Lipid Peroxidation and Oxidative Stress in Patients with Fibromyalgia Syndrome

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ABSTRACT:

BACK GROUND:

Fibromyalgia (FMS) is a common, chronic widespread pain syndrome usually associated with other somatic and psychologic symptoms including fatigue, sleep disturbances, cognitive difficulties Oxidative stress means an alteration in the delicate balance between free radicals and the scavenging capacity of antioxidant enzymes in favor of free radical in the body system.

OBJECTIVE:

To evaluate and compare the antioxidants and lipid peroxidation in patients with fibromyalgia and healthy control.

PATIENTS AND METHOD;

The study has included sixty patients with FMS (40 females and 20 males) and thirty healthy subjects. The subjects were selected from people attending the out patients clinic in Medical City-Baghdad Teaching Hospital- Rheumatology& Rehabilitation Consultation Unit. Laboratory parameters included: uric acid,albumin,caeruloplasmin,total thaiol,malondiaaldehyde(MDA) and peroxinitrate($ONOO^-$).

RESULTS:

MDA and uric acid levels in serum of patients with fibromyalgia were significantly higher than in the control group. While the levels of $ONOO^-$ GSH,CP,albumin in serum of patients with fibromyalgia were significantly lower than in healthy control.

CONCLUSION:

oxidative stress may have a role in the pathophysiology of fibromyalgia syndrome.

***KEYWORDS*:** lipidperoxide,$ONOO^-$,GSH,CP,uricacid,albumin, fibromyalgia.

INTRODUCTION:

Fibromyalgia (FMS) is a common, chronic widespread pain syndrome usually associated with other somatic and psychologic symptoms including fatigue, sleep disturbances, cognitive difficulties(memory problems,diminished mental clarity and concentration difficulties).The etiology and pathophysiology of FM has not been clearly understood and that makes the disease a frustrating condition for the patients and the physicians(Haynes,2005).

Oxidative stress means an alteration in the delicate balance between free radicals and the scavenging capacity of antioxidant enzymes in favor of free radical in the body system . recent study have shown some evidence that oxidative stress may have a role in the pathophysiology of fibromyalgia (haynes,2005).

Studies on depression elucidate the possible link between depression and lipid peroxidation . central nervous system cells are highly vulnerable to the toxic effect of free radicals when compared with the other organs of the body because they have a high rate of oxidative metabolic activity and a low level of protective antioxidant enzymes , a high ratio of membrane surface area to cytoplasmic volume a neuronal anatomical network vulnerable to disruption,and high concentration of readily oxidizable membrane PUFAS(2),lipid peroxidation may play an important role in depression and the peroxidation reducing effect of different selective serotonin reuptake inhibitors in major depression has been

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demonstrated by bilici et al (Bilici,2001). These authors reported a significant correlation between erythrocyte MDA level.which was in accordance with the results in FM(Bilici,2001). Additionally, Delibas et al. suggested that plasma MDA levels might be an important marker of cognitive deterioration in patients with dementia of al zherimer type(Delibas,2002.). Cognitive difficulties in FM patients have been well established.

SUBJECTS AND METHODS:

During the period from December 2008 to March2009 blood samples were collected from sixty patients with fibromyalgia and thirty apparently healthy subjects. with age range (18-72) years. The subjects were selected from the people attending the out patient clinic in Medical City – Baghdad Teaching Hospital – Rheumatology & Rehabilitation Consultation Unit.

Laboratory parameters included: uric acid,albumin,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 a .(Doumasetal,1971).

Malondialdehyde (MDA) was estimated by the method of Buege and Aust 1987.

Serum peroxynitrite level was measured 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< .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 MDA level in serum of patients with fibromyalgia 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. are shown in table (1) .

Table 1:Comparison of Pro-oxidant by products (MDA, and $ONOO^-$ for subjects studied (n=60)

Pro-oxidant By-product	Control (n=30) Mean ±SD	Patients (n=60) Mean ±SD	p-value	Sig.
MDA(m mol/ L)	1.19± 0.21	2.1± 0.3**	0.000	HS
ONOO (m mol/L)	1.13 ± 0.18	0.66± 0.1*	0.000	HS

The results showed that the GSH,CP,albumin levels in serum of patients with fibromyalgia were significantly lower than in healthy control,While uric acid was found to be significantly higher than in healthy controle are shown in table (2).

Table 2 :Comparison of Antioxidants Markers for subjects studied.

Antioxidant marker	Control(n=30) mean±SD	Patients(n=60) mean±SD	P-value	sig
CP(mg/dl)	24.67±2.0	21.58±1.69	0.000	HS
GSH(µmol/L)	0.596±0.102	0.368±0.083	0.000	HS
S.uric acid(mg/dl)	4.137±0.961	4.732±0.885	0.005	HS
s.albumin(g/dl)	4.307±0.867	3.602±0.596	0.269	NS

DISCUSSION:

Malondildehyde(MDA)level in serum of patients with fibromyalgia was higher and peroxynitrite was lower in patients with fibromyalgia than in control. This show the presence of oxidative stress in the patients, A limited number of in vivo or in vitro studies of blood of patients with fibromyalgia regarding the effects of antioxidant redox systems and LP levels on the etiology of fibromyalgia have been reported(Ozgocmen,2006,Altindag,2006,). In the current study, We compared the role of antioxidant vitamins with particular references to antioxidant redox systems in plasma of patients with fibromyalgia . In the current study, we compared the role of antioxidant vitamins with particular reference to antioxidant redox systems in plasma of patients with fibromyalgia. The etiology and pathogenesis of fibromyalgia are not clearly understood although it is characterized by activation of local ischemia injury(Ozgocmen,2006,andAltindag,2006). LP levels, reflecting oxidative degradation products of membrane PUFAs, are known to be related to ROS actions.In the present study, LP levels were higher in serum of patients with fibromyalgia than in control. Local ischemia leads to overproduction of ROS and interferes with the structure and ratio of PUFA leading to loss of biological membrane fluidity(Nazuoglu,2004). The role of ROS in patients with fibromyalgia is controversial, similar to the LP results of our current study. Altindag and Celic(Altindeg,2006), Ozgocmen et al(Ozgocmen2006), Reported that LP levels in serum of patients with active fibromyalgia were higher than in control. In contrasl, however ,Eisinger et al (Esinger,1994), measured LP levels, protein carbonyls, and antioxidant in female patients with fibromyalgia and found no difference in LP levels, as MDA, between controls and patients although they were able to show protein peroxidation in the patients. Signs of oxidative stress in fibromyalgia include high levels of oxidative damage to DNA in biopsy samples of patients with fibromyalgia.Reduced oxidative metabolism and mitochondrial abnormalities in fibromyalgia also support a mitochondrial defect as a cotributor (Ozgocmen,2006and Altindag,2006).Moreover, since mitochondria supply energy to the cell through oxidative phosphorylation, the lower level ATP that results from a low mitochondrial activity may explain the low exercise capacity and fatigue reported in patients with fibromyalgia(Altindag,2006). Glutathione is a compound classified as a tripeptide made of three amino acids: cysteine, glutamic acid, and glycine. Glutathione is an antioxidant that protects cells from toxins such as free radicalsa glutathione deficiency can have a devastating effect on the nervous system, causing such symptoms as lack of balance and coordination, and mental disorders(Fang,2004).The glutathione level of FM patients was significantly lower compared to the control group (Eisenger,1997) Moreover, symptoms that reflect an affected central nervous system such cognitive dysfunction, anxiety. stress and depression may be seen in FMS patients. Anxiety, stress and depression are also present in 30-45%of the patients with FMS(Yunus MB,2007), in there investigations, found decreased glutathione levels In the brains of mice accompanied by mood changes resembling anxiety following 6 hr of stress. Identical symptoms in FMS patients might have developed based on glutathione deficiency .Exposure of membrane lipids to free oxygen radicals in the presence of iron salts stimulates the process of lipid peroxidation(Akyol O,2001), one of the end products of lipid peroxidation is MDA, which reacts with thiobarbituric acid. Superoxide is spontaneously dismutated, to form H2O2 and O2.The possible mechanism of the increased MDA levels may be strongly related to the overproduction of ROS by the activated poly morphonuclear leukocytes(PMNL) in FM patients – similar to what has been emphasized in previous studies(KJ,2000). Uric acid, albumin account for the major contributions of total antioxidant capacity in human serum Contrary to what is traditionally considered a metabolically inert and waste compound of no physiological significance, uric acid can be oxidized following the nonenzymatic degradation ,and has been proven to be a selective antioxidant, capable especially, of reacting with hydroxyl radicals and hypochlorous acid.(Goldstein, 1979).Serum uric acid level had declined with the progression of the score, and also may be due to the usage of it as an antioxidant against peroxynitrite and other hypothesized FRs (Mattle,2004). 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 (Halliwell, 1988&Bourdon , 1999). 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 (Zilva&Philip, 2002).

CONCLUSION:

Patients with fibromyalgia are oxidatively streed according to change of LP and antioxidants. These result are consistent with the underlying hypothesis that there is an imbalance between ROS production and the antioxidant defense system in local ischemia of patientswith fibromyalgia.

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