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Letter to the Editor

## Increased oxidative stress suggested by low serum vitamin E concentrations in patients with chronic fatigue syndrome

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### Abstract

Serum  $\alpha$ -tocopherol concentrations were determined in 50 patients with chronic fatigue syndrome (CFS) and 40 control subjects (Control). Prevalence of each or any coronary risk factor was not significantly different between CFS and Control. CFS had significantly lower  $\alpha$ -tocopherol concentrations than Control. The concentrations were significantly lower in the subjects with any coronary risk factors than those without in CFS as well as Control. Even among the subjects with any coronary risk factors and also among those without, CFS had significantly lower  $\alpha$ -tocopherol concentrations than Control. In conclusion, CFS had significantly lower  $\alpha$ -tocopherol concentrations irrespective of coronary risk factors than Control, suggesting the presence of increased oxidative stress in CFS.

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Chronic fatigue often develops without any definite causes, frequently disturbs daily life severely, and is generally classified as chronic fatigue syndrome [1]. The etiology, risk factors and pathophysiology remain unclarified, although various factors have been implicated in the genesis [1,2]. Recently oxidative stress has been suggested to be involved in the pathogenesis of the chronic fatigue syndrome [3,4]. Oxidative stress affects physical and mental function through various redox-sensitive signaling systems [4]. Vitamin E is a major endogenous lipid-soluble anti-oxidative substance, and consumed during the lipid peroxidation process. A significant positive correlation between serum vitamin E ( $\alpha$ -tocopherol) concentrations and specific activity of superoxide dismutase, a major anti-oxidative enzyme, has been reported [5].

In the present study, serum vitamin E ( $\alpha$ -tocopherol) concentrations and presence of any coronary risk factors were determined in patients with chronic fatigue syndrome.

The study population comprised 50 patients (25 men and 25 women, younger than 50 years) with chronic fatigue syndrome (CFS) and age- and sex-matched 40 control subjects (19 men and 21 women) (Control). Subjects on vitamin E supplementation or receiving antioxidants were excluded. Also, subjects receiving antihypertensive, lipid-lowering, blood sugar-lowering or anti-depressive drugs have not been included. All enrolled participants gave informed consent and the study protocol was approved by the ethics committee of the institution.

CFS was diagnosed according to the revised case definition by Fukuda et al. [6].

Serum  $\alpha$ -tocopherol concentrations were determined using high-performance liquid chromatography and expressed as mg/g total lipids (total cholesterol and triglyceride) [7].

No significant difference was noted in the prevalence of any coronary risk factors including smoking, hypertension, hyper-LDL-cholesterolemia, hypo-HDL-cholesterolemia, hyper-triglyceridemia, fasting hyperglycemia and obesity, between the groups. Also, subjects with any coronary risk factors in CFS (60%) were as prevalent as in Control (60%).

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The  $\alpha$ -tocopherol concentrations (mg/g lipids) were significantly ( $p < 0.001$ ) lower in CFS ( $3.03 \pm 0.72$ ) than in Control ( $3.78 \pm 0.66$ ). The concentrations were significantly lower in the subjects with coronary risk factors than those without them in CFS as well as Control. The concentrations were significantly lower in CFS than in Control among the subjects without coronary risk factors ( $3.37 \pm 0.67$ ,  $n = 20$  vs.  $4.17 \pm 0.84$ ,  $n = 16$ ,  $p < 0.01$ ) and also among the subjects with coronary risk factors ( $2.80 \pm 0.67$ ,  $n = 30$  vs.  $3.52 \pm 0.35$ ,  $n = 24$ ,  $p < 0.001$ ).

Oxidative stress has been shown to be increased in the presence of various coronary risk factors such as smoking, hypertension, lipid metabolic disorders, diabetes mellitus and obesity. As we have reported previously [7,8], serum  $\alpha$ -tocopherol concentrations were low in the presence of various coronary risk factors as well as aging among apparently healthy subjects. The present study clearly demonstrated that oxidative stress indicated by serum  $\alpha$ -tocopherol concentrations was significantly greater in CFS than in Control among both subjects with and without coronary risk factors. Presence of coronary risk factors could not explain the reason for the exaggerated oxidative stress in CFS as compared with Control, although the presence of coronary risk factors should generally increase oxidative stress. Anti-oxidative therapy or oxidative stress reduction with administration of anti-oxidative drugs in addition to aggressive control of coronary risk factors including smoking cessation, exercise and diet, may be effective as a therapy for CFS. Whether augmented oxidative stress is one of the causes underlying the pathogenesis of CFS or effects by chronic fatigue remains unknown. It is possible that oxidative stress is an important mediator in the vicious cycle

aggravating chronic fatigue even if oxidative stress is not the primary cause for CFS. Further investigation will be needed to clarify the causal relationship between oxidative stress and CFS.

In conclusions, CFS had significantly lower serum concentrations of  $\alpha$ -tocopherol, antioxidant vitamin, suggesting the presence of increased oxidative stress in CFS. The low level of  $\alpha$ -tocopherol appeared to be not attributable exclusively to the presence of coronary risk factors. Increased oxidative stress may be involved in the pathogenesis of CFS.

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