β-Carotene Supplementation and Risk of Cardiovascular Disease

Subjects: Others

Contributor: Jiaqi Yang

β-carotene is widely available in plant-based foods. β-carotene supplementation had no beneficial effects on cardiovascular disease (CVD) incidence and potential harmful effects on CVD mortality.

β-carotene supplements | stroke | cardiovascular incidence | cardiovascular mortality

1. Introduction

Cardiovascular disease (CVD) is a major public health concern worldwide currently. It is the leading cause of death, accounting for about one-third of global death and premature death in 2019 [1]. Nutrient intake is an important modifiable risk factor for CVD prevention. Previous meta-analyses have consistently shown that vegetarian diets are beneficial for decreasing the risk of CVD mortality, especially for coronary disease mortality [2][3]. A high consumption of vegetables, fruits, whole grains, with low consumption of red meat, processed meat, and sodium reduces the incidence of heart failure and cerebrovascular disease, such as stroke [4][5]. Similar dietary patterns such as the Mediterranean diet also demonstrate protective effects towards lower death rates among patients with a history of myocardial infarction [6].

There are multiple nutrients which are highly available in plants and fruits, including vitamin C, folate, flavonoids, and β-carotene, which have been carefully examined in a few meta-analyses regarding their roles in CVD prevention and control [7][8][9][10][11]. β-carotene is a provitamin A carotenoid with antioxidant properties and the highest vitamin A activity. Nevertheless, the bioavailability of natural β-carotene in plants is low [12]. Some factors impacting bioavailability include change of cell wall structure when processing foods and interaction with other dietary ingredients and phytochemicals in the gastrointestinal tract [13][14]. Hence, more attention has been given to β-carotene supplementation, which has become an alternative for people to meet the recommended intake of β-carotene.

However, several studies have shown that β-carotene was associated with an increased risk of all-cause mortality [7][8][9]. The United States Preventive Services Task Force (USPSTF) in 2013 indicated a null effect of β-carotene on CVD prevention but an increased risk for lung cancer; thus, it was not recommended to use β-carotene supplements for prevention or treatment [7]. However, thus far, most previous studies have examined the combined effects of β-carotene with other antioxidants, and there are limited meta-analyses thoroughly discussing the effects of β-carotene treatment on different CVD outcomes specifically.

Previous studies have indicated a potential harmful effect of β-carotene acting as a co-carcinogen in different age and ethnic groups, while the conclusions were ambiguous when it comes to the single effects of β-carotene on CVD prevention [8][15].

2. β-Carotene Supplementation and Risk of Cardiovascular Disease

2.1. Effects of β-Carotene on CVD Incidence

β-carotene showed a 4% increased risk on overall CVD incidence and a 17% risk increment of β-carotene supplements for total stroke among adults compared with the placebo or controlled group. However, no effects were shown for major CVD events, other CVD, or myocardial infarction separately, which were in accordance with previous meta-analyses [7][9][10][11]. There is a 9% increased risk of CVD in the male population, while no effect was shown among female individuals; thus, gender might play a role in β-carotene's efficacy on cardiovascular incidence. There is an increased risk of total stroke among male smokers and intracerebral hemorrhage among male heavy drinkers [16][17]. However, in the Women's Health Study, no significant benefit or harm on stroke was observed among smokers (13% of female population at the baseline) [18]. Still, there was a possibility of random findings because of the small sample size. In addition, the gender differences may also be caused by the different health behaviors between men and women. Both cigarette smoking and heavy alcohol intake are established risk factors for stroke. Tobacco use facilitates the development of free radicals and atherosclerotic process [19]. It also increases the stroke risk by decreasing cerebral blood flow [19]. Studies also showed that, under certain conditions such as high oxygen concentration, β-carotene switched to a pro-oxidant effect [20][21][22]. This pro-oxidant mechanism generates the β-carotene radical cation, which requires vitamin C to repair. However, due to the low serum level of vitamin C in smokers, the β-carotene radical may lead to an increased risk of cardiovascular disease [21]. Heavy alcohol consumption (more than 3 to 4 drinks per day) causes harmful physiological responses and is associated with higher cardiovascular risk, which is apparent in both men and women [20]. Since smoking and drinking rates among male individuals are generally higher than female, these differences in proportion may lead to the discrepancy of β-carotene's efficacy on stroke or CVD incidence in sex groups. In general, the risk increment of CVD among smoking populations is 14%.

Results also indicated an increased risk of CVD in the subgroups of low-dose and single treatment of β-carotene. This result conflicts with previous meta-analyses which showed null effects [9]. However, this finding can be explained by previous literature. A previous study manifested that, besides the oxygen tension, the β-carotene concentration and interactions with other antioxidants also influenced the pro-oxidant effect of β-carotene [22]. Animal studies suggested that excess dietary intake of β-carotene facilitated the peroxidation in vivo, especially in an α-tocopherol-deficient diet since the presence of other antioxidants in the body might attenuate the pro-oxidant effect of β-carotene [22][23][24].

In nutrient-deficient populations, the effect of β-carotene supplementation is unclear. A study conducted in rural Nepal indicated beneficial effects of maternal β-carotene supplementation on decreased risk of hypertension

among their undernourished children with a high waist circumference, while no overall benefits on cardiovascular risk factors were observed [25]. To provide better recommended daily β-carotene intake in different populations, it suggests conducting further research focused on vitamin interventions in malnourished populations at different ages. In addition, thus far, although both China and the United States have set the tolerable upper intake level (UL) for preformed vitamin A, which is 3000 μg/day for adults [26][27], there is a lack of consideration regarding the specific effects of β-carotene intake. Knowing the populations' nutrient status and cardiovascular risk at baseline is essential for understanding the necessity of setting the UL for β-carotene.

2.2. Effects of β-Carotene on CVD Mortality

β-carotene was consistently associated with increased risk of mortality, including CVD mortality and all-cause mortality. Harmful effects were also observed in the single-treatment subgroup. Previous studies also indicated that high-dose, single or combined intervention of β-carotene increased the risk of all-cause mortality [8][9]. In at-risk and smoking populations, there are positive associations between β-carotene and CVD mortality. The USPSTF report also identified an increased risk of lung cancer in the high-risk population or smokers and hypothesized that the single supplementation of vitamins affected the physiologic system in an implicated way which could be either ineffective or could dose-harm to a certain disease risk [7].

3. Summary

β-carotene had no beneficial effects on CVD incidence and had potential harmful effects on CVD mortality. The use of β-carotene given singly for prevention purposes is not recommended. The daily supplemental use of β-carotene among individuals with CVD histories, cigarettes smokers, and heavy drinkers should be avoided. In the future, it is useful to further explore the combination effects of β-carotene use and antioxidants in multivitamin treatments in suboptimal populations with nutrient deficiencies and investigate the effects among different sex and age groups.

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