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Antioxidants and disease prevention; an obscure association with great significance

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Abstract

The human body has several mechanisms to combat oxidative stress by producing antioxidants, which are either naturally produced in situ, or externally supplied through food and/or supplements. Every time an antioxidant neutralizes a free radical, the antioxidant loses an electron and thereby loses its beneficial function. This signifies the magnitude of continuous re-supplying of our body with vitamins (and chemicals) that operate as antioxidants. If free radicals are left without any control, they can provoke cell damage in our body. These hazardous atoms can damage cells and lead to various diseases.

Introduction

Our body contains various types of antioxidants, which help us to decrease the concentration of oxidants. Oxidants are free radicals that can be detected in the environment. However, they could also be produced naturally in human body (1).

If free radicals would not be destroyed, they may accumulate in the body, which in turn could induce a phenomenon named oxidative stress. This process plays a leading role in the development of various diseases including cancer, diabetes, atherosclerosis, Alzheimer's disease, Parkinson's disease, ocular disease (2), motor neuron disease and other chronic diseases that are the cause of most cases of death nowadays (2-6).

Free radicals can lure low-density lipoprotein (LDL-C) in an artery wall and therefore commence the forming of an atherosclerotic plaque (7). Additionally, they can also damage the DNA and are able to influence the transportation of substances in cells. Moreover, physical assault can play a major role in the multiplication of free radicals. Some physical assaults from the environment, such as excessive alcohol consumption, cigarette smoke, air pollutants and UV-radiation can cause numerous free radicals, which can lead to the loss of control over the free radicals, by the body. Generally, the natural defense systems in the body which contain antioxidants are responsible for the neutralization of releasing free radicals in the body (7,8). However, if they release more than the amount that the body can neutralize, then they can overmaster the body's capability to nullify them, granting them to cause damage to the structure and operation of body cells (7,8).

Core tip
There is no doubt regarding the need for more research on antioxidants and their correlation with disease prevention.

Materials and Methods

For this mini-review, we used a variety of sources by searching through Web of Science, PubMed, EMBASE, Scopus and directory of open access journals (DOAJ). The search was performed using combinations of the following key words and or their equivalents such as; "antioxidant", "disease prevention" and "oxidative stress".

Significance of antioxidants

The human body has several mechanisms to combat with excessive free radicals. Through producing antioxidants, the body is capable to control the concentration of oxidants, by simply detoxifying them. Antioxidants are naturally produced in the body, just like as oxidants. However, they can also be obtained by antioxidant supplements.

It has been detected that antioxidants counteract oxidative stress in laboratory experiments (e.g. in cells or animal studies) (9). However, there is a controversy on whether consuming large amounts of antioxidant supplements are indeed helpful for the human health. There is also concern that excessive doses of these supplements may even have adverse effects (10,11). To put it briefly, many researchers have linked antioxidants with disease prevention (12,13), Nevertheless, the results are inconsistent (14). Hence, there is especially a great controversy among researchers on the effectiveness of dietary (antioxidant) supplements (14).

Many observational epidemiological studies, including cohort and case-control studies have implied that antioxidants could have a major role in preventing oxidative damage (15). However, as observational studies cannot sufficiently control for biases that might influence study outcomes, the results of each observational study must be viewed carefully (15). Randomized controlled clinical trials, on the other hand, are considered to provide the strongest and most reliable evidence of the benefit and/or harm of a health-related intervention, because they lack most of the biases, which make observational studies less reliable (15).

There have been many studies on the effectiveness of dietary antioxidant supplements regarding disease avoidance. In this mini-review, the results of two of the most important studies are discussed: supplémentation en vitamines et minéraux antioxydants (SU.VI.MAX) and selenium and vitamin E cancer prevention trial (SELECT).

It has always been suggested that a low dietary intake of antioxidant supplements increases the incidence of cardiovascular (CV) disease and cancer (16). In SU.VI.MAX study, the adequacy of nutritional doses of supplementation with a combination of antioxidant vitamins and minerals was assessed for reducing the incidence of cancer and ischemic cardiovascular disease in general population. The SU.VI.MAX study was a randomized, double-blind, placebo-controlled primary prevention trial (16). A total of 13017 French adults (7876 women aged 35-60 years and 5141 men aged 45-60 years) were included in this study. All participants were asked to take a single daily capsule with a combination of 120 mg of ascorbic acid, 30 mg of vitamin E, 6 mg of beta- carotene, 100 µg of selenium, and 20 mg of zinc, or a placebo. Median follow-up time was 7.5 years (16). This trial was carried out to investigate the effects of daily supplementation of a combination of antioxidants and minerals on the incidence of cancer and CV diseases in French men and women. The initial results showed that daily supplementation with vitamin C (120 mg), vitamin E (30 mg), beta-carotene (6 mg), and the minerals selenium (100 µg) and zinc (20 mg) for a median of 7.5 years had no effect on the incidence of cancer or CV diseases or on all-cause mortality (16,17). However, when the data for both male and female sexes were analyzed separately, antioxidant and mineral supplementation was associated with lower total cancer incidence and all-cause mortality among men but not among women. Striking was the observation of an increase in skin cancer incidence, including melanoma, among women but not among men. The favorable effects of the supplements for men disappeared within five years of ending supplementation, as did the increased risk of skin cancer among women (17). As a conclusion, after 7.5 years, low-dose dietary antioxidant supplementation lowered the total cancer incidence and all-cause mortality only in men. It was also assumed that supplementation might only be efficacious in men because of their lower baseline status of definite antioxidants, specifically the baseline status of beta-carotene (17). Likewise, the study regarding selenium and vitamin E cancer prevention trial (SELECT), was conducted with reasonable preclinical and epidemiological evidence that selenium and vitamin E may diminish the risk of prostate cancer (18). Hence, this clinical trial was conducted to find out whether daily supplementation of selenium (200 µg) and vitamin E (400 IU) could be beneficial in preventing cancer. The study began in 2001 and ended in 2004. A total of 35 533 men from 427 study spots in the United States, Canada, and Puerto Rico were investigated in a 3-year period. The primary analysis included 34 887 men who were randomly assigned to one of the four treatment groups; 8752 to receive selenium; 8737 to receive vitamin E; 8702 to receive both agents, and 8696, placebo (19,20). People with the following criteria were eligible to participate at the indicated randomized trial; black men (50 years and older) and all others (55 years or older) that had a prostate-specific antigen (PSA). In addition, men participated in this trial, were also required to prove that they were not suspected for prostate cancer, by undergoing a digital rectal examination (20). The initial results reported in 2008 revealed that the administration of these dietary supplements for a median period of 5.5 years did not decline the incidence of prostate and other cancers among the examined men. Moreover, new findings from the study (2011) even suggested 17% more cases of prostate cancer in the group of men taking vitamin E alone than the placebo-group after an average of 7 years. This difference in prostate cancer incidence between the group that only consumed vitamin E and the placebo-group was found to be statistically significant. Furthermore, men administered selenium alone, or both medications (selenium and vitamin E), were also more likely to develop prostate cancer than the group assigned to take a placebo. However those findings were found to be not statistically significant (20). After 7 years of being engaged in researching and monitoring, the final finding was that dietary supplementation with vitamin E significantly increases the risk of a prostate cancer among healthy men (20).

Conclusion

There is no doubt regarding the need for more research on antioxidants and their correlation with disease prevention. The human body has several mechanisms to

counteract oxidative stress, by producing antioxidants, which are either naturally produced in situ, or externally supplied through food and/or supplements (21). Every time an antioxidant neutralizes a free radical, the antioxidant loses an electron and thereby loses its beneficial function (22). This signifies the magnitude of continuous re-supplying of our body with vitamins (and chemicals) that operate as antioxidants. If free radicals are left without any control, they can provoke cell damage in our body. These hazardous atoms can damage cells and lead to various diseases.

As previously stated, there is a controversy on whether consuming large amounts of dietary antioxidant supplements are truly healthy. Many scientists have linked antioxidants with disease prevention. There have been numerous studies that aimed to test the efficacy of antioxidant supplements on disease prevention. In this review the results of two studies are discussed: SU.VI. MAX and SELECT, respectively. Yet, the results are still inconsistent.

Based on the results of these studies, antioxidant supplements may have different effects on men and women. Some dietary antioxidant supplements are assumed to be efficacious in men only, while the same supplements could have adverse effects on women. Conversely, some supplements are said to be more beneficial for women, whereas the same supplements could increase the chance to develop a cancer in men.

In order to learn more about antioxidants and their association with disease prevention, it is recommended that health organizations increase the number of clinics in both developed countries as well as in developing countries to investigate and to learn more about this issue of great importance. By cohort and case-control studies, more clarity can be obtained from the relationship between antioxidants and disease prevention.

Authors' contribution

Arman Amiri and Armin Amiri both searched and gathered the related articles, prepared the draft and edited the final manuscript equally. All authors read and signed the final paper.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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