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Antioxidant Status in Schizophrenic Patients

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Objective: To measure the concentration of total antioxidant status (TAS) in a number of chronic schizophrenic patients and to compare the results with those of healthy controls.

Design: Case-control study.

Setting: The College of medicine and Al-Salam hospital in Mosul.

Method: Twenty patients meeting DSM-IV criteria for schizophrenia, and twenty age and sex-matched healthy volunteers.

Total antioxidant status (TAS) was measured in both groups.

Result: Mean antioxidant status of the schizophrenic group was 1.15±0.39 mmol/l (Range 0.5 to 1.8 mmol/l) while those of the control group, mean was 1.96± 0.13 mmol/ l (Range 1.76 to 2.26 mmol/l). The difference between the two means was statistically significant (P<0.001).

Conclusion: The present study demonstrated that schizophrenic patients have low levels of TAS. It further emphasizes the growing consideration that oxidative damage may occur in schizophrenic patients that exhaust the antioxidant defense of the body leading to low levels of TAS.

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Oxygen free radicals are responsible for adverse effects of oxygen on living system. They produced from oxygen and include singlet oxygen, superoxide radical, peroxide ion, and hydroxyl radical[1].

A free radical is any chemical species possessing one or several mismatched electrons. These free radicals are in general, very active. They trigger chain reactions able to damage the different constituents of living organisms, including lipid, protein and DNA, it may be implicated in the occurrence of numerous diseases such as cancer, diabetes mellitus, atherosclerosis, neurodegenerative diseases (Alzheimer's disease and parkinsonism), rheumatoid arthritis, ischemic/reperfusion injury, obstructive sleep apnea, cardiovascular disease, hypertension and ageing[1-4].

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To this potential toxicity of free radicals the organism protects itself through different antioxidant defence systems[5]. The antioxidants neutralize the free radicals, stopping the chain of propagation and reducing their harmful effects on the body. They include a number of enzymes, notably superoxide dismutase, glutathione reductases and catalase, vitamin E and C, carotenoids, flavonoids, albumin, uric acid and glutathione[6,7]. In the case of a weakening of such an antioxidant defence or excess production of free radicals, a state of oxidative stress occurs[8].

Schizophrenia is a major mental disorder that has an incidence of 1% and affects young age in many cultures around the world. The etiology is unknown, the pathophysiology is complex, and most of the patients need treatment and care for the rest of their lives[9].

There is increasing evidence that oxidative injury contributes to pathophysiology of schizophrenia indicated by the increased lipid peroxidation products in plasma and CSF, altered levels of both enzymatic (superoxide dismutase, glutathione peroxidase and catalase) and non-enzymatic antioxidants (albumin, bilirubin and uric acid) in chronic schizophrenic patients[10]. Such abnormalities have been associated with certain clinical symptoms such as tardive dyskinesia, negative symptoms, neurological signs and poor premorbid function and CT scan abnormalities[11].

Studies to date concerning oxidative stress and schizophrenia been exploratory. Further elucidation of the role of free radicals and antioxidants in schizophrenia and its treatment will require systematic investigations[11].

Measurement of antioxidant status in schizophrenic patients have been performed in a number of studies by measuring an individual antioxidants such as glutathione, superoxide dismutase, glutathione peroxidase and catalase, uric acid, albumin or bilirubin.

Trial data evaluating the concentration of TAS in chronic schizophrenic patients are not available. Thus the present study was designed to measure the concentration of TAS in a number of chronic patients with schizophrenia and to compare the results with those of healthy controls.

METHOD

Twenty patients meeting DSM-IV criteria for schizophrenia and twenty age and sex-matched healthy volunteers were included in the study[12]. All participants gave consent form, and the study protocol was approved by the local research Ethics Committees of the University of Mosul and Mosul Health Administration. Each of the control and patient groups consist of 10 males and 10 females. They were 20 to 40 years in ages.

The patients are chronic schizophrenic on continuous neuroleptic therapy; the duration of the disease ranged between 3 to 17 years (mean 8.2±4.42). They are non-smokers non-alcohol drinkers with a good dietary intake.

No participant had a history of hyperlipidaemia, cardiovascular diseases, kidney disease, diabetes mellitus or any other systemic disease. Further exclusion criteria

were current use of antioxidants, vitamins and none of them had received medication during the study period and for 2 months before the study period other than neuroleptic drugs for the patients' groups. The total dietary intake of fruits and vegetables were good and not significantly different between the studied groups.

The study was carried out during fasting time in the morning.

Total antioxidant status (TAS) measurement was done in the immunology laboratory using antioxidant assay kit (Cayman Chemical Company-U.S.A.).

Statistical methods: Paired t-test was used to compare TAS of the patients and controls individuals and ages of the two groups. All values expressed as Mean $\pm$ SD and P value of ≤ 0.05 was considered to be statistically significant.

RESULT

The individuals in the schizophrenic and control groups were comparable in terms of age (Mean 29.65±6.40 year for schizophrenic group and 30±6.42 years for the control group ($P > 0.5$) and sex (10 males and 10 females in each group).

Mean antioxidant status of the schizophrenic group was 1.15±0.39 mmol/l (Range 0.5 to 1.8 mmol/l) while those of the control group, mean was 1.96± 0.13 mmol/l (Range 1.76 to 2.26 mmol/l). The difference between the 2 means was statistically significant ($P<0.001$).

DISCUSSION

This study revealed a low level of TAS in schizophrenic patients as compared to healthy controls. This may indicate that oxidative stress had occurred in such patients, which may have exhausted the antioxidant capacity of the body.

There is accumulating evidence of altered antioxidant enzyme activities (superoxide dismutase, glutathione peroxidase and catalase), increased lipid peroxidation products in plasma and CSF and low levels of esterified polyunsaturated essential fatty acids in schizophrenic patients[10]. This may indicate that oxidative injury contributes to pathophysiology of schizophrenia.

The brain is preferentially susceptible to oxidative damage since it is under very high oxygen tension and highly enriched in reactive oxygen species (free radicals), susceptible proteins, lipids and poor DNA repair[13].

Membrane dysfunction in schizophrenic patients can be secondary to free radical mediated pathology, and may contribute to specific aspects of schizophrenic symptoms and complications. Specifically, free radical mediated abnormalities may contribute to the development of a number of clinically significant consequences, including prominent negative symptoms, tardive dyskinesia, neurological signs and parkinsonian symptoms[14].

In the present study, level of TAS was measured in contrast to other studies which measured the antioxidant components of human body individually. Measuring total

antioxidant activity is better than measuring the individual antioxidant activity because the measurement of all known antioxidant in biological fluid is time consuming. Many antioxidants may be as yet undiscovered and the total activity may be greater than the sum of the individual antioxidants because of cooperative interaction[15].

The life style of some schizophrenic patients has pro-oxidative stress, such as, smoking, drinking, high caloric intake and no physical activity; added to that, treatment with pro-oxidant drugs[9]. The patients in this study were selected as non-smokers and non-drinkers, non-high caloric intake with a good fruit and vegetable nutrient consumption, in order to minimize the impact of these factors upon the results. The patients were on neuroleptic therapy only; no other drugs were taken by the patients that may interfere with the result.

In the present study, low levels of TAS were demonstrated in the schizophrenic patients. The patients were on anti schizophrenic (neuroleptic) therapy. Patients on Free drug therapy were not assessed because of ethical consideration; it is difficult to keep chronic schizophrenic patients for a period of time with no treatment. Some studies have assessed the concentration of some antioxidant component in drug free period and in drug therapy period. Akyol et al reported a decreased superoxide dismutase activity and an increased of thiobarbituric acid reactive substances levels in schizophrenic patients[16]. No effect of dose and duration of treatment with chlorpromazine on the results were observed. Reddy et al reported that a defect in the antioxidant defense system in schizophrenic patients occur early in the course of illness and is independent of treatment effects[17]. Yao et al showed that male patients with schizophrenia either during haloperidol treatment or in a drug-free condition had significantly lower levels of both plasma albumin and bilirubin compared with age- and sex-matched healthy volunteers[18].

CONCLUSION

The present study demonstrated that schizophrenic patients have low levels of TAS. It further emphasizes the growing concern that oxidative damage may occur in schizophrenic patients that exhaust the antioxidant defense of the body leading to a low levels of TAS.

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