Changes In Worker Fatigue After Vitamin C Administration

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Abstract

Objective : In recent research, the role of oxidative stress has been an important factor in fatigue. The principal objective of this study was to evaluate changes in fatigue in workers after vitamin C administration.

Methods : We consecutively examined 44 workers who work regularly. They were orally administered 6 g of vitamin C daily for 2 weeks. We then investigated the demographic data and assessed any changes in the patients' fatigue scale (VAS, FSS) and blood tests (vitamin C, HgA1c, CRP, AST, ALT, r-GTP, cortisol).

Results: In fatigue, both VAS and FSS improved after vitamin C administration ($p<0.005$). In blood tests, AST, ALT, r-GTP, HgA1c, CRP, and cortisol were reduced after vitamin C administration ($p<0.005$).

Conclusions : Vitamin C administration reduced fatigue symptoms and improved blood tests with fatigue in workers.

Key words : fatigue, vitamin C, workers, visual analog scale, fatigue severity scale

Introduction

Fatigue is extremely common in both primary and secondary care patients. Everybody experiences this symptom during life, even in the absence of any disease. However, doctors, as well as the general population, tend to neglect symptoms of fatigue, attributing it not to illness but to a normal response to the exertions of life.

The relevant rates of fatigue prevalence vary considerably, depending on whether the fatigue being examined is characterized by tiredness, weakness, or exhaustion. The phenomenon of fatigue is usually divided into fatigue, chronic fatigue, and chronic fatigue syndrome. The boundary between fatigue, chronic fatigue, and chronic fatigue syndrome is also fairly arbitrary, as these are obviously subjective terms.[1]

According to many researchers, the prevalence of fatigue was more than 27%, whereas chronic fatigue had a prevalence of 1-10%, and chronic fatigue syndrome evidenced a prevalence of 0.2-0.7% in the general population.[2-6] In Korea, Kim et al. reported that the prevalence of chronic fatigue was 8.4%, and that chronic fatigue syndrome occurred in 0.6% of the general population.[7]

The prevalence and severity of fatigue in workers is substantially higher than in the general population, due to the stress inherent to the modern work environment. Also, many workers have many diseases or risk factors of many diseases. If workers don't take early steps to reduce their fatigue, they may experience serious difficulty and reduced work efficiency.

Despite considerable worldwide efforts, no single etiology has been discovered to explain fatigue symptoms, and the pathophysiology of fatigue remains unclear. It appears likely that multiple factors promote its development, sometimes with the same factors both causing and being caused by fatigue.

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A great number of recent studies have demonstrated that oxidative stress may be involved in its pathogenesis. The role of oxidative stress in fatigue is an important area for current and future research, as it suggests the use of antioxidants in the treatment of fatigue. Specifically, the dietary supplements glutathione, N-acetylcysteine, alpha-lipoic acid, oligomeric proanthocyanidins, Ginkgo biloba, vitamin C, and Vaccinium myrtillus (bilberry) may exert beneficial effects.[8,9]

Vitamin C is a powerful antioxidant, and exists in a variety of fruits and vegetables. Fatigue is the initial symptom of experimental scurvy, and a marginal vitamin C deficiency may induce fatigue, lassitude, and depression, all of which have been shown to respond to supplementation.[10-13] Although some early reports have failed to find any evidence of decreased serum levels of vitamin C in chronic fatigue syndrome (CFS) patients, no current assay technique for the measurement of ascorbic acid is entirely satisfactory; therefore this single report of serum vitamin C levels arguably does not eliminate the possibility that a subset of chronic fatigue syndrome patients may be vitamin C-deficient.[14,15]

The principal objective of this study was to evaluate changes in fatigue in workers after vitamin C administration.

Materials and Methods

Study subjects

We consecutively examined 44 workers who work regularly from 9 am to 6 pm. The exclusion criteria included the following: pregnancy, cancer, cardiovascular diseases, and infection.

Method

Written consent was obtained from all study subjects. They were orally administered 6 g of vitamin C daily for 2 weeks. We then investigated the demographic data and assessed any changes in the patients' fatigue scale and blood tests.

The demographic data included the sex, age, and exercise status of the patients. The fatigue scales used included both a fatigue severity scale (FSS) and a visual analogue scale (VAS).[16] The blood tests conducted included: vitamin C, Hemoglobin A1c(HgA1c), C-reactive protein (CRP), aspartate aminotranferase (AST), alanine aminotranferase (ALT), r-GTP, cortisol.

Statistical analysis

The fatigue scale and blood test levels prior to and after vitamin C administration were compared via paired t-tests. A p-value of less than 0.05 was considered to be statistically significant.

Results

Demographic data

The demographic data (sex, age, smoking, alcohol, and exercise) are shown in **Table 1** (opposite). The subjects included 27 males (67.5%), 13 females (32.5%). The patients' mean ages were 33.83±5.63 years. No patients were excluded due to side effects of vitamin C.

Fatigue scale

The fatigue scales prior to and after vitamin C administration are shown in **Table 2** (opposite). VAS improved from 5.60±2.13 to 4.72±1.96 after vitamin C administration ($p=0.001$). Also, FSS improved from 5.04±1.41 to 3.44±1.06 after vitamin C administration ($p<0.005$).

Blood tests

The blood tests prior to and after vitamin C administration are shown in **Table 3** (opposite). The vitamin C level in the blood increased from 42.9±12.4 μmol/L to 68.60±26.57 μmol/L after vitamin C administration ($p=0.001$). In liver function tests, the subjects reported significantly lower levels of AST, ALT, and r-GTP following vitamin C administration ($p<0.005$).

Table 1. Demographic Data.

Demographic factor	No(%)	
Sex	Male	27.0(67.5%)
	Female	13.0(32.5%)
Age(mean±SD)		32.83±5.63 years
Smoking		20.0(50%)
Alcohol		32.0(80%)
Exercise		25.0(62.5%)

Table 2. Fatigue Scale after vitamin C administration.

	before vitamin C	after vitamin C	p-value
Fatigue Severity Scale	5.04±1.41	3.44±1.06	0.000
Visual Analogue Scale	5.60±2.13	4.72±1.96	0.011

Table 3. Blood test after vitamin C administration.

	before vitamin C	after vitamin C	p-value
Hemglobin A1c (%)	5.46±0.38	4.88±0.33	0.000
Cortisol (μg/dL)	11.64±3.83	8.80±2.75	0.000
Aspartate aminotranferase (U/L)	28.09±19.92	23.85±7.65	0.000
Alanine aminotranferase (U/L)	28.45±20.66	25.12±17.75	0.011
r-GTP (U/L)	32.59±28.92	25.93±18.05	0.000
C-reactive protein(mg/L)	0.11±0.20	0.05±0.07	0.033
vitamin C (μmol/L)	42.90±12.4	68.60±26.57	0.000

The cortisol levels in the blood were reduced from 11.64±3.83 μg/dL to 8.80±2.75 μg/dL, and CRP levels were reduced from 0.11±0.20 mg/L to 0.05±0.07mg/L after vitamin C administration ($p<0.005$). Also, HgA1C levels were reduced from 5.46±0.38% to 4.88±0.33% after vitamin C administration ($p<0.005$).

Discussion

Fatigue is a common experience, and most people experience feelings of fatigue during their regular lives. Thus, fatigue is a property both of normal experience and of certain diseases. We believe that fatigue should be considered a symptom or disease in cases in which the fatigued person perceives him- or herself to be ill. If an individual experiences fatigue symptoms for an extended period, that individual may be suffering from a disease of which fatigue is a symptom. Particularly in workers, the prevalence of fatigue symptoms is now growing at a rapid rate, due principally to the heavy stress inherent to the modern work environment.

The etiology of fatigue remains unclear; however, a number of recent studies have demonstrated that oxidative stress may be involved in its pathogenesis.[17] The role of oxidative stress in fatigue is an important area for current and future research, as it suggests that antioxidants might prove useful in the management of fatigue.[18]

In this study, the subjects reported significant improvements in fatigue following vitamin C administration. Vitamin C is a powerful antioxidant and an essential cofactor for carnitine biosynthesis.[19] Also, according to American reports, approximately 15% of American adults are deficient in vitamin C.[20] Twenty-five years ago, this percentage was far lower, at approximately 3-5% of American adults.[21] Thus, modern people appear to have an unfulfilled vitamin C requirement.

In this study, subjects evidenced improvements in some blood levels (AST, ALT, r-GTP, cortisol, CRP, HgA1c) after vitamin C administration.

AST, ALT, and r-GTP, which are associated with liver function and cortisol, were all hormone-related. Reduced blood levels of these compounds on these tests were associated with improvements in subjects' fatigue.

C-reactive protein (CRP) is an acute phase reactant which is secreted by the liver in response to inflammatory cytokines. It was identified recently as a stronger predictor of cardiovascular events than LDL cholesterol.[22] Recently, a meta-analysis indicated that individuals in the top third of CRP plasma concentrations (2.4 mg/L) were 2 times as likely to have coronary heart disease (CHD) as compared to those in the lowest third of CRP concentrations (1.0 mg/L).[23] In our study, the blood levels of subjects' CRP decreased after vitamin C administration. This result was reminiscent of several other studies showing that the antioxidant components in fruit and vegetables, i.e., carotenoids, vitamin E, vitamin C, and flavonoids, may contribute to this anti-inflammatory effect.[24,25] The consumption of a diet low in antioxidants was shown to result in inflammation, whereas antioxidant supplementation has been shown to ameliorate inflammation.[26]

HgA1c is an integrated measure of plasma glucose, and is intended to represent glucose concentrations in blood averaged over a 2-3 month period. In 1987, Cerami et al. summarized the interaction of glucose with protein and its association with human aging and diabetic disorders.[27] Additionally, a reduction in glycation has been suggested to prevent diabetic disorder and to retard the aging process. Although the duration of this study was only 2 weeks, the blood level of HgA1c was decreased by 0.58%. These results were reminiscent of those of other studies.[28,29] In the report of Khaw et al., a lowering of 0.2 in hemoglobin glycation in the population would reduce total mortality by 10%.[30]

In workers, fatigue is a very important problem. If workers can resolve this problem at an early time, they can help prevent fatigue-associated diseases and increase their work efficiency. We believe, after reviewing the relevant results, that antioxidants such as vitamin C may serve to reduce fatigue in workers.

Reference

1. Ranjith G: Epidemiology of chronic fatigue syndrome. *Occupat Med*, 2005; 55: 13-9.
2. Meltzer H, Grill D, Petticrew M, Hinds K: The prevalence of psychiatric morbidiy amongst adults living in private households. London: *HMSO,* 1995.
3. Lloyd AR, Hickie I, Boughton CR, Spencer O, Wakefield D: Prevalence of chronic fatigue syndrome in an Australian population. *Med J Aust,* 1990; 153: 522-8.
4. Bates DW, Schmitt W, Buchwald D, et al: Prevalence of fatigue and chronic fatigue syndrome in a primary care practice. *Arch Intern Med*, 1993; 153(24): 2759-65.
5. Kroenke K, Wood DR, Mangelsdorff AD, Meier

NJ, Powell JB. Chronic fatigue in primary care. Prevalence, patient characteristics, and outcome. *JAMA,* 1988; 260(7): 929-34.
6. Hickie IB, Hooker AW, Hadzi-Pavlovic D, et al: Fatigue in selected primary care settings: sociodemographic and psychiatric correlates. *Med J Aust,* 1996; 164(10): 585-8.
7. Kim CH, Shin HC, Won CW: Prevalence of chronic fatigue and chronic fatigue syndrome in Korea: community-based primary care study. *J Korean Med Sci,* 2005; 20(4): 529-34
8. Jung GC, Yeom CH, Cho BC, Choi JS: The effect of intravenous vitamin C in people with fatigue. *J Korean Acad Fam Med,* 2006; 27(5): 391-5
9. Grant JE, Veldee MS, Buchwald D: Analysis of dietary intake and selected nutrient concentrations in patients with chronic fatigue syndrome. *J Am Diet Assoc,* 1996; 96: 383-6.
10. Hodges RE, Hood J, Canham JE, Sauberlich HE, Baker EM: Clinical manifestations of ascorbic acid deficiency in man. *Am J Clin Nutr,* 1971; 24: 432-43.
11. Kinsman RA, Hood J: Some behavioral effects of ascorbic acid deficiency. *Am J Clin Nutr,* 1971; 24: 455-64.
12. Heseker H, Kubler W, Pudel V, Westenhoffer J: Psychological disorders as early symptoms of a mild-to-moderate vitamin deficiency. *Ann N Y Acad Sci,* 1992; 669: 352-7.
13. Gerster H: The role of vitamin C in athletic performance. *J Am Coll Nutr,* 1989; 8: 636-43.
14. Grant JE, Veldee MS, Buchwald D: Analysis of dietary intake and selected nutrient concentrations in patients with chronic fatigue syndrome. *J Am Diet Assoc,* 1996 Apr; 96(4): 383-6.
15. Lee W, Davis KA, Rettmer RL, Labbe RF. Ascorbic acid status: biochemical and clinical considerations. *Am J Clin Nutr,* 1988; 48: 286-290.
16. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The Fatigue Severity Scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol,* 1989; 46: 1121-3.
17. Logan AC, Wong C: Chronic fatigue syndrome: oxidative stress and dietary modifications. *Altern Med Rev,* 2001; 6(5): 450-9.
18. Werbach MR: Nutritional strategies for treating chronic fatigue syndrome. *Altern Med Rev,* 2000; 5(2): 93-108.
19. Reda E, D'Iddio S, Nicolai R, Benatti P, Calvani M: The carnitine system and body composition. *Act Diabetol,* 2003; 40: S106-113.
20. Hampl JS, Taylor CA, Johnston CS: Vitamin C deficiency and depletion in the United States: the Third National Health and Nutrition Examination Survey, 1988–1994. *Am J Pub Health,* 2004; 94: 870-875.
21. U.S. Department of Health and Human Services: Hematological and nutritional biochemistry reference data for persons 6 months-74 years of age. United States, 1976–.1980. In *Advance Data from Vital and Health Statistics, No. 83-1682* Hyattsville, Md. *National Center for Health Statistics;* 1982:124-139.
22. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR: Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. *N Engl J Med,* 2001; 347: 1557–65.
23. Danesh J, Whincup P, Walker M, et al: Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses. *BMJ,* 2000; 321: 199–204.
24. Calfee-Mason KG, Spear BT, Glauert HP: Vitamin E inhibits hepatic NF-B activation in rats administered the hepatic tumor promoter, phenobarbital. *J Nutr,* 2002; 132: 3178-85.
25. Meydani, SN, Wu D, Santos, MS, Hayek MG: Antioxidants and immune response in aged persons: overview of present evidence. *Am J Clin Nutr,* 1995; 62: 1462S–76S.
26. Sánchez-Moreno C, Cano MP, de Ancos B, et al: High-pressurized orange juice consumption affects plasma vitamin C, antioxidative status and inflammatory markers in healthy humans. *J Nutr,* 2003; 133(7): 2204-9.
27. Cerami A, Vlassare H, Brownlee M: Glucose and aging. *Sci Am,* 1987; 256(5): 90–6.
28. Krone CA, Ely JTA: Ascorbic acid, glycation, glycohemoglobin and aging. *Med Hypoth,* 2004; 62: 275-9
29. Sargeant LA, Warham NJ, et al: Vitamin C and hyperglycemia in the European prospective investigation in cancer- Norfolk (EPIC-Norfolk) study. *Diabetes Care,* 2000; 23(6): 726–32.
30. Khaw KT, Wareham N, et al: Glycated haemoglobin, diabetes, and mortality in men in Norfolk cohort of European Prospective Investigation of Cancer and Nutrition (EPIC-Norfolk). *BMJ,* 2001; 322: 1-6.