The Scientific Newsletter

N° 68 • June 2012

« RECENT KNOWLEDGE ON ANTIOXIDANTS »

Editorial

Are food-based dietary approaches the future of disease prevention?

In times of caloric over-nutrition, micronutrient intakes in Western societies mostly meet the dietary allowances. At the same time nutrition-related diseases still put a high demand on national health care systems. Despite this discrepancy between adequate micronutrient intakes on one side and the high prevalence of Western diseases on the other side, micronutrient supplements are still a popular means to prevent major diseases including cardiovascular diseases (CVD) and dementia.

Two articles in this issue emphasize the superiority of food-based approaches for disease prevention compared to a nutrient-based approach. *Nunez-Cordoba and Vina et al.* summarize the scientific evidence on the role of antioxidant supplements in the prevention of CVD and dementia. They conclude that most intervention trials with single or combined antioxidants failed to reduce disease risks. In contrast, plant-based dietary approaches providing antioxidants and other nutrients via high intakes of vegetables and fruit (V+F) effectively reduced disease risks.

On top of their preventive effects, V+F can make people look more beautiful. As *Gibault* reports in this newsletter, carotenoids from V+F accumulate in human skin. Within a short period of time after V+F intervention, a more attractive skin-coloration can be achieved. In addition, carotenoids from V+F protect the skin from UV damage.

In conclusion, this newsletter presents further arguments for a higher intake of V+F, and provides a wider perspective of the resultant health benefits from this course of action.

Bernhard Watzl
Max Rubner-Institute, Karlsruhe, Germany

© Philippe Desfray / INRA

IFAVA Contacts info

HEAD OFFICE
International Fruit And Vegetable Alliance
c/o Canadian Produce Marketing Association
162 Cleopatra
Ottawa, Canada, K2G 5X2

IFAVA CHAIR
Colleen Doyle - USA
e-mail : colleen.doyle@cancer.org

Antioxidant vitamin supplementation in Alzheimer's disease: is it useful?

— J. Vina, A. Lloret, E. Giraldo and G. Olaso —

Department of Physiology, Faculty of Medicine, University of Valencia, INCLIVA, Spain

Oxidative stress in Alzheimer's disease

All pathophysiological mechanisms involved in the onset and progression of Alzheimer's disease (AD) are related to oxidative stress[1]. Today, the amyloid beta (Aβ) cascade is the main hypothesis to explain the etiology of the disease. Deposits and accumulation of Aβ leads to extracellular plaques, which have been postulated to be more protective than damaging in terms of oxidative stress. More than a decade ago we reasoned that damage due to Aβ might be caused not by extracellular, but rather intracellular Aβ peptide interacting with normal cell metabolism. Aβ binds to heme and therefore partially blocks the passage of electrons through the respiratory chain and, as a consequence, the production of ROS is increased, thus we can propose a mechanism by which ROS are produced inside cells by interaction with Aβ peptide. Radical production in turn causes mitochondria to aggregate and then they release cytochrome c which is a well-known activator of the endogenous pathway of apoptosis[2]. The increased ROS production results in oxidative stress which provides the basis for a putative treatment of AD with antioxidants.

Antioxidant treatment in Alzheimer's disease

Antioxidant enzymes are over-expressed in hippocampus and parietal lobule but not in cerebellum in AD[3]. This can be a mechanism to prevent partially the occurrence of ROS in AD. In fact, activating the expression of the antioxidant enzymes is always a good strategy to prevent oxidative stress and therefore partially prevent the occurrence and progression of AD.

Many clinical trials have been developed to clarify whether antioxidants are beneficial in AD treatment. However, the results obtained in no way confirm that antioxidants are an effective AD therapy. Even though major efforts have been made in determining whether antioxidant supplementation could be a means of preventing, or even treating, AD this idea is far from being established. In this line, vitamin E has been suggested as a powerful antioxidant and thus may cause beneficial effects and lower the progression of AD. A decisive paper published in 1997[4] reported that vitamin E supplementation resulted in an improvement in the frailty of the patients but these authors did not observe a clear effect on cognition. We performed a study to correlate the administration of vitamin E to AD patients with the progression of the disease and with the blood oxidative stress status. We found that vitamin E does not cause a reduction of glutathione redox ratio in all patients. In those in whom it does not (non-respondent) vitamin E results in an even more pronounced loss of cognition than in patients treated with a placebo. For the patients who experimented a reduction in oxidative stress, cognition was maintained or slightly improved in the six months of the duration of the study[5]. We termed this the vitamin E paradox in Alzheimer's disease. The paradox is the fact that for some patients, vitamin E could even be detrimental whereas for others vitamin E treatment partially prevents the loss memory associated with the progression of the disease.

Moreover, the Rotterdam Study included 5,395 participants who were monitored for the incidence of dementia during ten years and had dietary assessment. The authors concluded that high dietary intake of vitamin C and E may lower the risk of AD[6]. But a more extensive analysis of the Rotterdam Study data (after multivariate adjustment) revealed that dietary intake levels of vitamin C were not associated with the risk of dementia and higher intake of foods rich in vitamin E may only modestly reduce AD[7].

Conclusions

We can state that healthy habits like correct nutrition based on vegetables containing vitamins, particularly vitamins C and E, as well as modest changes in lifestyle towards a healthier one like increasing daily exercise which activate the expression of antioxidant enzymes are beneficial in preventing onset, and more importantly to delay the progression of Alzheimer's disease. Thus, as a final conclusion, we recommend nutritional and physiological changes that activate the expression of antioxidant defenses rather than taking antioxidant vitamins as means of preventing Alzheimer's disease.

© Philippe Dutot / Inserel

REFERENCES:

1. Smith MA, Perry G, Richey PL, et al. Oxidative damage in Alzheimer's. Nature. Jul 11 1996;382(6587):120-121.

2. Lloret A, Badía MC, Mora NJ, Ortega A, Pallardó FV, Alonso MD, Atamna H, Viña J. Gender and age-dependent differences in the mitochondrial apoptogenic pathway in Alzheimer's disease. Free Radic Biol Med. 2008 Jun 15;44(12):2019-25.

3. Aksenov MY, Tucker HM, Nair P et al. The expression of key oxidative stress-handling genes in different brain regions in Alzheimer's disease. J Mol Neurosci 1998; 11:151-164.

4. Sano M, Ernesto C, Thomas RG et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. The Alzheimer's Disease Cooperative Study. N Engl J Med. 1997; 336:1216-1222.

5. Lloret A, Badia MC, Mora NJ, Pallardo FV, Alonso MD, Vina J. Vitamin E paradox in Alzheimer's disease: it does not prevent loss of cognition and may even be detrimental. J Alzheimers Dis. 2009;17(1):143-149.

6. Engelhart MJ, Geerlings MI, Ruitenberg A, van Swieten JC, Hofman A, Witteman JC, Breteler MM. Dietary intake of antioxidants and risk of Alzheimer disease. JAMA. 2002 Jun 26;287(24):3223-9.

7. Devore EE, Grodstein F, van Rooij FJ, Hofman A, Stampfer MJ, Witteman JC, Breteler MM. Dietary antioxidants and long-term risk of dementia. Arch Neurol. 2010 Jul;67(7):819-25.

It's been proven! Younger skin thanks to fruits and vegetables!

— Thierry Gibault —

Nutritionnist, endocrinologist – Paris, France

Our body constantly produces free radicals. This includes our skin where they are produced due to the effects of UV, visible and infrared light rays. To protect itself, our skin has its own defensive antioxidant mechanisms: Vitamins (A, C, E, D), carotenoids (β carotene, lycopene and luteine) and various enzymes. Lycopene is the most powerful antioxidant of all the carotenoids. Since most cannot be synthesized, carotenoids must come from a diet rich in fruits, vegetables, cocoa, tea... When free radical production exceeds antioxidant capacities, they can destroy cells and trigger premature skin aging. Currently, we know how to turn back the clock.

Many studies have shown that carotenoids represent a good marker for skin antioxidant potential. Several non invasive techniques (resonance spectroscopy) allow us today to measure in vivo the skin carotenoids concentrations. Fruits and vegetables are natural sources of antioxidants. Supplementation studies with individual antioxidants at high doses have not been conclusive, in terms of protection against cancer in particular.

Today we know that the most efficient protection involves a mix of antioxidants at physiological doses rather than one compound at high doses.

© Philippe Dufour / inter3d

We know how to measure carotenoids concentrations in the skin

Various non-invasive methods have been developed to measure in vivo carotenoid concentrations in human skin.

Reflection spectroscopy consists of irradiating the skin with light at various wavelengths. The amount of light absorbed by skin carotenoids is a reflection of their concentrations. This method is limited by numerous artefacts linked to the skin's optical properties and does not provide precise information.

A second method, Resonance Raman Spectroscopy is more precise. It uses an argon laser that emits two wavelengths: λ1 = 488 nm, absorbed by β carotene and lycopene and λ2 = 514 nm, mainly absorbed by lycopene. Thus the skin concentration of both carotenoids can be quantified.

How do carotenoids accumulate in skin?

Numerous studies using Resonance Raman Spectroscopy have shown that carotenoids found in foods – especially in fruits and vegetables – or dietary supplements, accumulate in skin. Their skin concentrations increase from the day after antioxidant-rich products are eaten. On the other hand, decrease is slower and can take a few days after stopping supplementation. This delay varies according to the initial amount ingested and patient lifestyle.

In addition, epidermal carotenoid distribution is heterogeneous. Carotenoid concentrations are maximal at the skin's surface since sweat carries them toward the superficial epidermal layers. On the contrary, when carotenoids are topically applied (skin cream), again sweat carries them from the skin's surface into the epidermis. Thus, cutaneous carotenoid concentrations are greater in areas where sweat glands abound such as the palms of the hands and feet and the forehead.

Amount ingested and ripeness: 2 important conditions

Experiments with volunteers have shown that non smokers who eat a lot of a fruits and vegetables have higher skin carotenoid concentrations than smokers who eat fewer fruits and vegetables. Seasonal increases of skin carotenoid concentrations (1.26 times) have been noted in summer and fall. Greater fruit and vegetable consumptions in summer and fall with respect to winter and spring are not the only explanation. Some people eat them year round. However, fruits come from local producers in summer and fall, whereas in winter and spring they are more likely to be imported and harvested before they are ripe. Thus, the fruits and vegetables are less rich in carotenoids. Hence, ingested amounts and produce ripeness represent two important factors that modulate skin carotenoid accumulation. On the contrary, situations such as stress, sun exposure, alcohol consumption or lack of sleep reduce skin carotenoid concentrations. Therefore, skin carotenoid accumulation reflects lifestyle.

Harmful UV effects

The impact of ultraviolet (UV) light on human skin has been widely studied. Following exposure to UV light, skin carotenoid concentrations diminish by roughly 35%. Lycopene concentrations rapidly drop between 0 and 30 minutes after exposure to reach trough concentrations after 1.5 to 3 hours. β carotene concentrations remain stable 30 to 90 minutes after exposure before dropping. It takes between two and four days for concentrations to return to normal.

Do these phenomena have an impact on skin aging? Yes. Studies including hundreds of volunteers have clearly shown that subjects with higher carotenoid skin concentrations look younger than their age. Measurements of fine line and wrinkle density and depth showed they were less evident and skin was smoother. Measures were clearly correlated with skin carotenoid concentrations. Unsurprisingly, UV light is a major cause of premature skin aging. Free radicals destroy collagen and elastin fibers. High local concentrations of antioxidants neutralize free radicals before they can cause any damage.

Of course, ladies, local cream applications can smooth rough skin and is helpful. However, above all, regular consumption of fruits and vegetables represents the best strategy in the fight against skin aging.

Just published :

"You Are What You Eat: Within-Subject Increases in Fruit and Vegetable Consumption Confer Beneficial Skin-Color Changes"

Whitehead RD, Re D, Xiao D, Ozakinci G, Perrett DI (2012)
PLoS ONE 7(3): e32988. doi:10.1371/journal.pone.0032988

BASED ON:

Lademann J et al, Carotenoids in human skin, Experimental dermatology, 20, 377-382, 2011

Is Antioxidant Vitamins Supplementation an Appropriate Population-wide Strategy for Primary Prevention of Cardiovascular Disease?

— Jorge M. Núñez-Córdoba —

1. Preventive Medicine Unit, Clínica Universidad de Navarra, Pamplona, Spain
2. Department of Preventive Medicine and Public Health, Medical School, University of Navarra, Pamplona, Spain

Cardiovascular disease (CVD) is the leading cause of death in the world and it requires an effective primary prevention approach to face this public health menace.

The hypothesis that oxidative events play a significant role in human atherogenesis has been considered the basis of a wealth of large-scale human observational studies and some clinical trials. The studies and trials have focused on linking the dietary antioxidant vitamins with a protective effect on CVD, one of the most important clinical manifestations of atherosclerosis, suggesting that antioxidant vitamins could help to block the atherogenic process and prevent CVD.

We have recently published a brief review in order to synthesize evidence from scientific literature of the relationship of antioxidants vitamins (specially vitamin C, vitamin E, and beta-carotene) and the risk of CVD.

Discrepancies between observational studies and clinical trials

Several observational cohort studies have shown an association between antioxidant vitamins C, E or β-carotene intake either from food or supplements and a protective effect against CVD. However, the evidence from most clinical trials evaluating single antioxidants, or the combination of a small number of these antioxidant vitamins in supplementation, have yielded disappointing results that are in clear disagreement with prior observational data.

Results from meta-analyses of randomized controlled trials evaluating the effect of antioxidant vitamins on cardiovascular events do not support the recommendation of antioxidant vitamins supplementation. In addition occasional data even discourages the use of these supplements because of the possibility that they may even slightly increase the risks of cardiovascular death.

Post-intervention studies

Longer-term effects after stopping antioxidant supplementations on cardiovascular outcomes have been studied in some of the main experimental studies of antioxidants and CVD prevention. These studies include the Alpha-tocopherol, Beta-carotene Cancer Prevention Study (ATBC) [Intervention: Alpha-tocopherol versus no alpha-tocopherol, and beta-carotene versus no beta-carotene; 6-year post-trial follow-up; CVD mortality as endpoint], the Beta-Carotene and Retinol Efficacy Trial (CARET) [Intervention: combination of 30 mg of beta-carotene and 25,000 UI of retinol versus placebo; 6-year post-trial follow-up; CVD mortality as endpoint], the Linxian General Population Nutrition Intervention Trial (NIT) [Intervention: vitamin C and molybdenum versus placebo, and selenium, vitamin E, and beta-carotene versus placebo; 10-year post-trial follow-up; stroke mortality as endpoint], and the Supplementation in Vitamins and Mineral Antioxidants (SU.VI.MAX) Study [Intervention: combination of 120 mg vitamin C, 30 mg of vitamin E, 6 mg of beta-carotene, 100 µg of selenium and zinc versus placebo; 5-year post-trial follow-up; ischaemic CVD incidence as endpoint]. None of these post-trial evaluations has shown any significant beneficial effect of antioxidant supplementation in CVD primary prevention.

Conclusions

Research findings on the potential role that antioxidant vitamins supplementation plays in preventing CVD have gone from promising observational studies outcomes to confusing clinical trials and post-intervention studies results. In the light of current evidence, the use of vitamin C, vitamin E or β-carotene routine supplementation as a population-wide strategy for primary prevention of CVD is not sufficiently warranted. Some authors have suggested the need of future studies using more potent antioxidants than vitamins used in prior evaluations, in addition to studies assessing the effect of these antioxidants in different subgroups of participants with characteristics that could affect the individual capacity to prevent oxidative stress.

For the time being, antioxidant-rich foods and diets, such as fruits and vegetables or the Mediterranean diet, rather than high-dose supplementation with single antioxidant compounds, should be recommended to prevent CVD.

REFERENCE:

Núñez-Córdoba JM, Martínez-González MA. Antioxidant vitamins and cardiovascular disease. Curr Top Med Chem 2011;11:1861-9