Oxidative Stress in Patients with Multiple Sclerosis on Interferon Therapy

Kassim Salih Abdullah, Hakki Mohammed Majdal**, Marwan Mohamad*.*
Department of Pharmacology, Mosul University, College of Medicine*
Department of neurology, Ibn Sina teaching hospital, Mosul, IRAQ*

Abstract

Controlled comparative clinical trial, conducted on the department of neurology , Ibin Sina teaching hospital, Mosul –Iraq, to evaluate the oxidative stress status in patient with multiple sclerosis. Thirty female patients diagnosed as multiple sclerosis enrolled in the study, thirty healthy individuals matched for age with patients group , kept as a control. Malondialdehyde (MDA) were measured in both groups as indicator of oxidative stress. The MDA level was higher in patients with multiple sclerosis than the control group. The present study demonstrated that patients with multiple sclerosis have exaggerated oxidative stress , and indicate that treatment with antioxidants might theoretically prevent propagation of tissue damage and improve both survival and neurological outcome of the disease.

Key words: multiple sclerosis , oxidative stress, antioxidants, malondialdehide

Introduction

Multiple sclerosis (MS) affects about 350,000 Americans and is about twice as common in women as in men (1). Multiple sclerosis (MS) is a progressive, invalidating pathological state the exact etiology of which is still uncertain (2). . It is considered as an autoimmune disease (3), that affects the myelin sheath (1), loss of myelin, the fatty tissue that surrounds and protects nerve fibres allowing them to conduct electrical impulses(4). although the reasons for the autoimmune demyelinization are far to be clear (5). One of these common features is the neuronal imbalance in oxidants/antioxidants (6).

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS). Central nervous system is particularly susceptible to Reactive oxygen species (ROS) induced damage due to the high oxygen demands of the brain and low concentration of endogenous antioxidants. Accumulating data indicate that oxidative stress (OS) plays a major role in the pathogenesis of multiple sclerosis (MS). Reactive oxygen species (ROS), leading to OS, generated in excess primarily by macrophages, have been implicated as mediators of demyelization and axonal damage in MS (7).

Oxidative stress is very high during active progression of multiple sclerosis when compared to those individuals whose multiple sclerosis is in remission or when compared with normal controls(8). 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 immuno-inflammatory processes in brain tissue(9). Others have suggested that excess free radicals trigger heightened T-cell activity via an arachidonic acid cascade, or that direct damage to myelin is caused by the free radicals themselves (10). According to the results of previous studies particular monocyte-derived macrophages are thought to play a central role in MS pathology, as macrophages produce various mediators (cytokines, nitric oxide, reactive oxygen species). (11). The exact mechanisms responsible for increased oxidative stress in MS patients needs to be further explored and there is not yet enough evidence to decide whether oxidative stress is a primary phenomenon inducing the progression of MS (12).

The aim of the study is to evaluate the oxidative stress status in patient with multiple sclerosis by measurement malondialdehyde (MDA) the end product of lipid peroxidation commonly used as indicator of oxidative stress.

Subjects and methods

Thirty females MS patients were included in this study. They were assessed clinically at the department of neurology in Ibn Sinna teaching hospital using the Extended Disability Status Scale score (EDSS), and they are on interferon therapy .

The control group consisted of 30 healthy women subjects, matched for age with the patients group. The study was approved by the local Ethic Committee in college of medicine – Mosul . In both patients and controls, Serum malondialdehyde (MDA) was estimated using thiobarbituric acid (TBA) assay (13).

Results

The individuals in the multiple sclerosis and control groups were females and comparable in terms of age, Mean 27.75±6.87 year and 27.65±6.67 year respectively, (P> 0.5). Mean MDA for the multiple sclerosis group (2.40±0.59 µmol/l)) was significantly higher (P<0.001) than that for the control group (1.44±0.22 µmol/l)), (table 1).

Discussion;

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS). It is characterized by loss of myelin, the fatty tissue that surrounds and protects nerve fibers allowing them to conduct electrical impulses, (4).

Free radicals are common outcome of normal aerobic cellular metabolism , oxidative stress (OS) leading to free radical attack on neural cells contributes calamitous role to neuro-degeneration. MS is characterized by a series of biochemical changes affecting neuronal functions (14). Particularly, one of these common features is the neuronal imbalance in oxidants/antioxidants (6). ROS cause damage to main cellular structures and components such as

lipids, proteins and nucleic acids (e. g., RNA, DNA), resulting in cell death by necrosis or apoptosis. In addition, weakened cellular antioxidant defense systems in the central nervous system (CNS) in MS, and its vulnerability to ROS effects may increase damage (15).

The present study was performed to evaluate the oxidative stress in a sample of multiple sclerosis patients, by measurement malondialdehyde (MDA) the end product of lipid peroxidation, the most commonly used as indicator of oxidative stress. The current study involved 60 individuals divided into 2 groups , 30 patients with multiple sclerosis, and 30 individuals kept as control group . The 2 groups were females and their ages was matched . This matching of individual groups may exclude any effect of the age factor on the results of this study.

In this study serum MDA levels were found significantly higher in MS patients than the healthy control subjects. Increased MDA level which is the consequence of lipid peroxidation and a marker of oxidative stress is an evidence of exaggerated oxidative stress in MS patients. This compound, originating from the irreversible decomposition of peroxidized polyunsaturated fatty acids of membrane phospholipids, is considered a reliable indicator of increased oxidative stress (16,17). Lipid peroxidation caused by reactive oxygen species has been hypothesized to damage white matter of the brain in MS. This hypothesis was supported by the findings that individuals with MS have increased concentrations of lipid peroxidation products in the plasma/serum of MS patients (18).

Increased levels of indicators of oxidative stress and/or decreased levels of antioxidant enzymes and antioxidants are observed in blood and cerebrospinal fluid during the active phases of MS (19).

A study done by Syburra and Passi 1999, by performing a multiparameter analysis of non-enzymatic and enzymatic antioxidants, showed significantly reduced levels of plasma antioxidant and significant oxidative stress in comparison to controls(20). Miller et al, (2010), and Hadzovic-Dzuvo et.al, (2011) measured the total antioxidant status (TAS) in patients with MS, demonstrated a significant decrease in plasma total antioxidant capacity in patients with MS compared to the controls(15,21). Tavazzi B, et.,al (2011) measured the concentrations of circulating MDA as an index of lipid peroxidation in MS patients and controls , showed that MDA in serum of MS patients (0.84 ± 0.53 µmol/L showed a tremendous 210 ± 132-fold increase in comparison with the concentration measured in serum of controls (0.004 ± 0.003 µmol/L serum(5).

Conclusion

The present study demonstrated that patients with multiple sclerosis have a high levels of MDA as compared to those of healthy control. It further emphasizes the growing concern that oxidative stress was enhanced in those patients and indicate that treatment with antioxidants might prevent propagation of tissue

damage and improve both survival and neurological outcome of the disease.

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Table 1 shows the Mean ± SD of age and MDA of studied groups.

Parameter	MS	Control
Age (years)	27.75 ± 6.87	27.65 ± 6.67
MDA(μmol/l)	2.40 ± 0.59	1.44 ± 0.22