# Nonpharmacological Interventions in the Treatment of Cancer-Related Fatigue

# **Abstract**

One of the most exhausting and common complications of cancer and its treatments is cancer-related fatigue. According to the results reported from various studies, non-pharmacological interventions are preferable to pharmaceutical treatments. The purpose of the present study was to investigate non-pharmacological approaches effective on cancer-related fatigue. Based on the results of various studies, there is much evidence of the positive effect of exercise and acupuncture on reducing cancer-related fatigue during and after treatments. Existing studies on psycho-social support, sleep modification, nutrition, and complementary and alternative medicine methods, such as massage and touch, yoga, relaxation and meditation, and herbal medicines, suggest that these methods can reduce or eliminate related fatigue. In general, it seems that all the methods discussed in this study are non-invasive, low-risk, and relatively cheap methods that can be used alongside common treatments or even replace pharmaceutical methods. It is hoped that such studies will be used for evidence-based performance in reducing fatigue in cancer patients.

**Keywords:** Nonpharmacological interventions, Fatigue, Cancer, Treatments

## Introduction

Today, various methods are used to treat cancer, the most common of which are surgery, chemotherapy, radiation therapy, and hormone therapy.<sup>[1, 2]</sup> Cancer-related fatigue is one of the common side effects of treatments, which is often more annoying than pain among cancer patients.<sup>[2]</sup> Studies report the incidence of this type of fatigue between 60-90% in patients.<sup>[3, 4]</sup>

According to the definition of the National Comprehensive Cancer Network, cancerrelated fatigue is a mental, unpleasant, and persistent symptom in the form of physical, emotional, and cognitive fatigue that is caused in connection with cancer or related treatments and interferes with the normal functioning of a person. Some of the aggravating factors are sleep disorders, anemia, and co-morbidities such as coronary artery disease, psychological problems, and drug side effects. [5, 6] CRF is also related to the type of cancer (lymphoma, breast, and pancreas) and its treatment regimen (single, combined treatment).<sup>[7]</sup> Fatigue associated with cancer is due to various causes, including the production of waste products following the destruction of tumor cells during treatment. The factors that cause or accelerate cancer-

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related fatigue are many and varied. Knowing these factors helps prevent, contract, or speed up the treatment of fatigue caused by cancer. Unlike normal fatigue, CRF does not resolve with rest. Experts have introduced four characteristics in the diagnosis and confirmation of CRF based on differentiation from normal fatigue: 1- decrease or lack of daily energy for at least two weeks or more, 2-discomfort and dysfunction, 3- presence of clinical evidence of Presence of CRF following cancer or related treatments, 4-Absence of psychiatric conditions such as depression.<sup>[7,8]</sup>

Cancer-related fatigue is characterized by symptoms of fatigue, decreased activity, lack of energy, and depressed mood. Associated disorders occur in the form of depression, sleep disorders, decreased concentration and memory, and nutritional disorders such as anorexia, decreased quality of life, decreased survival, and increased mortality.[8] The adverse effects of fatigue on the quality of life of sufferers develop in a wide range from the reduction of physical activity to its expansion in other dimensions such as loneliness or isolation.<sup>[9]</sup> The obvious effects of fatigue on different aspects

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of the patient's life, physical, psychological, and social, continue in the range of effects of CRF from the patient to the family and the community level. Costs that arise due to the reduction of the patient's activity, and the loss of the patient's job or his caregivers; make the treatment process more difficult.<sup>[8]</sup> Fatigue may appear as an initial symptom, before cancer diagnosis and during treatment, and it may remain stable in survivors long after the completion of treatment.<sup>[7,8]</sup> This type of fatigue is not only limited to the acute stage of the disease; Rather, it is a resistant and common symptom among 17-30% of cancer survivors.<sup>[10]</sup> However, many studies have mentioned the peak intensity of fatigue during the period of cancer treatments such as radiation therapy.<sup>[9]</sup>

The approaches that are used today in the treatment of fatigue related to cancer are placed in two categories pharmaceutical and non-pharmacological methods. Non-pharmacological treatments such as complementary and alternative medicine have many advantages compared to pharmaceutical treatments, which can be mentioned such as having a specific mechanism of action, ease of acceptance by everyone, and low cost.[11] It seems that compared to other complications of cancer or related treatments such as hair loss, pain, nausea, and vomiting, the category of fatigue related to cancer has been less studied by doctors, nurses, and researchers. Considering the complications of fatigue such as decreased performance and reduced quality of life in patients under treatment, the importance of finding new and less complicated approaches to eliminate or reduce it is obvious. The purpose of this study is to review the research conducted in the field of nonpharmacological approaches that have been evaluated so far on cancer-related fatigue.

## **Results and Discussion**

Considering that countless factors are involved in causing fatigue related to cancer; Fatigue should be treated before it becomes a chronic and problematic condition. According to the person's personality, mental state, and the extent of the disease, many and varied methods should be used in the treatment of fatigue. (8) A wide range of pharmacological and non-pharmacological interventions have been investigated to reduce cancer-related fatigue. The guidelines of the comprehensive National Cancer Network recommend many non-pharmacological approaches, including exercise and psychosocial interventions. [12]

### **Exercise**

Cancer treatments lead to a decrease in patients' activity and performance, resulting in fatigue. Exercise, by increasing muscle mass, increasing plasma volume, increasing lung ventilation and blood supply, and increasing heart capacity, ultimately reduces fatigue. Aerobic exercise has been recommended for the rehabilitation of cancer patients and to eliminate energy loss, as well as to increase the physical fitness of patients. Light to moderate walking relieves fatigue by increasing energy, stimulating appetite, and increasing performance capacity. Exercise ultimately increases the quality of life and has a positive effect on the psychological

aspects of the patient.<sup>[13]</sup> Winningham for the first time proposed the positive effect of exercise in breast cancer patients undergoing chemotherapy. He performed for ten weeks (three times a week) for 30 minutes. The findings of his research increased the physical performance capacity of patients. [14] Many studies have shown that a regular exercise program of aerobic or resistance type is effective in reducing fatigue in cancer patients. Cantarero-Villanueva et al.[15] investigated the effect of exercise on the fatigue level of 68 breast cancer survivors after completion of treatments. The participants of the intervention group attended the hot water pool 3 times a week for 8 weeks and each session was 60 minutes. The findings of this study showed a reduction in fatigue, an increase in mood, and improved abdominal and thigh muscle strength. From the results of this study, it can be concluded that exercise is an effective intervention in reducing resistant fatigue in cancer survivors. However, a few studies have provided conflicting results. Among the findings of the studies of Dodd et al.[16] as well as Husebø et al.[17] the implementation of an exercise program was ineffective in reducing the fatigue of breast cancer patients undergoing treatment. Looking at countless studies in this field, it can be said that the implementation of sports programs, both resistance and aerobic, such as walking, with ease of implementation, no side effects, and creating vitality among patients can be a suitable alternative method in the treatment of cancer-related fatigue.

# Complementary and alternative medicine

In recent years, complementary and alternative medicine has gained many fans in preventing diseases and promoting public health. The National Center for Complementary and Alternative Medicine defines CAM as a diverse group of medical and health care practices; Methods that are generally not considered part of common medicine. The researchers found the reasons for the increase in the use of complementary and alternative medicine approaches to be people's dissatisfaction with common treatment systems, accessibility, having fewer side effects, the existence of free will, the ability to be used by all social classes, and the involvement of participating and holistic people. They mention the existence of these treatments.<sup>[18]</sup> The increasing desire of cancer sufferers, especially breast cancer, to use these treatment methods is worthy of attention due to the insufficient response of common treatments and the cheaper nature of these methods.[19]

Recently, yoga has received attention from researchers as a non-pharmacological approach to the treatment of cancer-related fatigue. Bower *et al.* showed the positive effects of yoga on reducing resistant fatigue in cancer survivors in three studies. [20] The result of Bower's study indicated that yoga has a greater effect on reducing fatigue than other behavioral interventions in previous studies. [20] Sadja *et al.* [21] in a review, the study reviewed 10 articles regarding the effect of yoga on fatigue in cancer patients. There were 8 articles on breast cancer patients. The findings indicate that this non-invasive method is effective in reducing the fatigue of cancer patients. Kwekkeboom *et al.* [22] reviewed 43 studies conducted on the

effect of mind-body methods on reducing cancer pain symptoms, cancer-related fatigue, and sleep disturbance. The findings of this review study showed that meditation and music have led to the reduction or elimination of symptoms.

In a clinical trial in South Korea, 102 women with breast cancer were studied in two control and intervention groups. In the intervention group, 12 sessions of meditation therapy were held during six weeks of radiation therapy. The level of anxiety and fatigue in the intervention group was reduced compared to the control group, and the quality of meditation was introduced as a non-invasive method to relieve the symptoms of cancer patients.<sup>[23]</sup>

Mansky and Wallerstedt<sup>[24]</sup> also conducted a review of the methods used by complementary and alternative medicine among cancer patients to reduce fatigue symptoms. The results indicate that acupuncture and massage are more effective than other methods in reducing patients' fatigue. Acupuncture is a popular and popular method among cancer sufferers and a type of traditional Chinese treatment, in which special fine needles are inserted into the energy points along the channels of each disease, leading to its treatment. The findings of studies indicate the satisfactory effects of acupuncture or acupressure on relieving cancer-related fatigue symptoms. [25, 26] Decker et al.[27] investigated the effect of relaxation training on stress, anxiety, depression, and fatigue in patients undergoing radiation therapy. In this study, they randomly assigned 82 patients to the intervention group and 29 to the control group. The presence of symptoms in the intervention group is one of the findings of this study. Karagozoglu and Kahve<sup>[28]</sup> investigated the effect of touch therapy on the anxiety and fatigue of cancer patients undergoing chemotherapy in two intervention and control groups. The back massage was performed on 20 patients in the intervention group after chemotherapy. In the massage therapy group, fatigue the day after chemotherapy and anxiety immediately after the massage decreased significantly compared to the control group. The authors of this study say massage therapy is introduced as an effective nursing intervention in reducing the symptoms of cancer patients. Jeong et al. [29] during a clinical trial, 40 cancer patients into two intervention and control groups. The herbal medicine Bujun Tang (a traditional Chinese medicine) was administered for 2 weeks to the patients of the intervention group. No intervention was performed in the control group. The findings showed a significant reduction in cancer-related fatigue compared to the control group.

In a double-blind clinical trial, the effect of an herbal medicine called Shan Mani, which is a combination of three herbs, was investigated on the fatigue of cancer patients. The study was conducted in two intervention and control groups for 4 weeks, the results showed a reduction in fatigue.<sup>[30]</sup>

The favorable effects of laughter therapy on various aspects of the life of cancer patients have been noticed by researchers in the last decade. Studies have found laughing to be effective in reducing anxiety, stress, and depression and strengthening the immune system. However, only one clinical trial<sup>[30]</sup> was found

that examined laughter therapy on cancer-related fatigue. In this study, 58 patients with breast cancer were subjected to external radiation therapy in two groups, laughter therapy and usual care. Laughter therapy sessions focusing on comedy movies, jokes, and fun competitions were held twice a week (60 minutes each session) for four weeks for the intervention group. The results of this study showed that laughter therapy has reduced fatigue in cancer patients undergoing radiation therapy. It is necessary to conduct more research in this field.<sup>[30]</sup>

In a review article, Sood *et al.*<sup>[31]</sup> studied complementary and alternative medicine interventions to reduce cancer-related fatigue. The interventions included aromatherapy, massage therapy, music therapy, acupuncture, yoga hypnosis, touch therapy, relaxation and other methods. The authors of this study stated that there is still insufficient evidence on the certainty of the treatment of each complementary method in the treatment of cancer-related fatigue, and more studies should be conducted.

# **Psychosocial support**

Many factors are involved in a cancer patient suffering from anxiety and stress, including; Cancer type, treatments, related costs, pain, reduced social activities, and fear of death. Since the relationship between anxiety and depression with cancer-related fatigue has been confirmed, cancer patients should be able to control psychological factors such as stress, anxiety, and depression. Interventions related to reducing stress and increasing psychosocial support include education, support groups, individual counseling, methods of improving adaptation, methods of preserving and storing energy, management-guided stress, and cognitive behavioral interventions are approaches to deal with cancer symptoms and fatigue. [32, 33]

It should be kept in mind that education and counseling are key elements in support programs, and among the above techniques, only cognitive behavioral interventions require a specialist due to their specialization, and other techniques are easily performed at the bedside. They can execute. [8] Kangas *et al.* [34] conducted a systematic review and meta-analysis of 119 articles that examined non-pharmacological interventions (exercise and psychosocial interventions) on cancer-related fatigue. The research studies included clinical trials and non-clinical trial studies. The results of 41 clinical trial articles that dealt with the effect of psychosocial interventions on fatigue during and after cancer treatments; showed that these approaches had a small to moderate effect size on cancer-related fatigue.

Spiegel *et al.*<sup>[35]</sup> put 86 women with breast cancer into two groups of usual care and intervention. Support group meetings were held weekly for one year for the intervention group. By reducing the sample size, finally, the results of the data analysis of 30 people showed a decrease in fatigue scores and an increase in vitality in the intervention group compared to the control group. Despite the decline of research units in this study, the benefits of support groups on the dimensions

measured in the POMS questionnaire are important. Looking at the findings of the aforementioned studies, we can conclude that psychosocial support (individual or group) is effective in reducing fatigue in patients undergoing treatment or survivors of various types of cancer.

# **Sleep correction**

Sleep disorder is considered one of the most important side effects of cancer with a prevalence of 30-40% and related to its treatments. [36] This problem is so common among patients that about 25-50% of oncologists' prescriptions are sleeping pills. Although sleep disorders and fatigue related to cancer are two distinct conditions; their close relationship has been confirmed. [37] According to the clinical guidelines of the National Comprehensive Cancer Network, a patient who suffers from fatigue; initially, should be evaluated in terms of the factor that sleep disorder is one of these 5 factors. This guideline also recommends sleep modification as one of the non-pharmacological treatments for cancer-related fatigue. [12]

Graydon et al.[38] investigated strategies used by cancer patients to reduce fatigue. The research units of this study were 99 cancer patients undergoing chemotherapy and radiation therapy who participated in two interviews to determine the level of fatigue and the methods used to reduce it before and after the start of cancer treatments. The amount of fatigue in the patients after starting the treatment is more than before the treatment and the most used methods to reduce fatigue among the patients are to improve the sleeping position and exercise. [39] The results of this study are a good guide for nurses in providing fatigue reduction methods to patients. In a review article, Zee and Ancoli-Israel<sup>[40]</sup> studied 79 articles on cancer-related sleep disorders and fatigue up to 2009. The results of this study confirmed the effect of poor sleep or insomnia on the occurrence of fatigue and showed that improving sleep led to the reduction and control of fatigue. Based on the available evidence, Mitchell et al. recommend ways to improve sleep in relieving fatigue and insomnia in cancer patients.

Cognitive-behavioral interventions (individual or group) include activities in which a person uses relaxation along with some methods such as avoiding long sleep during the day or evening, controlling environmental stimuli, and reducing arousal before sleep. [41] Berger et al. [42] investigated the improvement of sleep and fatigue in cancer patients in a clinical trial using cognitive-behavioral methodology. They evaluated 219 breast cancer patients in stage I- III in two intervention and control groups. In this research, the intervention was in the form of cognitive-behavioral methods and included modified sleep restriction, control and reduction of external stimuli, relaxation, and sleep hygiene. Data collection was done before the start of chemotherapy, 7 days after each treatment, and 30 days after the last treatment. After the start of chemotherapy, fatigue was seen in both groups and sleep quality was better in the intervention group than in the control group. The results of this study showed that a decrease in sleep quality is not always associated with a decrease in fatigue.[42]

### **Nutrition correction**

Cancer patients are at risk of developing nutritional problems. Its symptoms include fatigue, anorexia, weight loss, and muscle wasting, which hurts a person's survival. On the other hand, nutritional problems lead to the creation or increase of fatigue in these patients. [43] Fatigue in people with cancer often occurs when the energy required by the body exceeds the supply of energy sources. Three main mechanisms may be involved: a change in the body's ability to process nutrients effectively, an increase in the body's energy requirements, and a decrease in the use of energy resources. [13]

According to the instructions published by the National Comprehensive Cancer Center, in the investigation and treatment of cancer-related fatigue, attention should be paid to the factors involved in the occurrence of cancer-related fatigue, and nutritional deficiency and its correction are some of these factors. [44] Nutritional disorders include malnutrition, anorexia, dehydration, and electrolyte disorders. [8] In a 2009 study, lifestyle modification, exercise, and diet and their relationship with cancer symptoms such as fatigue were examined in 227 cancer survivors. The findings of this study showed that more than half of the participants made positive nutritional and exercise changes after cancer diagnosis, and patients who consumed more fruits and vegetables experienced less fatigue. [45]

In another study in 2012, the relationship between diet and fatigue was evaluated in 40 breast cancer survivors, at least 12 months after completing treatments. The results showed that the average daily consumption of vegetables, especially with green leaves and tomatoes, was higher in patients with less fatigue than in those with moderate and severe fatigue. Also, patients who reported less fatigue had a higher intake of antiinflammatory foods. 3 Dietary habits of simple sugars, red meat, and a healthy diet were also investigated in patients, and the findings indicated that the possibility of severe fatigue in red meat and simple sugar consumers is much higher than that of a healthy diet. [46] One of the current treatments for cancer patients is fatigue relief. High-protein supplements, adequate hydration, vitamins, and fruits such as broccoli are foods recommended by doctors. In case of anemia, foods containing iron are prescribed.<sup>[47]</sup>

# **Conclusion**

With the increase in knowledge in the field of cancer treatments, many solutions without the need for pharmaceutical resources have been recommended to alleviate the symptoms of cancer-related fatigue. The ever-increasing population of cancer patients around the world makes it necessary to use these treatment strategies with minimal side effects. In the present study, there is much evidence of the effect of exercise on reducing cancer-related fatigue during and after treatments. This result is probably the result of increased cardiac capacity and better blood supply to body systems during exercise. Common methods mentioned in most of the studies have been aerobic exercises such as walking several times a week. In addition to its well-known benefits in

improving health, exercise is recommended as a suitable and safe way to reduce or eliminate fatigue in cancer patients. The findings of the studies on the effect of acupuncture also show the effectiveness of this method in the treatment of fatigue related to cancer. Needle stimulation of the energy points in the channels related to fatigue will reduce or eliminate it. The evidence on psychosocial support, sleep modification, nutrition, and some complementary and alternative medicine methods such as massage and touch, herbal medicine, yoga, relaxation, and meditation suggest that these methods can reduce or eliminate Fatigue related to cancer can be useful and effective. All the methods discussed in this study are non-pharmacological, non-invasive, low-risk, and relatively cheap methods that can be used alongside common treatments or even replace pharmaceutical methods. The cost-effectiveness of using these treatments for patients reduces treatment costs and eliminates the consequences. It is hoped that such studies will be used to reduce the fatigue of cancer patients and improve their quality of life by applying evidence-based practices.

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## **Conflict of interest**

None.

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## **Ethics statement**

None.

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