Role of antioxidants in generalised anxiety disorder and depression

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ABSTRACT

Background: Anxiety and depression form commonest stress-induced psychiatric disorders. To combat the biochemical changes which occur as a result of stress, there is antioxidant defence in the biological system. Secondary defence is by the nonenzymatic antioxidants like vitamins E (alphatocopherol), C (ascorbic acid), and β-carotene. Therefore, the authors interest was aroused to examine the status of these antioxidants in the biological system of patients suffering from stress-induced psychiatric disorders.

Aims: This study was carried out to find out whether patients with generalized anxiety disorder (GAD) and depression have any difference in blood serum levels of vitamins A (β-carotene), C, and E in comparison to the normal healthy control group and whether supplementation of adequate doses of vitamins A (β-carotene), C, and E leads to improvement in anxiety and depression and reduction in scores of the patients.

Materials and Methods: Eighty subjects in the age group of 20–60 years, who attended a psychiatric clinic of a private hospital and who met inclusion and exclusion criteria of the study and consented for psychological evaluation and blood screening to find out the serum levels of vitamins A, C, and E, were included in the study. Approval was sought from the institutional ethics committee for collecting the blood sample of these subjects before and after vitamins A, C, and E supplements given for a period of 6 weeks.

Statistics Analysis: It was observed that patients with GAD and depression had significantly lower levels of vitamins A, C, and E in comparison to healthy controls. After dietary supplementation of these vitamins for a period of 6 weeks, a significant reduction in anxiety and depression scores of patients was observed (P<0.001). A significant increase in the blood levels of antioxidants was observed in patients (P<0.05) except that of vitamin E in the group of depressed patients.

Results and Conclusion: The findings suggest that antioxidant supplement therapy as an adjuvant therapy is useful in patients with stress-induced psychiatric disorders and the results have been discussed.

Key words: Depression, generalized anxiety disorder, vitamin A, C, E

INTRODUCTION

In the era of scientific developments and technological advances, cut throat competitions, thrive for superiority, and increasing lifestyle demands have made human population more prone for stressful disorders and with the advent of media, the news of catastrophes and natural calamities across the globe has further increased the feeling of insecurity in human minds.

When we talk about stress in day-to-day life, we are not talking about disorders because now it is a part of life which may reflect in the form of aging but not disorders. Disorder
is said to be present when some of these stressors are continuously acting over a period of time and have started showing up in the form of certain symptoms/symptom clusters, which persist and reflect work efficiency, mood, sleep, and appetite.

There have been a number of studies which have evaluated the role of antioxidants and oxidative stress leading to varieties of health problems including leukemia,[1] thalassemia,[2] ischemic stroke,[3] hemodialysis,[4] myocardial infarction,[5,6] rheumatoid arthritis,[7] critically ill patients,[8] and postmenopausal women,[9] Schizophrenia[10,11,13] and depression.[12]

Although there are a wide range of stress-induced psychiatric disorders, anxiety is the core symptom of all stress-induced disorders and generalized anxiety disorder (GAD) is the commonest syndromal presentation. The majority of patients with GAD have an overlap of depressive symptoms vis-a-vis patients suffering from depression also have features of anxiety and a sizable numbers of patients suffer from mixed anxiety depression syndrome. Patients fulfilling the criteria of GAD (F 41.1) and depressive episode (F 32.0, F 32.1, and F 32.2) according to the ICD X classification fall under the category of these disorders.

Anxiety is a response to a threat that is unknown, internal, vague, or conflictual, it is an altering signal, it warns of impending danger and enables a person to deal with a threat. Depression (depressive episode) is another commonest psychiatric diagnosis in patients attending psychiatric clinics, psychiatric patients, departments, or mental health facilities.

Stress places an additional demand on the body, in terms of nutrition. In a condition of stress, there is an increase in adrenal production and mobilization, utilization of vitamins and minerals, e.g. vitamin C, vitamin E, magnesium, potassium, and micronutrients, which further accelerates metabolism of proteins, fats, and carbohydrates, producing quick energy to overcome stress.

To combat the biochemical changes which occur as a result of stress, there is antioxidant defence in the biological system. The primary defence is by enzymatic antioxidants such as superoxide dimutase, glutathione peroxidase, catalase, nicotanamide adenine diphosphate, glutathione transferase and glutathione reductase, while secondary defence is by the nonenzymatic antioxidants such as vitamin E (alphatocopherol), vitamin C (ascorbic acid), β-carotene, minerals, and trace elements like zinc.

Therefore, the authors’ interest was aroused to examine the status of these antioxidants in the biological system of patients suffering from GAD, depression, and of healthy individuals and to examine whether supplementation of antioxidants leads to change in their psychiatric status.

OBJECTIVES

In view of the above information and literature available on the subject, very little work has been done in India to explore the role of antioxidants in combating oxidative stress in GAD and depressive disorder (neurotic depression). Hence the study was carried out with the following aims:

1. To find out whether patients with GAD have any difference in blood serum levels of vitamin A, (β-carotene), vitamin C, and vitamin E in comparison to the normal healthy control group
2. To find out whether patients with depressive disorder have any difference in blood serum levels of vitamin A (β-carotene), vitamin C, and vitamin E in comparison to the normal healthy control group
3. To find out whether supplementation of adequate doses of vitamin A (β-carotene), vitamin C and vitamin E leads to improvement in anxiety and depression and reduction in scores of the patients.

MATERIALS AND METHODS

In order to achieve the above-mentioned goals, 80 subjects in the age group of 20–60 years, who attended the psychiatric clinic of a private hospital in Jaipur and who consented for psychological evaluation and blood screening to find out the serum levels of vitamins A, C, and E, were included in the study. Approval was sought from the institutional ethics committee for collecting the blood sample of these subjects before and after the vitamins A, C, and E supplements given for a period of 6 weeks.

Forty patients of GAD, 40 patients suffering from depression, and 20 healthy controls were included in the study. Patients attending the outpatient clinic of the hospital for treatment were included after obtaining informed consent.

The patients were diagnosed in the OPD of the hospital as per ICD-10 diagnostic criteria and a specially designed performa was filled up.

Inclusion criteria

All patients included in the study met the following inclusion criteria: diagnosis of GAD and depression as per ICD X (International Classification of Diseases X version, WHO), age range 20–60 years of age. All patients of Groups A, B, and C were matched on sociodemographic data (age, sex, education, and economic status) and were comparable and treatment naive for last 6 months was diagnosed for the first time.

Exclusion criteria

Any patient meeting one or more of the following were
excluded from the study: any chronic physical illness (diabetes, coronary artery disease, chronic lung disease, cancer, etc.), history of drug dependence, exposed to any antioxidant therapy in past and women with symptoms of postmenopausal syndrome (hot and cold flushes).

Patients fulfilling the above inclusion and exclusion criteria were subjected to psychiatric and nutritional evaluation. They were administered Max Hamilton Anxiety Rating Scale (HAM-A) and Max Hamilton Depression Rating Scale (HAM-D) to evaluate the level of anxiety and depression, a 24 h recall method and a food frequency questionnaire were employed to ensure that a patient consumed similar diet throughout the study period. Data were recorded at base time visit and after 6 weeks; however, patients were clinically evaluated by the psychiatrist once in 2 weeks and the investigator was blinded to the psychiatric evaluation.

All patients were divided in three groups.
• Group A: 40 patients with diagnosis of depression
• Group B: 40 patients with diagnosis of GAD
• Group C: 20 normal healthy subjects chosen from care givers of patients who were found to be not suffering from anxiety or depression on clinical evaluation by the psychiatrist.

Out of Group A which was further subdivided randomly into the control group and the experimental group. Patients in the control group were given regular antidepressant treatment (escitalopram, 10–20 mg per day) by the psychiatrist while patients included in the experimental group were given similar doses of antidepressants and supplementation of vitamins A, C, and E in a capsule and a tablet form. The antioxidant capsules induced 600 mg/day of vitamin A, 1000 mg of vitamin C/day, and 800 mg of vitamin E/day. Vitamins A and C were in the form of tablets containing 300 mg and 500 mg each, respectively, while vitamin E was in the form of capsules and 400 mg in each capsule, all of them were given twice a day at an interval of 12 h. Similarly, Group B was further subdivided into the control group and the experimental group. Patients in the control group were given regular antianxiety treatment by the psychiatrist while patients included in the experimental group were given regular antianxiety treatment (alprazolam 1–2 mg per day in divided doses) and supplementation of vitamins A, E, and C in capsule and tablet forms. The antioxidants included 600 mg/day of vitamin A, 1000 mg/day of vitamin C, and 800 mg/day of vitamin E. Vitamins A and C were in the form of tablets containing 300 mg and 500 mg of each, respectively, while vitamin E was in the form of capsules and 400 mg in each capsule all of them were given twice a day at an interval of 12 h. The antioxidants used for the study were prepared by a lab pharmacy as per authors’ requirements and it was not any company sponsored trial.

The blood sample was drawn to evaluate the serum levels of antioxidants, biochemical estimation of serum levels of vitamins A (β-carotene), C, and E were done using the standard techniques of estimations. Data were subjected to statistical evaluation.

RESULTS

The experimental groups (Group A patients with GAD, Group B patients with depression, and Group C healthy controls) were statistically comparable on socio-demographic data. Biochemical estimations and their comparison with the healthy control group are provided.

DISCUSSION

It is evident from Table 1 that administration of antioxidants for a period of 6 weeks to a patient with GAD led to increased levels of antioxidants to significant levels while comparison of pretest levels of antioxidants in the experimental group in vitamin A scores. All the antioxidant levels (vitamins A, C, and E) increased significantly after 6 weeks in the experimental group. In a group of depressed patients, preantioxidant administration scores of vitamins

| Table 1: Blood antioxidant levels in patients with GAD, pre- and post-therapy |
|---|---|---|---|---|---|---|---|
| N | Vitamins | Exp, N = 21 | Cont, N = 19 | t | df | P | Sig. |
| Pre | A | 39.20 | 82.93 | 9.97 | 18 | <0.001 | S |
| C | 0.61 | 0.62 | 0.00 | 18 | <1.00 | NS |
| E | 0.55 | 0.56 | 0.36 | 18 | <0.720 | NS |
| Post | A | 48.68 | 88.24 | 9.01 | 19 | <0.001 | S |
| C | 0.86 | 0.65 | 3.55 | 18 | <0.002 | S |
| E | 0.70 | 0.58 | 2.45 | 18 | <0.024 | S |

GAD - Generalized anxiety disorder

| Table 2: Blood antioxidant levels in patients with depression, pre- and post-therapy |
|---|---|---|---|---|---|---|---|
| N | Vitamins | Exp, N = 20 | Cont, N = 20 | t | df | P | Sig. |
| Pre | A | 90.99 | 84.69 | 0.39 | 19 | <0.789 | NS |
| C | 0.76 | 0.74 | 0.27 | 19 | <0.789 | NS |
| E | 0.54 | 0.48 | 0.69 | 19 | <0.495 | NS |
| Post | A | 140.56 | 89.2 | 81.42 | 19 | <0.011 | S |
| C | 0.89 | 0.80 | 1.54 | 19 | <0.139 | NS |
| E | 0.55 | 0.49 | 1.08 | 19 | <0.290 | NS |

| Table 3: Pre- and post-treatment scores of anxiety and depression in two groups |
|---|---|---|---|---|---|---|---|
| Psychological test score | Exp, N = 21 | Cont, N = 19 | t | df | P | Sig. |
| HAM A GAD | 36.57 | 37.29 | 0.51 | 16 | <0.611 | N |
| Post-treatment | 3.57 | 3.76 | 1.56 | 16 | <0.001 | N |
| Psychological test score | Exp, N = 20 | Cont, N = 20 | t | df | P | Sig. |
| HAM D score | 24.2 | 25.4 | 4.46 | 19 | <0.451 | N |
| pre-treatment | 2.15 | 12.10 | 15.93 | 19 | <0.001 | S |
A, C, and E were not significantly different and they were increased after 6 weeks administration. Vitamin A levels were significantly higher in the experimental group [Table 2]. Table 3 shows that pretreatment scores of GAD and depression were not significantly different; however, there was a reduction in anxiety and depression scores in both the groups but in the experimental group which received the combination of antioxidants and antidepressants/antianxiety medication the reduction in scores was at a significant level showing usefulness of adjuvant antioxidant therapy with regular psychotropic treatment as indicated.

REFERENCES

1. Ahmad R, Tripathi AK, Tripathi P, Singh S, Singh R, Singh RK. Malondialdehyde and protein carbonyl as biomarkers for oxidative stress and disease progression in patients with chronic myeloid leukemia. In Vivo 2008;22:525-8.
2. Ghone RA, Kumbar KM, Suryakar AN, Katkam RV, Joshi NG. Oxidative stress and disturbance in antioxidant balance in beta thalassemia major. Indian J Biochem 2008;23:337-40.
3. D’Souza B, D’Souza V, Sowmya S, Seema G, Hemalatha CN, Anu M, et al. A comparative study on oxidative stress and antioxidant status in ischemic stroke patients with and without diabetes. Indian J Biochem 2008;23:218-22.
4. Bhogade RB, Suryakar RN, Joshi NG, Patil RY. Effect of vitamin E supplementation on oxidative stress in hemodialysis patients. Indian J Biochem 2008;23:233-7.
5. Patil N, Chavan V, Karnik ND. Antioxidant status in patients with acute myocardial infarction. Indian J Biochem 2007;22:45-51.
6. Dwivedi VK, Chandra M, Misra PC, Misra MK. Effect of vitamin E on platelet enzymatic anti-oxidants in the patients of myocardial infarction. Indian J Biochem 2005;20:21-5.
7. Vijayakumar D, Suresh K, Manoharan S. Lipid peroxidation and antioxidant status in blood of rheumatoid arthritis patients. Indian J Biochem 2006;21:104-6.
8. Mishra V, Baines M, Wenstone R, Shenkin A. Markers of oxidative damage, antioxidant status and clinical outcome in critically ill patients. Ann Clin Biochem 2005;42(Pt 4):269-76.
9. Vural P, Akgül C, Cebaz M. Effects of menopause and tibolone on antioxidants in postmenopausal women, Ann Clin Biochem 2005;42(Pt 3):220-3.
10. Dadheech G, Mishra S, Gautam S, Sharma P. Evaluation of antioxidant deficit in schizophrenia. Indian J Psychiatry 2008;50:16-20.
11. Singh OP, Chakraborty I, Dasgupta A, Datta S. A comparative study of oxidative stress and interrelationship of important antioxidants in haloperidol and olanzapine treated patients suffering from schizophrenia. Indian J Psychiatry 2008;50:171-6.
12. Sathy aranayaya Rao TS, Asha MR, Ramesh BN, Jagannatha Rao KS. Understanding nutrition, depression and mental illnesses. Indian J Psychiatry 2008;50:77-82.
13. Dadheech G, Mishra S, Gautam S, Sharma P. Oxidative stress, a-ocopherol, ascorbic acid and reduced glutathione status in schizophrenics. Indian J Biochem 2006;21:218-22.

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