Increasing the Effectiveness of Intravenous Vitamin C as an Anticancer Agent

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Abstract *Vitamin C has been mentioned as an agent with chemotherapeutic potential since 1952. Physiological concentrations of vitamin C (L-ascorbate or L-ascorbic acid) in the body are controlled through intestinal absorption, tissue accumulation, and renal reabsorption and excretion. Therefore, intravenous administration is used to achieve pharmacologic doses not attainable by other means. In relation to intravenous administration of ascorbate, high-dose intravenous vitamin C (>0.5 g/kg body weight) has several effects: cytotoxicity for cancer cells but not for normal cells; improved quality of life for cancer patients; protection of normal tissues from toxicity caused by chemotherapy; reinforcement of the action of radiation and some types of chemotherapy; immune system enhancement; and strengthening of collagen and hyaluronic acid. In this article we discuss important therapeutic variables that the clinician faces that are key for increasing the effectiveness of intravenous vitamin C as an anticancer agent.*

Introduction

After over 60 years of experience with vitamin C and Cancer, what can we say about vitamin C as an anticancer agent? The extensive experience and published papers on vitamin C and cancer demonstrate that the use of high dose, both oral and intravenous (IV) vitamin C is remarkably safe.[1-7] Additionally, the vast number of publications confirm that it possesses many therapeutic benefits.

1. Improves quality of life of cancer patients:[8-10]

a. Decreases adverse effects of standard cancer treatments.
b. Reduces pain.
c. Increases energy.
d. Increases appetite.

2. Reduces many complications of the disease:[11-16]

a. Resolves ascorbate's insufficiency in the cancer patient.
b. Combats infections (viral, bacterial, fungi).
c. Decreases cancer-associated inflammation.
d. Prevents cancer associated sepsis.

3. Pharmacological doses of vitamin C have shown to have cytostatic or cytotoxic action in cancer cells through a variety of mechanisms:[17]

a. Fuel control of malignant cells by glucose antagonism.
b. Electron donor for the energy redox problem present in cancer.

c. Increases hydrogen peroxide formation.
d. Increases collagen formation.
e. Enhances immune parameters (cellular and humoral).
f. Sustains and improves the effect of standard antineoplastic agents.

Discussion

Many patients have shown impressive responses in tumor size reduction, improvement in pain control, increased energy levels and appetite, in general we can state that most patients improve their quality of life but nevertheless total effectiveness of the use of IV vitamin C as an anticancer agent has not been achieved. Results in some instances have been variable. This may be due to a number of direct interacting variables.

In order to consistently improve cancer patient outcomes, it is important to have a comprehensive evaluation of the therapeutic protocol that allows us to identify contributing factors that promote health deterioration and the barriers to achieve total healing. These must be identified and corrected.

These variables include but are not limited to:
1. Cell energy related metabolic derangements.[18-20]
2. Toxicities (e.g., tobacco, alcohol, pesticides, heavy metals, hydrocarbons, and food nitrosamines).[21-28]
3. Medications (i.e., opioids impair immune response, increase angiogenesis, and may even act directly on tumor cells to encourage their growth and spread. There are epidemiologic, animal, and cellular studies that suggest a role of mu opioid receptors on cancer growth and metastasis).[29-31]
4. Hormonal imbalances/endocrine disruptors.[32,33]
5. Excessive inflammation.[34,35]
6. Infectious agents and the balance of the body flora.[36,37]
7. Excessive psychological stress.[38,39]
8. Excessive exposure to radiation.[40,41]

Ten percent of invasive cancers are related to radiation exposure, including both ionizing radiation and non-ionizing radiation.

Relevant physiological/cellular variables to consider when improving the effectiveness of IV Vitamin C therapy

1. Level of tissue oxygenation: The level of tissue oxygenation may be the most important limiting factor in the anticancer activity of high dose IV vitamin C. As we are well aware of one of the most important mechanisms by which vitamin C exerts its anticancer action is by the production of hydrogen peroxide. For this to occur, the presence of sufficient oxygen is a requisite. Limited oxygen availability reduces the chances of the production of hydrogen peroxide from the conversion of ascorbic acid to dehydroascorbic acid. We propose the utilization of hyperbaric oxygen immediately after IV vitamin C therapy to increase its effectiveness as an anticancer agent, in order to increase the formation of hydrogen peroxide, and therefore enhance the anticancer effect of IV vitamin C.

In relation to ozone, it is known that vitamin C is antagonistic to ozone, although it has been shown that ozone does not to break down vitamin C in the body. Patients taking therapeutic doses of vitamin C either orally or via IV infusion, should take the ozone treatment first, then wait 30 minutes, and then take the vitamin C dose.

General Aspects of Oxygenation
a) Hyperbaric Oxygen: Increases oxygen to tissues.
b) Ozone: Increases oxygen. An Italian group postulates that a prolonged cycle of ozonated autohemotherapy may correct tumor hypoxia, lead to less aggressive tumor behavior. Improving oxygen levels would be expected to favor the anticancer effect of vitamin C.[42] Ozone therapy has been reported to produce an increase in red blood cell glycolysis rate. This leads to stimulation of 2, 3 diphosphoglycerate which then allows a rise of the oxygen released to the tissues. Ozone facilitates the Krebs's cycle by improving the oxidative carboxylation of pyruvate and promoting the synthesis of ATP. There is

also an increase in antioxidant enzymes that act as free radical scavengers (such as glutathione peroxidase, catalase and superoxide dismutase).[43] Vasodilation is also induced by ozone which leads to increased oxygen and nutrients and immune factors available to the cell.[44] Ozonized autohemotransfusion may be useful to improve both the poor rheological properties of the blood and the oxygen delivery to tissues[45] and therefore increase oxygen, immune factors and nutrients that improve healing and tumor response. Animal studies have shown very significant increased survival in advanced head and neck squamous cell carcinomas with the application of ozone. Although the mechanisms for this effect has not been totally elucidated, it is believed that various important immunemodulatory effects in macrophages, polymorphonuclear cells (PMN), NK cells, and cytotoxic T lymphocytes are involved as well as other metabolic modulatory effects.[46] Therefore, although at the present time there is no solid evidence that ozone can improve the anticancer activity of vitamin C, given the scope of its biological effects, it might be important to test this combination.

–Increases oxygen metabolism: More oxygen availability activates of the Krebs cycle, increases oxidative decarboxylation of pyruvate and ATP production. The additional supply of oxygen oxidizes the lipid layer of malignant cells and destroys them through cell lysis (apoptosis). Oxygen reacts with the unsaturated fatty acids of the lipid layer in cellular membranes, forming hydroperoxides. Lipid peroxidation products include peroxyl radicals and aldehydes that possess killer cell action.

–Increases circulation: Permits more oxygen, vitamin C and immune factors to be delivered to the tissues.

–Decreases bacteria/viral/fungi load: Microbes are important modulators of the immune system and, if not controlled, they can produce excess inflammation. Since inflammation is known to play a major role in the pathogenesis of cancer, microbial balance can influence tumor progression. This can occur by chronic activation of inflammation, alteration of tumor microenvironment, induction of genotoxic responses, reduction of immune action and metabolic derangements.[47]

c) Sodium bicarbonate: May correct tissue acidosis produced by increased fermentation. Sodium bicarbonate also has a specific ability that is, not possessed by other basic compounds to destroy fungi colonies.[48,49]

d) Dichloroacetic Acid: May improve mitochondrial function by facilitating oxidative phosphorylation which is lacking in the cancer cell.[49,50]

2. Level of Blood Glucose:[51,52] Excessive blood glucose can compete with vitamin C for the glut receptor sites. It is a good therapeutic approach to provide the high dose IV vitamin C in an empty stomach. Nevertheless we should be aware that sleepiness and hypoglycemia symptoms may arise. Receiving these IVs causes the body to produce insulin because it believes that the blood sugar is spiking. Patients might experience hypoglycemia-like symptoms. If their blood sugar is measured during the infusion of IV vitamin C, the meter reads an enormously high number because the body thinks that the vitamin C is sugar. So having a reduced level of blood sugar seems to be a necessary parameter to increase IV vitamin C's anticancer effectiveness.

3. Physiological Red-Ox balance:[53,54] The balance between oxidation and anti-oxidation is believed to be critical in maintaining healthy biological systems. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) play important roles in regulation of cell survival. In general, moderate levels of ROS/RNS may function as signals to promote cell proliferation and survival, whereas severe increases of ROS/RNS can induce cell death. Under physiologic conditions, the balance between generation and elimination of ROS/RNS maintains the proper function of redox-sensitive signaling proteins. Normally, the redox homeostasis ensures that the cells respond properly to endogenous and exogenous stimuli. However, when the redox ho-

meostasis is disturbed, oxidative stress may lead to aberrant cell death and contribute to disease development. Redox balance plays a critical role in maintaining the biologic processes under normal conditions. Disruption of redox homeostasis will result in a deregulation of apoptosis associated with various diseases, including cancer, degenerative diseases, and aging. In general, ROS at low levels act as signaling molecules that promote cell proliferation, which controls cell division and sustains cell survival. In contrast, a severe increase in ROS can induce cell death. There is continuous demand for exogenous antioxidants in order to prevent oxidative stress, representing a disequilibrium redox state in favor of oxidation. However, high doses of isolated reductive compounds may be toxic, owing to pro-oxidative effects at high concentrations or their potential to react with beneficial concentrations of ROS normally present at physiological conditions that are required for optimal cellular functioning. All this said, the physiological Red-Ox state may also influence IV vitamin C effectiveness as an anticancer agent. We do not recommend the concomitant application of agents with anti-oxidative potential (such as glutathione, B-complex vitamins) given at the same time with IV vitamin C since they may interfere with the pro-oxidative activity of vitamin C and reduce its anticancer potential.

Competing Interests

The authors declare that they have no competing interests.

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