E-ISSN: 2149-7222 (Online)

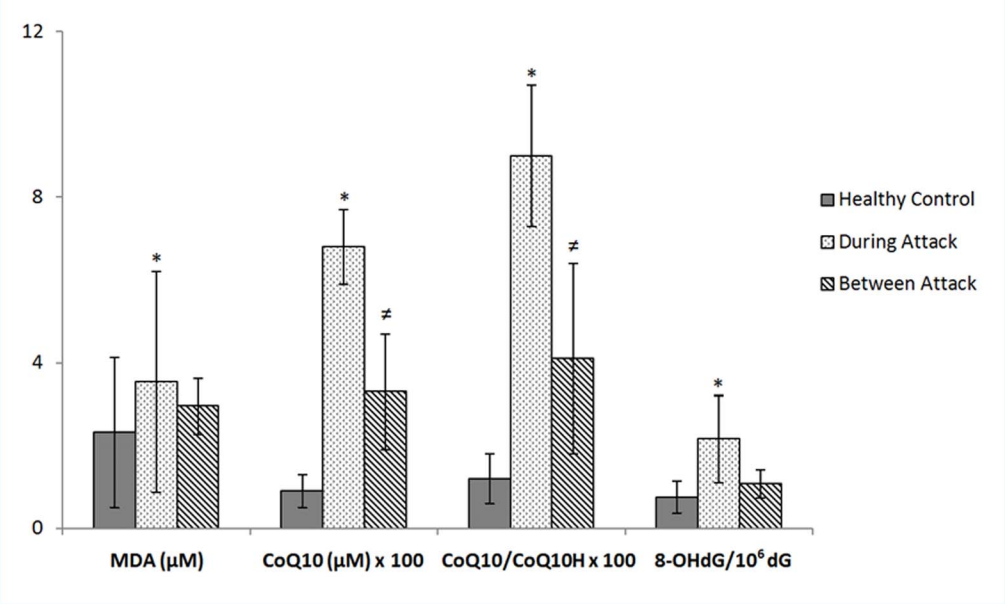
Journal of Cellular Neuroscience and Oxidative Stress

http://dergipark.gov.tr/jcnos

Former name; Cell Membranes and Free Radical Research

HSOD
Cellular Neuroscience and Oxidative Stress Society

An Official Journal of the Cell Membranes and Oxidative Stress Society
http://hsord.org.tr/en/



OPEN ACCESS and NO PUBLICATION FEE

Editor in Chief
Prof.Dr. Mustafa NAZIROĞLU

Volume 9, Number 1, 2017

Journal of Cellular Neuroscience and Oxidative Stress

http://dergipark.gov.tr/jcnos

An Official Journal of the Cell Membranes and Oxidative Stress Society

http://hsord.org.tr/en/

Formerly known as:

Cell Membranes and Free Radical Research (2008 - 2014)

Volume 9, Number 1, 2017

[CONTENTS]

Volume 9, Number 1, 2017
E-ISSN Number: 2149-7222 (Online)
Indexing: Google Scholar, Index Copernicus, Chemical Abstracts, Scopus (Elsevier),
EBSCOhost Research Database

AIM AND SCOPES
Journal of Cellular Neuroscience and Oxidative Stress is an online journal that publishes original research articles, reviews and short reviews on the molecular basis of biophysical, physiological and pharmacological processes that regulate cellular function, and the control or alteration of these processes by the action of receptors, neurotransmitters, second messengers, cation, anions, drugs or disease.

Areas of particular interest are four topics. They are;

A- Ion Channels (Na^+- K^+ Channels, Cl^- channels, Ca^{2+} channels, ADP-Ribose and metabolism of NAD^+, Patch-Clamp applications)

B- Oxidative Stress (Antioxidant vitamins, antioxidant enzymes, metabolism of nitric oxide, oxidative stress, biophysics, biochemistry and physiology of free oxygen radicals)

C- Interaction Between Oxidative Stress and Ion Channels in Neuroscience
(Effects of the oxidative stress on the activation of the voltage sensitive cation channels, effect of ADP-Ribose and NAD^+ on activation of the cation channels which are sensitive to voltage, effect of the oxidative stress on activation of the TRP channels in neurodegenerative diseases such Parkinson's and Alzheimer's diseases)

D- Gene and Oxidative Stress
(Gene abnormalities. Interaction between gene and free radicals. Gene anomalies and iron. Role of radiation and cancer on gene polymorphism)

READERSHIP

Biophysics	Biochemistry
Biology	Biomedical Engineering
Pharmacology	PhysiologyGenetics
Cardiology	Neurology
Oncology	Psychiatry
Neuroscience	Neuropharmacology

Keywords
Ion channels, cell biochemistry, biophysics, calcium signaling, cellular function, cellular physiology, metabolism, apoptosis, lipid peroxidation, nitric oxide synthase, ageing, antioxidants, neuropathy, traumatic brain injury, spinal cord injury, Alzheimer's Disease, Parkinson's Disease.

RESEARCH ARTICLE

J Cell Neurosci Oxid Stress 2017;9(1): 601-607.

Levels of leukocyte oxidative DNA damage (8-OHdG), serum coenzyme Q10 and lipid peroxidation in the formation attacks of patients with multiple sclerosis

Erdem Cokluk[1], Aysel Milanlıoğlu[2], Zübeyir Huyut[1], Vedat Çilingir[2], Hamit Hakan Alp[1]*, Mehmet Nuri Aydın[2], Mehmet Ramazan Şekeroğlu[3], Ragıp Balahoroğlu [1]

[1]*Department of Biochemistry, Medical Faculty, Yuzuncu Yıl University, Van, Turkey*

[2] *Department of Neurology, Medical Faculty, Yuzuncu Yıl University, Van, Turkey*

[3] *Department of Biochemistry, Medical Faculty, Sakarya University, Sakarya, Turkey*

Received February 23, 2017; ***Accepted*** March 5, 2017

Abstract

Multiple sclerosis (MS) is a demyelinating disease of the nervous system. Evidence about oxidative stress plays an important role in the pathogenesis of MS is increasing day by day. In our study, we aimed to investigate the effect of oxidative DNA damage and oxidative stress in the pathogenesis of MS disease. Blood samples were obtained from during an attack (Group 1), between attacks (Group 2) of MS patients (20 male and 10 female) and 30 healthy volunteers (Group 3). Malondialdehyde (MDA) levels as indicator of oxidized lipids were detected using flourescence dedector with high pressure liquid chromatograph (HPLC). DNA was extracted from leukocytes of control and patients with MS and then we measured 8-hydroxy-2' -deoxyguanosine (8-OHdG) and deoxyguanosin (dG) by using HPLC method with electrochemical and UV detector, respectively. Measurement of oxidized coenzyme Q10 (CoQ10) and reduced CoQ (CoQ10H) was performed by using UV detector with HPLC method. Serum MDA level of group 1 was significantly higher than those in group 2 and group 3 ($p< 0.001$). 8-OHdG/10^6 dG ratio of group 1 was significantly higher than those in group 2 and group 3 ($p< 0.001$). CoQ10/CoQ10H rates of group 1 were significantly increased compared with group 2 and group 3 ($p<0.001$). In conclusion, we observed that oxidative DNA damage, lipid and mitochondria oxidative damage were high in blood of patients with MS. It seems that oxidative stress acts a play role the pathogenesis of MS patients as well as induces attacks.

Keywords: Coenzyme Q10; Lipid peroxidation; Oxidative DNA damage; Multiple sclerosis

Author for correspondence :
Hamit Hakan ALP
Department of Biochemistry, Faculty of Medicine, Yuzuncu Yıl University Van, Turkey
Tel: +90 533 379 97 02 Fax: +90 432 236 1054
e-mail: hamithakanalp@gmail.com

List of Abbreviations;

8-OHdG, 8-hydroxy-2' –deoxyguanosine; **CNS**, central nervous system; **CoQ10**, coenzyme Q10; **EDSS,** expanded disability status scale; **ETC**, electron transport chain; **HPLC**, high pressure liquid chromatograph; **MDA**, Malondialdehyde; **MS**, multiple sclerosis; **ROS**, reactive oxygen species

Introduction

Multiple Sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) and characterized by re-activation of antigen-specific cells, microglia activation, recruitment of systemic immune-competent cells and production of cytotoxic mediators leading to neural tissue damage (Gonsette, 2008). Four different forms were found in terms of clinic progress in MS. These forms are called relapsing-remitting, secondary progressive, primary progressive and progressive relapsing form. The most frequently seen form is the relapsing-remitting form (Miller, 1999). Today, MS's reasons could not be fully understood. In MS pathogenesis, there are genetic factors and environmental factors (Lassmann et al., 2012). The studies conducted on MS stated that reactive oxygen species (ROS) could particularly play an important role in demyelinization in MS pathogenesis (Koch et al. 2006). ROS are formed in normal physiological process in the body. ROS are minimized by the antioxidant system and converted into harmless structures and this process constantly continues in balance. Along with the effect of the environmental factors, oxidant stress occurs when ROS-antioxidant balance shifts towards ROS. ROS affect biological molecules such as proteins, lipids and DNA (Frohlich et al., 2008). ROS attack on lipids and cell membrane lipids and lipid peroxidation products are formed due to ROS-mediated oxidation of cell membrane lipids. The most common and abundant lipid peroxide product is malondialdehyde (MDA) (Huyut et al., 2016a and 2016b). Therefore, MDA levels are widely used as an indicator of lipid peroxidation (Irshad and Chaudhuri, 2002).

ROS cause DNA damage such as strand breaks and base modifications, including the oxidation of guanine residues into 8-hydroxy-2' –deoxyguanosine (8-OHdG). Thus, 8-OHdG can serve as a sensitive biomarker of oxidative DNA damage (Arı et al., 2011). One of the sources of ROS in the body is the electrons which leak from the electron transport chain (ETC) in the mitochondria internal membrane. One of the proteins that transport electron in ETC is coenzyme Q 10 (ubiquinone). The main task of coenzyme Q10 (CoQ10) is to transport electrons between nicotinamide dinucleotide and succinate dehidrogenase in ETC (Ostman et al., 2012). CoQ10 is also used as supplementary in the treatment of some diseases such as diabetes and Parkinson (Chinnery et al., 2006; Litarru and Langsjoen, 2007). CoQ10 is found in two forms which are oxidized and reduced (Cobanoglu et al., 2011). Reduced form of CoQ10 is also known as ubiquinol-10 and it is the first defense against the oxidative damage of low-density lipoprotein (Mracoff and Thompson, 2007). Due to this antioxidant effect of CoQ10, ubiquinol-10/ubiquinon-10 ratio can be considered as a marker to determine oxidative damage (Huyut et al., 2016b). Plasma or serum CoQ10 concentration is usually used as the indicator for CoQ10 status in the human being.

We suggest that the oxidative DNA damage, lipid peroxidation and mitochondrial oxidative damage levels will be helpful in prognosis of these patients. In the current study, we aimed to investigate levels of leukocyte 8-OHdG, serum CoQ10 and MDA levels and ubiqinol10/ubiquinon-10 ratio in the during and between attack in MS patients.

Materials and Methods

Patients and Samples

The study was performed on the blood samples of 30 MS patients aged between 22-60 (34.85 ± 10.55) (20 male, 10 female) and 30 healthy control patients aged between 26-57 (33.46±9.54) (17 male, 13 female). The patients were elected among the patients who were diagnosed with MS and treated in the department of Neurology in Yuzuncu Yıl University Medical Faculty. MS was diagnosed based on McDonalds' criteria (McDonald et al., 2001) and only relapsing-remitting type MS patients were taken to the study. Whole blood samples were taken during the attack (group 1) and in minimum 1 month after the same patients' attack (group 2). Healthy control group (group 3) was made up of healthy individuals who did not have any chronic and acute disease. The study was approved by Human Ethics Committee of Yuzuncu Yıl University (REC number: 11/09.05.2013).

Biochemical Assays

Measurement of MDA

Analysis of MDA in serum was done by high-performance liquid chromatography (HPLC, Agilent 1200 Series system, Agilent Technologies, Waldbronn, Germany) as described by Khoschsorur et al., (2000).

Fluorometric detection was performed with excitation at 527 nm and emission at 551 nm. The peak of the MDA-TBA adduct was calibrated as a 1,1,3,3 tetraethoxypropane standard solution, carried out in exactly the same process as with the plasma sample. MDA levels were expressed as µM.

Reduced and oxidized CoQ10 analysis

Analyses of oxidized and reduced CoQ10 were performed according to Litarru et al. (Litarru et al., 2004; Litarru et al., 2007). The HPLC (Agilent 1200 Series system) was used to analyses of total CoQ10 and oxide CoQ10 levels. For HPLC measurement, octadecyl sulfonate (ODS) reversed phase supercoil LC 18 (15 x 0.46 cm i.d. 3 µm) colon was used. Oxidized and reduced CoQ10 were measured by electrochemical detector at 0.35V.

DNA isolation and hydrolization from leucocytes

Total DNA of leukocytes was extracted by used method of Ates et al., (2010). 2 ml of blood was mixed with 3 ml of erythrocyte lysis buffer, and incubation for 10 min in ice was followed by centrifugation (10 min at 1500 *xg*). The supernatant was decanted, and the pellet was resuspended thoroughly in sodium dodecyl sulfate (10%, *v*⁄v), proteinase K (20 mg⁄ml) and 1.9 ml leukocyte lysis buffer (4 M NaCI, 0.5 M EDTA). The mixture was incubated at 65 °C for 1 hour and then mixed with 0.8 ml of 9.5 M ammonium acetate. After centrifugation at 1500 *xg* for 25 min, the clear supernatant (2 ml) was transferred to a new sterile tube and DNA was precipitated by the addition of 4 ml ice-cold absolute ethanol. DNA samples were dissolved in Tris EDTA buffer (10 mm, pH 7.4).

DNA samples that were obtained for 8-OHdG analysis were hydrolyzed by using with formic acid at 150 °C for 30 minutes according to Kaur and Halliwell (1996). The hydrolysed DNA samples were dissolved in pure acetonitrile (final volume: 1 ml). 8-OHdG and dG levels were measured by using ECD and UV detector in the HPLC device, respectively. The reverse phase C-18 (RP-C18) analytical column was used as the column (250 mm × 4.6 mm × 4.0 µm, Phenomenex, CA). The mobile phase was prepared with mixed 0.05 M potassium phosphate buffer (pH: 5.5) and acetonitrile (97:3, v/v) and flow rate was set to 1 ml/min. The amount of 8-OHdG and dG was determined by using the ECD adjusted to 600 mV, and absorbance measurement at 245 nm with the UV detector, on the HPLC apparatus, respectively. For measurement of 8-OHdG and dG, 8-OHdG and dG standards were used (Sigma Aldrich). The oxidative DNA damage values were expressed as the number of 8-OHdG per 10^6 dG (8-OHdG/10^6dG) (Tarng et al., 2000).

8-OHdG and dG analyses

In the hydrolyzed DNA samples, 8-OHdG and dG levels were measured with high pressure liquid chromatography electrochemical detector (HPLC-ECD) and variable wavelength detector (HPLC-UV) systems according to used method by Kaya et al., (2012). The dG concentration was monitored based on absorbance (245 nm) and 8-OHdG based on the electrochemical reading (600 mV). Levels of dG and 8-OHdG were quantified using the standards of dG and 8-OHdG from sigma; the level of 8-OHdG level is expressed as the number of 8-OHdG molecules per 10^6 dG (Tarng et al., 2000).

Statistical analysis

Statistical analyses were done by using SPSS-15. The statistical significance was calculated using the ONE-Way ANOVA test. In the post-hoc analysis which was made in the statistical examination, the groups were compared between themselves. P-value of less than 0.05 was considered statistically significant. All the results were expressed as mean scores with their standard deviation (mean ± SD).

Results

Of all the patients, 66.7 % were males, while 56.7 % of the control group were males. The mean age of the patient group was 34.85±10.55 years, and the mean age of the control group was 33.46±9.54 years. The age and gender distributions of the patient and control groups did not significantly differ ($p > 0.05$) (Table 1).

Median level of EDSS scores of the patients was 2.66 and ranges were 1 to 6. The changes in all the parameters are shown in Table 2.

Table 1: Demographic characteristics of individuals

Groups	Male (%)	Female (%)	Age	Number
Healthy Control	56.7	43.3	33.46±9.54	30
Patients with MS	66.7	33.3	34.85±10.55	30

Table 2: Comparison of levels of MDA, CoQ10 and DNA damage in during attack and between attack of MS patients according to the healthy control.

				%95 CIM		P value
		Mean ± SD	Median	Lower Bound	Upper Bound	
	During attack	3.54 ± 2.67*	3.05	2.61	4.48	
MDA (µmol/L)	Between attack	2.95 ± 0.68	2.88	1.62	2.99	0.045
N=30	Healthy control	2.31 ± 1.82	1.64	2.69	3.21	
	During attack	2.16 ± 1.05*	1.84	1.80	2.53	
8-OHdG/10^6dG	Between attack	1.08 ± 0.34	1.02	0.95	1.21	0.001
N=30	Healthy control	0.75 ± 038	0.75	0.61	0.89	
	During attack	0.090 ± 0.017*	0.09	0.084	0.096	
CoQ10/CoQ10H	Between attack	0.041 ± 0.023≠	0.03	0.032	0.05	0.001
N=30	Healthy control	0.012 ± 0.006	0.011	0.01	0.015	
	During attack	0.068 ± 0.009*	0.067	0.065	0.071	
CoQ10 (µmol/L)	Between attack	0.033 ± 0.014≠	0.031	0.027	0.038	0.001
N=30	Healthy control	0.009 ± 0.004	0.0094	0.0081	0.01	

*: "It is statistically significant compared to other groups. ≠: It is statistically significant compared to the healthy control groups".

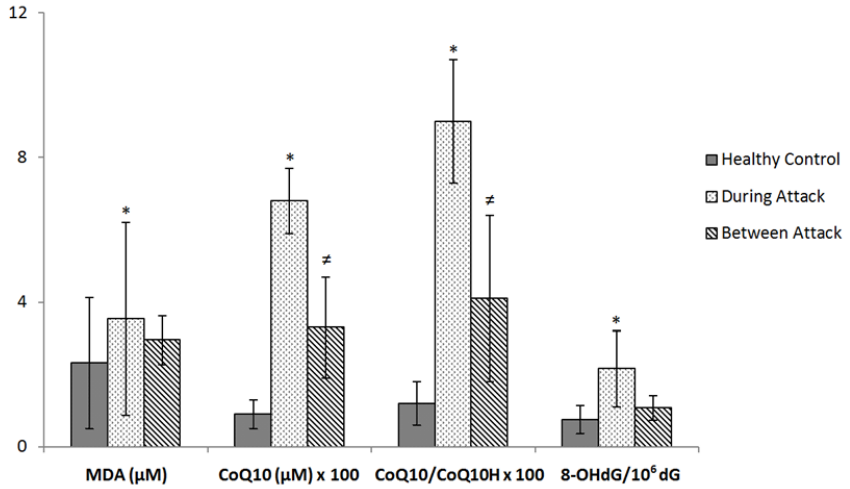


Figure 1. The comparison of all measured parameter values in between of healthy controls, during attack and between attack in patients with multiple sclerosis.

*: "It is statistically significant compared to other groups. ≠: It is statistically significant compared to the healthy control groups"

Serum MDA level of group 1 was significantly higher than those in group 2 and group 3 (Figure 1). The lowest MDA level was detected in group 3, but there was no significant difference between group 2 and 3. The level of oxidative DNA damage (8-OHdG/10^6dG) of group 1 (2.16±1.05) was significantly higher than those in group 2 and group 3 ($p<0.001$) (Figure 1). The lowest 8-OHdG/10^6 dG ratio was detected in group 3 but there was no significant difference between group 2 and 3. The CoQ10/CoQ10H ratio of group 1 was significantly increased when compared to those in group 2 and group 3 (group 1: 0.09±0.017, group 2: 0.041±0.023 and group 3: 0.012±0.006 respectively; $p<0.001$) (Figure 1). In addition, the serum CoQ10 levels were also significantly increased when compared to those in group 2 and group 3, respectively; $p<0.001$) (Figure 1). The lowest CoQ10 level was detected in group 3 and this difference was statistically significant.

As a result, it was observed that all measured parameter values in group 1 were very high compared to those in other groups and were parallel to each other in during attack. In addition, these increases in CoQ10, CoQ10/CoQ10H and oxidative DNA damage, were about 65-70% ratios in during attack according to the healthy control group.

Discussion

In demyelinating diseases including MS, the inflammation in the demyelinating area causes increase in the level of oxygen and nitrogen free radicals and the reason for this increase is substantially known as active macrophages (Mahad et al., 2015). There are studies that show that oxygen and nitrogen free radicals which are produced by macrophages intermediate axonal damage and demyelinization in MS (Gonsette, 2008).

Lipid peroxidation is the name given to the oxidative modification process which is created by ROS on lipids. Reactive aldehyde structures such as MDA, acrolein 4-hydroxy-2-nonenal and 4-hydroxy-2-hexenale develop as a result of lipid peroxidation. MDA is the second most frequently developing structure as a result of lipid peroxidation. It is used as the determinant of lipid peroxidation because of its easy measurement and availability (Grotto et al., 2009). In primary studies, it was found that there were lipid peroxidation products in the cerebrospinal liquids and plasma of MS patients (Gilgun-Sherki et al., 2004; Besler et al., 2002). We investigated the serum MDA levels and evaluated the results to compare the lipid peroxidation levels of relapsing-remitting MS patients during the attacks and after the attacks with the healthy control group in our study. We found that the MDA levels which were found in the samples taken from MS patients during the attack were significant when compared to the MDA levels found in the samples taken from the healthy control group ($p<0.045$). And no significant difference was found between the MDA levels of the patients and between the attacks and the MDA levels of the healthy control group in the results obtained. Our results were in harmony with the literature when compared to the studies in literature. Acar et al., (2012) have shown that the MDA levels were higher in the relapsing-remitting MS patient group when compared to the healthy control group. However, the MDA levels during the attacks were not studied in by Acar et al., (2012). Korpela et al., (1989) could not find significant difference on the MDA levels between the MS patient and healthy control groups (Korpela et al., 1989). We suppose that this different result can be probably associated with the changes in attack or remission phases of the patients at the time when the study was done (for example, exacerbation phase, beginning or end of relapse phase or remission phase).

One of the main sources of the ROS is the ETC in the mitochondria internal membrane. There is constant electron transportation in ETC and constant formation of ROS. The molecules in lipid structure in ETC act like an antioxidant. CoQ10 is the leading one among these structures. The main task of CoQ10 is to transport electrons between nicotinamide dinucleotide and succinate dehydrogenase (Ostman et al., 2012). In the experimental animal studies which were done on mitochondrial CoQ10, it was claimed that CoQ10 support had treating effect on Alzheimer disease and ischemia (Smith and Murphy, 2010; Manczak et al., 2010). In our study, we wanted to determine the reduced and oxidized CoQ10 levels in all groups and determine the oxidative damage in the mitochondria during the attacks and between the attacks of MS patients. In our study, we detected that the CoQ10/CoQ10H ratio which was found in the samples taken during the attack was higher than the other two groups. However, there was no significant difference between the CoQ10/CoQ10H ratio which was found in the samples taken during the

attacks and in the samples of the healthy control group. Based on these results, we can say that oxidative damage in mitochondria increases during attacks in MS patients. There are very few studies which are associated with the research on CoQ10 levels in MS patients in literature. In a experimental animal study, Mao et al., (2013) found that mitochondrial CoQ10 regulated some inflammatory associated genes and based on these results they stated that mitochondrial CoQ10 promises hope for the neuroprotective treatment in MS patients (Mao et al., 2013). Our study supports the results of Mao et al., (2013) in that CoQ10 level increases during the attack. Giving MS patients CoQ1O as a supplementary can be useful to reduce mitochondrial oxidative damage in these patients and it can also be useful due to its neuroprotective effect. However, the crucial point here is which CoQ10 (reduced or oxidized form) should be given. We believe that further studies are needed on this issue.

ROS, which plays a role in the pathogenesis of MS, leads to oxidative modifications in the nucleic acids on DNA. 8-OHdG is used as a biomarker in the determination of the oxidative DNA damage (Huyut et al., 2016b). Supposing that DNA synthesizes RNA and proteins, it is likely that the nucleic acids which are oxidized on DNA will lead to coding error and the proteins which are synthesized due to that process will lose their function or completely disrupt. Therefore, the damage which will be created by ROS in DNA can be severer and more permanent. 8-OHdG, which occurs under normal physiological conditions, gets into circulation and is excreted in the urine. Therefore, 8-OHdG is analyzed both in serum and urine. 8-OHdG concentration which is only found in serum and urine can only give us information about oxidative damage. And, the amount of 8-OHdG on DNA strand gives us information about mutation. There are very few studies which are similar to our 8-OHdG on MS patients. Therefore, results obtained on oxidative DNA damage in the pathogenesis of MS will provide important new information for the literature. We found the 8-OHdG/10^6dG ratios, which was determined in the samples that were taken during the attack statistically significantly higher when compared to the other two groups. Post-attack 8-OHdG/10^6dG ratios was also significantly higher than the level in the healthy control group. It is interesting that DNA damage is significantly higher. These datas showed that antioxidant system reduced the MDA levels and CoQ10/CoQ10H ratio. Even if the patients returned to their normal lives after the attack, the oxidative DNA damage continued. The study by Tasset et al., (2012) supports our study. Tasset et al., (2012) divided the MS patient group into two groups which are namely expanded disability status scale (EDSS)<5 and EDSS>5 and compared them with the healthy control group and found that 8-OHdG levels were higher than the healthy control group (Tasset et al., 2012). Tasset et.al. analyzed 8-OHdG in the plasma samples and as a result they stated that oxidative DNA damage increased in the MS patients. The datas which we obtained from our study have showed that guanine bases which are oxidized on DNA in MS patients can lead to severe complications if no antioxidant supplement is given.

In conclusion, we observed that oxidative DNA damage, lipid and mitochondria oxidative damage during attack in patients with MS were higher than those of healthy control group and after attack in MS patients.. In the light of these datas, we concluded that increased MDA, CoQ10 levels and oxidative DNA damage may play an important role in the pathogenesis of MS patients and they may be associated with attacks.

Acknowledgement

This study was done with opportunities of Department of Biochemistry and Neurology, Faculty of Medicine, Yuzuncu Yıl University.

The Roles of Authors

RB and RS researched literature and conceived the study. HHA, ZH and EC were involved in protocol development, gaining ethical approval, patient recruitment and data analysis. HHA, ZH, AM, VC and MNA wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Conflict of Interests

The authors declare, which they have no conflict of interest.

References

Acar A, Ugur Cevik M, Evliyaoglu O, Uzar E, Tamam Y, Arikanoğlu A et al. 2012. Evaluation of serum oxidant/antioxidant balance in multiple sclerosis. Acta Neurol Belg 112: 275-80.

Arı E, Kaya Y, Demir H, Cebi A, Alp HH, Bakan E, Odabası D, Keskin S. 2011. Oxidative DNA damage correlates with carotid artery atherosclerosis in hemodialysis patients. Hemodial Int 15: 453-459.

Ates O, Alp HH, Kocer I, Baykal O and Salman IA. 2010. Oxidative DNA damage in patients with cataract. Acta Ophthalmol 88: 891-895.

Besler HT, Comoglu S and Okcu Z. 2002. Serum levels of antioxidant vitamins and lipid peroxidation in multiple sclerosis. Nutr Neurosci 5: 215-20.

Chinnery P, Majamaa K, Turnbull D, Thorburn D. 2006. Treatment for mitochondrial disorders. Cochrane DB SYST Rev 1: article number CD004426.

Cobanoglu U, Demir H, Cebi A, Sayir F, Alp HH, Akan Z, Gur T, Bakan E. 2011. Lipid peroxidation, DNA damage and coenzyme Q10 in lung cancer patients--markers for risk assessment? Asian Pac J Cancer Prev. 12(6):1399-1403.

Frohlich DA, McCabe MT, Arnold RS and Day ML. 2008. The role of Nrf2 in increased reactive oxygen species and DNA damage in prostate tumorigenesis. Oncogene 27: 4353-4362

Gilgun-Sherki Y, Melamed E, Offen D. 2004. The role of oxidative stress in the pathogenesis of multiple sclerosis: The need for effective antioxidant therapy. J Neurol 251: 261-268.

Gonsette RE. 2008. Neurodegeneration in multiple sclerosis: The role of oxidative stress and excitotoxicity. J Neurol Sci 274:48-53.

Grotto D, Maria LS, Valentini J et al. 2009. Importance of the Lipid Peroxidation Biomarkers and Methodological Aspects for Malondialdehyde Quantification. Quim Nova 32: 169-174.

Huyut Z, Şekeroğlu MR, Balaharoğlu R, Karakoyun T, Çokluk E. 2016**a**. The relationship of oxidation sensitivity of red blood cells and carbonic anhydrase activity in stored human blood; Effect of certain phenolic compounds. BioMed Res Int Article ID 3057384

Huyut Z, Şekeroğlu MR, Balahoroğlu R, Alp HH, Çokluk E. 2016b. In stored human blood, the inhibitor effect of tannic acid and caffeic acid on lipid peroxidation and oxidative DNA damage. East J Med, 21(2): 88-93.

Irshad M, Chaudhuri PS. 2002. Oxidant-antioxidant system: role and significance in human body. Indian J Exp Biol 40:1233-9.

Kaur H, Halliwell B. 1996. Measurement of oxidized and methylated DNA bases by HPLC with electrochemical detection. Biochem J 318:21-23.

Kaya Y, Çebi A, Söylemez N, Demir H, Alp HH, Bakan E. 2012. Correlations between oxidative DNA damage, oxidative stress and coenzyme Q10 in patients with coronary artery disease. Int J Med Sci. 9(8):621-626.

Khoschsorur GA, Winklhofer-Roob BM, Rabl H, Auer T, Peng Z, Schaur RJ. 2000. Evaluation of a sensitive HPLC method for the determination of malondialdehyde, and application of the method to different biological materials. Chromatographia 52:181-184.

Koch M, Ramsaransing GS, Arutjunyan AV, Stepanov M, Teelken A, Heersema DJ, De Keyser J. 2006. Oxidative stress in serum and peripheral blood leukocytes in patients with different disease courses of multiple sclerosis. J Neurol 253:483-487.

Korpela H, Kinnunen E, Juntunen J, Kumpulainen J, Koskenvuo M. 1989. Serum selenium concentration, glutathione peroxidase activity and lipid peroxides in a co-twin control study on multiple sclerosis. J Neurol Sci. 91(1-2):79-84.

Lassmann H, van Horssen J, Mahad D. 2012. Progressive multiple sclerosis: pathology and pathogenesis. Nat Rev Neurol 8(11):647-656.

Mahad DH, Trapp Bruce D, Lassmann H. 2015. Pathological mechanisms in progressive multiple sclerosis. Lancet Neurol 14:183-193.

Manczak M, Mao P, Calkins MJ et al. 2010. Mitochondria-targeted antioxidants protect against amyloid-beta toxicity in Alzheimer's disease neurons. J Alzheimers Dis 20:609-631.

Mao P, Manczak M, Shirendeb UP and Reddy PH. 2013. MitoQ, a mitochondria-targeted antioxidant, delays disease progression and alleviates pathogenesis in an experimental autoimmune encephalomyelitis mouse model of multiple sclerosis. BBA Mol Basis Dis 1832: 2322-31.

McDonald WI, Compston A, Edan G, Goodkin D, Hartung HP, Lublin FD et al. 2001. Recommended diagnostic criteria for multiple sclerosis: Guidelines from the International Panel on the Diagnosis of Multiple Sclerosis. Ann Neurol 50:121-127.

Miller A. 1999. Continuum: Multiple Sclerosis (Part A). 5:7.

Ostman B, Sjodin A, Michaelsson K, Byberg L. 2012. Coenzyme Q10 supplementation and exercise-induced oxidative stress in humans. Nutrition 28: 403-417.

Smith RA and Murphy MP. 2010. Animal and human studies with the mitochondria-targeted antioxidant MitoQ. Ann NY Acad Sci 1201:96-103.

Tarng DG, Huang TP, Wei YH, Liu TY, Chen HW, Chen TW, Yang WC. 2000. 8-hydroxy-2 '-deoxyguanosine of leukocyte DNA as a marker of oxidative stress in chronic hemodialysis patients. Am J Kidney Dis 36:934-944.

Tasset I, Aguera E, Sánchez-López F, Feijóo M, Giraldo AI, Cruz AH, Gascón F, Túnez I. 2012. Peripheral oxidative stress in relapsing-remitting multiple sclerosis. Clin Biochem 45(6):440-444.

2nd International Brain Research School

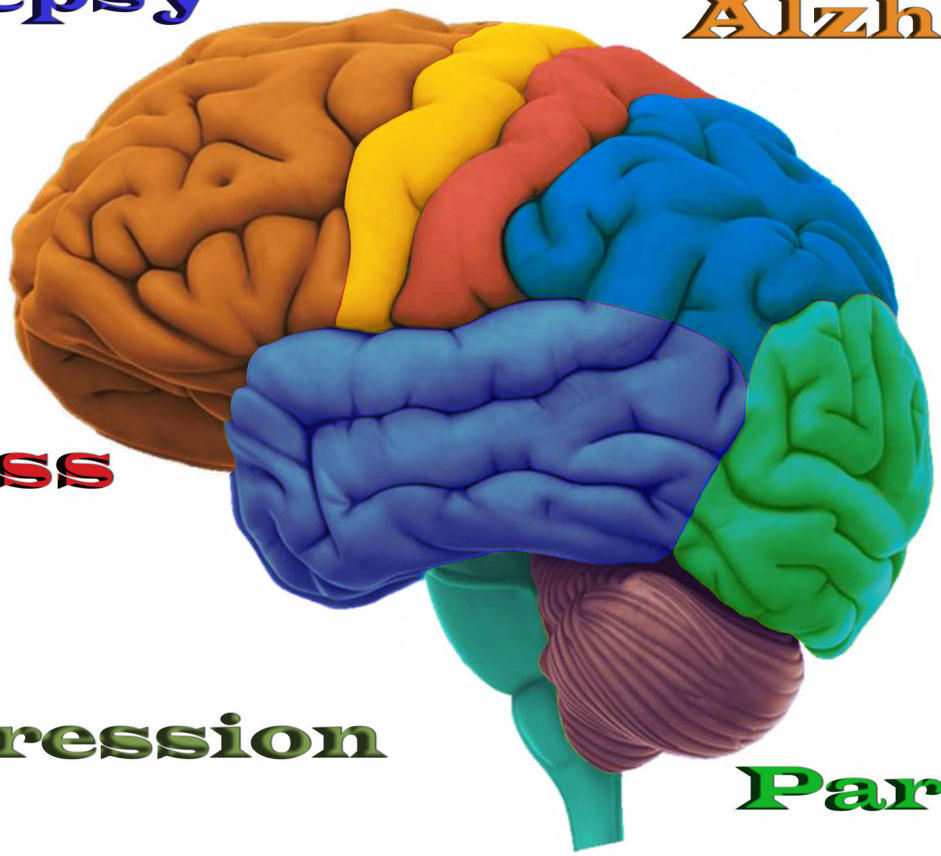
Cellular Neuroscience and Oxidative Stress Society

6 - 12 November 2017 - Isparta / TURKEY

www.cmos.org.tr/brs2017/

Epilepsy

Alzheimer



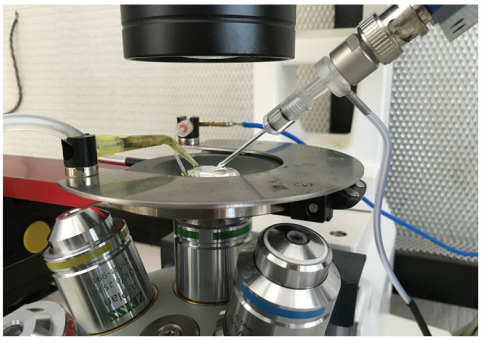
Pain

Stress

Depression

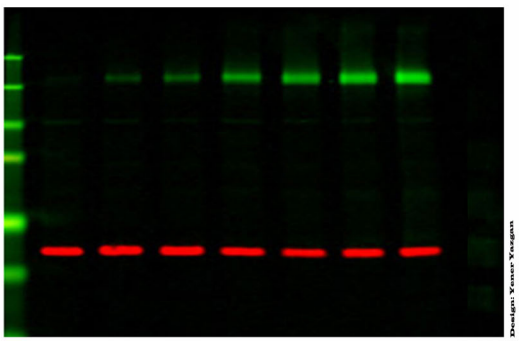
Paralysis

Patch Clamp & Calcium Signaling



Cell Culture

Western Blotting & RT - PCR



Design: Yaser Yazgan

Contact:

Neuroscience Research Center,
Suleyman Demirel University, Faculty of Medicine
Tel: +90 246 211 36 41 Isparta / TURKEY
Fax: +90 246 237 11 65 norobam@sdu.edu.tr

7th World Congress

Oxidative Stress, Calcium Signaling and TRP Channels

www.cmos.org.tr

20 - 23 April 2018
Alanya, Antalya
Turkey

HSOD Cellular Neuroscience and Oxidative Stress Society

EBSA Biophysics in Europe

INTERNATIONAL BRAIN IBRO RESEARCH ORGANIZATION Pan-European (IBRO-PERC)

ZEISS

Contact:
E mail: cmos@sdu.edu.tr
Tel: +90 246 211 36 41
Fax: +90 246 237 11 65

COPYRIGHT FORM

Journal of Cellular Neuroscience and Oxidative Stress

Date_____ Contributor Name _____

Contributer Address _____

Manuscripyt Number (if Know) _____

Re: Manuscript entitled _____

''For publication in **Journal of Cellular Neuroscience and Oxidative Stress** published by **Cellular Neuroscience and Oxidative Stress Society ''**

Submission of a manuscript implies:

- that the work described has not been published before (except in the form of an abstract or as part of a published lecture, review or thesis);
- that it is not under consideration for publication elsewhere;
- that its publication has been approved by all co-authors, if any, as well as by the responsible authorities at the institute where the work has been carried out;
- that, if and when the manuscript is accepted for publication, the authors agree to automatic transfer of the copyright to this publisher;
- that the manuscript will not be published elsewhere in any language without the consent of the copyright holders;
- that written permission of the copyright holder is obtained by the authors for material used from other copyrighted sources, and that any costs associated with obtaining this permission are the authors' responsibility. Copyright notice: The contributor and the company/employer agree that all copies the final published version of the contribution or any part thereof distributed or posted by them in print or electronic format as permitted herein will include the notice of copyright as stipulated in the journal and a full citation to the journal as published by **Cellular Neuroscience and Oxidative Stress Society** , Isparta, Turkey.

CHECK ONE BOX

☐ Contributor owned work: Contributor's signature_____ Date _____

Type or print name and title _____

Co-Contributor's signature_____ Date _____

Type or print name and title _____

☐ Company-Institution owned work _____

Company-Institution (Employer for here)_____ Date _____

Authorized signature_____ Date _____

☐ U.S. Government work _____

☐ U.K. Government work _____

☐ Other Government work _____

Journal of Cellular Neuroscience and Oxidative Stress

Principal Contact

Prof. Dr. Mustafa NAZIROGLU / Editor in Chief
Suleyman Demirel University, Faculty of Medicine, Department of Biophysics
32260 Cunur - Isparta / TURKEY
Phone: +90 246 2113641 Fax: +90 246 2371165
mustafanaziroglu@sdu.edu.tr
biophysics@sdu.edu.tr