Oxidative stress and lipid peroxidation in patients with multiple sclerosis

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Summary

Back ground: multiple sclerosis (MS) has a much higher incidence among Caucasians that in any other race. Females are much more susceptible than males and white females living in colder weather areas are much more susceptible than those living in warmer areas. Oxidative stress means an alteration in the delicate balance between free radicals and the scavenging capacity of antioxidant enzymes in favor of free radicals in the body system.
Objective: To evaluate and compare the antioxidants and lipid peroxidation in patients with MS and healthy control.
Patients and method: The study has included thirty patients with MS (16 females and 14 males) and thirty healthy subjects. The subjects were selected from people attending the out patients clinic of Baghdad Teaching Hospital in Medical City. Laboratory parameters included were: uric acid, albumin, and caeruloplasmin, total thaiol, malondiaaldehyde (MDA) and peroxinitrate ($ONOO^-$).
Results: MDA and $ONOO^-$ levels in serum of patients with MS were significantly higher than in the control group. While the levels of GSH, CP, albumin, uric acid, iron, copper and zinc in serum of patients with MS were significantly lower than in healthy control.
Conclusion: Oxidative stress may have a role in the pathophysiology of multiple sclerosis syndromes.
Keywords: lipidperoxide, $ONOO^-$, GSH, CP, uric acid, albumin, multiple sclerosis.

الخلاصة

الخلفية: ان نسبة حدوث مرض التصلب العصبي المتعدد في القوقازسيين اعلى من اي جنس اخر. وان اصابة الاناث أكثر بكثير مِنْ الذكوركما ان النساء البيض اللواتي يعشنِ في المناطقِ الباردة اكثر عرضة من اللواتي الذين يَعِشنَ في المناطقِ الأدفأِ. واخيرا فان الجهد التاكسدي يعني خللٌ في التوازن الدقيقِ بين وحدة انتاج الجذور الحرّةِ ومقدرة التخلص منها لصالح الاولى.
الهدف: لتَقييم ومُقَارَنَة مانعاتِ التأكسد وlipid peroxidation في المرضى والاصحاء.
المرضى والطريقة: تَضمّنتْ الدراسةُ ثلاثين مريضاً مَع إف إم إس (16 أنثى و14 ذكر) وثلاثين من الاصحاء وتم اخذ العينات من العيادة الاستشارية في مدينة الطب / مستشفى بغداد التعليمي. تَضمّنتْ البراميترات: الحامض البولي، زلال ,caeruloplasmin، يُجملُ ,malondiaaldehyde thaiol (إم دي أي) وperoxinitrate
النَتائِج: اظهرت مستويات $ONOO^-$,MDA في مصلِ المرضى مستويات أعلى جداً مِنْ الاصحاء. بينما اظهرت مستويات جي إس إتش، سي بي، زلال، حديدي حامضي بولي، نحاس وخارصين في مصلِ المرضى أوطأ جداً مِنْ الاصحاء.
المقترحات: وجد ان اكسدة الشحوم ومضادات الاكسدة لها دور كبير في متلازمة التصلب العصبي المتعدد.

Introduction

Multiple sclerosis (MS) has a much higher incidence among Caucasians than in any other race. Females are much more susceptible than males and white females living in colder, weather areas are much more susceptible than those living in warmer areas [1]. The cause, or causes, of M.S remains a mystery [2], and many different etiologies have been suggested, and theories of pathogenesis of the disease have gone through a long history. From the 19th century, the theories supposed many etiologies like that the disease

developed following an infection, anxiety, grief, stress shock and vexation [1].

It is now suggested that MS is caused by some interplay of the following factor [3]

1- Immunological factor.
2- Genetic factor.
3- Environmental factor.

The evidence of the above factors affecting the pathogenesis of M.S, supports the concept that the exposure of genetically susceptible individual to an environmental factor(s) during childhood (less than 15 years), e.g. to any common virus, leads eventually to an immune mediated inflammatory demyelination, and the precise inter-play between these factors remain to be elucidated [4].

Free radicals are unstable atom group in the body linked to tissue damage in a wide array of neurodegenerative disorders, including Parkinson's disease, dementia, and multiple sclerosis [5].

Different mechanisms have been proposed to explain how free radicals might specifically mediate the central nervous system damage in MS. Lower levels of antioxidants may promote increased activity of lipoxygenase, an enzyme which spurs the production of leukotrienes thereby increasing the immune-inflammatory processes in brain tissue [6]. Others have suggested that excess free radicals trigger height-ened T-cell activity via an arachidonic acid cascade, or that direct damage to myelin is caused by the free radicals themselves [7].

The mechanism behind lipid peroxide-tion is unknown precisely but it might be due to the accumulating ROS, that are hypothesized to be produced by numerous mechanisms, like the increased mitochondrial respiratory chain reaction [8], neutrophils [9], microglia and macrophages active-tion, and the peroxynitrite effect on lipids beside the already produced lipid peroxidation [10]. These generated ROS, in turn, cause further lipid peroxidation. In their studies, reported that lipid peroxidation end-products might be useful as an additional tool for clinical diagnosis of MS [10].

Subjects and Methods

During the period from December 2009 to March 2010, blood samples were collected from sixty patients with multiple sclerosis and thirty apparently healthy subjects with age range (18-72) years. The subjects were selected from the people attending the outpatient clinic of Baghdad Teaching Hospital in Medical City.

Laboratory parameters included: uric acid, albumin, and caeruloplasmin, total thaiol, malondiaaldehyde (MDA) and peroxinitrate ($ONOO^-$).

Caeruloplasmin activity was measured by the method modified by Menden, 1977. While total thiol concentration was determined by the method modified by Ellman, 1959.

Albumin was measured by the method of Doumasetal, 1971.

Malondialdehyde (MDA) was estima-ted by the method of Buege and Aust, 1987.

Serum peroxynitrite level was measu-red by modified of Vanuffelen, 1998.

Statistical Analysis

Descriptive statistics for all data of each set were expressed as mean ± S.D, and the percent of abnormal value in any test was calculated as above or below the mean ± S.D of the normal values for the matched control group, were compared using independent sample (t) test $P< 0.0005$, $P< 0.005$, $P< 0.05$ were considered statistically significant [18].

The overall predictive values for the results in the studied groups were performed according to program of office xp.

Results

The results showed that the GSH, CP, albumin, uric acid, iron, copper and zinc levels in serum of patients with MS were significantly lower than in healthy control are shown in table (1).

Table 1. Comparison of Antioxidants Markers for subjects studied.

Antioxidant Marker	patients mean±SD	Control mean±SD	Sig
CP(mg/dl)	24.67±2.0	21.58±1.69	NS
GSH(μmol/L)	0.596±0.102	0.368±0.083	S
S.uric acid(mg/dl)	4.137±0.961	4.732±0.885	S
s.albumin(g/dl)	4.307±0.867	3.602±0.596	S
S.iron(mg/dl)	4.137±0.961	4.732±0.885	S
s.copper(mg/dl)	4.307±0.867	3.602±0.596	S
S.zinc(mg/dl)	4.137±0.961	4.732±0.885	S

p<0.005 as compared with group control.

The results showed that the MDA level in serum of patients with MS was significantly higher than in the control group. While the level of $ONOO^-$ was significant lower in serum of patients compared with the control group as shown in table (2).

Table 2. Comparison of Pro-oxidant by products (MDA, and $ONOO^-$

Pro-oxidant By-product	patients Mean ±SD	control Mean ±SD	Sig.
MDA(m mol/ L)	2.463± 1.493	0.981± 0.169	S
ONOO (m mol/L)	0.116 ±0.006	0.054± 0.005	S

P<0.005 as compared with group control.

Discussion

The increase in caeruloplasmin levels may provide increased antioxidant activity against O_2. This lacked into extracellular space [11]. Caerulo-plasmine can serve as a scavenger of super oxide radicals and protect cells against oxidative damage [12].

Glutathione is a tripeptide. Its oxidized form is a dimer - GSSG which is involved in the transport of certain amino acids, is coenzymes for various enzymes and protects against oxygen radicals and toxic compounds [13].

Results obtained in the present study agree with others, like Plam et al who found that the levels of iron, copper and zinc were lower in patients with MS compared to controls. In younger patients low serum copper possibility that malabsorption of the metals causes the low serum concentrations is discussed [14].

Uric acid works by inactivating peroxynitrite, a toxic compound that may causes damage to the central nervous system in MS patients. Researchers report that they found lower levels of uric acid in the blood of MS patients than of people without the disease. It appears that high serum uric acid levels protect against the development of MS [14].

Albumin serum level was shown to be decreased with the increased disability and score, and it might be due to the more consumption and utilizing in front of the FRs and its oxidizing environmental effects [15, 16].

The plasma levels of proteins depends on the balance between their synthesis and their catabolism or loss from the body, many plasma proteins are synthesized in the liver ,but the plasma cells and lymphocytes of the immune

system synthesis immunoglobulin's, and proteins of the complement system are synthesized by macrophages as well as hepatic cells. Total protein levels may be misleading, and may be normal in the face of quite marked changes in the constituent proteins, only low albumin levels are of clinical importance [17].

In conclusion this study showed that oxidative stress plays an important role in pathogenesis of multiple sclerosis. This finding also suggests the importance of antioxidants in diet and therapy of MS patients.

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