Case Study

Effects of High Doses of Vitamin C on Cancer Patients in Singapore: Nine Cases

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Abstract

Introduction. Intravenous high-dose vitamin C therapy is widely used in naturopathic and integrative oncology; however, a study reviewing its effects has never been performed in Singapore. This article serves to document administration of supportive vitamin C therapy for cancer patients in Singapore. *Methods.* The clinical response of 9 cancer patients of differing stages to the regular administration of large doses (25-100 g/d) of intravenous vitamin C (IVC; ascorbic acid) is outlined. Tumor pathology and patient health were verified by doctors who do not practice vitamin C treatment. *Results.* Cases suggesting survival beyond prognosis, improvement in quality of life, safe coadministration with and improved tolerance of conventional therapy, and deterioration in clinical condition following withdrawal of vitamin C therapy are documented clinically. Some patients experience the Jarisch-Herxheimer reaction—the release of endotoxin from microorganism death resulting in pimples, fever, and body odor—for a few hours after the therapy, but these are resolved quickly with no lasting effects. *Conclusion.* Randomized trials of IVC therapy are recommended because it has minimal side effects and has shown promising results.

Keywords

intravenous vitamin C, ascorbic acid, cancer, nutrition therapy, high-dose vitamin C therapy

Introduction

Cancer remains the top cause of death worldwide, despite continuing advances in research and development in the past decade.[1] In the United States, cancer accounts for 23% of the total death rate.[1,2] In Singapore, 1 in 3 Singaporeans dies of cancer,[3] and 33 people are diagnosed with cancer every day.[4] In 2005, the global incidence of cancer was 11 million, with an estimated mortality rate of 7.6 million.[5] This has been forecast to increase to an incidence of 15.5 million with 11.5 million deaths by 2030.[5]

Intravenous vitamin C (IVC) therapy for cancer patients was first developed by Linus Pauling.[6,7] Soon after, Pauling and Cameron documented their findings.[6] IVC therapy has a controversial history because clinical trials done at the Mayo Clinic failed to show any benefit; it was thus discarded by subsequent mainstream oncologists.[7,8] Although similar doses of vitamin C were used in the Cameron-Pauling study and at the Mayo Clinic, the administration of vitamin C for the Cameron-Pauling study had been performed intravenously, whereas that at the Mayo Clinic had been through the oral route.[9,10] More recent studies undertaken by the United States of America National Institute of Health showed that vitamin C showed cytotoxicity in cancer cells at high serum levels achievable only through intravenous administration.[10] Furthermore, studies show that oral administration of large doses of vitamin C can increase serum levels to a maximum of 220 μmol/L, but with IV administration, serum levels reach as high as 14 000 μmol/L.[10] Concentrations of 1000 to 5000 μmol/L are selectively cytotoxic to tumor cells in vitro.[10,11] Many recent studies have also highlighted the benefit of high intravenous doses of ascorbic acid.[11]

IVC therapy for cancer is not well known in Singapore. However, it is available for aesthetic purposes, such as in skin whitening or skin rejuvenation.[12] In this study, vitamin C infusion was used as one component of a nutritive support program for cancer patients. Vitamin C does not have the status of an alternative cancer therapy in Singapore because the suggested benefits of vitamin C have not been confirmed by controlled clinical trials. Most cancer patients in Singapore have received some form of alternative treatment such as Chinese medicine, herbal medicine, acupuncture,

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bioresonance therapy, Gerson therapy, macrobiotic diets, and raw food diets in addition to their conventional medical treatment.[13] Most of these alternative therapies are not well documented, and thus, the extent of effectiveness of these treatments remains largely unknown. Therefore, the aim of this study is to document the effects of IVC therapy in a series of cases from a Singaporean family medical practice with specialization in occupational medicine.

Methods and Procedures

Patients were given IVC therapy and other nutritional supplements at the Hosanna Clinic where Dr Yuen CFR (family physician and specialist in occupational medicine) is in charge. Patients seen at the clinic are normally treated and managed by conventional oncology centers. Most of the patients come to Dr Yuen for advice on medical nutrition and to improve general health status. Before the treatment, patients' consent was obtained for the disclosure of the medical information in this article. The vitamin C infusion protocol was adapted from the University of Kansas Medical Centre General Oncology Protocol, updated in August 2009.[14]

Eligibility for Therapy

The patients documented in this case study were selected from the pool of patients that regularly visited the clinic for vitamin C therapy. Patients who were documented had a wide variation in the severity and type of cancer they were affected with. A standard protocol of IVC administration for all patients was provided despite wide variation in disease type and severity.

For patients to be eligible for therapy at Hosanna Clinic, they had to possess a histologically or cytologically diagnosed neoplasm and also have care approved by their main oncologist. Furthermore, their medical history, physical information, and all copies of laboratory tests had to be submitted to the doctor administering IVC therapy. Patients with a newly diagnosed or relapsed neoplasm with histological or cytological confirmation had to also ensure that all relevant information was provided and documented. Patients could be simultaneously undergoing chemotherapy and/or radiation therapy.

Treatment Plan

History, physical examination, and all laboratory analyses, including a complete blood count, were done before commencing therapy. This included glucose-6-phosphate dehydrogenase testing. All patients desiring to undergo IVC therapy were first subjected to a screening visit and review of their condition. Decisions for follow-up visits were then made on the basis of the initial visit and were mutually agreed on by the patient and the treating physician.

Each patient would receive IVC and oral supplements, including laetrile, at the discretion of the treating physician based on cancer stage and status. IVC was then allocated in dosages (25-100 g) based on plasma vitamin C levels. The desired plasma concentration that had to be attained was approximately 350 to 450 mg/dL. Because we do not have a test to monitor the levels of vitamin C in patients, we followed the Kansas IVC therapy protocol strictly. For patients with active cancer, an initial recommendation of 21 days of daily IVC therapy was followed by continuing infusions every 2 to 3 days weekly. For patients who were using therapy as a maintenance routine, weekly infusions were recommended.

The patient was encouraged to take oral nutrient supplementation and adhere to a modified Gerson diet (low sugar, carbohydrate, and meat diet with high vegetable and fruit intake, especially through juicing) as soon as they started IVC therapy. Oral supplements included supplements for digestive health, including pancreatic enzymes (400-1200 mg/d) and probiotics (3-9 billion CFU); antioxidants, including α-lipoic acid (600-1200 mg/d), niacin (500-1500 mg/d), and resveratrol (10-20 mg/kg/d); energy boosting supplements, including CoQ10 (150-300 mg/d), cobalamin (80-100 mg/d), folic acid (0.5-1 mg/d), and thiamine B1 (5-30 mg/d); immune function supplements, including vitamin D (5000-10 000 IU/d), vitamin E (40-80 IU/d), selenium (200 µg/d), zinc (50 mg/d), colostrum (1-2 g/d), echinacea (1.2-3.6 g/d), and β-1,3/6D glucan (100-200 mg/d); and anti-inflammation supplements, including curcumin (1-3 g/d), flaxseed oil (3-6 g/d), quercetin (500-1000 mg/d), boswellia (1.2-2.4 g/d), and silymarin (300-900 mg/d). The dosages of supplements depended on individual needs and cancer status of the patient. These supplements play a supportive role to IVC treatment.

For the first 2 IVC doses, the initial infusion rate was 0.5 g/min, starting at 15 g of vitamin C with an appropriate amount of carrier fluid (sterile water and ringer's lactate, depending on the concentration of ascorbic acid infused). For the next 2 doses, 25 g of vitamin C was given at 0.5 g/min, with an appropriate amount of carrier fluid, with addition of 200 mg of magnesium chloride to prevent vascular spasm. For the subsequent 2 doses, 50 g of vitamin C was given at 0.5 g/min with an appropriate amount of carrier fluid and 200 mg of magnesium chloride. After the first 6 doses, 75 g of vitamin C was given at 0.5 g/min with an appropriate amount of carrier fluid and 200 mg of magnesium chloride. Vitamin C dosage was then increased to 100 g with 400 mg of magnesium chloride for patients with extremely aggressive tumors.

Patient 1 (P1)

P1, a 41-year-old Caucasian woman, was diagnosed with stage I breast cancer in July 2014. Her core biopsy revealed

an invasive ductal carcinoma, provisional grade 2 out of 3, ER and PR positive, and cerbB2 negative. An ultrasound showed an ill-defined heterogeneous lesion with hypervascularity located at the 10:00 position, measuring 1.3 × 0.8 × 1.2 cm^3 with enlarged right axillary lymph nodes. Her oncologist recommended surgery or localized radiation therapy, but she refused. She began to modify her diet by excluding meat and carbohydrates, mainly consuming fruits and vegetables, began exercising, and quit her 15-year smoking habit. After 2.5 months of a holistic lifestyle change, her tumor started shrinking. The patient's condition remained stable, and she enjoyed a good quality of life. On October 15, 2014, P1 started IVC therapy. Her most recent ultrasound report dated November 11, 2014—3 weeks after therapy commenced—showed that her tumor had undergone a sizable reduction, now measuring 0.8 × 0.6 × 0.9 cm^3 (a 55% reduction compared with the scan in September). The patient experienced the Jarisch-Herxheimer reaction during the initial phase of IVC therapy. She had a pimple outbreak around the face, neck, and thoracic area and strong odor in perspiration that lasted for 2 to 3 weeks. Despite the improvements seen in her ultrasound reports, the patient was still encouraged to consider surgical removal of the tumor. However, P1 is an overseas patient and follow-ups were not done when she left the country.

Patient 2 (P2)

P2, a 44-year-old Chinese man, was diagnosed with nasopharynx carcinoma stage III in May 2013. He had previously completed 33 cycles of radiotherapy and a single dose of chemotherapy before collapsing in a seizure as a result of a panic attack at the oncology clinic. In October 2013, a PET scan showed the spread of cancer to the submandibular lymph node. In January 2014, the spread to the lymph node was confirmed as a submandibular tumor. The patient refused further chemotherapy and surgery because of the traumatic experience of radiotherapy. He had been afflicted with many side effects after radiotherapy, including dryness in mouth, eyes, and nose; muscle and bone ache; toothache; hair loss; loss of taste; and frequent nosebleeds. In January 2014, the patient was started on IVC therapy because he had not recovered from his prior psychological stress and, therefore, was not able to complete his course of chemotherapy. Just before treatment commenced, another PET scan showed that the lesion in the right nasopharynx was largely resolved, with mildly increased FDG activity near the roof of the right nasopharynx, coupled with an interval reduction in size and metabolic activity of the previously noted FDG avid lymph nodes in the bilateral level II of the neck. In April 2014, 4 months after the start of therapy, a PET scan demonstrated marked cancer regression. There was no remaining abnormal tumor enhancement in the nasopharyngeal areas, oropharynx, and parapharyngeal space and pterygopalatine fossae. The previously mildly enlarged cervical lymph node on level II of the right side of his neck also showed necrotic changes. The patient feels more energetic and cheerful after the change of treatment from radiotherapy to IVC therapy, with most of the radiotherapy side effects not seen or felt. To date, the patient is well, without any swelling felt on his neck. A follow-up scan was scheduled in January 2015. However, because of psychological side effects, the patient did not return for further PET scans. The patient is well to date and is enjoying good quality of life.

Patient 3 (P3)

P3, a 54-year-old Chinese woman, was diagnosed with stage IV lung cancer, left-lower lobe bronchoalveolar lavage adenocarcinoma in December 2012. Multiple FDG-avid pulmonary nodules were noted in the right lung, and a moderately FDG-avid mass-like consolidation with multiple adjacent nodular opaque regions was seen in the lower lobe of the left lung. She was given a prognosis of 7 months to live. Her oncologist suggested oral chemotherapy but the patient initially refused. The patient then sought other alternative therapies and eventually started IVC therapy on November 16, 2013. Despite high doses of vitamin C, her cancer still progressed, shown through chest X-rays and pleural lung effusion, with no decrease in the levels of lung fluids. She was prescribed gefitinib, a targeted therapy drug for non-small-cell lung cancer. The patient started to feel very weak after beginning drug therapy and was unable to walk without a walking aid. Soon after, the patient decided to continue with IVC therapy along with gefitinib. By September 2013, P3's CT scan showed a large decrease in the consolidation in her lungs—from covering 75% of the total lung field to only affecting the lining at the base of her lungs. This combination therapy elicited an effective response with minimal side effects of the chemotherapy drug, which was mild dryness in mouth. The patient was also able to gain strength to walk on her own once again after a few IVC infusions. A follow-up report done by the National Cancer Centre, Singapore, dated September 11, 2014, showed an interval decrease in the size of her pretracheal lymph node (1 cm reduced to 0.2 mm) as well as an interval resolution of the majority of pulmonary nodules and bilateral consolidation.

Patient 4 (P4)

P4, a 48-year-old Chinese woman, was diagnosed with stage IV ovarian cancer in March 2013. A well-defined rounded lesion with mild enhancing rim was found situated in a posterolateral manner to the left submandibular gland and lateral to the left carotid vessels. Soon after, oophorectomy and hysterosalpingectomy were performed. She then proceeded with 6 cycles of chemotherapy after surgery.

Subsequent reports showed that the patient was cleared of cancer cells. A complete blood count done on September 21, 2013, showed the presence of tumor markers within the normal range. From her full blood count, hemoglobin levels were 9.7 g/dL (12.0-16.0 g/dL) and white blood cell count was 2.9×10^9/L ($4\text{-}10 \times 10^9$/L). Her oncologist warned P4 that there was a 70% chance of her cancer relapsing within a year. The patient decided to try IVC therapy on November 13, 2013, to improve her health and immune system and prevent cancer relapse. From her full blood count in March 2015, hemoglobin levels increased to 11.3 g/dL, and white blood cell count increased to 5.8×10^9/L. Though these results were on the lower end of the reference range, IVC therapy, in addition to the diet and supplemental therapies prescribed, did improve her overall health. Her most recent ultrasound of the pelvis in March 2015 shows no pelvic mass or free fluid, with unremarkable urinary bladder status. Her most recent blood test (April 20, 2015) had shown normal tumor markers—CA125 (cancer antigen) of 6.1 U/mL (<36 U/mL)—revealing no relapse of her cancer. After the implementation of vitamin C therapy, P4 has been travelling, spending time with her family, and leading a normal life.

Patient 5 (P5)

P5, a 49-year-old Chinese woman, was diagnosed with stage II/III breast cancer, ER and PR positive, cerbB2 negative in August 2013. On her right breast, histopathology of hyalinized fibroadenoma—multiple hypoechoic masses—were seen at the 10:00 to 1:00 position measuring between 6 to 16 mm. The mass at the 1:00 position was lobulated. On her left breast, histopathology of invasive ductal carcinoma—2 ill-defined inhomogeneous masses—were seen at the 10:00 to 2:00 position measuring $4.3 \times 4.3 \times 3.4$ cm^3 and $5.9 \times 4.3 \times 3.7$ cm^3. A smaller hypoechoic mass was also seen at the 2:00 position measuring $0.9 \times 0.8 \times 0.8$ cm^3. Her oncologist suggested surgery with breast reconstruction. She tried traditional Chinese medicine, but the tumor was growing 1 cm each month despite treatment. In August 2013, metastatic carcinoma from the left breast spread to the left axillary lymph node. The patient subsequently commenced IVC therapy in January 2014. From January to February 2014, all her tumors shrank by 30% to 53%. She was referred to an oncology surgeon to remove the breast tumors, but the cancer had metastasized to her sternum, and thus, the surgery could not be performed. In June 2014, the patient agreed to also start on oral hormonal therapy with tamoxifen. Unfortunately, tamoxifen did not result in any improvement. The patient initially thought that the IVC therapy might have been preventing the absorption of tamoxifen, and therefore, she chose to undergo IVC therapy less than once in 10 days (recommended once every alternate day initially). After this, her condition rapidly deteriorated while the patient remained on tamoxifen. A bilateral breast ultrasound was done on November 25, 2014. This showed an increase in the mass at the 12:00 position on her left breast, measuring $6.6 \times 6 \times 3.7$ cm^3 (vs $6 \times 5.6 \times 4.2$ cm^3) previously. There was also an interval increase in the size and number of metastatic left axillary nodes, measuring 1.7×1.3 cm^2, 1.3×0.7 cm^2, and 0.9×0.8 cm^2. The patient has since discontinued IVC therapy.

Patient 6 (P6)

P6, a 57-year-old Chinese woman, was diagnosed with stage I nasopharynx cancer (T2N1M0) in May 2014. There was a FDG-avid lesion on the right side of her nasopharynx abutting the clivus. The lesion extended across the midline and posterior margin of the right nasal cavity. The patient went for 33 sessions of radiation therapy. On July 12, 2014, P6 decided to start on IVC therapy to speed up the healing process. Her blood test result (July 12, 2014) showed high serum tumor markers—positive Epstein Barr virus (EBV) IgA of 291.6 (>126.5), low lymphocyte count of 0.61×10^9/L (1.50-4.00)—coupled with altered liver function— serum glutamic-pyruvic transaminase (SGPT)/alanine aminotransferase (ALT) of 56 U/L (<37), Serum glutamic-oxaloacetic transaminase (SGOT)/aspartate aminotransferase (AST) of 56 U/L (<41), and gamma GT of 65 U/L (<51). By October 24, 2014, after 3 months of IVC therapy along with other therapies given at the study clinic, the patient's lymphocyte count had increased to 0.88×10^9/L. Her liver profile similarly demonstrated improvement and was found to be within the healthy range—SGPT/ALT 17 U/L (<37), SGOT/AST 25 U/L (<41), and gamma GT 43 U/L (<51). Her tumor markers also decreased, with an EBV IgA positive 201.6 (>126.5). On November 17, 2014, the patient underwent an EBV quantitative PCR at Singapore General Hospital. The results showed that her EBV levels were undetectable, an extremely good prognosis. The patient continues to undergo IVC therapy to boost her immunity and also to prevent the relapse of cancer.

Patient 7 (P7)

P7, a 46-year-old Chinese female, was diagnosed with an early stage of breast cancer in March 2012: right breast cancer in situ and invasive lobular carcinoma, ER and PR positive, cerbB2 negative. Three irregular hypoechoic solid nodules were detected on her right breast. Lesion 1 measured $1.3 \times 1.1 \times 0.5$ cm^3, lesion 2 measured $0.6 \times 0.6 \times 0.3$ cm^3, and lesion 3 measured $2.2 \times 1.0 \times 0.6$ cm^3. These lesions had irregular margins together with an electrography distance ratio of 1.5 to 1.9. Biopsy was done in March 2012 as well; core biopsy was done, showing foci of lobular carcinoma in situ and an extensive invasive lobular carcinoma consisting of E-cadherin-negative tumor cells infiltrating a sclerotic breast into fat. Lobular carcinoma was

seen on her right breast. Her blood report before the commencement of IVC therapy on April 3, 2012 showed low serum tumor markers—α fetoprotein 3 μg/L (<16), carcinoembryonic antigen (CEA) <0.5 μg/L (<5.0), CA19.9 15 U/mL (<38), and CA15.3 9 U/mL (<32.1). However, her serum tumor markers were insensitive and did not show the presence of her breast tumors. P7 began IVC therapy on April 5, 2012. By May 2012, her largest lesion (2.2 × 1.0 × 0.6 cm^3) had shrunk to 2.1 × 0.8 × 0.6 cm^3. On October 8, 2012, the patient had a cytopathology report done by Parkway Health Laboratory. The report showed indeterminate right breast lesions, features of benign changes, and no malignant cells seen. The patient was successfully relieved of the cancer and is still cancer free as of December 2014.

Patient 8 (P8)

P8, a 53-year-old Chinese woman, was diagnosed with stage II breast cancer in November 2013: an infiltrative ductal carcinoma grade 3, ER and PR positive, cerbB2 negative. The patient's mammography report (December 2013) showed a 1.1 × 1.0 × 0.7 cm^3 solid nodule on her right breast and an indeterminate node that measured 1.5 × 1.3 × 0.9 cm^3 in the right axilla. The patient was referred to have the 2 breast nodules removed by her oncologist. P8 had a lumpectomy done on January 21, 2014, but a mass in the axilla was not removed. Her scan after the operation (end January) showed a 5.0 × 3.1 × 4.1 cm^3 mass with irregular margins at her right axilla, a v-shaped mixed-echo lesion measuring 3.9 × 1.7 × 1.1 cm^3 at the 12 o'clock position on her right breast with dilated ducts, and numerous cysts ranging from 0.3 to 0.7 cm in diameter. She began IVC therapy in end January. After 21 days of intensive therapy (April 23, 2014), P8 immediately went for her scan. Her scan showed a lesion of 2.1 × 2.2 × 0.8 cm^3 (a reduction of 49.3% from 3.9 × 1.7 × 1.1 cm^3). The mass in her right axilla had also been reduced to scar tissue. She went for another scan in March 2014 (March 11, 2014), and this showed a continual shrinkage of her tumor, seen now to be 1.8 × 0.3 × 0.5 cm^3 (a reduction of 92%). An ultrasonic review performed on April 23, 2014, showed another reduction of 66% (0.6 × 0.3 × 0.5 cm^3). On July 1, 2014, only postsurgical scarring was found, together with the absence of a small postoperative seroma previously seen. A follow-up was performed a month later in August 2014, and again, no unusual masses and lesions were seen. Her most recent full blood count in October 2014 showed normal results with cancer markers well within healthy range.

Patient 9 (P9)

P9, a 72-year-old Chinese man, was diagnosed with early-stage liver cancer in February 2001. He subsequently had a cholecystectomy and transarterial chemoembolization performed, spanning the period of February to June 2001. P9's liver was found to be normal in size and echogenicity. On August 7, 2009, an ultrasound was done at Medical Imaging X-Ray and Diagnostic Centre, Singapore. An 11.3 × 10.7 × 7.5 cm^3 large solid mass with internal calcifications was seen with no hepatomegaly. Three cysts were found in the right kidney—2 at the midpoint of the kidney, measuring 3.2 × 2.9 × 2.6 cm^3 and 2.6 × 2.1 × 1.7 cm^3, respectively, and 1 at the upper pole measuring 2.8 × 2.4 × 2.1 cm^3. In the left kidney, 2 cysts were also seen—the first measuring 2.6 × 2.4 × 1.7 cm^3 at the midpoint, and the second measuring 5.4 × 4.5 × 4.2 cm^3 at the lower pole. The cancer relapsed, and the patient was given a prognosis of 9 months. The patient commenced IVC therapy on that same day. Two months later, a report dated October 1, 2009, showed that the lesion in the liver had undergone a reduction in size to 8.2 × 7.9 × 6.7 cm^3, with poorly outlined borders, and isoechoic to hypoechoic lesions seen in the right lobe of the liver (segment 5/6). However, multiple simple renal cysts were still present bilaterally. On November 3, 2009, the patient had another abdominal ultrasound performed at the National Healthcare Group Singapore. This ultrasound showed that the larger liver mass had shrunk to 7.1 × 6.6 × 6.0 cm^3, and it was stable in appearance and size. P9's liver masses had responded well to the nutrition therapy, and his general condition had improved, with a slight gain in body weight. The patient decided to stop IVC therapy and just maintain a healthy diet. In September 2010, 2 large hepatic masses were seen on the right lobe (segment 5 and 6). The mass at segment 5 was 11.1 × 10.2 × 7.6 cm^3 in size, with internal calcification. The second mass was 6.7 × 5.6 cm^3 in size. To date, the bilateral renal cysts are still present, but the patient is able to live with the cysts and enjoy an increased quality of life.

Discussion

Pharmacokinetics of Vitamin C

The pharmacokinetics of IVC differ from orally administered vitamin C.[15] Studies found that the oral absorption of vitamin C can vary up to 70-fold lower compared with that of intravenous administration.[16]

There is increasing evidence that IVC is selectively toxic to some types of tumor cells by inducing tumor cell apoptosis, inhibiting angiogenesis, and reducing inflammation.[17] Vitamin C at normal physiological concentrations takes on a water-soluble antioxidant role.[17] However, at high concentrations (350-450 mg/dL), vitamin C dissociates in extracellular fluid to become an ascorbate radical ($AscH^-$), causing iron to be reduced to the ferrous form ($AscH^- + Fe^{3+} \rightarrow Fe^{2+} + AscH^- + H^+$) The ferrous iron then reacts with oxygen, producing a superoxide anion (O_2^-), which reacts with hydrogen to form H_2O_2.[15] As the concentration

of H_2O_2 increases in these tumor cells, these cells are left vulnerable to the cytotoxic effects of H_2O_2, and hence, apoptosis is successfully induced, killing the cells.[11,15,18,19] At the same time, a high concentration of serum vitamin C suppresses the reduction of glutathione, causing it to be present in its oxidized form (GSSG). As a result of this reaction, H_2O_2 gets accumulated. H_2O_2 is easily metabolized into oxygen and water by the enzyme catalase in normal, healthy cells. However, the enzyme catalase is missing in tumor cells. This process of selective cytolytic activity allows the effective targeting of tumor cells without simultaneously affecting the body's immune cells.[15] In addition to the absence of catalase, tumor cells selectively take up more vitamin C compared with normal cells because of the upregulation of glucose transporters to facilitate their metabolic needs.[20-22]

Tumor angiogenesis is the development of new blood vessels toward and into a tumor.[17] It is known to be critical for the growth and metastasis of tumors because it provides a supply of nutrients and a removal system for waste products.[17] Studies suggest that vitamin C enhances collagen synthesis, which in turn inhibits the formation of new vascular tubules, stopping tumor angiogenesis.[17]

Inflammation was found to be an ongoing issue in cancer patients.[17] Studies have shown that this inflammation can be effectively modulated with IVC therapy.[15,17] Vitamin C decreases inflammation by suppressing the expression of both COX-2 (cyclo-oxygenase) and nuclear factor κ-light-chain-enhancer of activated B cells (NF-κB).[15] C-reactive protein (CRP), one of the markers of inflammation, was used in certain studies to monitor the effects of IVC therapy.[17] It was found that high levels of CRP correlated with poor prognosis of patients, but this can be controlled with IVC therapy.[23]

Effects of Vitamin C Therapy

The effects of IVC therapy have been studied in this article. For most patients, the side effects of IVC therapy comprised mainly signs and symptoms of Jarisch-Herxheimer reaction. This is a reaction of the body to endotoxins produced by the necrosis of harmful cells in the body.[24] Side effects felt by patients were similar to the Jarish-Herxheimer reaction, but definite conclusions could not be drawn because Jarish-Herzheimer reactions were linked to antimicrobial effects. We suggest that IVC therapy results in a similar Jarish-Herzheimer reaction, but more research will be needed to be done in this field. These transient effects were usually reversible. This reaction usually manifests as fever, chills, strong body odor, and pimples on the body and neck.[24] This reaction commonly occurs within 2 hours after IVC therapy and resolves after 2 to 3 hours. However, P1 experienced the most side effects because her outbreak of pimples and strong perspiration odor lasted for 2 to 3 weeks. Thus, this therapy is relatively safe compared with radiotherapy and chemotherapy. In contrast, the patients who underwent chemotherapy and/or radiotherapy experienced many side effects such as dryness in the mouth, eyes, and nose; muscle and bone ache, toothache, hair loss, loss of taste and frequent nosebleeds, lethargy, weakness, and low immunity.

For most patients, IVC therapy has improved their quality of life and may have prolonged their life expectancy. For example, P3 was unable to walk initially because of the weakness in her lower limbs as a side effect of gefitinib; however, with the combination of IVC therapy, the patient gained strength to walk again. P4 has been free of recurrence following completion of conventional treatment from stage IV ovarian cancer since September 2013 and with nutritive support of IVC therapy, she now enjoys a good quality of life. Also, P9 has been living with his cancer comfortably till today despite being given a 9-month-prognosis previously (dated August 7, 2009).

IVC therapy may stabilize cancer and reduce risk of metastasis. P9's doctor commented that it was unusual for an aggressive tumor (such as a hepatoma) to remain stable in size despite the tumor being large ($7.1 \times 6.6 \times 6.0$ cm^3).

Instances of tumor regression likely attributable to IVC therapy were observed. After IVC treatment, P2 showed necrotic activity in his abnormal enlarged cervical lymph nodules that had not been removed by previous radiotherapy. The invasive breast carcinoma in P7 disappeared after 6 months. Most remarkably, the tumor P8 had been afflicted with shrank by 49.3% in the first 21 days of intensive IVC therapy. This was followed by a 93% shrinkage after approximately 6 weeks. The patient was totally cleared 10 months later. P9 also showed remarkable tumor shrinkage. After the relapse of cancer in 2009, the patient did not seek conventional treatment and decided to solely focus on IVC therapy. For P9, his tumor also shrank from $11.3 \times 10.7 \times 7.5$ to $7.1 \times 6.6 \times 6.0$ cm^3 for the whole duration of IVC therapy. On the other hand, when P5 stopped IVC therapy, her breast tumor growth started to worsen. Her tumor grew from $6 \times 5.6 \times 4.2$ to $6.6 \times 6 \times 3.7$ cm^3 in a span of less than 5 months. When P5 initially started IVC therapy, her 3 tumors showed consistent results: shrinkage of 30% to 53%. These improvements of her tumor were seen in a span of 1 month. P5's tumor growth only started to worsen after the removal of IVC therapy and illustrated the likelihood of tumor regression attributed to IVC therapy.

Two cases illustrate the results of concomitant use of IVC and conventional drugs. P3 utilized gefitinib in conjunction with IVC therapy. This drug is known to cause acute dyspnea, interstitial lung disease, diarrhea, nausea, mouth ulceration, pancreatitis, rash, aches, dry skin, anorexia, weight loss, peripheral edema, amblyopia, conjunctivitis, hemorrhage into the central nervous system, and even death in pediatric patients.[25] She did not suffer from

any of these side effects. The patient had a strong response to gefitinib, suggesting no impairment of its activity by IVC. P5 utilized tamoxifen in conjunction with IVC therapy. This drug may result in endometrial adenocarcinoma and polyps, uterine sarcoma, vaginal bleeding and discharge, musculoskeletal inflammation, hypercalcemia, elevation in liver function tests, thrombocytopenia, leukopenia, ocular toxicity, and even an increase in thromboembolic risks.[26] However, P5 similarly did not suffer any side effects from this hormonal therapy, although admittedly, all these are rather rare and might not have been encountered in the relatively short observation period. While tamoxifen and IVC were being used concurrently, the patient did not experience any improvement, and she was persuaded to cease IVC to facilitate the activity of tamoxifen. After IVC was withdrawn, the patient experienced an increase in the size and number of breast tumors.

IVC therapy is an alternative treatment for cancer for some patients. P2 had a very bad experience with radiotherapy and chemotherapy and was unable to undergo these treatments without experiencing a panic attack. IVC therapy was the only therapy that the patient was willing to be treated with. Although IVC therapy is known mainly as a supportive therapy, the patient refused professional advice and only underwent IVC therapy. The results were shrinkage in cervical lymph nodules and, eventually, necrotic changes.

However, there were also cases when IVC therapy was not the best therapy. For example for P3, high doses of vitamin C did not prevent her cancer from progressing or decrease the pleural effusions.

Observations on the Use of IVC Therapy by Cancer Patients

With the advances in medicine and the advent of many therapies, patients now have a wide variety of treatments to choose from. The use of complementary therapies has been increasing over the years, from 1990 to 2006.[27] Most patients visiting the Hosanna Clinic for IVC therapy are extremely well educated and make well-informed decisions. Many patients do not simply rely on chemotherapy and radiotherapy but seek alternative treatments as well. P3 only decided to consume gefitinib after researching about its side effects and drug mechanisms and used it alongside IVC. Although P4 has a strong belief in alternative medicine, she still believes in conventional medicine to a certain extent—for example, going in for a lumpectomy. Thus, patients are knowledgeable and do not simply make decisions based on advice given by professionals.

The purpose of this case study is to document the effects of IVC therapy and to increase awareness about IVC therapy as a supportive therapy for cancer treatment. There are many limitations to our study. The size of the cohort for this case study was 9 patients, which was insufficient to rule out the outliers in our study. This study was also not a controlled or prospective study, which results in the inability to fully distinguish effects of IVC therapy from that of other therapies such as diet and supplements given. However, it was observed that the combination of diet, supplements, and IVC therapy results in substantial positive results. Also, the diet of each patient was not strictly monitored. An inclusion of a diet questionnaire or a chart for patients to record their daily diet would be helpful in a future study.

Conclusion

Compared with chemotherapy, IVC therapy, in combination with a diet and supplement regimen, is tolerated well, appears to have antitumor activity in some cases, has been administered alongside conventional therapy without impairing response, is safe for most patients, and is inexpensive. It also appears to increase the quality of life for patients. IVC therapy has the potential to become an important chemotherapeutic method to combat cancer. This, however, this can take place only through further research and clinical study.

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Declaration of Conflicting Interests

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