

Chemoprevention with Vitamins and Minerals: There's Still A Lot to Learn

Maarten C Bosland and Alan M Diamond*

Department of Pathology, University of Illinois at Chicago, Chicago, IL 60612, USA

*Corresponding author: Alan M Diamond, Department of Pathology, University of Illinois at Chicago, Chicago, IL 60612, USA, Tel no: 312-413-8747; E-mail: adiamond@uic.edu

Received Date: 26 June 2015; Accepted Date: 27 June 2015; Published Date: 30 June 2015

Copyright: © 2015 Bosland MC. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Editorial

The health benefits of adequate intake of vitamins, minerals and a host of other natural products are supported by extensive epidemiological data and have become a mainstay of nutritional counseling. The potential for some of these nutrients to reduce cancer mortality is particularly important for patients whose cancer has metastasized and have poor prognosis. Furthermore, efforts to develop vitamins and minerals as dietary supplements to reduce cancer incidence have been ongoing for decades, yet in recent years there has been a decline in both interest and effort in this area. A major reason for this has been the lack of success of large supplementation trials investigating the efficacy of individual supplements in preventing either the development or progression of a variety of cancer types. The failure to detect benefits has been compounded by data obtained from the same trials indicating that for several of the most promising supplements intake was associated with elevated cancer incidence [1]. For example, two large randomized supplementation trials, the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study (ATBC) and the Beta-Carotene and Retinol Efficiency Trial (CARET) both reported significant increases in lung cancer incidence and mortality among high risk individuals provided beta-carotene. In the largest prostate cancer prevention trial ever conducted, the randomized Selenium and Vitamin E Chemoprevention Trial (SELECT), approximately 35,000 men over the age of 50 were provided vitamin E, selenium, or both and the incidence and grade of prostate cancers developing over a 7 year period were compared to those in men provided placebo. The results of this study indicated that the risk of prostate cancer was increased by 17% in those provided the vitamin E supplement and in the selenium supplemented group, those men who had the highest baseline selenium status experienced an increased risk of high grade prostate cancer by 91% [2]. In a prospective study of men diagnosed with prostate cancer, use of selenium supplements was associated with a significant increase in prostate cancer-specific mortality [3]. More and more, supplementation studies are revealing what is described as a "U shaped dose-response curve" [4], where a supplement is beneficial when provided to individuals with low baseline levels of that substance, but detrimental when provided to those at adequate or above adequate levels.

Because of the failure of the trials described above and others to find a consistent benefit to vitamin and mineral supplements, research

in this area has lost popularity. This, in our opinion, is unfortunate and a wasted opportunity. The failure of the tested substances to prevent cancer or reduce associated mortality does not erase the epidemiology that supports their intake, indicating that benefits could be achieved, but probably not when provided to certain high risk individuals or over only a limited period of time. Moreover, data indicating an increased risk of getting and/or dying of cancer in sub-groups taking these supplements indicates there are undiscovered mechanisms of cancer progression that could be very reasonable targets for interventions. Instead of moving forward with large and expensive trials, mechanistic and conceptual research using appropriate animal and *in vitro* models could focus on how specific supplements can increase or decrease cancer risk depending on baseline status of the supplement agent, genetic polymorphisms in molecular pathways affected by the agent, and timing and duration of the intervention in relation to the process of carcinogenesis and cancer progression. The increased prostate cancer risk found in men taking vitamin E supplementation in a randomized clinical trial was reproduced in a rat model that also reproduced the lack of preventive activity of selenomethionine supplementation [5]. Important insights are likely to emerge from such research efforts that can inform the design of future clinical trials, including small scale phase II-type studies that address mechanistic aspects of the action of supplement agents.

References

1. Jerome-Morais A, Diamond AM, Wright ME (2011) Dietary supplements and human health: for better or for worse. *Mol Nutr Food Res* 55: 122-135.
2. Kristal AR, Darke AK, Morris JS, Tangen CM, Goodman PJ, et al. (2014) Baseline selenium status and effects of selenium and vitamin E supplementation on prostate cancer risk. *J Natl Cancer Inst* 106: 1-8.
3. Kenfield SA, Blarigan ELV, DuPre N, Stampfer MJ, L Giovannucci E, et al. (2015) Selenium supplementation and prostate cancer mortality. *J Natl Cancer Inst* 107: 360.
4. Chiang EC, Shen S, Kengeri SS, Xu H, Combs GF, et al. (2009) Defining the Optimal Selenium Dose for Prostate Cancer Risk Reduction: Insights from the U-Shaped Relationship between Selenium Status, DNA Damage, and Apoptosis. *Dose Response* 8: 285-300.
5. McCormick DL, Rao KV, Johnson WD, Bosland MC, Lubet RA, et al. (2010) Null activity of selenium and vitamin E as cancer chemopreventive agents in the rat prostate. *Cancer Prev Res (Phila)* 3: 381-392.