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Changes of Terminal Cancer Patients' Health-related Quality of Life after High Dose Vitamin C Administration

Over the years there has been a great deal of controversy on the effect of vitamin C on cancer. To investigate the effects of vitamin C on cancer patients' health-related quality of life, we prospectively studied 39 terminal cancer patients. All patients were given an intravenous administration of 10 g vitamin C twice with a 3-day interval and an oral intake of 4 g vitamin C daily for a week. And then we investigated demographic data and assessed changes in patients' quality of life after administration of vitamin C. Quality of life was assessed with EORTC QLQ-C30. In the global health/quality of life scale, health score improved from 36±18 to 55±16 after administration of vitamin C (p=0.001). In functional scale, the patients reported significantly higher scores for physical, role, emotional, and cognitive function after administration of vitamin C (p<0.05). In symptom scale, the patients reported significantly lower scores for fatigue, nausea/vomiting, pain, and appetite loss after administration of vitamin C (p<0.005). The other function and symptom scales were not significantly changed after administration of vitamin C. In terminal cancer patients, the quality of life is as important as cure. Although there is still controversy regarding anticancer effects of vitamin C, the use of vitamin C is considered a safe and effective therapy to improve the quality of life of terminal cancer patients.

Key Words : *Neoplasms; Cancer; Ascorbic Acid; Quality of Life; Terminal Care*

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INTRODUCTION

Numerous studies explored the efficacy of vitamin C in the treatment of cancer, but their mixed findings caused a great deal of controversy. In 1949, Klenner first suggested the possibility of using vitamin C for the treatment of cancer. In 1952, McCormick asserted that vitamin C has been proposed as a chemotherapeutic agent. Hundreds of articles including an array of in vitro, in vivo, cell culture, animal, and human studies have been published on this topic. As a result, it is believed that vitamin C might have anti-cancer effects (1-3).

Twenty-six years ago, Cameron et al. reported that they increased the time of survival of cancer patients and improved their quality of life by administrating high doses of vitamin C (4). As a result, Pauling and Cameron continuously asserted the effect of vitamin C on cancer. However, Moertel et al. (Mayo Clinic) reported that high-dose vitamin C therapy was not effective against advanced cancer (5). This finding is critical because it may prevent clinicians from using vitamin C for cancer patients.

A critical point of both studies (Cameron et al. and Moertel et al.) is that they used a different administration method, intravenous route in the former and oral route of vitamin C in the latter. Oral absorption of vitamin C cannot achieve plasma concentrations comparable to those obtained by intravenous administration. Moreover, it has been recently reported that vitamin C acts as a toxic agent against cancer cells when given intravenously (6).

Unlike most mammals, human and other primates cannot synthesize vitamin C from glucose due to L-gulonolactone oxidase deficiency. Therefore, we must be obtained adequate amounts of this nutrient from foods and supplements. Vitamin C plays a crucial role in the synthesis of L-carnitine from lysine, neurotransmitters synthesis, cytochrome p-450 activity, cholesterol metabolism, detoxification of exogenous compounds and as an antioxidant (7-10). In addition, when given in large doses, vitamin C may function as an ergogenic agent (11). Because the levels of vitamin C in the blood of the cancer patients were significantly decreased compared to healthy persons, cancer patients required larger amounts of vitamin C (12, 13).

Improved health-related quality of life is important as much as a cure of cancer in terminally ill cancer patients who have an estimated survival of less than 6 months. The objective of this study was to examine changes in the quality of life in terminally ill cancer patients after administration of high-doses of vitamin C.

MATERIALS AND METHODS

Study subjects

Outpatients with terminal cancer who were treated in the Department of Family Medicine, Myungji-Hospital, Kwandong University College of Medicine from 1 February 2004 through 31 August 2005, were included in the study. The study included 39 cancer patients (male: 20, female: 19) after excluding those who were undergoing chemotherapy.

Assessment of cancer patients' life-related quality

A written consent was obtained from all patients. They were given an intravenous administration of 10 g vitamin C twice with a 3-day interval and an oral intake of 4 g vitamin C daily for a week. And then we investigated demographic data and assessed changes in patients' quality of life 1 week after administration of vitamin C.

Demographic data included sex, age, cancer diagnosis, anticancer therapy, recurrence, metastasis and performance status (Eastern Cooperative Oncology Group, ECOG). Quality of life was assessed by the European Organization for Research and Treatment of cancer (EORTC). This was a self-administrated questionnaire (EORTC) that was used to assess the quality of life of the patients. When a patient was unable to self-administer the questionnaire, an interviewer or the patient's caregiver completed the questionnaire after finding out answers from the patient. The Korean version of the European Organization for Research and Treatment of cancer core quality-of-life questionnaire (EORTC QLQ-C30) was used as the questionnaire. It was designed to ask clinical symptoms experienced by the patients during the previous week. The questionnaire consists of 30 items, that comprise a global evaluation of health status and quality of life, five functions (physical, role, emotional, cognitive, and social), three symptoms (fatigue, pain, and nausea/vomiting), and six additional single items (dyspnea, appetite loss, sleep disturbance, constipation, diarrhea, and financial impact of the disease and treatment) (14). Scores for each scale on the EORTC QLQ-C30 questionnaire were calculated as suggested by the EORTC Study Group on Quality of Life. All of the scales and single-item measures ranged in score from 0 to 100. A high scale score represents a higher response level. Thus a high score for the global health status/quality of life represents a high quality of life and a high score for a functional scale represents a high/health level of functioning. But a high score for a symptom scale/item represents a high level of symptomatology/problems.

Statistical analysis

The EORTC scales scores before and after administration of vitamin C, were compared using the Wilcoxon signed rank-test. A p-value of less than 0.05 is considered statistically significant.

RESULTS

Demographic data

The demographic data (age, sex, cancer diagnosis, anticancer therapy, metastasis, performance status) are shown in Table 1. All patients were stage IV, and 12 (30.8%) patients experienced a recurrence of their cancers. No patients were excluded due to side effects of vitamin C.

Quality of life (EORTC)

The quality of life before and after administration of high dose vitamin C, are shown in Table 2. In the global health/quality of life scale, health score improved from 36 ± 18 to 55 ± 16 after administration of vitamin C (p=0.001). In functional scales, the patients reported significantly higher scores for physical, role, emotional, cognitive, and social function after administration of vitamin C (p<0.005). In symptom scales, the patients reported significantly lower scores for fatigue, nausea/vomiting, pain, sleep disturbance, and appetite loss after administration of vitamin C (p<0.005). The other symptom scales such as dyspnea, constipation, diarrhea, financial impact were not significantly changed after adminis-

Table 1. Demographic data

Characteristics	Number (%)
Sex	
Male	20 (51.3)
Female	19 (48.7)
Age (mean±SD, yr)	53.5±10.5
Cancer diagnosis	
Stomach	10 (25.6)
Lung	7 (17.9)
Liver	1 (2.6)
Breast	4 (10.3)
Cervix	1 (2.6)
Colo-rectal	9 (23.1)
Biliary	2 (5.1)
Other	5 (12.8)
Previous anticancer therapy	
Surgery	1 (2.6)
Chemotherapy (CTx)	11 (28.2)
Radiotherapy (RTx)	1 (2.6)
Surgery+CTx	19 (48.7)
CTx+RTx	3 (7.7)
Surgery + CTx+RTx	4 (10.3)
Recurrence	12 (30.8)
Metastasis	39 (100.0)
Performance status (ECOG)	
0-1	26 (66.6)
2-4	13 (33.4)

Table 2. Change of terminal cancer patients' health-related quality of life (EORTC) after high dose vitamin C adminstration

	EORTC (Mean±SD)		*p*-value
	Before	After	
Global Health Scale			
Global health	36±18	55±16	0.001
Function scale			
Physical	66±20	72±15	0.037
Role	59±31	73±22	0.002
Emotional	68±24	78±19	0.001
Cognitive	69±23	80±16	0.002
Social	62±34	71±24	0.049
Symptom scale			
Fatigue	52±24	40±19	0.001
Nausea/Vomiting	24±25	11±15	0.001
Pain	30±32	21±25	0.013
Dyspnea	23±28	15±20	0.051
Sleep disturbance	32±35	26±25	0.029
Appetite loss	50±43	31±29	0.005
Constipation	19±26	16±25	0.390
Diarrhea	16±24	11±18	0.218
Financial impact	25±27	23±24	0.914

tration of vitamin C.

DISCUSSION

In terminal cancer patients, the quality of life is as important as cure. The treatment for terminal cancer patients was particularly focused on the patient's well-being in addition to the efforts to minimize symptoms. Thus, the ultimate goal of treatment for terminal cancer patients can differ from those pursued in treatments designed to cure.

If terminal cancer patients were concerned about emotional changes and functional impairment and if the patients' quality of life did not improve, the treatment that they underwent should not be considered successful even though it extended their life expectancy. Although investigators are divided in their opinions on whether vitamin C is effective for the treatment of cancers, many of them reported that cancer patients showed improvement in their quality of life.

This study also demonstrated improvement in global health/quality of life in terminal cancer patients after administration of vitamin C along with improvements in all functions (physical, role, emotional, cognitive, and social) and some symptoms (fatigue, nausea/vomiting, pain, sleep disturbance, and appetite loss).

The therapeutic impacts of vitamin C, expected when administered to terminal cancer patients, include anticancer effects, positive impact on the central nervous system and mental ability, pain relief and contribution to energy generation. The anticancer effects of vitamin C boost cytotoxicity of tumor cells, collagen synthesis, antioxidant action, immunity system and low concentration of certain amino acids. First, the mechanism underlying the action of vitamin C in combating cancer cells explains that vitamin C in blood is oxidized to dehydroascorbate acid, which passes freely back and forth through the cell membranes via glucose transport. When dehydroascorbate acid enters cancer cells, glutathione turned the dehydroascorbate back into ascorbic acid (vitamin C), which is not allowed to move out of cancer cells. This ascorbic acid is converted to dehydroascorbate again and produces H_2O_2, which destroy cancer cells (15). Higher levels of ascorbic acid were observed around cancer cells when compared to normal cells (16). Casciari et al. study reported tumor cells apoptosis occurred in 42.9% of total patients and necrosis in 24.4% when patients' blood level of vitamin C was 11.2 mM. They said apoptosis increased to 57.6% and necrosis to 33.1%, respectively, when patients' blood level of vitamin C rose to 33.7 mM (17). Secondly, an increase in the synthesis of collagen inhibits the growth of cancer cells, leading to apoptosis and necrosis in cancer cells (18). That is, cancer cells releases collagenase and dissove collagen between cells/tissues. This means that these enzymes dissolve basement membranes, an organization of collagen and extracellular matrices, enabling cancer cells to infiltrate and destroy adjacent normal tissues. An increase in collagen synthesis due to vitamin C would however increase membrane mechanical integrity and cohesion and eventually prevent the growth of cancer cells. Thirdly, antioxidant properties of vitamin C inhibit cancer growth induced by free radicals (3, 19). It is however an interesting fact that vitamin C is taken up in oxidized form by cancer cells. Fourthly, vitamin C enhances the immune system by elevating the production of infection-fighting white blood cells and interferon levels, so cancer cells are suppressed or eliminated (20, 21). Last, the vitamin C can change the levels of certain amino acids in body fluids and may deplete the bioavailability of lysine and cyteine, 2 amino acids that required for rapidly growing tumors (22, 23).

The impact of vitamin C on the central nervous system and mental ability is based on the following mechanisms: First, increased c-AMP enables vitamin C to block phosphodiesterase, so the breakdown of c-AMP can be prevented (24). An increase in blood c-AMP levels therefore boosts mental ability. Secondly, vitamin C also prevents the formation of toxic neurotransmitters. Vitamin C deficiency triggers the oxidation of adrenalin and noradrenalin, and adrenochrome and noradrenochrome are generated, respectively, and their toxic effects pose various problems (25).

The impact of vitamin C on pain relief is explained by various mechanisms (26). First, vitamin C has anti-inflammatory effects by stimulating c-AMP production, which in turn elevates production of steroid in the ACTH. Secondly, vitamin C works to help decrease blood calcium levels and enhances calcium uptake in bone. As a result, bone pain is relieved (27).

It was recently discovered that vitamin C also supports the body's energy generation (28). The mechanism of ergogenic activity of vitamin C is probably due to vitamin C's oxidation

reduction potential, capable of providing necessary electrons to the electron transport system in the mitochondria for increased energy production.

Since Szent-Gyorgyi reported the efficacy of vitamin C for the first time in 1928, studies in the same area have continued and anticancer effects of vitamin C are still under debate. While Cameron et al. suggested beneficial effects of vitamin C on the treatment of cancer (4), the Mayo Clinic study reported no anticancer effects of vitamin C (5). Investigators cited the different administration method as the reason for such opposite results. The former used intravenous vitamin C administration at a dose of 10 g and subsequent oral administration, whereas the latter used oral administration only. Padayatty et al. proved that it was difficult to increase vitamin C level to more than 220 M/L in blood through oral administration and that blood levels of vitamin C that are required for combating cancer could be achieved through intravenous adminstration (6). Their findings provided the scientific basis for using intravenous administration in cancer patients.

Vitamin C is a water-soluble and remarkably nontoxic at high levels. Nevertheless, this treatment should be administered with caution to patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency (29). When given high doses of vitamin C, these patients may have the risk of developing hemolysis. Before applying vitamin C therapy, patients should be screened for this deficiency.

Although there is still controversy regarding anticancer effects of vitamin C, the use of vitamin C is considered the safe and effective therapy to improve the quality of life in terminal cancer patients. The further study is required to compare effects of vitamin C in between placebo and vitamin C group in terminal cancer patients with well-designed experimental strategy.

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