False Presumptions and Continued Surprises: How Much Do We Really Know about Nutritional Supplements and Cancer Risk?


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Studies of dietary supplementation and cancer risk are full of surprises. Ten years ago, most epidemiologists and nutritionists sincerely believed that β-carotene was the leading candidate for evaluation in chemoprevention trials. We now know that β-carotene supplementation among smokers increases the risks of lung cancer, cardiovascular disease, and total mortality (1, 2). Although the story is incomplete, the recent findings on selenium supplementation were equally unanticipated. Until recently, few scientists would have argued that selenium supplementation was likely to be a chemopreventive agent active against a variety of cancers. However, in a large clinical trial, selenium supplementation reduced total cancer incidence by 59% (3). There are other less extreme examples of where our expectations about dietary supplements were off the mark. Consider the Finnish study of β-carotene and α-tocopherol to prevent lung cancer, in which α-tocopherol supplementation reduced the incidence of prostate cancer by 32% (4). It is simply hubris to make definitive statements about the effects of dietary supplementation on cancer risk without exhaustive and careful study.

The study by Vinceti et al. (5) provides more data (again unexpected) on the association between selenium exposure and cancer risk. They report a 3.9-fold increased risk of melanoma in a cohort exposed to high selenium in tap water. This increased risk was observed both for men and women over a 10-year period of follow-up. There are many potentially important differences between the two large selenium supplementation trials (3, 6) and this natural experiment. The supplementation trials enrolled participants living in selenium-poor areas, who were at high risk of certain cancers, whereas the participants in the present report resided in a selenium-replete area. The supplementation trials used higher doses (50 and 200 μg) of organic selenium (selenomethionine) in Brewer’s yeast, compared to a low dose (10–20 μg/day) of inorganic selenium (selenate) in tap water (the average intake from food alone in the United States is 60–110 μg/day, primarily as organic selenium). Exposure was also comparably short (5–6 years) in the supplementation trials compared to at least 11 years, and perhaps up to a lifetime, in the natural experiment.

Vinceti et al. (5) hypothesize that selenium ingested as inorganic selenate in drinking water is better absorbed, more bioavailable, and has different biological activity than selenium ingested as organic selenium (SeMet and SeCys) in foods. However, our understanding of selenium bioavailability and biological activity is far from complete. Selenium metabolism varies according to the form ingested and the selenium status of the individual. Most studies of selenium bioavailability in humans have been done in selenium-poor areas such as New Zealand and Finland. These studies suggest that organic selenium has greater bioavailability than inorganic selenium due to lower renal clearance (7) and increased reutilization (8). In these populations, supplementation with organic selenium results in higher plasma levels (9) and sustains increases in plasma glutathione peroxidase longer than supplementation with selenate (10). It is still not known, however, if there are differences in the metabolic activities of SeMet and selenate that are relevant to cancer risk.

Exposure to selenium as selenate is quite common in the United States. The most commonly used multivitamins contain 20 μg of selenium as sodium selenate. It seems likely that this small amount of selenium will not be harmful, but careful evaluation is warranted. Several brands of multivitamin supplements contain over 100 μg of sodium selenate, and the impact of this much higher level of supplementation is unknown.

New and carefully targeted research on the impact of vitamin supplement use is needed. About half of adult Americans use supplemental vitamins or minerals (11), on which they spend about 12 billion dollars per year (12). Cohort studies are almost certainly the best approach to this research, because they allow us to examine exposures to different combinations of supplements at a variety of doses. Results from cohort studies would support the rational selection of specific agents for new clinical trials. It is likely that observational studies on high intakes of β-carotene, particularly among smokers, may have allowed us to make more rational decisions about its use as a chemopreventive agent.

References


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