KASTAMONU MEDICAL JOURNAL

Original Article / Özgün Makale

DOI: 10.51271/KMJ-0001

Kastamonu Med J 2021; 1(1): 1-4

Investigation of some trace element levels in multiple sclerosis

Multiple sklerozda bazı eser element düzeylerinin incelenmesi

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ABSTRACT

Purpose: In this study, it was aimed to investigate the relationship between multiple sclerosis (MS) and the homeostatic state of trace elements, and to reveal the relationship between Fe and Zn in MS pathology

Material and Method: Total of 40 (20 patients and 20 control) subjects were participated to this study. Blood samples were taken and analysed plasma iron and zinc levels using an atomic Absorption Spectrophotometer. Kolmogrow-Smirnov Z test used to analyse statistically significance of the data. $P<0.05$ was accepted as significant.

Results: The plasma iron and Zn levels were found to be significantly lower in MS patients compared to control.

Conclusion: Considering the important beneficial effects of iron and zinc against neurodegenerative disease and increased oxidative stress, reduced level of these trace elements should be considered in MS treatment.

Keywords: Trace element, iron, zinc, multiple sclerosis

ÖZ

Amaç: Bu çalışmada multipl skleroz (MS) ile eser elementlerin homeostatik durumu arasındaki ilişkinin araştırılması, MS patolojisinde demir ve çinko arasındaki ilişkinin ortaya konması amaçlanmıştır.

Gereç ve Yöntem: Toplam 40 denek (20 hasta ve 20 kontrol) bu çalışmaya katılmıştır. Kan örnekleri alınmış, plazma demir ve çinko seviyeleri atomik absorpsiyon spektrofotometresi kullanılarak analiz edilmiştir. Unpaired-t testi verilerin istatistiksel olarak anlamlılığını analiz etmek için kullanılmıştır. $P<0.05$ istatistiksel olarak anlamlı kabul edilmiştir.

Bulgular: Plazma demir ve çinko düzeylerinin MS hastalarında kontrole göre istatistiksel olarak anlamlı oranda düşük olduğu bulunmuştur.

Sonuç: Demir ve çinkonun nörodejeneratif hastalıklara ve artmış oksidatif strese karşı önemli faydalı etkileri göz önünde bulundurularak, bu eser elementlerin MS tedavisinde dikkate alınması gerektiği önerilmektedir

Anahtar Kelimeler: Eser element, demir, çinko, multiple skleroz

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Received / Geliş: 21.03.2021 **Accepted / Kabul**: 30.03.2021

Cite this article as / Bu makaleye atıf için: Algül S, Kapan O, Bengü AŞ. Investigation of some trace element levels in multiple sclerosis. Kastamonu Med J 2021; 1(1): 1-4

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INTRODUCTION

Multiple sclerosis (MS) is an unpredictable, chronic, inflammatory, demyelination disease of the central nervous system that interrupts the connection between the brain and the body and nerve conduction (1). Inflammation is evident in all stages of the disease, but is more common in the acute stage than in the chronic stage. Although the etiology of this disease is still unknown, it is believed that various immunological, smoking, obesity and genetic factors contribute to the pathogenesis of MS (2-4).

It is thought to be one of the most common cause of neurological disorders in young people (5). More than 2.5 million people are affected by this disease in all around the world. The studies showed that incidence of MS in women are significantly higher than in men (6). MS has four subtypes: Relapsing-remitting MS (RRMS), primary progressive MS, secondary progressive MS, and progressive relapsing MS (7).

Trace elements could be found in various environments including soil, plants and living organisms. The beneficial roles of trace elements in many physiological and metabolic functions of biological systems have been shown in the literature. Trace element levels should be kept within optimal limits to support the metabolic functions of body systems (8,9). Marked variation in levels of trace elements including iron and zinc, response to the exercise induced increased metabolic stress has been shown (10). Some trace elements are essential for bodily functions such as enzyme systems, energy metabolism. All trace elements are toxic in high concentrations, some of which cause neuron inflammation and degeneration. Additionally, the deficiency of trace elements can affect some aspects of immunity. In relation to MS patients, inflammation and immune system involvement are vital in the pathology of the disease, and trace elements can affect a variety of diseases, including neurological disorders.

It has been reported that trace elements are associated with pathophysiological mechanisms related to MS (11). They are necessary not only for the synthesis and stability of myelin, but also for the normal function of the central nervous system (12). It is one of the important trace elements responsible for the functions of various enzymes and proteins that have important roles In addition, an imbalance in the regulation of iron and zinc can cause serious consequences regarding cell function. This leads to increased oxidative stress and neurodegenerative disorders. Zinc contains a group of various major myelin proteins including essential myelin proteins with important functions in myelin regulation of the immune system, neuronal and oligodendrocyte death, and therefore has a broad role in the pathogenesis of MS (13-15). Iron is critically important for normal neuronal metabolism, such as mitochondrial energy production and myelination (16,17). However, excessive iron levels in the brain can cause iron-induced oxidative stress and thus contribute to the neurodegeneration seen in MS (18).

In this study, it was aimed to investigate the relationship between MS and the homeostatic state of trace elements, and to reveal the relationship between Fe and Zn in MS pathology.

MATERIAL AND METHOD

The ethical approvement for this study has been taken from Elazığ Training and Research Hospital Ethical Committee (date: 14.12.2017, number:17-21).

Patients who applied to the Neurology Polyclinic of Şehir University, Elazığ Training and Research Hospital and diagnosed with MS were included in this study. In the study, 20 MS patients and 20 controls participated. A signed ethical approvement forms were obtained from patients and control subjects before participation to this study.

Inclusion Criteria

The patient with MS who was newly diagnosed and medical treatment has not been applied, voluntarily participated to this study.

Exclusion Criteria

Persons with diseases such as cardiovascular disease, diabetes and metabolic syndrome, cancer that may affect the level of trace elements were not included in the study.

Control Group

Individuals without any neurological, metabolic, cardiovascular disease, diabetes and diseases such as metabolic syndrome, cancer were included.

Taking a sample to do this study was done as follows; after an overnight fasting, 2 cc of venous blood samples were taken between 08:00 and 10:00 in the morning from patients diagnosed with MS. The bloods taken were centrifuged at 4500 rpm for 5 minutes and their plasma was separated. After separation, the plasmas were stored at -80 degrees until they were analysed. During the study, demographic characteristics (weight, height, age, gender) and BMI of the patients were also reported.

Plasma Iron and Zinc Analysis

Atomic absorption spectrophotometer was used to determine the amount of metal elements. The principle of this method is based on the excitation of free atoms of the element by absorbing ultraviolet or visible rays. Determination of Fe, Zn levels in plasma was carried out in Atomic Absorption Spectrophotometer (Perkin Elmer AAS 800, USA). With the flame atomization technique, measurements were made twice for each illuminated sample at 248.3 nm, 324.8 nm and 213.9 nm wavelengths, respectively, for the elements. The levels of the mentioned elements are determined as ppm.

Statistical Analysis

Data are given as mean (±SD). As a statistical method, Kolmogrow-Smirnov Z test was determined whether the data showed normal distribution or not. Since the data showed normal distribution, unpaired t-test was used to determine whether there was a difference between the patient and control groups. $P<0.05$ will be considered statistically significant.

RESULTS

Fe Level

When the plasma iron levels of MS patients and the control group were compared, it was determined that the plasma iron level in MS patients (471.45±26.3 ppm) was statistically significantly lower than the plasma iron level (429.56±23.7 ppm) of the control group ($p<0.05$).

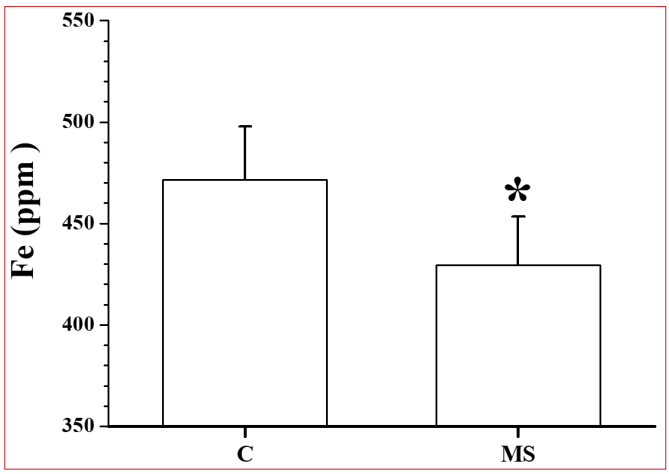

Figure 1. The mean (±SD) values of iron for the control (C) and for the multiple sclerosis (MS) patients. * represent statistically y significant differences

Zn Level

When plasma zinc levels of MS patients and control group were compared, it was determined that plasma zinc level in MS patients (9.76±1.45 ppm) was statistically significantly lower than plasma zinc level (7.24±1.01 ppm) of control group ($p<0.05$).

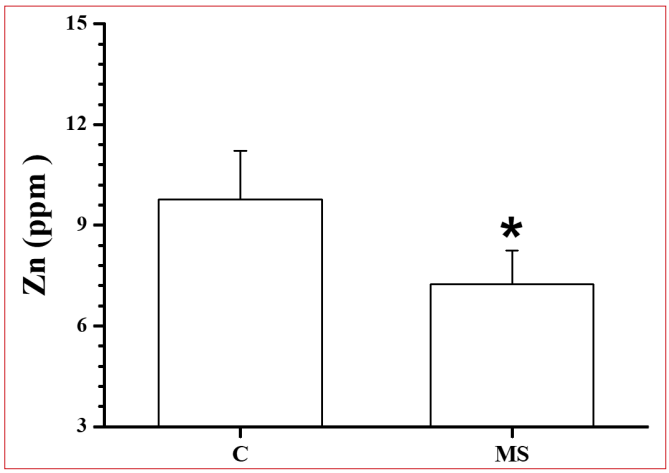

Figure 2. The mean (±SD) values of zinc for the control (C) and for the multiple sclerosis (MS) patients. * represent statistically significant differences

DISCUSSION

MS is the most common chronic demyelinating disease of the central nervous system. It is an irreversible and severe clinical disorder characterized by autoimmune and neurodegeneration (19,20). Low or high levels of trace elements among environmental factors are effective in the pathogenesis of various neurological disorders including MS (21,22). In this study, Fe and Zn levels were compared in MS patients and healthy controls. Both trace elements were found to be lower in MS patients compared to the control group. It is known that iron homoeostasis has great importance for the prevention of muscle injury and inflammation (23). Iron supplementation causes significant reduction in oxidative stress parameters (24). Thus, the observation of lover iron levels in MS patients indicates the existence damage of neuromuscular system. However, unchanged iron and zinc levels in MS patients compared to the control in MS patient has been reported (25).

It is a cofactor for more than 300 enzymes including zinc matrix-metalloproteinase and is an essential trace element in the brain. It is found in many proteins, such as the essential myelin protein (26). Therefore, it plays an important role in MS pathophysiology. The lower zinc level in MS patients than the control group is consistent in some studies in the literature (27). The important beneficial effects of zinc supplementation on metabolic stress have been reported (28).

Iron is a cofactor of various enzymes in normal brain metabolism (16). Abnormal iron homeostasis may contribute to the neurodegeneration associated with MS aetiology. The lower iron level in MS patients than the control group is consistent with many other studies in the literature. It suggests that iron plays a key role in MS pathogenesis. Because it is suggested that it causes neuronal damage by triggering oxidative stress (29). Importantly, nutrition status and antioxidant capacity has significant impact on prognosis in MS patients (30).

CONCLUSION

The observation of lower levels of iron and Zn could be related with the severity of disease. Clinicians should be considering trace elements levels for treating MS patients. Measurements of these two important trace elements in blood and other body tissues in large number of patients with different stage will provide better information with regarding the involvement of iron and zinc with the severity and pathogenesis of MS disease.

ETHICAL DECLARATIONS

Ethics Committee Approval: The ethical approvement for this study has been taken from Elazığ Training and Research Hospital Ethical Committee (date: 14.12.2017, number:17-21).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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