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Concerns about safety of vitamins E and C unfounded

Editorial

Recent reports suggesting that more people die when they take antioxidant supplements than when they don't [1, 2] have caused quite a stir in healthcare circles, and made health-conscious individuals think again about their supplementation habits. They have also brought cries of outrage from other nutrition experts, who have strongly criticised the way their colleagues have handled the data at their disposal, and are disappointed with the exaggerated conclusions drawn by others in their published commentaries.

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The fact is that most adults could consume up to 1600 IU vitamin E (about 1000 mg) and 2000 mg vitamin C daily without any risk of adverse effects. This is the conclusion reached by an international group of experts after considering all the available evidence [3]. Since the Food and Nutrition Board (FNB) of the US Institute of Medicine established its system of dietary reference intake values five years ago, no revolutionary new evidence has emerged that would make it necessary to modify the findings of its authoritative safety evaluations.

Evidence for the safety of vitamin E supplements comes from 25 studies involving more than 80'000 people who took a daily dose of up to 2000 IU (in one study for as long as 8 years). Most studies found no major adverse effects at all, and laboratory tests, when done, remained normal. Although it has been reported that vitamin E supplements can increase the risk of bleeding, most evidence indicates that this only occurs in people with a vitamin K deficiency. Even a study in patients taking the anticoagulant warfarin found no effect of vitamin E supplementation on coagulation parameters. The increased mortality from haemorrhagic stroke found in the ATBC Study in Finland [4] was dismissed as "not convincing" by the FNB panel that established the US DRI values for vitamin E.

The FNB also examined in detail the reports suggesting that high intakes of vitamin C can lead to oxalate and kidney stone formation, excess iron absorption, increased uric acid concentrations, reduced vitamin B-12 concentrations, systemic conditioning (induced scurvy) and prooxidant effects, and found they have no substantive basis. Although vitamin C does facilitate iron absorption when taken at the same time as iron-containing foods, it has little effect at intakes above 50 mg daily. The only adverse effects of vitamin C supplementation in healthy adults that are generally recognised are gastrointestinal discomfort and diarrhoea; and these only occur after massive doses (above 3000 mg).

It should be remembered that upper intake limits are designed to protect the most sensitive individuals in the general population. They do not apply to the most sensitive persons in sensitive subpopulations. Although millions of people regularly take vitamins E and C at amounts higher than the RDA, adverse effects are rarely reported. On the other hand, low intakes might increase the risk for chronic disease and accelerate the aging process.

A. Bowley

1. Miller ER III, Pastor-Barriuso R, Dalal D, et al. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med* 2005; 142: 37–46.
2. Bjelakovic G, Nikolova D, Simonetti RG, Gluud C. Antioxidant supplements for prevention of gastrointestinal cancers: a systematic review and meta-analysis. *Lancet* 2004; 364: 1219–1228.
3. Hathcock JN, Azzi A, Blumberg J, et al. Vitamins E and C are safe across a broad range of intakes. *Am J Clin Nutr* 2005; 81: 736–745.
4. Leppala JM, Virtamo J, Fogelholm R, et al. Controlled trial of alpha-tocopherol and beta-carotene supplements on stroke incidence and mortality in male smokers. *Arterioscler Thromb Vasc Biol* 2000; 20: 230–235.

NUTRITION IN PREGNANCY AND LACTATION

Folic acid supplementation policy to reduce NTDs ineffective

Survey

To test whether the policy of telling women of childbearing age to take folic acid supplements as protection against giving birth to a child with a neural tube defect (NTD) is effective, Botto et al. studied birth defects registries in 13 countries (in Europe and Israel) for trends in NTD rates before and after the recommendations were implemented.

Between 1992 and 1998, 8636 cases of anencephaly (no brain) and spina bifida (open spine) were registered among over 13 million births in the countries studied. NTD rates showed no detectable change associated with recommendations to consume more folic acid.

Conclusion

These findings show that existing recommendations for women to increase folic acid intake are not working. In countries that have increased the folic acid status of the population through flour fortification, NTD rates have fallen significantly. Flour fortification would therefore be a reasonable and urgently needed strategy to reduce suffering.

Source

Botto LD, Lisi A, Robert-Gnansia E, et al. International retrospective cohort study of neural tube defects in relation to folic acid recommendations: are the recommendations working? Brit Med J 2005; 330: 571–573.

PREVENTION OF CANCER

Vitamin D may reduce colorectal cancer risk

Review

To examine the role of vitamin D in the aetiology of colorectal cancer, Grant and Garland analysed relevant epidemiological studies. Most of the research that measured either solar, dietary and supplemental sources of vitamin D together or levels of the active form in the body found a reduced risk with higher vitamin D levels. Studies involving measurement of dietary intake only generally showed no correlation.

Conclusion

Available evidence suggests that vitamin D can reduce the risk of developing colorectal cancer. Further studies are needed to elucidate the mechanisms and develop guidelines for achieving an optimal status.

Source

Grant WB, Garland CF. A critical review of studies on vitamin D in relation to colorectal cancer. Nutr Cancer 2004; 48: 115–123.

PREVENTION OF CARDIOVASCULAR DISEASE

Antioxidant supplements might slow hardening of the arteries**Intervention**

Based on the hypothesis that levels of C-reactive protein (CRP), an acute phase protein produced by the liver in response to inflammation, might be a marker of cardiovascular disease risk, Block et al. investigated the effect of antioxidant supplementation on plasma CRP in active and passive smokers. Participants (healthy men and women exposed to cigarette smoke) took 515 mg vitamin C, an antioxidant mixture (containing 515 mg vitamin C, 371 mg α -tocopherol, 171 mg γ -tocopherol, 252 mg mixed tocotrienols and 95 mg α -lipoic acid) or placebo daily for two months. The analysis was done on 160 participants who completed the study within the limits of the protocol.

After vitamin C supplementation, plasma CRP fell by 24% compared to controls; after the antioxidant mixture CRP fell by 4.7% (nonsignificant), while after placebo it rose by 4.3%.

Conclusion

Evidence suggests that plasma CRP may directly influence the progression of atherosclerosis. In this study, the CRP-lowering effect of vitamin C was comparable to that seen with statin drugs. If the results reflect a true impact of vitamin C, the public health benefit could be significant. To confirm if this is so, further investigations are required.


Source

Block G, Jensen C, Dietrich M, et al. Plasma C-Reactive Protein Concentrations in Active and Passive Smokers: Influence of Antioxidant Supplementation. J Amer Coll Nutr 2004; 23: 141–147.

Effect of folic acid on homocysteine levels depends on genes**Intervention**

High blood levels of homocysteine are recognised as an independent risk factor for cardiovascular disease. They can be caused by a poor vitamin B status or a mutation in the methylenetetrahydrofolate reductase (MTHFR: a central enzyme in the breakdown of homocysteine to methionine) gene. To investigate how the MTHFR genotype influences the effect of supplementation, Liu et al. measured the homocysteine-lowering effect of 5 mg folic acid daily in 23 patients suffering from cardiovascular disease, and linked the results to their specific genotype.

After eight weeks of supplementation, plasma total homocysteine levels fell 40% in TT genotype patients, 23% in those of CT genotype, 10% in those of CC genotype, and 23% in carriers of the T allele (one of the possible alternative forms of a gene at a specific location on the chromosome). The effect was statistically significant only in patients of the CT genotype and carriers of the T allele. (Genotype: under normal circumstances, an individual

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has two copies of each gene. The genotype is determined by which alleles of that gene the individual has inherited. For example, a person with two TT alleles is therefore TT genotype).

Conclusion

High doses of folic acid significantly lower plasma homocysteine in cardiovascular patients with CT and T alleles. The effect may be determined by the MTHFR polymorphism (natural differences in the DNA sequence), and the T allele may play an important role.

Source

Liu C-S, Chiang H-C, Chen H-W. Methylentetrahydrofolate reductase polymorphism determines the plasma homocysteine-lowering effect of large-dose folic acid supplementation in patients with cardiovascular disease. Nutrition 2004; 20: 974–978.

NUTRITION AND EYE HEALTH

Vitamins B1, B2 and E influence cataract progression

Survey

To establish the influence of nutrition on changes in lens opacity in women with age-related cataract, Jacques et al. calculated usual nutrient intakes and supplement use in 408 women participating in the Nurses Health Study, based on food frequency questionnaires collected over 13–15 years before the first measure of lens nuclear density. Then, using computer-assisted analysis methods, they measured the change in nuclear lens density during a five-year follow-up period.

The mean five-year change in nuclear lens density was inversely associated with intake of thiamin (vitamin B1) and riboflavin (vitamin B2), and with duration of vitamin E supplement use.

Conclusion

Long-term use of vitamin E supplements and higher intakes of vitamins B1 and B2 may reduce the progression of age-related cataract.

Source

Jacques PF, Taylor A, Moeller S, et al. long-term nutrient intake and 5-year change in nuclear lens opacities. Arch Ophthalmol 2005; 123: 517–526.

Many US ophthalmology patients use vitamins and herbs

Survey

The use of complementary and alternative medicines has become popular in the USA. To get an indication of their use at the University of Michigan Kellogg Eye Center, West et al. surveyed 397 ophthalmology patients between September 2002 and March 2003.

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Two hundred and thirty-two (58.4%) of them took a vitamin supplement (mostly multivitamins) almost daily; only 19 (4.8%) had discussed their use with an ophthalmologist. Thirty-two patients (8%) used herbal products regularly. None of the patients used vitamins or herbs for a particular eye condition, but mainly for general health benefits.

Conclusion

Vitamin and herb supplements are widely used by ophthalmology patients. Ophthalmologists should therefore systematically ask about their use.

Source

West AL, Feters MD, Hemmila MR, et al. Herb and vitamin supplementation use among a general ophthalmology practice population. Am J Ophthalmol 2005; 139: 522–529.

NUTRITION AND BONE HEALTH

Vitamin K important for healthy bones and blood vessels**Review**

In November 2002, European vitamin K experts met in Paris to review available data on vitamin K, and formulate recommendations for dietary intake and use of supplements. Apart from its classical role in blood coagulation, vitamin K is important for bone, vascular and other cell functions. Accumulating evidence suggests that usual intakes of vitamin K are insufficient for healthy bones and arteries.

Conclusion

Dietary intakes of 200–500 µg/day vitamin K (or 100 µg/day as a supplement) may be required for optimal metabolism, and to benefit bone health. Vitamin K may act synergistically with vitamin D, calcium and other micronutrients to maximise bone mineral density and prevent calcification of the arteries. Health benefits may therefore be expected by taking supplemental vitamin K with vitamin D and minerals. More work is needed to increase understanding for the various roles of vitamin K.

Source

Vermeer C, Shearer MJ, Zittermann A, et al. Beyond deficiency: potential benefits of increased intakes of vitamin K for bone and vascular health. Eur J Nutr 2004; 43: 325–335.

GENERAL NUTRITION

Ascorbic acid most efficient enhancer of iron absorption**Review**

Ascorbic acid is the most widely studied enhancer of iron absorption. It acts by reducing ferric iron to ferrous iron, which is more soluble. Both nutrients

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must be consumed at the same time for enhancement to occur. Ascorbic acid is stable in the dry state, but it oxidises rapidly in solution. Oxidation can be limited by encapsulation or air-tight packaging. Losses during storage/cooking may be considerable.

Conclusion

Ascorbic acid is the most efficient enhancer of non-haeme iron absorption when its stability in the food vehicle is ensured. Its effect depends on the type and amount of iron used as fortificant, and the levels of iron-absorption inhibitors and other enhancers in the meal, among other things.

Source

Teucher B, Olivares M, Cori H. Enhancers of iron absorption: ascorbic acid and other organic acids. Int J Vitam Nutr Res 2004; 74: 403–419.

THERAPEUTIC APPLICATIONS

Antioxidants improve success of kidney transplants

Intervention

In an effort to minimize renal dysfunction in five patients with kidney transplants, Loong et al. gave them an antioxidant supplement (500 mg vitamin C and 500 mg vitamin E) for 1–3 months.

Supplementation resulted in a 20% reduction in serum creatinine levels (an indicator of renal function).

Conclusion

Supplementation with vitamin C and vitamin E appears to improve the stability of renal transplant function. Further studies are needed to confirm this.

Source

Loong CC, Chang YH, Wu TH, et al. Antioxidant supplementation may improve renal transplant function: a preliminary report. Transplantation Proc 2004; 36: 2438–2439.

Thyroidectomy patients may need vitamin D supplements

Intervention

To predict the need for postoperative vitamin D supplementation after thyroid surgery, Quiros et al. measured levels of parathyroid hormone intraoperatively in 72 patients, and monitored serum hormone and calcium levels for one month.

Fourteen patients had intraoperative parathyroid hormone levels below 10 pg/ml; 11 of them needed vitamin D supplementation because of persistent hypoparathyroidism or hypocalcaemia. None of the patients with higher intraoperative parathyroid hormone levels needed supplementation after one month.

Continued 

Conclusion

Thyroidectomy may increase the risk for hypocalcaemia. Thyroidectomy patients with parathyroid hormone levels below 10pg/ml at surgery should therefore be given vitamin D supplementation to prevent development of tetany.

Source

Quiros RM, Pesce CE, Wilhelm SM, et al. Intraoperative parathyroid hormone levels in thyroid surgery are predictive of postoperative hypoparathyroidism and need for vitamin D supplementation. Am J Surg 2005;189: 306–309.

Daily vitamin K injections could influence antithrombotic effect of warfarin

Review

Since the year 2000, the US FDA asks that parenteral multivitamin preparations used in hyperalimentation include vitamin K at a dose of 150µg daily. Concerned that this increase in dosage (previously a weekly dose of up to 10 mg was more common) could influence other physiological systems dependent on vitamin K, and might also complicate the use of warfarin as antithrombotic therapy, Berner reviewed the available research for relevant information.

Conclusion

It became apparent how complex vitamin K systems are. Because studies on warfarin done so far have not considered the possible effects of vitamin K, further investigations are warranted.

Source


Bern M. Observations on possible effects of daily vitamin K replacement, especially upon warfarin therapy. J Parenter Enteral Nutr 2004; 28: 388–398.

Diving apnoea a model for measuring oxidative stress

Intervention

Cellular hypoxia (lack of oxygen) and subsequent reoxygenation, which occur in conditions such as sleep apnoea, various circulatory disorders, organ transplantation and chronic obstructive pulmonary disease, are a source of oxidative stress that can cause extensive damage to body tissues. To test diving apnoea (divers hold their breath under water) as a model for studying the mechanisms involved, Sureda et al. gave seven professional divers 1 g vitamin C or a placebo for one week and measured relevant parameters in blood and neutrophils before and after a diving session. Ten days later, they repeated the procedure, giving the divers the opposite supplement.

Diving apnoea induced oxidative stress, and initiated neutrophil reactions that resemble the acute-phase immune response. Vitamin C supplementation reduced production of nitric oxide (NO) and levels of inducible nitric oxide synthase (indicators of oxidative stress) in neutrophils.

Continued 

Conclusion

Diving apnoea is a good human model to study the mechanisms of oxidative stress induced by hypoxia/reoxygenation and their consequences.

Source

Sureda A, Batley JM, Tauler P, et al. Hypoxia/reoxygenation and vitamin C intake influence NO synthesis and antioxidant defenses of neutrophils. Free Rad Biol Med 2004; 37: 1744–1755.