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Estimation of Trace Elements (Zinc and Copper) in Serum of Multiple Sclerosis Patients in Baghdad City

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Abstract

Background Multiple Sclerosis (MS) also known as demyelinating disease, is a condition in which the insulating coverings of nerve cells in the brain and spinal cord are damaged. This injury impairs the nervous system's ability to transfer messages, resulting in a variety of signs and symptoms, including physical, mental, and psychiatric issues. Double vision, blindness in one eye, muscle weakness, and problems with sensation or coordination are all possible symptoms. MS comes in a variety of ways, with new symptoms appearing in isolated attacks (relapsing forms) or gradually over time (progressive forms), the progressive forms symptoms may go away completely between attacks. The exact cause is unknown.

Objective To determine trace elements (zinc and copper) and discuss their relation and effect on MS patients.

Methods The study was performed during the period March 2021 to August 2021, involved 50 samples divided into two groups the first 25 samples from normal individuals (16 males and 9 females) and the second 25 sample of MS patients (12 males and 13 females) collected with help of (Sa'ad Al-Watrai Hospital), (Neuroscience Hospital) in Baghdad City. Samples obtained as serum due to venipuncture considering that patients did not use any treatment during the period of samples collection that may affect analysis results other feature like age, gender and other chronic disease has been recorded in this study.

Results The patients with progressive MS disease showed significant higher copper level than non-progressive MS patients and control samples, when we compare it with control group p = <0.0001. Also, patients with non-progressive MS disease showed a lower zinc level compared with progressive MS and control samples (p =0.005 and p = 0.001) respectively.

Conclusion The level of serum copper in progressive MS patients is higher than both healthy people and non-progressive MS patients. Additionally, it showed a lower zinc level in non-progressive than progressive MS patients. Therefore, this study showed a success to compare trace elements level (Zinc and Copper) between progressive and non-progressive MS patients. Also, discriminate between healthy people samples and MS patient's samples has been found.

Keywords Multiple Sclerosis, Copper (Cu), Zinc (Zn)

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List of abbreviations: CIS = Clinically isolated syndrome, MS = multiple sclerosis, PPMS = Primary progressive multiple sclerosis RRMS = Relapsing remitting multiple sclerosis, SPMS = Secondary progressive multiple sclerosis

Introduction

Multiple sclerosis (MS) is a chronic and an unpredictable central nervous system illness that affects more than 2.3 million people globally. It impairs the flow of information within the brain, as well as

between the brain and the rest of the body, due to the breakdown of myelin, the insulating coverings of nerve cells in the brain and spinal cord. Although the cause is uncertain, the failure of myelin-producing cells or immune system deterioration is thought to be the underlying mechanism [(1)].

MS is usually diagnosed based on the presenting signs, symptoms and the findings of supporting medical testing. Proposed causes include genetics and environmental variables being caused by a viral infection [(2)]. Recent research suggests that MS is caused by an autoimmune reaction. Scientists believe that immune cells, which normally protect the body against bacteria and viruses, target the myelin layer, tearing it away, and exposing the nerve fibers underneath. Furthermore, axon destruction occurs early in the disease progression [(3)]. Once injured, nerve cells in the brain and spinal cord lose their ability to communicate with each other and with the rest of the body.

MS can divide into four types:

1- Clinically Isolated Syndrome (CIS)

Inflammation and demyelination in the central nervous system cause CIS, which is a first episode of neurologic symptoms. The occurrence, which by definition must continue at least 24 hours, is a characteristic of MS but does not yet meet the requirements for an MS diagnosis because people with CIS may or may not go on to develop MS. When CIS is combined with lesions on a brain Magnetic Resonance Imaging (MRI) that are identical to those found in MS, a second episode of neurologic symptoms and a diagnosis of relapsing-remitting MS is quite likely. When CIS isn't accompanied with MS-like lesions on a brain MRI, the person's chances of developing MS are substantially reduced [(1)].

2- Relapsing Remitting MS (RRMS)

The most common sickness is characterized by episodes of new or worsening neurologic symptoms. Attacks that are followed by intervals of partial or complete recovery are known as relapses or exacerbations (remissions). During remissions, all symptoms could disappear or some might linger and last permanently. However, there is no discernible disease development when the patient is in remission. RRMS can be categorized as active (with relapses and/or evidence of new MRI activity over a given period of time) or not active, as well as deteriorating (a proven increase in disability following a relapse) or not worsening, with approximately 85% of cases falling into the latter category [(1)].

3- Secondary Progressive MS (SPMS)

At first, SPMS exhibits a relapsing-remitting pattern. Some RRMS patients will eventually transition to a secondary progressive course, in which their neurologic function gradually declines over time (resulting in disability accumulation). SPMS can also be classified as active (with relapses and/or evidence of new MRI activity over a set period of time) or not active, as well as with or without progression (evidence of disability accumulation over time, with or without relapses or new MRI activity) [(1)].

4- Primary Progressive MS (PPMS)

From the outset of symptoms, PPMS is marked by declining neurologic function (accumulation of disability), with no early relapses or remissions. Additionally, PPMS can be categorized as active (with an occasional relapse and/or evidence of new MRI activity over a specified length of time), not active, with progression, or neither (evidence of disability accumulation over time, with or without relapse or new MRI activity). PPMS is a kind of MS that affects about 15% of patients with MS [(1)].

The objectives of this study is To determine trace elements (zinc and copper) and discuss their relation and effect on MS patients.

Methods

This study was performed during the period March 2021 to August 2021. It included 50 subjects divided into two groups:

Group I: included 25 samples from normal individuals (control) (16 males and 9 females). Their age ranged from 35 to 40 years.

Group II: included 25 samples from MS patients (12 males and 13 females).

These groups were collected from Sa'ad al-Watri Hospital and Neuroscience Hospital in Baghdad city. Their age ranged from 35 to 40 years.

The exclusion criteria of these groups were:

A. Patients do not have any kind of diseases that may affect in the results of this study.
B. Patients did not use any kind of therapy in the period of samples collection.

The colorimetric biochemical methods performed by using:

1. Copper kit (Biosam \UAE), which depends on released from ceruloplasmin in an acidic medium, react with Di-Br-PASA to form a colored complex, intensity of complex formed is directly proportional to the amount of copper present in the sample.
2. Zinc kit (BioSystem\Spain); Zinc in the sample reacts with 5-Br-PAPS in the alkaline medium forming colored complex that can measure by spectrophotometry.

Statistical analysis

Statistical package for social science (SPSS) version 21 was used for data analysis of this study. Mean and standard deviation (SD) were used to compare between zinc and copper value in both healthy individuals and MS patients. Comparison among study groups was done by using ANOVA and post hoc Tukey test.

Results

Results are shown in table 1. The mean±SD of age is (37.36±8.29 year) for control, (36.091± 7.077 year) for non-progressive MS and (42.429±32.110 year) for progressive MS. The results showed there is no significant difference in age between control, non-progressive and progressive MS. Likewise, there was no significant difference in weight between all groups, as it was (74.04±10.19 Kg) for control and (78.64±9.51 Kg) for non-progressive MS and (79.64±8.2 Kg) for progressive MS.

Moreover, copper (mean±SD) was (182.16±59.58 µg/dl), (167±104.65 µg/dl) and (626.5±250.07 µg/dl) for control, non-progressive MS and progressive MS, respectively. These results showed a significant difference between (control and progressive MS) and (control and non-progressive MS). Furthermore, zinc (mean±SD) was (131.40±49.57 µg/dl), (66.64±55.44 µg/dl) and (191.7±123.62 µg/dl) for control, non-progressive MS and progressive MS, respectively. Here, the output illustrated a significant decrease of zinc level in non-progressive MS compared with both control and progressive MS.

The concentration of copper has significantly elevated in progressive MS in comparison with non-progressive MS and control where p value <0.0001. Also, zinc has a significant decrease in non-progressive MS in comparison with progressive MS and control, p value is 0.001.

Table 1. Mean and standard deviation of age, weight, copper and zinc between MS (progressive & non-progressive) patients and control group by ANOVA

Parameter	Control Mean± SD	Non progressive MS Mean± SD	Progressive MS Mean± SD	P value
Age (yr)	37.36±8.29	36.091±7.077	42.429±32.110 b,c	0.02
Weight (kg)	74.04±10.19	78.64±9.51	79.64±8.20	0.069
Cu (µg/dl)	182.16±59.58	167.0±104.65a	626.5±250.07b,c	<0.0001
Zn (µg/dl)	131.40±49.57	66.64±55.44a	191.7±123.62b,c	0.001

a: comparison between control with non-progressive MS by post hoc Tukey test, b: comparison between control with progressive MS by post hoc Tukey test, c: comparison between non-progressive with progressive MS by post hoc Tukey test

Discussion

The majority of people with MS is diagnosed between the ages of 20 and 50 years old, while it can affect both young and old people [4]. Current result showed a minor relationship between age and MS disease, which agreed with Manouchehrinia et al. findings [5].

Weight shows No significant difference between control, progressive MS and non-progressive MS These results showed in agreement in somehow with Pilutti and her partners [6].

In this study, the patients with non-progressive MS had a low level of zinc in comparison with control, while progressive MS patients had a higher level of zinc in on comparing with control samples and that close to Bredholt and Frederiksen opinion [7].

The zinc is second to iron in its concentration in the body. It plays a role in cell division, cell growth, wound healing, and the breakdown of carbohydrate. Zinc is also needed for the senses of smell and taste. During pregnancy, infancy, and childhood the body needs zinc to grow, it is also enhancing the action of insulin. Zinc is found in cells throughout the body and needed for the body's defensive (immune) system to properly work. For instance, it is involved in releasing tumor necrosis factor alpha (TNFα), which activates the immune system. It was shown that even a mild zinc deficiency can weaken the function of the immune system [8].

Copper is an essential trace mineral. It is found in all body tissues and plays a role in making red blood cells and maintaining nerve cells and the immune system It also helps the body to form collagen and absorb iron, and play role in energy production. Most copper in the body is found in the liver, brain, heart, kidneys, and skeletal muscle Both too much and too little, copper can affect how the brain works. Impairments have been linked to Menkes, Wilson's, and Alzheimer's, deficiency of copper can result in cardiovascular disease and other problems in central nervous system [8].

As a result, the values indicate to high level of copper in progressive MS patient's serum in comparison with control samples, the value also high in comparison between progressive and non-progressive MS patients, whilst no remarkable change has been found in the value between control and non-progressive MS patients, that in agreement with other studies [9-11].

In conclusions, patients with progressive MS had an elevated level of copper and zinc than healthy people, while patients with non-progressive MS had a low level of copper and zinc than healthy people.

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Author contribution

Dr. Al-Saeed put the research plan and supervised the work. Jabbar did the sampling,

wrote the manuscript in addition to statistical work.

Conflict of interest
None.

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