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Preface

The number of individuals with stress-related diseases, such as chronic fatigue or burn-out syndrome, continues to increase. As a consequence, the World Health Organization (WHO) has now declared stress to be the biggest health hazard in the 21st century.

The Literature Service of Orthomol® Vital has collected current information material for health professionals on this subject. The enclosed summaries of various publications from renowned scientific journals will give you a general overview.

The supplementation of micronutrients for the specific support of individuals with stress-related diseases is an essential part of an extensive treatment approach. Therefore physicians and pharmacists should inform stress patients about the options of a sufficient micronutrient supply.

Psychosocial stress and myocardial infarction

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Psychosocial risk factors and risk of acute myocardial infarction in 52 countries (INTERHEART Study): case-control study

Association of psychosocial risk factors with risk of acute myocardial infarction in 11,119 cases and 13,648 controls from 52 countries (the INTERHEART study): case-control stud.
Rosengren A, Hawken S, Ounpuu S, et al. Lancet 2004;364(9438):953-62.

Background

Psychosocial risk factors are associated with the occurrence of coronary heart diseases. The aim of this study was to analyze the psychosocial risk factors for myocardial infarction in 24,767 subjects in 52 countries.

A total of 11,119 patients with myocardial infarction and 13,648 controls without infarction were enrolled in the study. An age- and gender-matching control was assigned to each infarction patient. Psychosocial stress was assessed based on questions about the subjects' work, family, recreation and money.

Results

Patients with myocardial infarction demonstrated a higher prevalence of all stress factors ($p < 0.0001$). It was found that permanent stress at work increases the risk of myocardial infarction more strongly than transient stress at work (Odds Ratio 2.14 vs. 1.38). 11.6% of infarction patients had temporary stress in their private lives compared with 8.6% of controls, and thus also a higher infarction risk (Odds Ratio 1.52). These effects of stress on myocardial infarction were similar in men and women, in persons of various ages and in all geographical world regions that had been examined.

Conclusion

The study results suggest that psychosocial stress is associated with a higher risk of acute myocardial infarction, and permanent stress is related to a higher infarction prevalence than transient stress.



Work stress and the risk of cardiovascular mortality: a prospective cohort study of industrial employees

Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees

Kivimäki M, Leino-Arjas P, Luukkonen R, et al. *BMJ* 2002;325(7369):857-60.

Background

Work stress has implications for health, especially the risk of coronary heart diseases. The “job strain model” claims that the combination of high demands at the work place and low salary (in terms of money, social approval, work place safety, career opportunities) represents a health risk for employees. Using the “effort-reward imbalance model”, the authors Kivimäki and colleagues evaluated the effect of labor market conditions on employees’ health.

The aim of the study was to establish to which extent these two work stress models may explain the risk of cardiovascular mortality.

In total 812 employees who at baseline did not suffer from any cardiovascular disease were enrolled in the study and followed-up over a period of 25 years. By means of a questionnaire the stress at the work place was recorded. In addition, cardiovascular risk factors, such as systolic blood pressure, serum cholesterol level or Body Mass Index (BMI), were measured.

Results

For the evaluation of study findings, the subjects were categorized according to age, gender and work load. It could be shown that employees with combined high job strain and low job control had a 2.2-fold higher cardiovascular mortality risk than their colleagues with low job strain. Employees with an effort-reward imbalance (low salary, lack of social approval) had a 2.4-fold higher mortality risk.

These ratios remained statistically significant even after additional adjustment for occupational groups, biological factors and behavior at baseline. At the 5-year follow-up, high job strain was associated with an elevated serum total cholesterol level, at the 10-year follow-up effort-reward imbalance had led to an additional increase in body mass index.

Conclusion

High job stress and an “effort-reward imbalance” seemed to increase the mortality risk of cardiovascular diseases. Permanent high job stress and effort-reward imbalance increases the mortality risk more than temporary strain.

Nutritional strategies for treatment of the Chronic Fatigue Syndrome (CFS)

Nutritional strategies for treating chronic fatigue syndrome

Werbach MR. Altern Med Rev 2000;5(2):93-108.

Summary

Probably there are many factors that promote the development of the Chronic Fatigue Syndrome. Studies have demonstrated that also marginal nutritional deficiencies have etiologic relevance. These include deficiencies of various B vitamins, vitamin C, magnesium, zinc, L-tryptophan, L-carnitine, coenzyme Q₁₀, and essential fatty acids. It is likely that these deficiencies not only contribute to clinical manifestation, but also are detrimental to the healing process.

It is difficult, however, to detect these marginal deficiencies. Therefore it seems rational to consider supplementing CFS patients with the nutrients discussed above in combination with other high-potency vitamin-mineral substances. Thus, in CFS patients a nutritional supplementation should be recommended.

Conclusion

In CFS patients a supplementation of vitamins and other micronutrients is beneficial.

Vitamin B status in patients with Chronic Fatigue Syndrome (CFS)

Vitamin B status in patients with chronic fatigue syndrome
Heap LC, Peters TJ, Wessely S. J R Soc Med 1999;92:183-5.

Background

The Chronic Fatigue Syndrome (CFS) is characterized by physical and mental exhaustion after minimal physical strain. Studies show that a supplementation of vitamin-mineral combinations, in particular vitamin C, B vitamins and beta-carotene, relieved the symptoms.

The aim of this study was to determine the status of B vitamins (pyridoxine, riboflavin, and thiamin) which are essential for energy metabolism in untreated CFS patients and to compare it with that of control subjects.

The status of B vitamins (pyridoxine, riboflavin and thiamin) was examined in 12 CFS patients and 18 age- and gender-matched healthy controls. The activity of enzymes the co-factors of which are the respective vitamins were measured in erythrocyte hemolysate, before and after the relevant vitamin had been added in vitro.

Results

In individuals suffering from CFS, the basal and activated enzyme activities were lower than in healthy controls. This suggests a functional defect of B vitamins, especially of pyridoxine. A particularly low activity was shown for pyridoxine which may be relevant to the development of depressions associated with CFS. It is assumed that these deficiencies cannot be ascribed to a low dietary intake or malabsorption, as CFS patients are usually well nourished. Excessive losses, catabolic processes or increased requirements are therefore more likely.

Conclusion

CFS patients demonstrate a reduced B vitamin status. This is especially true for vitamin B₆ (pyridoxine).

Low serum zinc levels in Chronic Fatigue Syndrome (CFS): correlation with immune dysfunction and oxidative stress status in CFS

Lower serum zinc in Chronic Fatigue Syndrome (CFS): relationship to immune dysfunctions and relevance for the oxidative stress status in CFS

Maes M, Mihaylova I, De Ruyter M. *J Affect Disord* 2006;90(2-3):141-7.

Background

The Chronic Fatigue Syndrome (CFS) is defined as permanent and recurrent tiredness lasting for at least 6 months. Its cause is still unclear, although first studies suggest that the pathophysiology of CFS has to be seen in relation to disorders of the immune system. A zinc deficiency is able to affect cellular and humoral immunity and thus may be an explanation for individual symptoms of CFS.

The authors of this study wanted to examine whether CFS patients, in comparison with healthy controls, have a lower serum zinc concentration and, if so, whether the lower zinc level is correlated with symptoms of CFS (depression, tiredness or attention disorders) or with various immunological and inflammatory alterations observed in such patients.

Therefore 21 patients with CFS and 12 controls were examined. In order to quantify the CFS symptoms, a fibro-exhaustion scale was used. The zinc levels in serum were determined by an atomic absorption method. Additionally, alpha-2 protein concentration as inflammation marker and the expression of CD69+ on CD3+ as well as CD3+CD8+ T-cells were measured to assess the activity of the immune system.

Results

Compared to control subjects, serum zinc levels in CFS patients were significantly lower ($p < 0.001$). Researchers found a significant negative correlation between serum zinc level and severity of CFS ($r = -0.39$). There also was a significant negative correlation between serum zinc level and alpha-2 protein fraction ($p < 0.002$). PHA*-induced CD69+ expression on CD3+ T-cells was significantly reduced in CFS patients ($p = 0.008$). Furthermore, the authors found a significant correlation between serum zinc level and PHA-induced percentage of CD3+CD69+ cells ($r = 0.54$, $p = 0.04$) and the Con-A*-induced percentage of CD3+CD8+CD69+ cells ($r = 0.53$, $p = 0.04$). These results show that CFS is accompanied by a low serum zinc status and that the latter is related to signs of inflammation and defects in early T-cell activation pathways.

Conclusion

The study results suggest that some patients with CFS should be treated with antioxidants, including zinc supplements.

* PHA (phytohemagglutinin) and Con-A (concanavalin A), are mitogens.



Oxidative stress levels are raised in Chronic Fatigue Syndrome (CFS) and associated with clinical symptoms

Oxidative stress levels are raised in chronic fatigue syndrome and are associated with clinical symptoms.

Kennedy G, Spence VA, McLaren M, et al. *Free Radic Biol Med* 2005;39(5):584-9..

Background

The Chronic Fatigue Syndrome (CFS) is a state characterized by permanent exhaustion and various unspecific symptoms, the pathophysiology of which is unknown. However, oxidative stress, in particular lipid peroxidation, seems to be involved in the development of the disease and its symptoms.

The aim of the study was to investigate levels of 8-iso-prostaglandin-F(2 alpha)-isoprostanes together with other plasma markers of oxidative stress in CFS patients and control subjects, in order to examine their relationship with clinical CFS symptoms.

A total of 47 CFS patients and 34 healthy volunteers who were matched for age and gender were enrolled. Investigators measured the plasma concentration of 8-Iso-prostaglandin F2 α , glutathione, oxidized LDL (LDLox) and HDL cholesterol. The CFS patients also completed a questionnaire in which they rated the degree of their complaints, e.g., headache, joint pain, muscle pain, according to intensities "no", "mild", "moderate" or "severe pain".

Results

Based on their medical history, CFS patients were divided into two groups.

Group 1 had previously defined cardiovascular (CV) risk factors of obesity and hypertension (CHD risk group), and group 2 were normotensive and nonobese (non-risk group). Patients had significantly increased levels of isoprostanes (group 1, $p=0.007$; group 2, $p=0.03$, compared to controls) and oxidized low-density lipoproteins (group 2, $p=0.02$). CFS patients also had significantly lower high-density lipoproteins ($p=0.011$) and glutathione ($p=0.023$) compared to the control group.

The non-risk group showed significantly higher levels of LDLox ($p=0.02$), higher 8-Iso-prostaglandin F2 α ($p=0.03$) and lower HDL levels ($p=0.005$) than the controls.

In patients of the non-risk group 8-iso-prostaglandin-F2 α levels correlated positively with the scores of joint pain (correlation coefficient $r=0.546$).

Conclusion

Irrespective of their cardiovascular risk factors, CFS patients demonstrated raised isoprostane levels and thus increased oxidative stress which was associated with clinical CFS symptoms. Therefore supplementation of specific antioxidants might help to relieve symptoms in these patients.



Relationship between musculoskeletal symptoms and markers of oxidative stress in patients with Chronic Fatigue Syndrome (CFS)

Relationship between musculoskeletal symptoms and blood markers of oxidative stress in patients with chronic fatigue syndrome
Vecchiet J, Cipolline F, Falasco K, et al. *Neurosci Lett* 2003;333:151-4.

Background

The Chronic Fatigue Syndrome (CFS) is defined as a persistent and recurrent state of tiredness which has been present for at least 6 months. Next to symptoms such as headache and attention disorder, muscle and joint pain is very common. A new hypothesis suggests that oxidative stress may play an essential role in CFS development.

In the present study oxidative stress parameters were determined in CFS patients compared to healthy subjects. Also the association between pain perception and muscular exhaustion was examined.

Twenty-one CFS patients and 20 healthy controls participated in the study. Levels of vitamin E and plasma LDL cholesterol as well as the lag phase were measured. The TBARS* plasma concentration served as marker of oxidative stress. In addition, patients' muscular exhaustion and pain perception were quantified.

Results

Compared with the controls, the blood vitamin E levels and LDL cholesterol level in CFS patients were significantly lower. Also higher TBARS concentrations and a delayed lag phase were found in CFS patients. The degree of tiredness was significantly increased, the electrically induced threshold pain level was significantly decreased.

The study results showed that CFS patients, compared with healthy individuals, have an increased oxidative stress and a lower antioxidative defence potential. In all subjects examined, all measured parameters of the oxidant-antioxidant balance correlated significantly with muscular symptoms.

Conclusion

Increased oxidative stress and a low antioxidative defence are related to more severe symptoms of CFS so that a supplementation of antioxidants is recommended.

* TBARS: thiobarbituric acid reactive substances

Be vital, not stressed.

Micronutrients

- anti-stress combination
- balanced dosage

Micronutrients	Features and Characteristics
B vitamins, chromium, zinc	<ul style="list-style-type: none"> • Regeneration of the nervous system • Support the energy metabolism
Magnesium	<ul style="list-style-type: none"> • Supporting the cardiac function • Stability for nerves and muscles
Omega-3 Fatty Acids (content higher in Orthomol® Vital m)	<ul style="list-style-type: none"> • Regulation of lipid metabolism (triglycerides) • Protection of heart and vessels
Folic acid, vitamin B ₁₂ , vitamin B ₆	<ul style="list-style-type: none"> • Lowering the vessel-damaging homocysteine
Folic acid, vitamin B ₆ , vitamin B ₁₂ , iron, copper	<ul style="list-style-type: none"> • Important for blood formation and cell growth
Vitamins A, C and E, mixed carotenoids, selenium, zinc	<ul style="list-style-type: none"> • Strengthening the immune defence • Antioxidants for the protection against the stress-related increase in free radicals
Bioflavonoids	<ul style="list-style-type: none"> • Natural antioxidants, supporting the effect of vitamin C
Vitamin A, pantothenic acid, biotin, zinc	<ul style="list-style-type: none"> • Important for skin, hair and mucous membranes
Vitamins D ₃ and K, calcium (in Orthomol® Vital f)	<ul style="list-style-type: none"> • Strengthening the bones
Manganese	<ul style="list-style-type: none"> • Formation and stability of connective tissues

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