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ANTIOXIDANT SUPPLEMENTS MAY INCREASE MORTALITY

"Mortality in Randomized Trials of Antioxidant Supplements for Primary and Secondary prevention; Systematic Review and Meta-analysis"

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Many people take antioxidant vitamin supplements every day as they are in the hope that they will be beneficial by improving their health, preventing diseases and slowing down the aging process. Many clinical trials have investigated the effect of antioxidants on health. There have been research studies that have suggested that antioxidant supplements are neither beneficial nor harmful to health, and studies have reported that the supplements can be harmful to health with some trials showing increases in mortality.

According to background information in a recent article, antioxidant supplements may be harmful rather than beneficial. The meta-analysis and review article was published in the February 28 issue of the *Journal of the American Medical Association* and the research team was lead by Dr Goran Bjelakovic.

Meta-analysis is a method used to integrate and summarise the findings from several research studies. Goran Bjelakovic and his colleagues conducted an analysis of previous studies to investigate the effects of antioxidant supplements on all-cause death of adults included in primary prevention (including healthy adults) and secondary prevention trials (including participants with specific disease but excluding acute, infectious and malignant diseases). They included all primary and secondary prevention published trials in adults randomised to receive beta-carotene, vitamin A, vitamin C, vitamin E, or selenium vs. placebo or no intervention.

Following the Cochrane Collaboration method, Dr. Bjelakovic and his associates searched the medical literature to identify relevant articles dated up to October 2005. The sources of data included studies of antioxidants that were used in any dose and administered individually or in combination with other vitamin supplements. The researchers identified and included 68 randomised trials with a total of 232,606 participants that were randomly assigned in the trials for the review and meta-analysis. The range of ages of the subjects was between 18-103 yrs and the mean age was 62.

The authors classified and analysed the trials according to the risk of bias based on the quality of the methods used in the study. The groups were "low-bias risk" (high methodological quality) or "high-bias risk" (low methodological quality) trials. Out of the 68 trials, 21 trials fell into the category of high bias risk trials and 47 trials (with a total of 180,938 participants) were low bias risk trials, which the authors say highlights the validity of their results.

STUDY RESULTS

In the analysis that combined all of the low-bias risk and high bias risk trials, the results showed that there was no significant association between the use of antioxidant supplements and mortality. However, in trials with low bias risk, mortality was significantly increased. The risk of mortality had a statistically significant difference between the low bias risk trials and the high bias risk trials. Among the 47 low-bias trials, the antioxidant supplements were associated with a significantly increased risk of mortality and beta-carotene, vitamin A and vitamin E were all associated with increased mortality at the doses studied, when used alone or in combination. Vitamin A and beta-carotene had a dose-related effect, with mortality increasing as doses increased, whereas vitamin E did not have a dose-related effect, as all doses were associated with increased mortality. Vitamin C and selenium had no significant effect on mortality. Among low-bias trials, use of beta carotene, vitamin A, and vitamin E was associated with a 7 percent, 16 percent and 4 percent (respectively) increased risk of mortality, whereas there was no increased mortality risk associated with vitamin C which had no effect, and or selenium use which had no significant effect (tabulated below).

Agent investigated	**% Increased Risk of Death**
Taking beta-carotene	7
Vitamin A	16
Vitamin E	4
Vitamin C	Nil effect on risk of death
Selenium	Nil effect on risk of death

Table 1. The percentage of increased risk of death associated with the use of supplements.

BETA CAROTENE

The study indicated that Beta Carotene used alone, without combining it with any other supplements, significantly increased the risk of mortality. Only high-quality trials demonstrated an increase in mortality associated with the use of Beta Carotene both singly and combined with other supplements.

VITAMIN A

Vitamin A used alone or in combination with other supplements did not significantly affect mortality. When high-quality research was examined alone, Vitamin A alone or combined significantly increased mortality.

VITAMIN E

Vitamin E given alone or in combination therapy did not significantly affect mortality. Also, given alone in high or low dosages did not significantly affect mortality. However only high-quality trials demonstrated that vitamin E used either alone or combined significantly increased mortality.

VITAMIN C

Vitamin C used alone or in combination with other supplements had no significant influence on mortality. It did not appear to be harmful or beneficial. This effect was unchanged even after analysing the high quality trials.

SELENIUM

Selenium was associated with a slight reduction in mortality overall, however this outcome was excluded when the high-quality trials were examined alone, indicating no significant benefit or harm when used alone or in combination.

POSSIBLE EXPLANATIONS FOR EFFECT ON MORTALITY

Oxidative stress is the build up of destructive molecules called “free radicals”,that circulate in the blood. Free radicals are linked to tissue damage, accelerate the aging process, and is a factor in most diseases. Oxidative stress can result from many factors, including exposure to alcohol, poor nutrition, medications, cold, trauma, and excessive exercise. Antioxidants are substances which reduce the oxidative damage caused by free radicals.

According to the researchers, antioxidants may increase mortality, as eliminating free radicals could interfere with the defence mechanism.

By eliminating free radicals from our organism, we interfere with some essential defensive mechanisms” “Antioxidant supplements are synthetic and not subjected to the same rigorous toxicity studies as other pharmaceutical agents. Better understanding of mechanisms and actions of antioxidants in relation to a potential disease is needed," the researchers conclude.

CONCLUSION

The comprehensive collection and analysis of data on antioxidant supplements showed that beta-carotene, vitamin A, and vitamin E may increase the risk of death. The two other antioxidant agents vitamin C and selenium had no effect on mortality.

The reviews and guidelines suggest that antioxidant supplements may be of no benefit to health. However, the authors of the study emphasise that they evaluated the effect of only synthetic antioxidants, so their "findings should not be translated to potential effects of fruits and vegetables." Nutritionists suggest that rather than taking antioxidant supplements, the best way to protect your health is to improve lifestyle by being physically active, being in the healthy weight range and eating a healthy, balanced diet to obtain the vitamins needed, naturally from food.