Antioxidant Supplementation Increases Skin Cancer Risk, or, Why Zinc Should Not Be Considered an Antioxidant

Dear Editor,

The increased skin cancer risk among the female participants of the SU.VI.MAX (Supplementation en Vitamines et Mineraux Antioxidants) trial (1) indeed suggests, as the authors point out, that “...dietary supplementation with vitamins and trace element antioxidants may not always provide beneficial effects.” However, a question that lies at the heart of the above trial is whether zinc (Zn) can be rightfully claimed to be an “antioxidant mineral” in view of its host of essential functions that are clearly not associated with any antioxidant activity. Zinc is required for growth and, as a component of the zinc finger proteins, it plays a pivotal role in controlling of cell division and oncogene activation. There is evidence that zinc may favor the malignant transformation of normal cells: in tumor-bearing animals, supplemental Zn stimulated tumor growth and shortened life span; Zn is also a selenium (Se) antagonist and has been shown to abolish its anticarcinogenic effects (2,3).

In the SU.VI.MAX trial, the experimental subjects were required to take 1 capsule containing 20 mg Zn as the gluconate per day, on average for ~7.5 y. Together with the Zn in their diet, the experimental subjects thus obtained ~35 mg Zn/d. This is 3 times the daily requirement of Zn, an amount that could not have been obtained under normal dietary conditions, and probably sufficient to greatly impede, or to abolish, any anticarcinogenic effect of the 100 μg of supplemental Se provided in each capsule.

In previous correlational studies (4), the age-corrected mortalities from cancers of the skin in 27 countries were shown to be inversely correlated with Se intakes; the associations were weak, but stronger for men ($r = -0.28, P = 0.10$) than for women ($r = -0.19, P = 0.33$). However, significant direct associations between skin cancer mortality and dietary zinc intakes were reported for both men ($r = 0.65, P = 0.0001$) and women ($r = 0.60, P = 0.001$). Other major forms of cancer were also inversely associated with dietary Se intakes and directly associated with dietary Zn intakes (3). For example, breast cancer and dietary Se intakes in 27 countries were negatively correlated ($r = -0.80, P = 0.0001$), whereas the corresponding association with Zn intakes was positive ($r = 0.54, P = 0.005$). Using an empirically derived equation$^1$ linking the estimated dietary Zn and Se intakes with the age-corrected breast cancer mortalities, it is estimated that the presence of Zn in the capsules actually raised the breast cancer risk, whereas without the Zn, the amount of Se supplied might have been sufficient to render its anticarcinogenic effect observable. In a recent study (5), elevated Zn levels in benign human breast tissue were associated with increased risk of subsequent breast cancer development. It follows that the SU.VI.MAX trial primarily tested the effects of a long-term, daily supra-nutritional dose of zinc on a population with generally adequate dietary Zn intakes, and it now becomes apparent that the risk associated with this measure outweighs any possible benefit it might otherwise have.

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Literature Cited


$^1$ Breast cancer mortality = 0.00215 $\times$ (Zn) $– 0.351 \times$ (Se) $+ 34.21$, wherein (Zn) and (Se) denote the estimated intakes of the elements per capita per year and the age-adjusted female breast cancer mortality is expressed per 100,000 population.

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