning of the brain and central nervous system (13). Zinc deficiency increases copper concentrations, which can increase anxiety, irritability and emotional instability (14, 15). The role of zinc has been implicated in depressive disorders, but the possible association of zinc with schizophrenia has not been sufficiently studied (16). Although studies on zinc supplementation for the treatment of schizophrenia have been somewhat promising, further studies are required to understand the disease and to improve treatment methods (17). As mentioned earlier, results of studies on the level of zinc and other trace elements in patients with schizophrenia have been contradictory (18-21). A meta-analysis in 2018 reported that serum zinc levels are notably lower in patients with schizophrenia than in healthy individuals (16). Another study claimed that there is a relationship between low serum zinc levels and high-risk and abnormal behaviors in patients with schizophrenia (22). In a study on the relationship of trace elements with schizophrenia and the effects of antipsychotics therapy, serum zinc concentrations were lower after risperidone therapy. The mentioned studies also reported that the patients had significantly higher concentration of magnesium and phosphorus and significantly lower concentrations of iron, calcium and zinc compared to healthy controls. Age was positively correlated with iron and copper concentrations and negatively correlated with calcium, phosphorus and zinc concentrations in the control group (23). In this study, we aimed to compare the level of serum zinc in patients with schizophrenia and healthy individuals.

MATERIALS AND METHODS

This was a case-control study that included 55 patients (37 men and 18 women) with schizophrenia who were admitted to the psychiatric ward of 5 Azar Hospital in Gorgan, Iran. The control group consisted of 55 healthy persons accompanying patients referred to the hospital. The groups were matched in terms of age, gender and ethnicity. Written consent was obtained from all individuals. The sample size was estimated based on the study of Chen et al. using the G.Power application and considering type I error of 5% (α) and test power of 95% (β) (22). The patients were selected based on convenience sampling method using the Positive and Negative Syndrome Scale (PANSS), while the control subjects were enrolled based on the General Health Questionnaire-28 (GHQ-28) (23).

The patients were either not receiving any medication or had stopped taking their medication for at least a year .Inclusion criteria were confirmed diagnosis of schizophrenia by a psychiatrist according to the DSM-5 criteria, hospitalization in the psychiatric ward of the hospital, age of 20 to 55 years and discontinuation of medication for at least one year. Exclusion criteria were presence of any other mental illnesses, having autoimmune, cardiovascular, hepatic, renal and allergic diseases, pregnancy, a history of drug abuse and consumption of medications that affect the metabolism of zinc i.e. tetracycline, fluoroquinolones, bisphosphonates, some anticonvulsants, contraceptives and glucocorticoid. Fasting blood samples (3 ml) were taken between 7 and 9 am. Next, serum was separated and stored at -80 ^{o}C. Serum concentration of zinc was measured using a commercial colorimetric assay kit (5-Br-PAPS method).

Statistical analysis of data was carried out using the SPSS 16 software package. Demographic and laboratory data were analyzed using descriptive statistics. Normality of data was assessed by the Shapiro-Wilk test. The independent t-test and Mann-Whitney non-parametric test were used to compare serum zinc levels between the study groups for normally and not normally distributed data, respectively. The Pearson correlation test was used to evaluate the association between variables. All statistical analyses were performed at significance of 0.05.

RESULTS

The mean age of male patients was 36.81 ± 10.86 years and the mean age of female patients was 42.94 ± 10.15 years. The mean age of patients and controls were 38.82 ± 10.93 and 39 ± 10.70, respectively. In terms of ethnicity, the case group included 35 Persians (63.6%), 8 Turkmen (16.4%) and 11 Baluchis (20%).

The serum concentration of zinc did not differ significantly between the patients (76.87 ± 15.43 μg/dl) and healthy controls (76.42±22.05 μg/dl) (P=0.93). Based on the results of the independent t-test, serum concentrations of zinc were significantly higher in men than in women in both study groups (Table 1).

Table 1. Comparison of serum zinc levels between patients with schizophrenia and healthy controls based on gender

Group	Serum zinc level (mean ± standard deviation)		P-value
	Men	Women	
Patients	79.92±13.27 µg/dl	70.61±17.94 µg/dl	0.035
Control	80.49±21.60 µg/dl	68.06±21.13 µg/dl	0.049

The serum concentration of zinc did not differ significantly between the three ethnic groups of patients (P=0.16). There was no significant correlation between age and serum concentration of zinc (r=-0.16, P=0.08). However, there was a significant negative correlation between age and serum zinc level in the patients (r=-0.22, P=0.02).

DISCUSSION

In the present study, the mean age of male and female patients was 36.81 and 42.94 years, respectively. Previous studies have also shown that men develop schizophrenia at a younger age compared to women (5).

We found no significant difference in the serum zinc levels between the patients and healthy subjects, which is consistent with findings of some previous studies (19, 20). However, in a meta-analysis by Joe et al., serum zinc levels in schizophrenics were lower than in the healthy individuals. In the mentioned study, serum zinc levels of patients treated with antipsychotics did not differ significantly from those of healthy individuals (16). However, it should be noted that the mentioned study was performed on schizophrenics under treatment with antipsychotics, while we enrolled newly diagnosed or non-treated patients. It has been reported that newly diagnosed schizophrenics generally have lower serum zinc levels than healthy people (17), but we observed no such difference in our study. Because schizophrenia is a heterogeneous disorder, not all patients are expected to have a serum zinc abnormality as part of the syndrome, which may explain the conflicting results of different studies. In a study by Chen et al., at time of admission, schizophrenic patients had lower serum zinc levels compared to healthy controls, which is inconsistent with our findings. They also reported that serum zinc levels were inversely correlated with the age of patients, which is in line with our findings (5). The inverse correlation between age and serum zinc levels might be due to the age-related downexpression of membrane zinc transporter genes (24).

It has been well-established that zinc has a vital role in the proper functioning of physiological systems, such as the nervous system. Convergence of clinical, molecular and genetic data plays a major role for zinc homeostasis in relation to depression and mental disorders. Intracellular zinc deficiency as well as circulating zinc deficiency may be due to poor diet or impaired absorption related to aging or a medical condition, such as alcoholism. Various medications including anticonvulsants, diabetes medications, hormones, anti-acids and anti-inflammatory drugs that are commonly prescribed to patients with neurological disorders also affect zinc absorption. In addition, genetic zinc transporter defects can affect zinc concentrations. Clinical studies have indicated the beneficial effects of zinc supplementation in relieving depression, which signifies the importance of investigating the effectiveness of zinc as a potential treatment option for mental illnesses (17).

CONCLUSION

The results of the present study showed that the mean serum concentration of zinc does not differ significantly between schizophrenic patients and healthy individuals. In both patients and controls, serum zinc level is significantly higher in men than in women. Moreover, serum zinc level has a significant, negative correlation with age in schizophrenics. Based on the results, it is recommended to pay more attention to the diet of patients with schizophrenia.

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Ethics approvals and consent to participate

The study has been approved by the ethics committee of the Golestan University of Medical sciences, Iran (ethics code: IR.GOUMS.REC.1398.249). Written consent was obtained from all participants.

Conflict of interest

The author declares that there is no conflict of interest regarding publication of this article.

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