Estimation the Level of Metals (Lead, Cadmium, Copper and Zinc) In Multiple Sclerosis Patients in Basra\ Iraq

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Abstract

Multiple sclerosis (MS) is a demyelinating inflammatory disease of the central nervous system white matter that displays a triad of pathogenic symptoms. The toxicity of heavy metals can disrupt or damage central nervous systems. Long-term exposure of human population to heavy metals has shown neurological impairments. The degenerative processes are similar to Alzheimer's disease; Parkinson's disease.This study compared the serum level of Lead, Cadmium, Copper and Zinc in MS patients with their levels in a control group. **Methods:** prospective study of cohort includes fifty Iraqi people selected from the Southern area of Multiple Sclerosis Clinic Center divided into two groups, in which the first group contains twenty five patients with MS and twenty five people without MS. Serum level of Lead, Cadmium, Copper and Zinc have been measured. **Results:**In the present study, there was a significant increase in the concentration of (cupper - lead –cadmium) in patients with multiple sclerosis as compared with normal people *($p<0.05$)*. There is a significant decrease in the concentration of zinc in patients with multiple sclerosis as compared with normal people *($p<0.05$)*.**Conclusion:** Lead, copper, cadmium and zinc could affect on the susceptibility of patients to induce MS attack.

Keywords: *heathy metals, health; Patients; critical levels*

Introduction

Multiple sclerosis (MS) is a chronic autoimmune, inflammatory neurological disease of the central nervous system (CNS)[1]. MS attacks the myelinated axons in the CNS, destroying the myelin and the axons to varying degrees [2]. In most patients, the disease is characterized initially by episodes of reversible neurological deficits, which is often followed by progressive neurological deterioration over time[3], and 50% of patients will need help walking within 15 years after the onset of the disease[4].

Twice as many women are affected as men, and persons of Northern European descent appear to be at highest risk for MS[5].The disease is diagnosed on the basis of clinical findings and supporting evidence from ancillary tests, such as magnetic resonance imaging (MRI) of the brain and examination of the cerebrospinal fluid (CSF). MS typically presents in adults 20 to 45 years of age; occasionally, it presents in childhood or late middle age[6].

The cause is unknown, but it appears to involve a combination of genetic susceptibility and a non-genetic trigger, such as a virus, metabolism, or environmental factors, that together result in a self-sustaining autoimmune disorder that leads to recurrent immune attacks on the CNS[7].

The term "heavy metals" refers to any metallic element that has a relatively high density and is toxic or poisonous even at low concentration. Heavy metals is a general collective term, which applies to the group of metals and metalloids with atomic density greater than 4 g/cm3, or 5 times or more, greater than water[8].

Cadmium and lead are among the most abundant heavy metals and are particularly toxic. The excessive

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content of these metals in food is associated with etiology of a number of diseases e such as chronic obstructive pulmonary disease, lung cancer, nephrotoxicity and mild anemia[9].

Nonessential heavy metals and metalloids (e.g. arsenic [As], lead [Pb], mercury [Hg] and cadmium [Cd]) are xenobiotic and theoretically are capable of exerting toxic effects at any level of exposure[10].

Some metals (e.g. copper [Cu], zinc [Zn], selenium [Se] and chromium [Cr]) serve as micronutrients and are essential to normal metabolic function as trace elements but are toxic at high levels of exposure[11]. A few metals are not known to be essential to human health but may have some beneficial effects at low levels of exposure. These include silicon, nickel, boron, and vanadium[12].

Heavy metals usually enter the human body via different food chains, inhalation, and ingestion. In addition, heavy metals have been used for long time by humans for making metal alloys and pigments for paints, cement, paper, rubber, and other materials[13]. The toxicity of heavy metals can disrupt or damage central nervous systems[14], change blood composition,[15] damage lungs [16], kidneys[17], livers.[18] The long-term exposures of human population to heavy metals have been shown many degenerative diseases like Alzheimer's disease[19], Parkinson's disease [20].

Subjects and Methods

A cross section study of 25 MS patients and 25 healthy participants without MS. They were selected from the Multiple sclerosis center in Basra Governorate.

Exclusion Criteria: The exclusion criteria include the Patients with renal failure, Patients with congenital condition, Patients live near high way, gas station and industrial factory, Patients taking food supplement containing zinc and other elements.

Blood sampling:

Blood sample (10 ml) taken from each participant studied groups , centrifuged to isolate the serum that be used for estimation of trace elements ,and the remaining of the sample put into Ethylene diaminetetraaceticacid (EDTA) tubes to keep whole blood for estimation of heavy metals[21].

Biochemical assay

Frozen serum was allowed to thaw at room temperature, assessment of inorganic elements (Zn, Cu) [22].Refrigerated (Whole blood Pb) was performed by Flam Atomic Absorption Spectrophotometry(FAAS) [23], while(Cd) was performed by Graphite Furnace Atomic Absorption spectrophotometry (GFAAS)[24].

Statistical Analysis

Numerical data were expressed as mean± standard deviation (SD). The data were analyzed by utilizing computerized statistical package for the social sciences SPSS program. Unpaired student t-test was performed for each group pair includes comparison between two groups (*P-values<0.05*) were considered to be statistically significant. Chi-square test was used to assess the statistical significance in distribution between different discrete variable.

Ethical Consideration: All administrative approvals were taken from the Participants, the administrative team of the hospital. Also we take patients concern.

Results

In table (1), there are no significant differences in age and weight when compared between the patients with multiple sclerosis and normal individuals *(p>0.05)*. In the table (1), there were no significant relationship in sex, marital status and residency when compared between the patients with multiple sclerosis and the people without multiple sclerosis meanwhile there was significant differences in job status between the patients with multiple sclerosis when compared to the people without multiple sclerosis.

Table (1): Demographical information of patients with multiple sclerosis and healthy participant without MS.

Characters		Patients with multiple sclerosis	Normal people	p-value
Age (in years)		42.46±9.3	41.12±10.11	0.491734
Weight (in kg)		75.12±12.39	78.1±10.27	0.380247
Sex	Male	10(40%)	11(44%)	0.834558
	Female	15(60%)	14 (56%)	
Marital status	Single	7(28%)	9(36%)	0.7125553
	Married	18(72%)	16(64%)	
Residency	Center	13(52%)	9(36%)	0.517219
	Rural	10(40%)	13(52%)	
	Urban	2(8%)	3(12%)	
Job status	employee	8(32%)	23(92%)	1.24034E-05
	Not-employee	17(68%)	2(8%)	

Clinical information of patients with multiple sclerosis

In table (2), the onset of multiple sclerosis in the patient was around (82.8±39.3) months, the classes of multiple sclerosis was differ in which the patients with Primary progressive multiple sclerosis was 6(24%) , patients with Relapsing Remitting Multiple Sclerosis was 16(64%) meanwhile the Secondary Relapsing Multiple Sclerosis was 3(12%) .

Table (2): Clinical information of patients with multiple sclerosis

Characters		Patients with multiple sclerosis
Onset of disease (months)		82.8±39.3
Type of multiple sclerosis	Primary progressive Multiple Sclerosis	6(24%)
	Relapsing Remitting Multiple Sclerosis	16(64%)
	Secondary Relapsing Multiple Sclerosis	3(12%)

Biochemical results of heavy metals

In table (3), lead, cadmium and cupper concentration for the patients with multiple sclerosis was significantly higher when compared to normal peoples *(p<0.05)*, meanwhile zinc concentration for the patients with multiple sclerosis was significantly lower when compared to normal peoples *(p<0.05)*. Cadmium concentration for both groups was within normal values, lead concentration for both groups was higher than normal values, cupper concentration for both groups was lower than normal values and patients with multiple sclerosis have zinc concentration lower than normal values meanwhile normal peoples have zinc

concentration within normal values

Table (3): Blood Heavy Metal Concentration

	Patients with multiple sclerosis	Normal peoples	p-value
Lead concentration (µg/dl)	25.67±2.9A	14.8±2.8B	1.85×10-05
Cadmium concentration (µg/L)	0.312±0.05A	0.126±0.02B	5.82×10-10
Cupper concentration (µg/dl)	161.56±15.9A	116.4±19.5B	0.006134
Zinc concentration (µg/dl)	66.7±7.6A	93.3±7.1B	0.000256

- Data are expressed as mean±S.D.

- Values with non-identical capital letters superscripts (A,B) consider significant different when compared between tests groups (P>0.05)

- Normal value of cadmium is less than 1.2(µg/dL), Normal value of copper is between (72-166) (µg/dL), Normal value of zinc is between (80-120) (µg/dL), Normal value of lead is less than 10 µg/dL

Discussion

Multiple sclerosis (MS) is a demyelinating inflammatory disease of the CNS white matter that displays a triad of pathogenic symptoms: mononuclear cell infiltration, demyelination, and scarring (gliosis)[25].

Toxicity by heavy metals has been shown to be affected by individual susceptibility, genetic factor, nutritional and health[26].

Lead plays a crucial role in the redox-reactions which generate free radical species by participating in the transfer of electrons. The molecular mechanism of lead toxicity is multifactorial as it generates free radical species, decreases glutathione antioxidant sulphydryl pools; inhibits enzyme activity and blocks important trace element absorption[27]. Other report study has described a patient with MS treated for neurological symptoms which were thought to be a progression of his disease but which were subsequently found to be caused by lead poisoning; his clinical signs improved with oral chelation therapy[28].

In this ecological study, there are evidences that lead positively correlated with MS incidence. Thus, further investigation is suggested for the effects of lead poisoning on MS patients[29].

Zinc (Zn) has a key role in regulation of the immune system. For instance, Zn is involved in releasing tumor necrosis factor alpha (TNFα), which activates the immune system. It was shown that even a mild Zn deficiency can weaken the function of the immune system[30]. Copper (Cu) is used in the synthesis of myelin; thus, the deficiency may potentially cause myelinopathy[31]. Furthermore, its influence on auto-immune diseases through the catalyze of prostaglandins (anti-inflammatory drugs) has been known. In addition, it is documented that there is an interaction between Zn and Cu. This means that a high level of Zn could be a reason for Cu deficiency and vice versa. Moreover, Cu and some other elements, such as cadmium, may compete with Zn[32].

Many studies have been focus on the role of heavy metals in the pathogenesis of MS. One study showed that an increase in Cu and a decrease in Zn might stimulate the immune system toward MS [33], other studies also highlighted the etiological role of zinc and Cu. This study suggested that impaired Cu and Zn homeostasis may be a cause of MS disease [34]. Cadmium is one of the most important toxic metals[35]. The precise molecular mechanisms of Cd toxicity are not known however, it has been suggested that Cd indirectly enhances the free radical generation and participates in oxidative

stress via Fenton reaction[35].].Cd induces neurological abnormalities, neonatal cerebral edema and cerebral hemorrhage in animal experimental studies[36].

As Cd has been increased the production of reactive radicals and interferes with antioxidant enzymes activity in adult rat brain. This effect in turn results in alteration of membrane-bound enzymes including Na+/K+ ATPase and structural lipids integrity[37]. In developing rat, it has been observed that initially Cd changes the vascular endothelium permeability resulting in focal edema, brain oxygen and nutrient uptake interference and finally the necrotic changes in neuronal components which are secondary to this effect[38]. A previous study has been found that, blood cadmium level was higher in multiple sclerosis patients in comparison with healthy individuals also the researchers suggested the possible relation between premature mortality and tobacco smoking in MS patients[39]. On the other hand, other study was shown that there is a significantly elevated cadmium level in patients' blood sample. It could be inferred that various cadmium exposure might be affected susceptibility to multiple sclerosis and could increase its risk of development[40].

Conclusions

1-Patients with MS show high level of Lead, Cadmium, Copper, and low level of Zinc.

2-There could be a role of Lead, Cadmium, Copper, and Zinc in pathogenesis of MS.

3-There is increase in concentration of Lead, Cadmium, Copper in healthy participant without MS.

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Conflict of Interest: Non

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