

vitamin supplements

Do vitamin supplements improve health?

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PROFILE Each month we present a clinical problem encountered in general practice together with a commentary from an expert in the field. If you meet an interesting or puzzling case you would like considered in this series please send it to us.

Commentary

There is a vast amount of new information about micronutrients (vitamins and elements) and human health which needs to be taken into account in clinical practice. The difficulty for health practitioners is, as always, when is the evidence sufficient to justify change, and have our views changed in a revolutionary or evolutionary way?

Antioxidants have become a paradigm of the review of appropriate micronutrient intakes. Antioxidant vitamins include the fat soluble carotenoids (provitamin A), the vitamin E family of compounds (tocopherols and tocotrienols) and the water soluble ascorbic acid (vitamin C). But the antioxidants in food include scores of

other compounds, like flavonoids, tannins and various phenolic compounds.¹ Some that are currently attracting particular attention are present in legumes (e.g. soya contains genistein, which is also oestrogenic, immunomodulatory, and antiangiogenic), tea (tannins) and red wine (phenolic substances).²

The first question that emerges is: can any one of these antioxidants substitute for another, and will a large dose of it be preferable to a spectrum of antioxidants? Increasingly, it is clear that there is an interplay between antioxidants, that they

have different time frames over which they operate after an oxidant challenge, and that their sites of action are often quite different.³ For example:

- vitamins E and C are complementary
- a spectrum of carotenoids and vitamin E isoforms (transported with LDL) is required to protect LDL
- intracellular antioxidation may depend to a relatively greater extent on metalloenzymes like superoxide dismutase (which requires copper, zinc and manganese) or glutathione peroxidase (which requires selenium) than does extracellular antioxidation
- antioxidation in the portal circulation after a meal (e.g. in Kupffer cells) may differ significantly from that in the myocardium or skeletal muscle during exercise.

All of this points to the intake

Clinical problem

■ Over the years I have always reassured my patients that they do not require vitamin or mineral supplementation if they have a balanced diet. However, recently it would seem that the evidence that this is so has been shaken by epidemiological studies showing that vitamin E supplementation has a protective effect against ischaemic heart disease. There also appears to be increasing evidence that antioxidants are protective against various sorts of malignancy. Am I doing my patients a disservice?

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of a wide variety of food being more likely to achieve appropriate antioxidation than micro-nutrient supplementation.

Another area of concern about supplementation is how to determine the level of oxidation suppression that may be compatible with good health, since toxic oxygen species and free radicals are required for defence mechanisms. As yet, there are no clear guidelines on dose-response relationships for antioxidants *in vivo* from the literature.

So, do micronutrient supplements actually improve health and decrease the risk of disease where food cannot? We cannot yet answer this question from available studies. Willett and colleagues observed health care professionals in relation to their vitamin E and other micronutrient intakes from food and supplements.^{4,6} Their results suggest a benefit from vitamin E supplements in terms of coronary heart disease prevention (however, the same was not found of other antioxidant vitamins in these studies). The benefit may be realised at up to or about 100 IU of vitamin E a day on average. Whether this result is a cause and effect relationship or attributable to some other health-seeking behaviour by those subjects with higher vitamin E intakes we cannot say from the study.

One distinct possibility is that, given their health care professional status, the subjects modified their diets in other putatively healthy directions, such as increasing polyunsaturated fat intake, which may actually increase the requirement for vitamin E. In this event, increasing vitamin E intake to a level above that usually allowable from food may be a conditional requirement not ordinarily seen with traditional mixed diets. It would be possible to go on creating a patchwork of changing nutrient requirements in this fashion. This is likely to be an emerging difficulty in an environment of rapidly changing food intake – polyunsaturated fat intake has only been at present level for about 25 years. In any case, in a more community-based report (NHANES supplement study), vitamin supplementation was not associated with health protection.⁶

Vitamins are being found to have more functions than previously appreciated. For example, retinoic acid (derived from vitamin A) regulates genes, vitamin D has a role in macrophage function, vitamin K has a role in bone metabolism, and vitamins E and B₆ enhance immune responsiveness. There are more examples from a recent paper by Jeff Blumberg for the WHO Cyprus Food

Based Dietary Guidelines Workshop.⁷ Sooner or later, health practitioners will wish to exploit these functions, but physiology is one thing and pharmacology another. Clinical decision making will require ongoing respect for traditional food culture and risk-benefit analysis of new opportunities in preventive nutrition and nutrition therapy. We are at the beginning of a new era, with new uncertainties. In the meantime, we know that we can optimise health by encouraging the consumption of a wide variety of nutrient dense foods. ■

References

1. Krinsky NI. Mechanism of action of biological antioxidants. *Proc Soc Exp Biol Med* 1992; 200: 248-254.
2. Frankel EN, Kanner J, German GB, Parks E, Kinsella JE. Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine. *Lancet* 1993; 341: 454-457.
3. Esterbauer H, Striegl G, Puhl H, Rotheneder M. Continuous monitoring of *in vitro* oxidation of human low density lipoprotein. *Free Radic Res Commun* 1988; 6: 67-75.
4. Rimm EB, Stampfer MJ, Ascherio A, Giovannucci E, Colditz GA, Willett WC. Vitamin E consumption and the risk of coronary disease in men. *N Engl J Med* 1993; 328(20): 1450-1456.
5. Stampfer MJ, Hennekens CH, Manson JE, Colditz GA, Rosner B, Willett WC. Vitamin E consumption and the risk of coronary disease in women. *N Engl J Med* 1993; 328(20): 1444-1449.
6. Kim I, Williamson DF, Byers T, Koplan J. Vitamin and mineral supplement use and mortality in a US cohort. *Am J Public Health* 1993; 83(4): 546-550.
7. Blumberg J. Background report: Role of vitamins in health promotion and the preventive of non-communicable diseases. Nicosia, Cyprus: World Health Organization, 1995.