

Nutritional Supplementation and Fatigue in an Ovarian Cancer Patient

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Abstract

Fatigue associated with chemotherapy can range from mild to severe depending on the regimen administered and the specific type of cancer. The etiology of fatigue is not well understood and many causes are proposed including a deficiency in the body to effectively utilize dietary nutrients. Therefore, the case of a 47 year old female recently diagnosed with Stage I ovarian carcinoma for which she received chemotherapy along with dietary supplementation was reviewed. Baseline fatigue levels were obtained prior to initiation of nutritional therapy and monitored for at least 3 months. During the treatment and supplement period, significant improvement in fatigue, nausea, vomiting, diarrhea, and over all general well being was reported. Additionally, hematological monitors and cancer markers were also followed and evaluated. The patient tolerated chemotherapy without any significant complications and reported her fatigue to be decreased upon nutritional supplementation.

Introduction

Fatigue is a common complaint of oncology patients who receive chemotherapeutic agents (1-5). Depending upon the chemotherapeutic regimen, the degree of fatigue reported by patients is variable, ranging from mild(2) to severe (4). It is not surprising then, that Buckingham et al reported fatigue as the most common and troublesome side effect in ovarian cancer patients who received carboplatin for treatment(6). Similarly, fatigue was reported as a significant toxicity in 33% of patients treated with docetaxel for pancreatic cancer(1).

The factors that affect the level of fatigue in patients with cancer have not been formally recognized. However, in 1997, based on the results of a quality of life survey, Pater et al concluded that female patients, those with metastatic disease, and those with poor performance status were more likely to experience fatigue. In addition, older patients and those with breast cancer were found to report less fatigue. While patients with ovarian and lung cancer experienced greater degrees of fatigue. Also of importance, patients who were controlled with anti-emetics experienced less fatigue (7).

However, there is no proven or recognized therapy for fatigue, regardless of its etiology. As healthcare providers struggle with quality of life issues (including fatigue), many may look to nutritional supplements to increase the body's inherent defenses against disease, medications, and the assault of aggressive radiation.

Objective

To evaluate the effectiveness of nutritional supplementation for decreasing fatigue in an oncology patient undergoing treatment with chemotherapeutic agents documented to produce or exacerbate fatigue.

Case History

A pelvic ultrasound for a 47 year old white, female revealed a 2.5 cm complex cyst in her left ovary. It was also noted that the cyst had a 0.8cm internal cyst with small

amounts of debris collected within it. At this time, differential diagnosis included hemorrhagic cyst, endometrioma, ectopic pregnancy, and ovarian neoplasm. A follow-up ultrasound after her next menstrual cycle was recommended.

Upon follow-up, one month later, ultrasound confirmed the presence of a complex cyst with internalized debris. However, the cyst had increased to 5.1 cm in diameter. Since the patient had recently had a negative pregnancy test, differential diagnosis included ovarian neoplasm, endometrioma, and hemorrhagic cyst.

Biopsy of fallopian tubes, cyst, and left ovarian specimens resulted in a diagnosis of invasive well-differentiated papillary serous carcinoma (Stage I-C Ovarian Cancer). In addition, a 60-cc sample of cyst fluid reported scattered irregular papillary fragments of atypical epithelial cells consistent with a serous neoplasm.

Laparoscopic left salpingo-oophorectomy was performed on the patient without any complications. Post operative chest x-ray was normal with postoperative pneumoperitoneum. Three days later she was returned to surgery where she underwent the following procedures: right salpingo-oophorectomy, appendectomy, bilateral pelvic and periaortic lymphadenectomy, supracolic omentectomy, and left subclavian intravenous port insertion. Specimens collected during the surgery indicated no malignancies of omental tissue or fibrous connective tissue, no histopathologic changes of the appendix, and no metastatic tumors in any of the lymph nodes biopsied. In addition, sections of the ovary revealed papillary serous carcinoma involving the surface of the ovary with minimal stromal invasion, unremarkable fallopian tube, fibrous adhesions of the uterine serosa, chronic and acute cervicitis, benign endometrium, and superficial adenomyosis was present.

An additional specimen of abdominal fluid was studied for malignancy. The fluid contained mesothelial cells, many with reactive changes, neutrophils, fat, and skeletal muscle. There were rare clusters of atypical columnar epithelial cells present. However, no malignant cells were identified.

Patient underwent first treatment of chemotherapy with paclitaxel, carboplatin, and gemcitabine on 7/3/99 without any complications during infusion. She was discharged on 7/8 with prescriptions for estrogen and propoxyphene for pain. To assess the perspective of her fatigue and general well-being, the patient completed a survey at day 1, 5, 35, 45, 55, 65, 111, and 121. Day 1 of the survey was actually 10 days after the 1st dose of chemotherapy was administered. Based on this initial survey, her fatigue could be classified as occurring all of the time. In addition, the patient made note of frequent vomiting and diarrhea. Subsequently, the nutritional supplement, Propax, was initiated. At day 5 of the survey (15 days post chemotherapy), her fatigue appeared to be improving and she noted an improvement in the regulation of her bowel movements.

Sometime later, she developed a severe global rash with lesions that required treatment with steroids. At this time gemcitabine was discontinued for the next scheduled chemotherapeutic regimen. Pathological evaluation of the lesions showed microscopic features most consistent with lymphocytic angitis. The epidermis was normal with no apoptosis identified. However, within the subjacent dermis, a predominant superficial perivascular inflammatory infiltrate consisting of lymphocytes and extravasated red blood cells was present. Microscopic differential diagnosis included drug eruption,

viral exanthem, and id eruption. The lesions were not consistent with those of erythema multiforme or gamma benzene hexachloride (GBH) eruption.

Laboratory values obtained on 7/12 reported SEGS, WBC, RBC, Hg, and Hct below the normal ranges while monocytes and lymphocytes were above the normal ranges. MCV, MCH, MCHC, RDW, platelets, bands, and eosinophils were within normal limits. In addition, serum carcinoembryonic antigen (CA-125) of 51 U/mL was above the reference range (See figures 1 - 4).

A complete blood count (CBC) was obtained on 7/21 with abnormally low values for RBC and Hct with high WBC, RDW, and platelets. All other values were normal. She received her second dose of chemotherapy with paclitaxel and carboplatin with no complications.

CBC for 8/18 reported decreased RBC, Hg, Hct, and segs; increased RDW; normal WBC, MCV, MCH, MCHC, platelets, monocytes, eosinophils, lymphocytes, and basophils. All other parameters were insignificant. Third regimen of chemotherapy was administered on 8/20/99, again without any complications. In addition, the CA-125 decreased to 6 U/mL. At survey day 35, she documented fatigue as occurring only part of the time. A significant improvement was noted when compared to the initial survey where fatigue was recorded as occurring all of the time. She also noted that she was generally feeling "very strong". This trend in improvement of fatigue continued throughout survey day 45. However, she noted muscle and joint aches; and indicated she might be catching a cold. By survey day 55, notations of the upcoming cold were absent. Her indicators of fatigue continued to show a trend towards improvement.

CBC for 9/13 reported low RBC, Hg, Hct; high RDW; all others were normal. In addition, a serum chemistry for BUN, serum creatinine, glucose, sodium, potassium, chloride, and carbon dioxide were also within normal limits. CA-125 continued to decrease to 4 U/mL. She received her 4th dose of chemotherapy on 9/15. She reported major joint aches and fatigue with the administration of this chemotherapy dose. She indicated on survey day number 65 that she napped 2 hours for 3 - 6 days post chemotherapy.

CBC for 10/5 was significant for low WBC, RBC, Hg, Hct, and segs. All other values were considered normal. During this scheduled office visit, the absence of blood return for her subclavian port was noted. As a result, the fifth dose of chemotherapy was administered on 10/7 via peripheral infusion. Patient admitted to initiating yoga exercise that required strenuous upper body stretching. Under fluoroscopic control, further evaluation noted the proximal end of the catheter was actually underneath the clavicle entrapped within the fascial layer of tissue. A new port a cath was attached during operative procedure with no complications. Patient was sent home on propoxyphene for pain. CA-125 continued to decrease to 3 U/mL

On 10/29, CBC was significant for decreased WBC, RBC, Hg, Hct, and segs. Since her Absolute Neutrophil Count (ANC) was less than 1500, chemotherapy was delayed. Increased parameters were noted for RDW and lymphocytes. All other values were within normal limits. Survey day 111 recorded a return trend towards fatigue improvement. She documented in the survey that she felt good despite the delay of therapy. She received her 6th dose of chemotherapy without incident on 11/8.

Survey entry for day 121, continued with a trend towards fatigue improvement. She

also noted insomnia post chemotherapy on 11/8. But overall, she reported feeling stronger.

Medications administered during treatment

The patient was started on famotidine for stress ulcer prophylaxis upon diagnosis in July. In addition, she received azithromycin for a suspected bacterial infection as noted in August, acetaminophen as needed for muscle and joint aches and pain in August and September, temazepam temporarily for insomnia in November, and docusate for post operative constipation. Accordingly, Propax was administered by the patient and her compliance was self reported to be about 95% throughout the study period.

Discussion

In many cases, the antineoplastic regimens used to treat ovarian carcinoma may produce a number of unpleasant or intolerable adverse effects that can affect the therapy. Thrombocytopenia associated with gemcitabine is well documented and dose limiting. Neutropenia is also common, but not dose-limiting. Cumulative effects of gemcitabine commonly produce anemia. Additionally, it has a low potential for emesis. About two-thirds of patients experience an increase in hepatic transaminases. Commonly, an acute flu-like syndrome consisting of fever, fatigue, chills, headache, and arthralgia is reported in patients who received gemcitabine. Erythematous pruritic maculopapular rashes of the neck and extremities are also frequently reported and respond to treatment with topical glucocorticosteroids.

Carboplatin, a derivative of cisplatin, is also associated with dose limiting myelosuppression with thrombocytopenia occurring more frequently than leukopenia. Twenty-five percent of previously treated patients and 35% of previously untreated ovarian cancer patients experience thrombocytopenia when treated with carboplatin. Additionally, 90% of patients will have anemia (40% requiring transfusions and 5% hemorrhaging). Diarrhea, abdominal pain, and constipation are reported in 6 - 17% of patients who receive treatment. Unlike gemcitabine, carboplatin's emetic potential is considered high to moderate.

Neutropenia associated with paclitaxel is the dose-limiting toxicity. In combination with cisplatin, paclitaxel commonly produces peripheral neuropathy. Like gemcitabine, it has a low emetic potential. Mucositis is dose-dependent and alopecia has an abrupt onset that can occur for up to 2 weeks.

Overall, the patient described tolerated her chemotherapy regimens well. There were no unusual or unexpected myelosuppressive episodes. During the study period, chemotherapy was delayed only once as a result of neutropenia. In addition, arthralgia, diarrhea, and constipation were reported by the patient as mild and controllable. Nausea and vomiting were not identified by the patient as severe or moderate.

The protective effects of fat-soluble and other natural antioxidants are well known⁽⁸⁾. These antioxidant defenses are important in determining immune cell integrity and functionality of membrane lipids, cellular proteins, and nucleic acids. Additionally, antioxidants are believed to control signal transduction and gene expression in immune cells⁽⁹⁾. There are several stages where antioxidants may control the progression and malignancy of disease. Antioxidants may also provide protection even when cancer-infected viral activity is present.

Therefore, dietary introduction of these nutrients may stimulate host immunological defenses and damage malignant cells directly by cycling with consequent oxygen radical production. The unique dietary supplement, Propax, addresses the nutritional concerns of oncology patients without resorting to mega dosing as in many immunosuppressive types of disease states. The formulation is composed of the complete antioxidant group and trace minerals, combined with water-soluble nutrients and essential fatty acids. To aid in the production of ATP, the formulation also includes phospholipids & creatinine, creatinine phosphate, tyrosine, and alpha glutarate. Finally, the formulation utilizes a unique delivery system that mimics the way the body utilizes nutrients₍₁₀₎. These properties may be of benefit in treating the fatigue and mylaise commonly seen in patients with immunosuppressive disease, similar to the one previously described. Although, well-controlled, blinded, clinical studies are required to draw definitive conclusions on the effectiveness of nutritional supplements like Propax, it may correlate with the positive results for decreased fatigue, vomiting, nausea, and diarrhea experienced by the patient.

Summary of CBC parameters

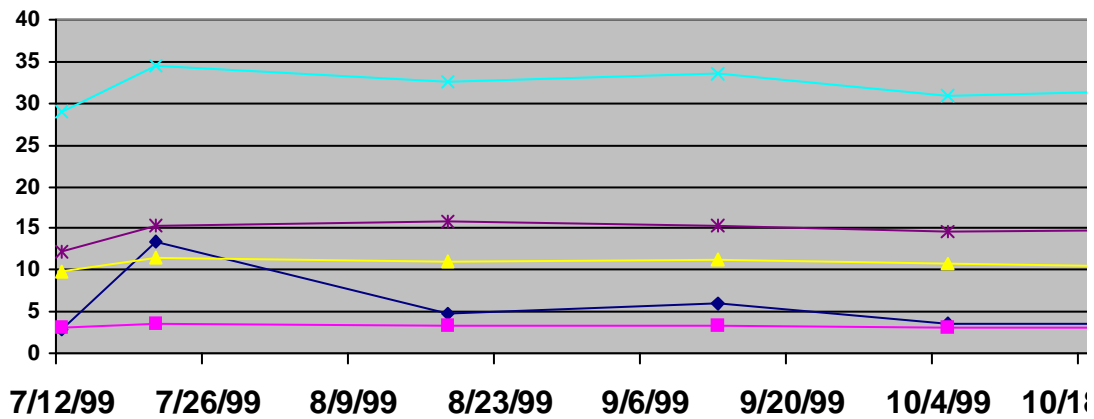


Figure 1. Summary of selected CBC parameters during treatment regimen.

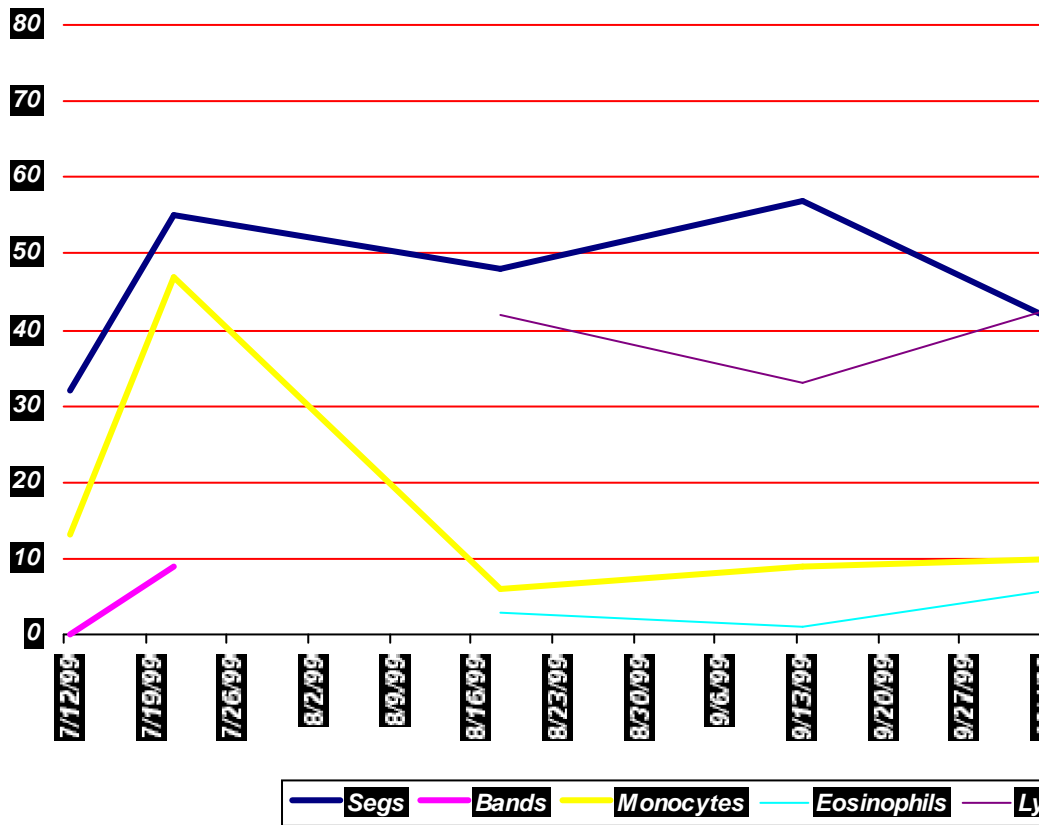


Figure 2. Summary of differentials during treatment regimens.

Summary of CA-125 during therapy

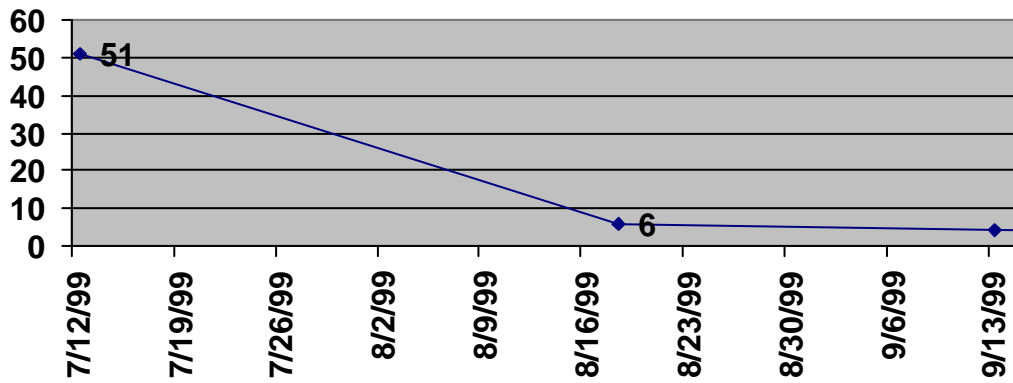


Figure 3. Summary of CA-125 during therapy.

Fatigue Survey During Treatment

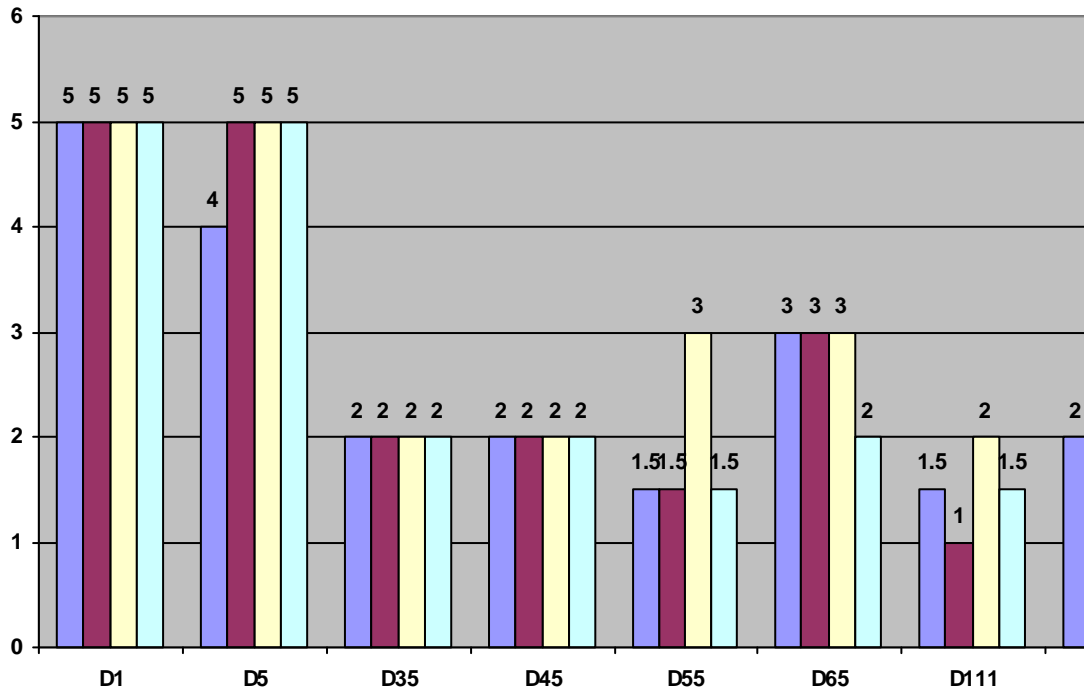


Figure 4. Summary of fatigue indicators per patient survey.

Legend: 1 = Does your tiredness / fatigue keep you from doing your housework / job/ work?
 2 = Does your fatigue keep you from your social life?
 3 = Do you take naps everyday because of tiredness / fatigue?
 4 = Does your fatigue interfere with your mental focus ?

Rated 1 thru 5:
 1 = None of the time
 2 = Part of the time
 3 = Half of the time
 4 = Most of the time
 5 = All of the time

Commonly used abbreviations in the Case Presentation

Abbreviation	Definition
SEGS	Segmented neutrophils
WBC	White Blood Cells
RBC	Red Blood Cells
Hg	Hemoglobin
Hct	Hematocrit
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hematocrit
RDW	Red (cell) Distribution Width
CBC	Complete Blood Count

Note: Dr. Colodny is clinical coordinator at Broward General Medical Center in Ft. Lauderdale, Florida. She is also assistant clinical professor at Nova Southeastern University School of Pharmacy.

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