

Cancer-related fatigue as a major problem in patients with cancer; a systematic review

Farhad Azadmehr¹, Roghayeh ESmaeili², Ziba Borzabadi Farahani^{3,*}, Zahra Arabborzu⁴

¹MSc Student in Nursing, Student's Research Committee, Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of medical Sciences, Tehran, Iran, ²Assistant Professor in Medical Surgical Nursing Filed, School of Nursing and Midwifery, Shahid Beheshti of Medical Sciences University, Tehran, Iran, ³Assistant Professor, Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran, ⁴PhD Student in Biostatistics, School of Paramedical Sciences, Shahid Beheshti University of medical Sciences, Tehran, Iran.

Correspondence: Ziba Borzabadi Farahani, Assistant Professor, Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of medical Sciences, Tehran, Iran.

ABSTRACT

Introduction: Cancer is a non-communicable disease that has a widespread incidence compared to other non-communicable diseases. Fatigue is an unusual, continuous, and subjective feeling of illness that is related to cancer. In this study, we reviewed the published articles in the field of fatigue due to cancer done in Iran society. **Method and materials:** In this study, internal databases for Persian articles, including SID, MagIran, IranMedex, and also www.irandoc.ac site for dissertations were reviewed as well as PubMed, ISI web of knowledge and Google Scholar databases were assessed to study English articles by June, 2018 and 12 articles were entered into the study. **Results:** In this review, 957 individuals were analyzed in the 12 selected articles, 6 articles in Persian and 6 articles in English. Anemia caused by chemotherapy and low quality of life were among the most important factors affecting cancer-related fatigue. There was no steady way to measure the fatigue of cancer. **Conclusion:** This review indicated that improving the quality of life, massage, laughing, exercise and work-out can be an effective factor in reducing fatigue in patients.

Keywords: Cancer, Fatigue, Iran.

Introduction

Cancer is a non-communicable disease that has a widespread incidence compared to other non-communicable diseases [1, 2]. It is due to the manifestation and abnormality of the gene and is one of the major causes of mortality in developed and developing countries [3]. Cancer is the second leading cause of death in the world [4], and currently the five-year prevalence of cancer is 32.6 million people [4]. Based on the performed modeling, due to the demographic trends and the increase in life expectancy in our country, Iran, the incidence of cancer from 84800 people in 2012 will reach to 129700 people in

2025. In fact, we will have a 35% increase in the incidence of cancer patients [4].

According to recent statistical and epidemiological studies in Iran, cancer after cardiovascular disease and accidents is placed in the third most common cause of death [5]. Cancer is a very unpleasant and unbelievable experience for anyone, which affects the various aspects of the quality of life of patients such as psychological, social, physical, sexual status, and family life [6]. Fatigue is one of the most common and debilitating problems associated with cancer, which is experienced by patients at each stage of cancer, and about 72 to 99 % of the patients suffer from it. In these patients, fatigue may be happening due to illness and treatment, which is called cancer-related fatigue [7]. In fact, fatigue is an unusual, continuous, and subjective feeling of illness that is related to cancer [8].

Cancer-related fatigue is a multidimensional phenomenon that can be examined from physical, psychological and social aspects [9], and fatigue itself can jeopardize the quality of life of cancer patients [10]. The issue of fatigue among cancer patients is a controversial issue worldwide and is considered as a diagnosis in the revision of the International Classification of Diseases [11]. Post-diagnosis fatigue can be controlled with non-

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drug strategies such as training ^[12]. In this study, we reviewed the published articles in the field of fatigue due to cancer done in Iran society.

Method and Materials

Search strategies of literatures

In order to study the published articles in this field, internal databases for Persian articles, including SID, MagIran, IranMedex, and also www.irandoc.ac site for dissertations were reviewed as well as PubMed, ISI web of knowledge and Google Scholar databases were assessed to study English articles by June, 2018. The key words used in this search were cancer, fatigue, cancer fatigue, psychological fatigue, chemotherapy and Iran, or a combination of them in medical subject indexes or abstracts. The list of references in the specified articles were also reviewed for further relevant studies.

Inclusion criteria

After collecting articles, their characteristics and abstracts were entered into the reference software, and duplicates were removed using this software as well as the re-reading of the titles. In the next step, by reviewing the titles, the studies that are not related to the purpose of this study were excluded and then, from the remaining studies, referring to the abstract of the article as well as the full text the relevance of the articles was assured. Studies were limited to studies that were performed only on humans. Finally, the studies published in Persian and English were included in this systematic review. When several studies from a single cohort or population are published, only the results from the latest study find the conditions necessary to enter this analysis.

Data extraction

Information about publication (first author's surname, year of publication, etc.), study design, number of samples studied, results of each article were extracted by two independent researchers. The observed differences in the evaluation of studies were solved by a third researcher. Based on the type of design study, specific qualitative methodology checklist for Quality Assessment was used. Whenever 95% confidence interval was reported, we also reported it. If we did not have a confidence interval of 95%, we reported P value.

Results

Twelve studies were eligible for this review. Six articles were published in Persian language journals and six articles were published in English-language journals. Five observational studies and seven were experimental Table 1 indicates the results of the study eligible for the study.

The first study, carried out by Safaei et al. in 2010 ^[7], which was a cross-sectional study on a randomized 119 case of breast cancer patients treated with chemotherapy in Namazi Hospital of Shiraz. All patients with definite diagnosis of breast cancer

were identified as eligible for the study based on pathology findings that lasted at least two months from the date of their diagnosis. In this study, the Persian version of QLQ-C30 and QLQ-BR23 questionnaires were used to assess the fatigue and quality of life in patients. These questionnaires were assessed and validated in terms of validity and reliability. The results of this study showed that 78% of patients had a different level of fatigue. The mean fatigue score was 41.44 ± 26.91 . Among functional areas, fatigue had a great influence on people's social performance. Linear regression analysis showed that pain, appetite loss, body image and type of treatment were the most important factors affecting fatigue.

In the study of Zeighami Mohammadi et al. in 2011 ^[10] entitled "The Relationship between Anemia and Severity of Fatigue and Quality of Life in Cancer Patients Undergoing Chemotherapy", 121 patients with cancer undergoing the third chemotherapy period were selected using purposive sampling method. The data collection tool in this study was a sample selection form, a personal profile form, a disease and treatment information form, Visual Fatigue Scale, and a European Quality of Life Scale for Cancer Research and Treatment. In this study, the EORTC QLQ-30 assessed the quality of life. The quality of life scale was 30 questions, which examined two-point, four-point, seven-point, physical, cognitive, emotional, social, and role play dimensions. The results of the study showed that the prevalence of anemia in cancer patients under chemotherapy was 63.6%. and 57% of patients had mild anemia and 6.4% had moderate to severe anemia. There was a significant difference between the level of hemoglobin and the level of hemoglobin in the mean fatigue ($P < 0.001$) and quality of life ($P = 0.003$) as well as quality of life and severity of fatigue ($P < 0.001$).

In the study of Chehrehgosha et al. in 2013 entitled "Cancer-Related Fatigue and Its Relationship with Demographic and Clinical Characteristics", which was analytical study, 150 patients with cancer referred to the oncology and radiotherapy center of Shafa Hospital in Azargagan Educational Center were selected by purposive sampling during 4 months. Demographic and clinical demographic questionnaire and a Multidimensional Fatigue Inventory (MFI) questionnaire were used for collecting the data of interest and 51.3% of patients received chemotherapy-surgical-radiotherapy treatment, 24.7% had surgical-chemotherapy, 14% chemotherapy, 7.3% radiotherapy and 2.7% surgery. The mean total fatigue score was 54.56 ± 8.78 . The duration of marriage ($P = 0.018$), type of regimen ($P < 0.001$) and family status ($P = 0.001$) were significantly correlated with fatigue.

A prospective study was designed by Haghghat et al. in 2003 ^[13] to investigate the factors predicting fatigue in breast cancer patients using the Cancer Fatigue Scale (CFS) in addition to the Hospital Anxiety and Depression Scale and a questionnaire containing items on demographic and clinical data, and measures of patients' physical symptoms. The CFS measures total fatigue score was from 0 (lowest level) to 60 (highest level) and included three subscales namely: physical, affective and cognitive fatigue. All 112 patients were participated and the

mean age was 45.7 ± 11 years with stage II breast cancer (67%) and had completed their initial treatment (45%). The mean total fatigue score was 18.7 ± 13.5 as well as overall 49% reported different type of fatigue to some degree. Severe anxiety and depression were reported approximately 16% and 32%, respectively. The results showed that fatigue was predicted by depression ($P=0.003$), pain ($P=0.005$), current tamoxifen use ($P=0.001$), undergoing mastectomy ($P=0.03$) and anxiety ($P=0.04$).

Another study was conducted by Faragollahi in 2004 entitled "Strategies Used by Patients Receiving Chemotherapy to Relieve Fatigue", on 120 cancer patients under chemotherapy who were selected by continuous sampling from the central chemotherapy departments of Imam Khomeini Hospital, Tehran, the feeling of tiredness was recorded and examined during a 21 or 28 days' chemotherapy cycle. The results of this study showed that the units used different methods to relieve their fatigue severity, with the most used methods, lying (20.8%) and stopping work (11.7%) and the least used methods, exercise (3.3%) and walking (4.2%) as well as 85.2% of the samples used a constant method to relieve their fatigue during a chemotherapy cycle^[9].

Rahmani et al., in their study entitled "The Effect of Group Mindfulness-Based Stress Reduction Program and Conscious Yoga on the Fatigue Severity and Global and Specific Life Quality in Women with Breast Cancer" done as a quasi-experimental study with control group and 24 patients with breast cancer referring the Division of Oncology and Radiotherapy of Imam Hossein hospital in Tehran were selected using convenience sampling, and randomly assigned into the intervention and control groups. All the participants completed the Fatigue Severity Scale, Global Life Quality of Cancer Patient and Specific Life Quality of Cancer Patient questionnaires. Data were analyzed using multivariate repeated measurement variance analysis model and results showed the mindfulness-based stress significantly improved the overall quality of life, role, cognitive, emotion, social functions and pain and fatigue symptoms in global life quality in the intervention group. It also significantly improved the body image, future functions and therapy side effects in specific life quality of the experimental group compared to the control group. In addition, fatigue severity caused by cancer was reduced significantly.

Another study was done by Rad et al. in 2016 entitled "The Effect of Humor Therapy on Fatigue Severity and Quality of Life in Breast Cancer Patients Undergoing External Radiation Therapy". This clinical trial study conducted on 58 patients with breast cancer receiving radiation therapy for 5 weeks in the two groups of intervention and control and patients in the intervention group attended humor therapy sessions twice a week for one month. Fatigue questionnaires were completed at the end of the first week as the pre-test and at the end of following weeks as the post-test. There was a statistically significant differences between intervention and control groups regarding fatigue severity in both groups after humor therapy

showed ($P=0.001$). There was a mild fatigue interfering with normal activities in the humor group and a severe fatigue interfering with making relationship with others and enjoyment of life in the control group which was significant ($P=0.001$).

In another study done by Aghili et al. "A Pilot Study of the Effects of Programmed Aerobic Exercise on The Severity of Fatigue in Cancer Patients During External Radiotherapy", At the 4th and 5th days of the first week, two 30-min teaching sessions were held for the training group describing fatigue, its causes, its importance and the advantages of walking. Patients were also given a notebook about the training plans. The training plans included daily walking for 20 min (or 10 min twice daily for frail patients), which began at the second week and lasted for 21 days (3 weeks). At the first week of assessment (before start of exercise) moderate fatigue (scores of 4–6) in the training and comparison group patients were 56% and 43%, respectively. The severity of current fatigue had no difference in the two groups at the start of the study. At the fourth week, most patients (44%) in the training group had mild fatigue whereas 57% of the patients in the comparison group reported severe fatigue.

In a quasi-experimental study done by Shariati, et al. in 2010, 36 adults with colorectal cancer were enrolled. The place of study was adult hematology and chemotherapy wards of Shefa Hospital in Ahwaz. Data were collected using a demographic form and a questionnaire in order to measure the severity of fatigue. Then, the patients had 40-minute exercise, 3 times a week for 4 weeks. The effect of exercise versus fatigue intensity was measured at the end of every week. The mean fatigue severity after exercise was significantly different compared to the before. The mean fatigue severity was 3.69 on the week zero (before the exercise), and decreased to 3.57 on the first after exercise, 3.46 on the second, 2.58 on the third, and 1.69 on the fourth week.

A study by Aghabati et al. in 2010 entitled "The Effect of Therapeutic Touch (TT) on Pain and Fatigue Of Cancer Patients Undergoing Chemotherapy" which was a randomized by three-groups of experimental, placebo, and control (usual care) has included 90 patients undergoing chemotherapy, exhibiting pain and fatigue of cancer in the Cancer Center of Imam Khomeini Hospital in Tehran, Iran. Data were recorded before and after the intervention for 5 days (once a day). The intervention consisted of 30 minutes TT given once a day for 5 days between 10:00 a.m. and 10:30 a.m. The Visual Analogue Scale (VAS) of pain and the Rhoten Fatigue Scale (RFS) were completed for 5 days before and after the intervention by the subjects. TT was more effective in decreasing pain and fatigue of the cancer patients undergoing chemotherapy than the usual care group.

In a study of Narimani et al. in 2015 which was quasi-experimental, the population were all females suffering from breast cancer and were introduced themselves to Shafa Partov Clinic in Ardabil province to do radiotherapy during 2011-2012. Patients (45 subjects with 16-45 years) were selected using convenience sampling (because of the lack of total list of

patients), and the Cancer Fatigue Scale (CFS) was used for data collection. Both treatment methods reduced the degree of fatigue ($P < 0.001$).

In a study of Mofid et al. in 2016 entitled "The effect of Processed Honey and Royal Jelly on Cancer-related Fatigue", 52 patients who visited the oncology clinic of Shohada-e-Tajrish hospital in Tehran during 2013-2014 were selected and divided into two groups. The intervention group (26 patients) received processed honey and royal jelly, while the control group

received pure honey. Both groups used their 5mL supplement twice daily for 4 weeks. Both groups were assessed at the beginning of the study, after 2 weeks, and then at the end of 4 weeks of treatment. Fatigue was measured using a visual analogue fatigue scale (VAFS) and fatigue severity scale (FSS). The mean age of patients was 54.84. After two and four weeks, VAFS and FSS due to treatment was better in the intervention group compared to the control group ($P < 0.001$ and $P < 0.001$)^[14-26].

Table 1. The detail of studies entered into systematic review in Iran society

| Reference | Sample size | Design | Age (Mean±SD) | Conclusion |
|-------------------------------------|-------------------------|----------------------|---|---|
| Safaei et al. 2010 [14] | 119 | Cross-sectional | 48.28±11.42 | Necessary Factors to reduce fatigue prescribing by physicians are effective in improving the quality of life in cancer patients. |
| Zeighami Mohammadi et al. 2010 [15] | 121 | Analytic-descriptive | - | Anemia in cancer patients undergoing chemotherapy is common and the hemoglobin levels and quality of life decrease with increased fatigue. |
| Chehrehgosha et al. 2013 [16] | 150 | Analytic | 48.39±1.50 | Providing physical care and nursing interventions, paying attention to the socioeconomic components of the life of cancer patients e.g. fatigue is important. |
| Haghighat et al. 2003 [17] | 112 | Prospective | 45.7±11.1 | Physical and psychological symptoms have a more important role in cancer-related fatigue. |
| Faragollahi et al. 2004 [18] | 120 | longitudinal | 44.83±9.01 | Cancer patients during several chemotherapy cycles choose different methods to reduce or eliminate the severity of their fatigue, and they are compatible with one method.... |
| Rahmani et al. 2015 [19] | Test= 12 Control= 12 | Quasi- experimental | Control =44.8 ±3.28 Test= 43.25 ±3.07 | The mindfulness - based stress reduction treatment can be effective in improving global and specific life quality and fatigue severity in women with breast cancer. |
| Rad et al. 2015 [20] | 58 | Clinical trial | - | Laughter therapy is effective in decreasing the fatigue severity of patients with breast cancer. |
| Aghili et al. 2007 [21] | 30 | Pilot | - | Exercise for patients undergoing cancer treatments have positive results. |
| Shariati et al. 2010 [22] | 36 | Quasi-experimental | - | Exercise and work-out can be an effective factor in reducing fatigue in patients. |
| Aghabati et al. 2010 [23] | 90 | Randomized trial | Test=36.86±13.15 Placebo=42.70±24.4 Control=43.30±12.83 | Therapeutic touch was more effective in decreasing pain and fatigue of the cancer patients undergoing chemotherapy. |
| Narimani et al. 2015 [24] | 45 | Experimental | - | Progressive muscles relaxation and music technique to decrease fatigue in cancer patients are effective. |
| Mofid et al. 2016 [25] | 52 | Randomized trial | Test=55.42 Control=54.27 | The use of processed honey and royal jelly to ameliorate Cancer-related fatigue is useful. |

Discussion

In cancer patients are accompanied with many mental and psychological problems such as anxiety, disappointment as well as lower quality of life affect the amount of fatigue caused by cancer, so these subjects will also be mentioned in this section^[26]. In a study conducted by Bahrami et al., in 2013, the anxiety and its relationship with the quality of life of women with cancer were examined. In this cross-sectional study, 276 women with definite diagnosis of cancer participated. A questionnaire containing three sections of demographic characteristics, Templer death anxiety inventory and McGill quality of life were used for collecting data. The median score of death anxiety was 48 and the mean score for their quality of

life was 103.07 ± 25.11 . There was a significant relationship between death anxiety and quality of life ($r = -0.35$). Also, there was a correlation between death anxiety with mental dimension of quality of life ($r = -0.38$), age ($r = -0.13$) and reading frequency ($r = -0.14$). Anxiety, social support and education level were predictors of quality of life in cancer patients. The development of a comprehensive care plan for cancer patients will be possible considering the factors affecting their quality of life. Reducing anxiety, increasing social support and raising the level of education is one of the things that can improve the quality of life of women with cancer^[27].

In a study by Mao et al., in 2016, the effect of infrared radiation on the amount of fatigue associated with head and neck cancer was studied. In this double blind clinical trial, 78 patients were admitted. In the control group, routine therapy and in the

intervention group 10.6 In infrared radiation was used three times a week for up to 4 weeks for 20 minutes. Fatigue was also examined at the fourth weekend and also for the probable study of the remaining effects of treatment in the eighth week. In the group treated with infrared radiation, fatigue in the fourth week showed significantly lower levels compared to the control group. Improvement in fatigue associated with cancer in the eighth week was also significantly lower in the intervention group than in the control group [28].

In a study by Iwase et al., in 2015, the fatigue associated with cancer, pain, and quality of life in cancer patients was examined. In this study, a short form of Fatigue and Pain Questionnaire and European Cancer Agency Quality of Life Questionnaire were used. Of 183 patients enrolled in the study, 85.8% of the patients had metastatic cancer, which 42.6% of the patients had lung cancer. The mean score of patients' quality of life in this study was 41.4. The mean fatigue score was 4.1. The use of short fatigue questionnaire, like pain, can provide an accurate assessment of the fatigue of cancer patients [4].

In a study conducted by Beydag et al., in 2012, factors affecting the anxiety of cancer patients were investigated. In this descriptive study, 106 patients underwent chemotherapy. In this study, Templar death anxiety scale was used and 36.6% of the participants were more than 45 years old, 57.5% were female and 65.1% were married. There was a significant difference in gender, age and duration of treatment in this study. Anxiety was significantly higher in women in the age group of 17-39 years [29].

In a study done by Demir et al. in 2015, factors affecting anxiety, pain and fatigue in cancer patients treated with a reiki method were studied. In this study 80 patients underwent a clinical trial. In the intervention group, 71.4% were women, 40% were married and 40% had elementary education. In the control group 72.7% were women, 60% were married and 60% had elementary education. The control group received routine nursing care. In the intervention group, five sessions of reiki each night were performed for 30 minutes. In the face-to-face interview, they were collected in a personalized and related profile. Pain, stress and fatigue were evaluated based on the numerical reticulation scale. The results showed a significant difference in control group regarding pain ($P = 0.002$), stress ($p = 0.001$), and fatigue ($p = 0.001$) in the control group compared with the intervention group. Reiki method can be used as an alternative method with routine therapies in this regard [26].

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