# THE RELATIONSHIP BETWEEN CANCER CHEMOTHERAPY AND FATIGUE: A REVIEW

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## Abstract

**Fatigue is a subjective experience that affects cancer patients who treated with chemotherapy. In healthy individuals, it can be considered a physiological response to physical or psychological stress. In people with cancer diseases; fatigue often represents one of the most significant problems. Fatigue can be caused by many factors, both intrinsic to the patient and extrinsic, such as therapeutic (chemotherapy). This review, based on published studies, has been conducted between 2005 and 2012 with the aim of presenting a critical analysis of the available information on the characteristics, causes and potential treatments of fatigue in cancer patients receiving chemotherapy. Furthermore, in the absence of a clear demonstration of the efficacy of some therapies, the management of cancer-related fatigue remains poorly defined (except for the treatment of anemia-related fatigue). New randomized clinical trials are necessary to indicate the best strategies for overcoming this problem among cancer patients.**

**Key words:** **chemotherapy, fatigue, exercise, and cancer.**

## Introduction

Fatigue is one of the most common side-effects of cancer and its treatments (Hofmana et al., 2007, Prue, Rankin, Allen & et al. 2006). Fatigue is a common problem in patients receiving treatment for cancer. This type of fatigue, defined as cancer- or therapy-related, is different from everyday tiredness, which can be reversed by rest or sleep. Results of a multi-centre patient survey revealed that cancer patients identify fatigue as an important problem which affects their daily activities for more of the time than either nausea/vomiting or cancer pain. CRF is usually characterized as an overall lack of energy, cognitive impairment, somnolence, mood disturbance, or muscle weakness (The National Comprehensive Cancer Network (NCCN), 2012). These symptoms occur with cancer and cancer therapy and are not relieved by rest or additional sleep and often interfere with daily activities.

Cancer-related fatigue that associated with chemotherapy has been associated with other symptoms, including pain, difficulty sleeping and muscle weakness (Cleeland, 2007). Cancer-related fatigue may interact with other common adverse effects of chemotherapy drugs, such as nausea and vomiting, by increasing their perceived severity. This could increase their impact on patient activity, and challenge patients' ability to complete their recommended treatment on the optimal schedule. In addition to having a significant influence on the quality of life (QOL) during chemotherapy, CRF may be present even before treatment begins; it can increase during the course chemotherapy; and it can persist at a higher-than-baseline rate, sometimes for years, after cancer treatment is finished (Nail & King (1987).

Cancer-related fatigue has been under-reported, under-diagnosed and under-treated (NCCN, 2012). Health care professionals have been challenged in their efforts to help patients manage this distressful symptom and to maintain the quality of patients' life.

Compared with other health care providers, nurses spend most of their time with patients and their families (Dickinson, Clark, & Sque, 2008).

Nurses play a major role in the care of individuals and their families in all stages of cancer, from diagnosis to death. Nurses deal frequently with cancer patients and trying to maintain high quality of care, alleviate suffering, decreases side effect and complications of cancer treatment (Dickinson, Clark, & Sque, 2008). Nurse's knowledge and experience about CRF can shape their attitudes toward care for cancer patients (William, Dale, Godley, & Neimeye, 2003). In addition, nurses are in the most immediate position to provide care, comfort and counseling for patients and families at the stage of cancer management (Dickinson, Clark, & Sque, 2008). Successful symptom management for patients can help maintain effective chemotherapy, physical/social wellbeing, and reduce emotional distress of patients. Thus, the purpose of this paper is to determine factors that have been associated with treatment of cancer and to identify the risk factors associated with methods of treatment of cancer with chemotherapy that causes fatigue.

## Methodology

In order to review the body of knowledge related to fatigue among patients receiving cancer chemotherapy, a comprehensive literature review was conducted using the electronic databases of CINAHL, EBSECO, MEDLINE, and PUBMED, for articles published between 2006 and 2012. The following key terms were used to search the electronic databases: fatigue, cancer, exercise, and chemotherapy.

Many articles obtained and reviewed, only 18 research articles that achieved the inclusion criteria for the purpose of this study. The inclusion criteria were the following: (1) it is a research-based study; (2) written in the English language; (3) investigated the pain experience among patients receiving cancer treatment; and (4) recently published article. Each article will be read and analyzed, to identify the main themes/findings of the studies. Articles then will be systematically compared for common concepts to recognize similarities and differences in scope and findings across the studies. The articles that included in this study were quantitative and qualitative studies that published in peer reviewed nursing and medical journals. Countries within which the studies for this review were conducted include the United States, Australia, Japan, China, Greece, and Jordan.

The 18 studies composing this integrative research review were seven quantitative studies and seven qualitative studies. Although only 18 studies were included in this research review, a wide variety of instruments were used to measure concepts related to cancer pain experience. The most common questionnaires used in these studies are the piper fatigue scale. The sample sizes in the 18 studies in this review ranged from 11 to 360 adult cancer patients aged between 18 and 82 years.

### Finding

More than half of the patients had suffered fatigue every day or almost every day. Nevertheless, even social activities, concentration and caring for the family were more difficult for >50% of patients on the days when they suffered from fatigue. An analysis of the financial impact of this syndrome revealed that 75% of patients had changed their employment status. Bed rest, exercise, and relaxation techniques were the treatments most widely advised by health care provider; nevertheless, 40% of patients were not provided with any advice or recommendation.

### Cancer-related fatigue

Cancer-related fatigue (CRF) is a universal distressing symptom among cancer patients who are receiving cancer treatments (Gibson,et al.2005). The National Comprehensive Cancer Network (NCCN) defined CRF as: "distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" (NCCN, 2012, p.FT1). Cancer-related fatigue has been reported as the most important symptom that impairs the quality of life and daily patients' activities (Rayan, et al. 2007). According to NCCN, 70% to 100% of cancer patients experience CRF and most cancer patients suffer from CRF while receiving chemotherapy, radiation, or bone marrow transplant (NCCN, 2012). Cancer patients experience CRF resulting from the disease process, treatment modalities, psychological burdens, and worsen during chemotherapy course and persists for months after completing the treatment (Mustian, Morrow & Carroll, 2007).

A study conducted by Erickson, et al. (2010) aimed to explore factors affecting fatigue. The researchers recruited 20 adolescents with cancer receiving chemotherapy. Twelve cancer patients in the study reported brief peaks of moderate to severe CRF that occurred one to four days after each week of chemotherapy administration. In addition, the researchers found that the factors that made CRF worse included "not being able to eat before procedures, going to the bathroom a lot, getting chemotherapy in the morning, and just getting chemotherapy".

Alison Richardson & Margeret Evison (2005) mentioned that patients with cancer have identified CRF as symptom that causes them major distress as they live with the disease and its treatment squeal. Many did experience physical, social, and psychological distress as a result of having fatigue.

**Relationship between Chemotherapy and Fatigue**

Wielgus, Berger, & Hertzog (2009) found that higher CRF is associated with chemotherapy treatment. Hofman and colleagues (2007) found that more than 80% of patients receiving chemotherapy report CRF as a significant side effect of treatment. At the same study they found that 88% of patients who had chemotherapy reported that CRF had affected their activities of daily living.

Lucia and colleagues (2003) explain the relation between cancer and CRF and found that 70% of people with cancer report feelings of CRF during and after adjuvant chemotherapy.

Hwang, et al. (2003) in their study proposed a conceptual model with three dimensions (situational, biological, and psychological dimensions) that predict cancer-related fatigue. The situational dimension represents demographic information including age, gender, stage of cancer, active cancer treatment, and caregiver status. The biological dimension can be described by serum chemistry profile to identify anemia caused by chemotherapy or radiotherapy (Berndt, et al. 2005). The impact of anemia on CRF may be different depending on onset time, patient age, and co-morbidity (Berndt, et al. 2005). Psychological factors, such as depression and anxiety, may contribute to the development of chronic CRF before and after chemotherapy among patients with solid tumors (Wasteson, et al. 2009). Distress after a diagnosis of cancer can be caused by the initial fatigue, and other side effects of upset, like insomnia which may also increase in patients undergoing chemotherapy (Wasteson, et al. 2009).

Furthermore, Yeh, et al. (2008) investigated the relationships between clinical factors (including hemoglobin value, chemotherapeutic agents, and corticosteroid use) and changing patterns of CRF before and for the next 10 days following the start of a new round of chemotherapy in children with cancer. The researchers found that CRF levels were changed significantly over time; patients have more problems with CRF in the first few days after the start of chemotherapy. Also, the researchers reported that Corticosteroid use and hemoglobin value were associated with significant increases in CRF that were sustained for several days and reached the highest level of CRF at day 5 for those receiving concurrent steroids. In addition, Yeh, et al. (2008) reported that the association of chemotherapeutic agents with CRF varied between patient self-report and parent report, but the type of chemotherapeutic agents used was not associated with most changes in fatigue.

This study supports that lower hemoglobin level as a significant contributor to fatigue, thus, frequent hemoglobin check might increase the nurses' understanding of CRF that accompanies chemotherapy treatment.

Berger, Lockhart, &Agrawal, (2009) examined the relationships among cancer-related fatigue, physical and mental quality of life (QOL) and different chemotherapy regimens in patients prior to, during, and after treatment. The researchers reported that CRF and mental (QOL) changed significantly over time for all regimens, but the patterns of change did not differ based on regimen. Physical (QOL) changed significantly over time for all regimens. Higher CRF was correlated with lower physical and mental (QOL) prior to and 30 days after the final treatment, regardless of regimen. The results of this study assure that higher CRF associated with lower (QOL) regardless of the chemotherapy regimens. Thus, study recommended that nurses should screen patients for CRF using a visual analog scale (VAS), assess for contributing factors and to integrate evidence-based CRF interventions as early as possible to reduce CRF and prevent lower quality of life during treatment.

**Evidence-Based Treatment for Cancer-Related Fatigue**

Despite the high prevalence of cancer-related fatigue and its documented negative effects on patients' quality of life, limited evidence is available to support interventions to prevent or treat cancer-related fatigue. Both pharmacologic and non-pharmacologic interventions have been tested, with aerobic exercise programs and anemia correction by erythropoietin demonstrating greatest effectiveness. This article reviews the available evidence and describes gaps in knowledge regarding cancer related fatigue.

Yurtsever (2007) studied the experience of CRF in patients receiving chemotherapy. The researcher focused on measures taken by patients to cope with fatigue. Cancer-related fatigue was found to be affected by patients' daily activities, age, gender, treatment, and symptoms related to the chemotherapy.

Yurtsever (2007) found that the majority of cancer patients receiving chemotherapy (86%) experienced fatigue; and73 % stated that they coped with CRF by decreasing their activities and resting more. In addition, taking care with their nutrition (12%), exercising (5%), reading a book or newspaper (3%), listening to music (3%), drinking lots of fluids (3%), watching television (3%), trying to cope with the pain (3%), and massage (3%). Additionally, when the patients used these measures, 26% stated that the measures were "partially effective" in decreasing their CRF and 37% stated that they were "ineffective." Age was not found to be a significant contributing factor that is affecting the level of fatigue. However, other related factors including gender, length of illness, number of chemotherapy courses, and patients' symptoms were found to have an effect on level of fatigue. The findings of Yurtsever may refer to the majority of patients experiencing CRF, coped with less activity and more resting.

On the contrary, Kuchinski, Reading, & Lash (2009) did a systematic review to determine the effect of exercise in decreasing CRF for patients receiving chemotherapy and radiation.The researchers found that eight out of ten studies showed regular committed exercise (walking, bicycling or swimming) resulted in less CRF among patients participating in exercise programs. Participants who walked at least 60 minutes per week in three or more sessions demonstrated an increased functional capacity and activity level, with minimal increase in CRF compared to the control group.

In another study done by Blaney, et al. (2010) who explored the barriers of using exercise among patients recently diagnosed with cancer and suffering of fatigue.

The researchers reported that Cancer-related fatigue was associated with barriers such as physical problem, social isolation, and difficulty of making a routine exercise.

Lee, Tsai, Lai, and Tsai (2008), explored the relationship between fatigue, hemoglobin, and the coping strategies used by cancer patients receiving chemotherapy. The researchers found that majority of patients had a baseline hemoglobin level of 12 g/dl and a significantly greater mean cancer-related fatigue score than patients with hemoglobin >12 g/dl. Cancer-related fatigue levels were significantly higher in patients receiving a third course of chemotherapy than in those receiving first course.

The most commonly used management strategy was energy conservation (sitting and lying down). However, participants rated exercise, sleep, going to bed early and walking as the most effective. Distraction techniques, such as listening to music, reading books and visiting with friends had low-to-moderate effectiveness. The most effective coping strategy was chatting with others; back massage and relaxation training which were found to be moderately effective in reducing chemotherapy-induced fatigue. Thus, implementation of these coping strategies may prevent CRF and promote the quality of life.

Yesilbalkan, (2009) did a quasi-experimental, descriptive study to determine whether a nursing educational interventions decreased the perception of CRF among gastrointestinal (GI) cancer patients receiving chemotherapy for the first time. The researcher assessed cancer-related quality of life by using the Fatigue Inventory, Piper Fatigue Scale, and the European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ C-30) scale before their first cycle of chemotherapy, on the 10th day after (T1), and again 10 days after the second cycle of chemotherapy (T2). Patients received an individual educational intervention at baseline, T1, and T2 based on the results of their CRF assessment. Patients were given an educational booklet on CRF prior to treatment and symptom specific booklets as required atT1 and T2. The researcher found that at baseline, patients generally reported moderate levels of fatigue for each subscale of the (PFS) (behavioral, affective, sensory, and cognitive), but the levels decreased with each subsequent intervention (i.e., at T1 and T2). Following the educational intervention, mean scores in the functional domain of the EORTC QLQC-30 (physical, role, cognitive, emotional, social, and global QOL) have been increased while symptoms (fatigue pain, lack of appetite) have been decreased at both T1 and T2, compared to baseline.

## Recommendation

These findings emphasized the importance of developing a nursing educational program regarding CRF assessment. This is crucial for the provision of appropriate educational interventions to patients prior to chemotherapy in order to help in reducing severity of CRF and improve quality of patient's life. There is need to expanded nursing educational programs regarding CRF assessment and possible management options to reduce severity of CRF and improve their quality of life. New randomized clinical trials are necessary to indicate the best strategies for overcoming this problem among cancer patients.

## Summary and Conclusion

Cancer-related fatigue is the most commonly reported side effect of cancer and its associated treatment options, mainly chemotherapy. Cancer-related fatigue differs from that induced by other causes, such as sleep disturbance and exertion, as the latter are typically alleviated by a period of rest. This literature review considered the effect of several factors including exercise on CRF among patients treated with chemotherapy. Evidence from these studies supports the inclusion of scheduled exercise in the care plan of patients undergoing chemotherapy. Patients with cancer may be challenged to do exercise with nursing support.

This support can be made more effective if the recommended exercise program is regularly adjusted to the patients' health status with consideration to other factors such as level of hemoglobin, age, course of chemotherapy. Nurses' awareness of the role of exercise in managing related CRF can provide better education that benefits patients. Results of included studies indicated that exercise and psychological interventions provided reductions in cancer-related fatigue.

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