A New Theory to Explain the Benefits of High-Dose Antioxidants in Cancer Treatment

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Abstract *Extensive research and clinical trials have shown that high-dose antioxidants generally benefit rather than harm people with cancer. Many mechanisms have been proposed to explain why antioxidants provide such benefits, including selective cytotoxity, reducing side effects of chemotherapy, and improving quality of life. This report proposes yet another potential mechanism. Cancer cells are known to produce large numbers of free radicals leading to the creation of new mutations, some of which will likely be resistant to treatment. By quenching many of these free radicals, high-dose antioxidants may reduce the numbers of treatment-resistant mutations, enabling better control of existing cancers through conventional and alternative therapies.*

Introduction

Contrary to the prevailing opinion of allopathic oncology, high-dose antioxidant therapies usually benefit rather than harm cancer patients. The positive effects of antioxidant therapies have been borne out in numerous clinical trials and review articles.[1-3]

Many reasons have been proposed for the benefits of high-dose antioxidants as a complementary therapy for cancer patients. In the 1950s, McCormack wrote that vitamin C might reduce the spread of cancer by enhancing surrounding collagen formation.[4,5] In 1972, Cameron suggested that large amounts of vitamin C could enhance the body's ability to destroy cancer cells.[6] Cameron and Pauling subsequently expanded on these concepts.[7] Levine et al showed that, in large concentrations, intravenous vitamin C generates large amounts of hydrogen peroxide in cell cytoplasm, in effect functioning as a mild and nontoxic form of chemotherapy.[8-17] Other studies have demonstrated that various antioxidants can correct nutritional deficiencies (which are common in cancer patients),[18] interrupt the life cycle of cancer cells and induce apoptosis,[19] reduce side effects from chemotherapy,[20-22] control inflammation,[23] inhibit free radical production,[23] ease pain,[24] improve appetite and overall quality of life,[24] and often extend life expectancy.[8,15]

Hypothesis

I propose an additional mechanism to explain the benefits of high-dose antioxidants as a complementary therapy in cancer treatment. My hypothesis is that high-dose antioxidants reduce the spontaneous generation of treatment-resistant cancer mutations.

Cancers develop from gene mutations,[25] epigenetic aberrations,[26] chromosomal derangements (aneuploidy),[27] and from at least some types of chemotherapy.[28] Once created, cancers generate large numbers of their own free radicals, leading to ongoing damage to their deoxyribonucleic acid and the propagation of new mutations. [29,30] Inevitably, some of these mutations will be of little consequence and have a null clinical effect, and some of these mutations will be treatment sensitive. However, some of these mutations invariably will be treatment resistant and

pose difficulties for both conventional and orthomolecular cancer treatment.

Any therapy will by its very nature select for the evolutionary survival of treatment-resistant cancer cells, making that treatment less effective over time. To use a common analogy, treating cancer is often like shooting at a moving target. Conventional oncologists typically respond to this situation by using different chemotherapy regimens or radiation treatments to destroy recurrent and secondary tumors. Orthomolecular physicians often follow a similar strategy, although their specific methods differ from those of conventional oncologists. For example, the late Robert C. Atkins, M.D., best known for his high-protein, low-carbohydrate diet plan, treated many cancer patients. He used as many as fifty different modalities because cancer patients would eventually become resistant to their current treatment (personal communication, April 28, 1995). When one treatment ceased to provide benefits, Atkins would switch patients to a different treatment regimen. In effect, he was shifting from a treatment-resistant protocol to a treatment-sensitive protocol.

Antioxidants are known to quench free radicals and reduce the formation of mutations, some of which may lead to cancer.[31] In general, this role of antioxidants has been seen in light of cancer prevention. However, the same role of antioxidants—particularly high-dose antioxidants—likely provides a similar benefit in existing cancers. By dampening the production of free radicals by cancer cells, antioxidants may reduce the creation of further mutations, some of which would be resistant to treatment. The benefits likely include sustained treatment sensitivity and longer life expectancy, which have been documented in clinical trials and review articles.

Conclusion

To my knowledge, I am the first to propose this mechanism for the anticancer effect of high-dose antioxidants. Furthermore, this theory is not mutually exclusive with any of the other postulated ideas explaining why high-dose antioxidants benefit cancer patients. It is likely that high-dose antioxidants provide benefits by supporting a variety of biochemical pathways and gene-regulating activities.

Competing Interests

The author declares that he has no competing interests.

References

1. Simone CB 2nd, Simone NL, Simone V, et al: Antioxidants and other nutrients do not interfere with chemotherapy or radiation therapy and can increase kill and increase survival, part 1. *Altern Ther Health Med,* 2007; 13: 22-28.
2. Simone CB 2nd, Simone NL, Simone V, et al: Antioxidants and other nutrients do not interfere with chemotherapy or radiation therapy and can increase kill and increase survival, part 2. *Altern Ther Health Med,* 2007; 13: 40-47.
3. Block KI, Koch AC, Mead MN, et al: Impact of antioxidant supplementation on chemotherapeutic efficacy: a systematic review of the evidence from randomized controlled trials. *Cancer Treat Rev,* 2007; 33: 407-418.
4. McCormick WJ: Cancer: the preconditioning factor in pathogenesis. *Arch Pediat,* 1954; 71: 313–322.
5. McCormick WJ: Cancer: a collagen disease, secondary to a nutritional deficiency? *Arch Pediat,* 1959; 76: 166–171.
6. Cameron E, Rotman D: Ascorbic acid, cell proliferation, and cancer. *Lancet,* 1972; 1: 542.
7. Cameron E, Pauling L: *Cancer and Vitamin C.* Updated edition. Philadelphia, PA. Camino Books, Inc. 1993.
8. Padayatty SJ, Riordan HD, Hewitt SM, et al: Intravenously administered vitamin C as cancer therapy: three cases. *CMAJ,* 2006; 174: 937-942.
9. Duconge J, Miranda-Massari JR, Gonzalez MJ, et al: Pharmacokinetics of vitamin C: insights into the oral and intravenous administration of ascorbate. *P R Health Sci J,* 2008; 27: 7-19.
10. Duconge J, Miranda-Massari JR, González MJ, et al: Vitamin C pharmacokinetics after continuous infusion in a patient with prostate cancer. *Ann Pharmacother,* 2007; 41: 1082-1083.
11. Chen Q, Espey MG, Sun AY, et al: Pharmacologic doses of ascorbate act as a prooxidant and decrease growth of aggressive tumor xenografts in mice. *Proc Natl Acad Sci USA,* 2008; 105: 11105-11109.
12. Chen Q, Espey MG, Sun AY, et al: Ascorbate in pharmacologic concentrations selectively generates ascorbate radical and hydrogen peroxide in extracellular fluid in vivo. *Proc Natl Acad Sci USA,* 200; 104: 8749-8754.
13. Chen Q, Espey MG, Krishna MC, et al: Pharmacologic ascorbic acid concentrations selectively

kill cancer cells: action as a pro-drug to deliver hydrogen peroxide to tissues. *Proc Natl Acad Sci USA,* 2005; 102: 13604-13609.
14. Padayatty SJ, Sun H, Wang Y, et al: Vitamin C pharmacokinetics: implications for oral and intravenous use. *Ann Intern Med,* 2004; 140: 533-537.
15. Drisko JA, Chapman J, Hunter VJ: The use of antioxidants with first-line chemotherapy in two cases of ovarian cancer. *J Am Coll Nutr,* 2003; 22: 118-123.
16. Challem J: Medical Journal Watch. Should vitamin C be used as an adjunctive treatment in cancer? *Alternat Complement Ther,* 2009; 15: 42-46.
17. Challem J, Gonzalez MJ, Levy TE, et al: Roundtable: intravenous vitamin C for treating cancer. *Alternat Complement Ther,* 2009; 15: 81-86.
18. Rumelin A, Humbert T, Luhker O, et al: Metabolic clearance and the antioxidant ascorbic acid in surgical patients. *J Surg Res,* 2005; 129: 46-51.
19. Zi X, Feyes DK, Agarwal R: Anticarcinogenic effect of a flavonoid antioxidant, silymarin, in human breast cancer cells MDA-MB 468: induction of G1 arrest through an increase in Cip1/p21 concomitant with a decrease in kinase activity of cyclin-dependent kinases and associated cyclins. *Clin Cancer Res,* 1998; 4: 1055-1064.
20. Ladas EJ, Kroll DJ, Oberlies NH, et al: A randomized, controlled, double-blind, pilot study of milk thistle for the treatment of hepatoxicity in children with acute lymphoblastic leukemia (ALL). *Cancer,* 2010; 116: 506-513.
21. Al-Tonbary Y, Al-Haggar M, El-Ashry R, et al: Vitamin E and N-acetylcysteine as antioxidant adjuvant therapy in children with acute lymphoblastic leukemia. *Adv Hematol,* 2009; 2009: 689639.
22. Pace A, Giannarelli D, Galie E, et al: Vitamin E neuroprotection for cisplatin neuropathy. *Neurology,* 2010; 74: 762–766.
23. Goel A, Kunnumakkara AB, Aggarwal BB: Curcumin as "Curecumin": from kitchen to clinic. *Biochem Pharmacol,* 2008; 75: 787-809.
24. Yeom CH, Jung GC, Song KJ: Changes of terminal cancer patients' health-related quality of life after high dose vitamin C administration. *J Korean Med Sci,* 2007; 22: 7-11.
25. Harman D: The aging process. *Proc Natl Acad Sci USA,* 1981; 78: 7124-7128.
26. Teegarden D, Romieu I, Lelièvre SA: Redefining the impact of nutrition on breast cancer incidence: is epigenetics involved? *Nutr Res Rev,* 2012; 25: 68-95.
27. Duesberg P: Chromosomal Chaos and Cancer. *Sci Am,* 2007; 296: 52-59.
28. Sun Y, Campisi J, Higano C, et al: Treatment-induced damage to the tumor micro- environment promotes prostate cancer therapy resistance through WNT16B. *Nat Med,* 2012 [Epub ahead of print].
29. Valko M, Izakovic M, Mazur M, et al: Role of oxygen radicals in DNA damage and cancer incidence. *Mol Cell Biochem,* 2004; 266: 37-56.
30. Marnett LJ: Oxyradicals and DNA damage. *Carcinogenesis,* 2000;21: 361-370.
31. Harman D: Nutritional implications of the free-radical theory of aging. *J Am Coll Nutr,* 1982; 1: 27-34.