The antioxidants controversy: Are vitamin E and beta carotene supplements beneficial?

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The prevalence of dietary supplements in today's society is a symptom of our excessively health-conscious mentality. Many people take dietary supplements in the belief that they boost immune function and offer some form of protection against certain diseases. The National Health and Nutrition Examination Survey estimate nearly half the adults in the United States take dietary supplements, a substantial proportion of which are antioxidants [2]. Antioxidants have been thought to confer protection against the harmful effects of free radicals [4]. Diseases such as lung cancer have been associated with oxidative stress resulting from free radical activity [3]. If free radical damage can be limited, it may be possible to prevent these diseases. "Scientists assumed that these antioxidants were protective, and that taking them as supplements or in fortified foods should decrease oxidative damage and diminish disease," says Barry Halliwell, who has spearheaded studies in free radicals and diseases [3]. But the mechanism by which antioxidants operate is complex and still unknown; scientists can only speculate how they might work in the body. Researchers do know, however, that many antioxidants happen to also be pro-oxidants, which can generate toxic oxygen species. "In the right context and the right dose, they may be able to cause problems rather than prevent them," warned Dr Peter Gann, director of research in the pathology department of the University of Illinois [4].

One of the most popular and well-known antioxidants is beta carotene. Beta carotene showed much promise in the early 1980s when epidemiological evidence suggested that diets which were rich in carotenoids such as fruits and vegetables were associated with a reduced risk of developing lung cancer. Originally known only as a pre-cursor to vitamin A, beta carotene is also a powerful antioxidant in laboratory conditions and extensive research has been conducted to investigate its properties.

However, much controversy has arisen given the conflicting findings by studies conducted on the effects of beta carotene over the past few decades. Although proponents assert that scientific data support the intake of beta carotene supplements decreases the risk of developing lung cancer, critics are convinced otherwise. Studies with contrary findings have raised doubts concerning the protective association of the antioxidant.

Betacarotene and lung cancer
The association between beta carotene and a decreased risk of lung cancer did not happen by chance, but by the cumulative agreement of more than 30 observational studies [15,16]. The studies suggested that diets rich in carotenoids, which are organic pigments naturally present in dark green, yellow and orange vegetables, corresponded with a reduced risk of developing lung cancer [17,18]. They also found the converse to be true – low dietary intake of fruits and/or vegetables was linked to an increase in lung cancer incidences. Upon the analysis of carotenoid classes, numerous studies have noted that a particular carotenoid - beta carotene may be primarily responsible for the association [19]. For instance, it was observed that relative risk of lung cancer rose from between 50% to 150% for dietary intake of vegetable/fruit categories with the lowest beta carotene content in comparison to those with the highest beta carotene content [15]. The results from these observational studies represents "perhaps the most persuasive evidence for an association available in the diet-cancer epidemiologic literature today, both with respect to the magnitude and consistency of the protective association," says Demetrius Albanes, author of a review on beta carotene and lung cancer [15].

Yet in spite of such compelling evidences from observational studies, findings from large-scale clinical trials strongly challenged the association. Instead of showing a decline in risk of lung cancer, the consumption of beta carotene supplements in smokers corresponded to higher incidences of lung cancer. The ATBC trial was a major pioneer trial which aimed to test the effect of beta carotene (and alpha-tocopherol) on lung cancer after epidemiological evidence suggested that diets which were rich in carotenoids may be associated with reduced incidences of lung cancer [7]. The trial, which started in 1985, tested a total of 29,000 male smokers from Finland. When the findings were published in 1994, the results were unexpected because rather than showing a reduction in lung cancer cases, it indicated that men who took beta carotene supplements had an 18 percent greater risk of developing lung cancer. The authors acknowledged that there was "statistical significance" in the higher incidences of lung cancer, but the lack of data from studies on smokers at that time led them to attribute the unanticipated difference to chance.
Further doubts were cast when results from a later clinical trial suggest that the increased risk may not be due to chance after all. The Carotenoid and Retinol Efficacy Trial (CARET), initiated by the US National Cancer Institute, engaged more than 18,000 people with high risk of developing lung cancer, having either a history of smoking or asbestos (a harmful mineral) exposure [20]. These people were then randomly assigned to take either beta carotene supplements or its placebo. The trial was intended to run for 6 years from 1992 but the researchers intervened in 1996 (just 2 years short of completion) and stopped the trial prematurely. Participants were also instructed to discontinue their supplements intake. What prompted the scientists to take such abrupt measures? Statistics showed a 28 percent increase in lung cancer among those who took beta carotene, with overall mortality rate up by 17 percent. Besides being consistent to the findings from the ATBC trial, the results from CARET also strongly indicated that beta carotene supplements “not only did no good but had the potential to do harm,” says biochemist Halliwell from the National University of Singapore [3].

Worse still, it has been suggested by researchers that the adverse effect of beta carotene may persist even after consumption of its supplements has ceased [21,22]. The scientists continued to monitor the health of participants of both ATBC and CARET trials for at least 6 years after they stopped taking beta carotene supplements. Scientists of the study groups reported that risk of lung cancer started to decrease not long after participants ceased their beta carotene intake in both cases. It took 4 years after the ATBC trial ended for the risk of developing lung cancer to be equal in both treatment and control groups. The CARET trial, on the other hand, reported a gradual decrease in lung cancer incidences over time among those in the treatment group, but their risk of developing lung cancer was still slightly higher (although statistically insignificant) than those in the control after 6 years. Researchers of the CARET trial suggest that the higher dosage of beta carotene administered in CARET as compared to ATBC resulted in increased storage of beta carotene in body fat tissues, hence prolonging the adverse effects. Beta carotene supplements may therefore have potential long-term adverse effects in smokers, especially if taken in high doses.

Fortunately, beta carotene supplements have not been shown to have any adverse effects in non-smokers. The Physicians’ Health Study found that the supplements appeared to have no effect on lung cancer incidences in healthy men [23]. One explanation could be that beta carotene more likely accelerates the progression of lung cancer rather than initiates carcinogenesis [24]. If so, it would mean while beta carotene supplements promote the development of lung cancer, it is not the direct cause for lung cancer growth. This would serve to explain why the increase in incidences of lung cancer among the smokers who took beta carotene was not reflected in healthy men.
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It is highly doubtful that the consumption of beta carotene supplements reduces the risk of lung cancer in smokers despite the contrary findings of preliminary observation studies. Some have proposed that the presence of another micronutrient (besides beta carotene) found in carotenoid-rich diets, is responsible for the reduced risk of lung cancer [15]. Unfortunately, no such compound has been discovered. While observational studies may be helpful in suggesting the association between beta carotene and lung cancer, they are nonetheless unable to substitute the role of well-designed clinical trials which must be conducted to establish the claims. In light of the ATBC and CARET clinical trials, it is evident that beta carotene supplements are likely to increase the risk of lung cancer in smokers.

Conclusion

The antioxidant properties of beta carotene appear to be ineffective and perhaps even harmful in the body despite being a powerful antioxidant in test tubes. Despite the association that beta carotene supplements decrease the risk of lung cancer by early observation studies, the apparent adverse effect of beta carotene supplements on lung cancer in smokers makes for a persuasive and unsettling argument. Overwhelming evidence from both the ATBC and CARET clinical trials, suggest that smokers avoid beta carotene supplements.

Even though the consumption of beta carotene supplements might not have similar adverse effects in non-smokers as compared to their smoking counterparts, awareness of the lack of substantial evidence supporting the beneficial claims of beta carotene should prompt unvirtuous consumers to cease patronising the supplements. Not only would they be spared the disappointment of unfulfilled expectations, they would also not incur needless financial costs.

Admittedly, it is unfortunate that beta carotene is probably not the “miracle” cure for the many diseases which plague the human race. In the face of limited support and a myriad of contrary evidences, the hope that beta carotene supplements may starve off diseases remains wishful thinking.

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References

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