Review: Vitamin E, vitamin C, and possibly coenzyme Q10 are ineffective for preventing or treating cardiovascular disease

Shekelle P, Morton SC, Hardy M, et al. **Effect of supplemental antioxidants vitamin C, vitamin E, and coenzyme Q10 for the prevention and treatment of cardiovascular disease.** Evid Rep Technol Assess (Summ). 2003 Jun;(83):1-3. http://www.ahrq.gov.

Shekelle P, Morton SC, Jungvig LK, et al. **Effect of supplemental vitamin E for the prevention and treatment of cardiovascular disease.** J Gen Intern Med. 2004;19:380-9.

QUESTION

What is the effectiveness of vitamin C, vitamin E, and coenzyme Q10 in preventing and treating cardiovascular disease (CVD)?

DATA SOURCES

Studies were identified by searching 13 databases, reviewing the reference lists of relevant articles, searching the personal libraries of project staff and their associates, and contacting experts in the field.

STUDY SELECTION AND ASSESSMENT

Studies in any language were selected if they were randomized controlled trials (RCTs) or systematic reviews evaluating vitamin C, vitamin E, or coenzyme Q10 in the prevention or treatment of CVD and assessing clinical outcomes. Trial quality was assessed using the Jadad scale.

OUTCOMES

All-cause and CVD mortality, fatal and nonfatal myocardial infarction (MI), and lipid levels.

MAIN RESULTS

156 reports of 144 trials met the selection criteria, and 87 assessed the outcomes of interest. Vitamin E: Compared with placebo, vitamin E alone or in combination did not reduce all-cause or CVD mortality or fatal or nonfatal MI (Table). Similarly, no difference was seen for change in lipid levels (21 trials). Coenzyme Q10: 1 meta-analysis reported improvements with Q10 on indices of cardiac function. 5 RCTs gave mixed results: 2 showed favorable outcomes with Q10 and 3 did not. Vitamin C: 4 placebo-controlled RCTs comparing vitamin C, mostly in combination with vitamin E, showed no benefits for CVD with vitamin C.

CONCLUSIONS

Vitamin E is not effective for preventing or treating cardiovascular disease. Evidence does not support vitamin C and is insufficient to support or refute the use of coenzyme Q10.

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Vitamin E (vit E) alone or in combination (combo) vs placebo for secondary prevention of cardiovascular disease (CVD)*

Outcomes	Comparisons	Number of trials (number of patients)	Follow-up	RRR (95% CI)
All-cause mortality	Vit E vs placebo	5 (17 543)	1.4 to 7 y	4% (–10 to 16)
CVD mortality	Vit E vs placebo	5 (26 446)	1.4 to 5.3 y	3% (–19 to 20)
				RRI (CI)
	Vit E combo† vs placebo	4 (27 251)	3.2 to 5.3 y	3% (–19 to 32)
				RRR (CI)
Fatal MI	Vit E vs placebo	5 (18 301)	1.4 to 5.3 y	3% (–27 to 26)
				RRI (CI)
	Vit E combo† vs placebo	4 (27 231)	3.2 to 5.3 y	2% (–23 to 37)
				RRR (CI)
Nonfatal MI	Vit E vs placebo	5 (18 301)	1.4 to 5.3 y	28% (–2 to 49)
	Vit E combo† vs placebo	4 (27 231)	3.2 to 5.3 y	1% (–10 to 11)

*Abbreviations defined in Glossary. A random-effects model was used. All comparisons are not significant.
†Vit E plus any of the following: vitamin C, β-carotene, selenium, niacin, statin drug, and n_3 polyunsaturated fatty acids.

COMMENTARY

Laboratory and animal research has unveiled the role of oxidative processes in atherogenesis. Thus, a summary of human clinical antioxidant interventional data is of interest. Unfortunately, this well-done synthesis of the literature by Shekelle and colleagues indicates that antioxidant therapy in the form of vitamins C and E and coenzyme Q10 does not seem to substantially affect cardiovascular risk. This review was part of a larger work that helped inform the U.S. Preventive Services Task Force recommendations on vitamin use (1).

Several potential explanations exist why antioxidant therapies have not been proven to affect clinical outcomes. First, these trials were done in patients who already had advanced atherosclerosis (either secondary prevention or primary prevention in older high-risk patients) before antioxidant therapy was initiated. It is possible that antioxidant therapy needs to be implemented at earlier stages of atherosclerosis development in order to inhibit its progression. Second, antioxidant therapy in the form of supplemental pills may not provide the optimal antioxidant activity necessary to affect human pathobiological processes. Perhaps we should be looking to the more biologically active antioxidants found in fruits and vegetables, as opposed to the limited forms of antioxidants so widely available. Third, atherosclerosis is a complex process. The actual effect and dose response, if any, of antioxidants on each of the individual atherogenic processes and overall progression of atheroslcerosis has yet to be fully clarified.

Future research is necessary to evaluate the antioxidant theory in younger patients with less advanced stages of atherosclerosis, but at this point we should not be recommending antioxidant therapy to reduce cardiovascular risk until the proper translational clinical research is available providing enough evidence that its use is worthwhile in improving meaningful clinical outcomes.

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Reference

1. **U.S. Preventive Services Task Force.** Ann Intern Med. 2003;139:51-5.