Current stand on supplementation with antioxidant vitamins in cardiovascular disease

Farouk M. El-Sabban, MS, PhD.

Cardiovascular diseases (CVD) are leading causes of death in many developed and developing countries. Numerous experimental studies supported the role of low-density lipoprotein (LDL) oxidation in the development of atherosclerosis, which led to the hypothesis that antioxidants can be of benefit in preventing and treating coronary artery disease, stroke, peripheral vascular disease, and other vascular-related diseases.[1] Observational and some experimental studies indicated that supplementation with vitamin E, beta-carotene, and vitamin C, either separately or in selected combinations of 2 or all 3, can be beneficial against CVD. In contrast, data of conducted randomized-controlled clinical trials did not produce solid evidence for the benefit of supplementing such antioxidant vitamins. At present, there is a discrepancy among existing scientific data regarding an evident benefit of administering antioxidant supplementation to CVD patients or towards its prevention for those who are at risk. This communication explores recent relevant reports and expresses current recommendations, which rely mostly on naturally-occurring antioxidants in the diet.

Conducted clinical studies. In the past few years, several controlled clinical studies have reported the effects of antioxidant vitamin and mineral supplements on CVD risk. These studies have been the subject of some recent reports.[1,2] Trials involved large numbers of subjects, either healthy or with different disease conditions, and lasted for periods between 1–12 years. Supplementation of antioxidant vitamins involved intake of an individual vitamin or in combination of others, either 2 or more in a mix. The prevention goal of these studies was either primary or secondary.

Critical appraisal. Variable outcomes resulted from conducted clinical trials. Some studies showed a beneficial effect, others showed no effect, and some indicated an adverse effect.[2] Trials differed in many respects with regard to: subject populations studied, type and dose of antioxidant vitamin/cocktail given, length of study, and study end points. Although some studies involved healthy subjects, most of these studies were carried out on post–myocardial infarction subjects or on those at high risk for CVD. Also, the synthetic form of vitamin was used in some of the trials and the natural form of the vitamin was used in others. Other antioxidants (beta-carotene and vitamin C) were used alone in different doses and the antioxidant cocktail combinations used also varied. Subjects of these trials were followed up for varied durations. Therefore, such factors and variability make it difficult to assess the real value of such vitamin supplementation in CVD.[2]

Recent meta-analyses showed the lack of efficacy of these antioxidant vitamins in varied population groups. Analysis of relevant studies on treatment with vitamin E showed no statistical significance, or clinical importance of such supplementation.[3] Meta-analysis revealed that high doses of vitamin E supplementation (greater than 150 IU/d) may progressively increase all-cause mortality.[4] This conclusion created a stir among specialists in the field and the debate over this subject is likely to continue until concrete and conclusive evidence is found.

While a wealth of information has been gained from these studies, the overall outcome of these trials does not seem to be clearly cut, as clinical trials failed to demonstrate a beneficial effect of antioxidant supplements on CVD morbidity and mortality. This failure may be attributed to the following reasons: 1) only known antioxidant vitamins were used, but not most antioxidant therapies (for example, phytochemicals) were tried, and 2) trials may have not lasted long enough, as heart diseases are chronic. Failure of clinical trials to provide an evidence of beneficial effects of antioxidant vitamin supplementation does not necessarily rule out a role for oxidative mechanisms in the pathogenesis of human atherosclerosis. Further, antioxidant research should continue to determine the relevance of oxidative modification hypothesis to this disease process and associated events in the arterial wall. Also, antioxidant compounds differ quantitatively, and qualitatively from one another and there is a need to find biochemical markers with which to evaluate each. Apparently, treatment with supplemental doses of antioxidants may need to begin earlier in life to be effective. Furthermore, the discrepancy between the data of randomized clinical trials and population studies needs to be explained. It is possible that the positive findings from observational studies with regard to vitamin E supplementation and lower rates of CVD, for example, may be a reflection of the generally healthy lifestyles and dietary intakes of supplement users – namely, among health-conscious individuals. Also, the discrepancy between the observational data and the results of clinical trials could reflect the difference between a lifelong exposure to an antioxidant-rich diet and a limited 5-year exposure, for example, to antioxidant supplements.[2]

For the purpose of medical practice, existing data do not support the routine use of antioxidant supplements for the prevention and treatment of CVD; thus, there is a little reason to prescribe them at present. Lack

of solid evidence of beneficial effects in this regard would logically mean reliance on dietary sources for such antioxidants. Current recommendations are for consumption of a diet high in plant food sources of antioxidants and other cardio-protective nutrients, such as: fruits, vegetables, whole grains, vegetables oils, and nuts, instead of antioxidant supplements to reduce the risk for CVD.[5] These recommendations were also among several that emphasized an active and healthy lifestyle, for an overall health benefit.

In conclusion, collective data of all types of studies are inconsistent and do not provide solid evidence that supports the supplementation with one or more antioxidant vitamin, as being beneficial against CVD.[5] Until more clinical trials are conducted and become sufficient in number for evidence-based analysis, the current stand is not to administer supplements in medical practice. This means that emphasis would be directed to healthy dietary aspects that would be of benefit in this regard. Recent recommendations focus more on the naturally-occurring antioxidant vitamins and plant-based phytochemical antioxidants found in food items, such as carotenoids, catechins, and flavonoids. At present, it seems that daily consumption of adequate amounts of food items that contain antioxidants would be the remedy to follow against CVD in the long run.

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From the Department of Family Sciences, College for Women, Kuwait University, Safat, State of Kuwait. Address correspondence and reprint requests to: Dr. Farouk M. El-Sabban, Department of Family Sciences, College for Women, Kuwait University, PO Box 5969, Safat 13060, State of Kuwait. Tel. +965 (2498) 3081. Fax. +965 (2251) 3929. E-mail: farouk.elsabban@cfw.kuniv.edu

References

1. Willcox BJ, Curb JD, Rodriguez BL. Antioxidants in cardiovascular health and disease: key lessons from epidemiologic studies. ***Am J Cardiol*** 2008; 101: S75-S86.
2. Kris-Etherton PM, Lichtenstein AH, Howard BV, Steinberg D, Witztum JL. Antioxidant vitamin supplements and cardiovascular disease. ***Circulation*** 2004; 110: 637-641.
3. Steinhubl SR. Why have antioxidants failed in clinical trials? ***Am J Cardiol*** 2008; 101: S14-S19.
4. Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. ***Ann Intern Med*** 2005; 142: 37-46.
5. Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, et al. Diet and lifestyle recommendations revisions 2006: a scientific statement from the American Heart Association Nutrition Committee. ***Circulation*** 2006; 114; 82-96.

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Alkhenizan AH, Al-Omran MA.The role of vitamin E in the prevention of coronary events and stroke. Meta-analysis of randomized controlled trials. ***Saudi Med J*** 2004; 25: 1808-1814.