Original Article

Effect of standardized exercise program on reported fatigue in patients of cancer receiving chemotherapy

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ABSTRACT

Context: Fatigue is an important symptom of cancer as well as a major side-effect of chemotherapy and is one of the main causes of decrease in physical performance brought on by the disease and its treatment. Several researches have been conducted to study the effect of exercise on relieving cancer related fatigue (CRF). This study will look into the effectiveness of exercise in reducing fatigue in patients of cancer undergoing chemotherapy. **Aims:** The aim was to study effect of a standard exercise program on fatigue in cancer patients on chemotherapy. **Settings and Design:** This was a case-control study conducted in a rural hospital setting. **Materials and Methods:** The case group was given an exercise intervention for 15 days and the control group was not given any intervention. The fatigue scores of both groups were assessed with the help of a Fatigue Severity Scale questionnaire 3 times during this time and compared. **Statistical Analysis Used:** An independent samples *t*-test was done to compare fatigue scores. **Results:** Fatigue scores collected from case and control group on the 15th day showed statistical significance ($t = 3.40$ and $P = 0.002$). **Conclusions:** The study suggested that exercise was an effective intervention is reducing CRF in cancer patients undergoing chemotherapy. Further research is required to establish the type and duration of exercise that can provide optimum relief and alleviate the effects produced by CRF.

Key words: Cancer, cancer related fatigue, chemotherapy, fatigue

INTRODUCTION

According to the International Agency for Research on Cancer, the Global Incidence of Cancer per year exceeds 12 million. Over the years, the treatment of cancer has improved and advanced greatly resulting in cancer patients living longer and the cure of more patients from cancer. This also means that more patients have to live with the consequences of cancer and the long-term effects of its treatment. Subsequently, they seek palliative care to cope with effects of this disease and its treatment. Along with the treatment of cancer therefore it becomes imperative that its adverse effects be recognized, managed and supportive care for it be incorporated into the strategy for cancer patients care.

One of the most common and earliest symptoms of a malignant condition reported by more than 50% individuals at diagnosis and more than 90% patients after treatment is initiated is fatigue.[1,2] Cancer related fatigue (CRF) can be defined as "persistent, subjective, sense of tiredness-related to cancer and cancer treatment that interferes with usual functioning."[3] CRF can be characterized with generalized lack of energy and is different from typical weakness and tiredness by the fact that it is not relieved by rest or even associated to the patient's level of exertion. Fatigue, like pain is a self-perceived state. The patient may complain of feeling tired, drained, exhausted with no energy to even wake up from bed. The effect of fatigue on the patient is considerable as it interferes in the normal activities of the individual and therefore can be considered as one of the most distressing symptom reported by cancer patients. As a result often patients even show reluctance toward adhering

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.138053

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to treatment thus compromising with treatment schedules.[4] This may get in the way of patient's remission owing to the fact that patient loses interest in continuing treatment. Even though, the effect of CRF is acknowledged the exact etiology of this condition is largely unknown.

In order to relieve from CRF, doctors often recommend rest. However, this approach often acts counterproductive as lack of activity leads to "atrophy of muscles and loss of cardio-respiratory fitness."[5] However, if mild aerobic exercise was incorporated into the management strategy of cancer, it would prove to be of more effect and benefit in relief from CRF. This research will look into the effect of exercise on patients reporting CRF and its assessment would be studied.

MATERIALS AND METHODS

Ethics

The procedures followed were in accordance with the ethical standards of the Institutional Ethics Committee, and this study was initiated after the approval of the committee. Informed consent was taken from all participants involved in the study.

This study was carried out on cancer patients in a rural hospital in the state of Maharashtra.

Type of study

This was a Quasi Experimental Study (case-control). The patients undergoing chemotherapy were the study participants. The case group involved patients undergoing chemotherapy who received exercise intervention and the control group received no intervention. Both their fatigue scores were collected and compared.

Study participants

The exercise population was 30 patients diagnosed with any form of cancer. The study evaluated the effect of exercise on CRF in patients of both sexes belonging to age group 12-70 years undergoing any type of chemotherapy.

Exclusion criteria

- Non consenting patients
- Bed ridden patients
- Patients with bone malignancies
- Patients below the age of 12 and above the age of 70 years
- Patients with central nervous system malignancies
- Patients with co-morbidities where exercise is contraindicated.

Sample size

The intervention group was 15 patients diagnosed with any form of cancer undergoing chemotherapy and the control group included 15 patients diagnosed with any form of cancer undergoing chemotherapy.

Duration of study

This study was conducted for 2 months - during the months of June and July 2013.

Proposed intervention

It included a standardized exercise program of aerobic exercise. Participants were asked to walk for 10 min twice a day for 15 days. The intervention was delivered in a group and to individual participants in the hospital setting.

Data collection

For both case and control groups, fatigue scores were collected and compared. Cox regression technique was used to adjust for patient characteristics.

Fatigue score

The assessment of fatigue in the patients was done through the help of the "Fatigue Severity Test"[6] and measured with a Liker scale shown in [Table 1].

Fatigue severity scale questionnaire

The Fatigue Severity Scale Questionnaire contains 9 statements that rate the severity of the fatigue symptoms. After reading the statement, a number from 1 to 7 was circled depending on how accurately it described the condition of the patient where 1 is the lowest signifying strong disagreement with the statement and 7 is the highest showing strong agreement. Any score above 36 indicates presence of fatigue.

The study participants were asked to fill this form thrice:

- At the beginning of the intervention
- At the end of 7 days
- At the end of 15 days.

Steps to reduce bias

In order to reduce bias, the study was a Single Blind Study (Assessor Blind) where the assessment of fatigue was conducted by a third person and the assessor conducted the intervention without being involved in fatigue assessment.

Table 1: Fatigue severity scale

During the past week I have found that	Disagree↔Agree
My motivation is lower when I am fatigued	1 2 3 4 5 6 7
I am easily fatigued	1 2 3 4 5 6 7
Fatigue interferes with my physical functioning	1 2 3 4 5 6 7
Fatigue causes severe problems for me	1 2 3 4 5 6 7
My fatigue prevents sustained physical functioning	1 2 3 4 5 6 7
Fatigue interferes with carrying out certain duties and responsibilities	1 2 3 4 5 6 7
Fatigue is among my most disabling symptoms	1 2 3 4 5 6 7
Fatigue interferes with my work, family or social life	1 2 3 4 5 6 7
Exertion brings on my fatigue	1 2 3 4 5 6 7

As the population is prevalently rural, the fatigue assessment was conducted in the patient's first language - Marathi. The participants were randomly assigned to case and control. This was done by assigning the first patient into one of the groups by coin toss and then allotting every alternate patient into case or control.

RESULTS

Characteristics of participants

During the study period (June-July 2013), a total of 30 participants who fit the inclusion criteria and agreed to participate were asked to fill the questionnaire out of which 15 patients in case group had undergone intervention and the other 15 were control. There were no dropouts during the study and all 30 questionnaires were valid for analysis. Significance testing was done on baseline for demographic and medical characters in control and intervention group.

Patient characters were adjusted by Cox regression using the IBM SPSS statistical software version 20.0. None of the baseline parameters were shown to have significant effect on fatigue scores.

Table 2: Patient characteristics

Characteristics	*n*=15		*P* value
	Cases	Control	
Age (mean±SD)	41.6 (10.56)	47.87 (11.34)	0.1283 NS
BMI (mean±SD)	20.5 (2)	20.8 (1.9)	0.6768 NS
Diagnosis (%)			
Ca. Breast	10 (66.66)	6 (40)	0.14 NS
Ca. Ovary	1 (6.66)	2 (13.3)	0.54 NS
GI malignancies	1 (6.66)	3 (20)	0.28 NS
Ca. Lung	1 (6.66)	2 (13.3)	0.54 NS
Lymphomas	1 (6.66)	1 (6.66)	1 NS
Sarcomas	1 (6.66)	1 (6.66)	1 NS
Chemotherapy cycle (%)			
Cycle I	5 (33.33)	3 (20)	0.4 NS
Cycle II	4 (26.66)	3 (20)	0.66 NS
Cycle III	3 (20)	6 (40)	0.23 NS
Cycle IV	2 (13.33)	1 (6.66)	0.54 NS
Cycle V	0 (0)	1 (6.66)	0.3 NS
Cycle VI	1 (6.66)	1 (6.66)	1 NS
Operated patients (%)	9 (60)	8 (53.33)	0.75 NS
Comorbidities (%)			
Hypertension	1 (6.66)	3 (20)	0.28 NS
Anemia	5 (33.33)	4 (26.66)	0.69 NS
Fatigue scores (mean±SD)			
Day 1	54±5.7	52±12	0.56 NS
Day 15	28.4±4.9	37.9±9.2	0.002 S

Values are number of patients unless stated otherwise. Ca: Cancer, GI: Gastrointestinal, BMI: Body mass index, SD: Standard deviation, NS: Nonsignificant, S: Significant

Changes in patient reported outcome

An independent samples *t*-test was conducted to compare fatigue scores in both case and control group both on the 7th day of intervention and on the 15th day of intervention shown in [Table 2]. It was found that there was No statistically significant difference in the fatigue scores of case (mean [M] =43.6 and standard deviation [SD] =10.45) and control (M = 41.86 and SD = 6.43) measured on the 7th day of intervention ($t = 0.54$ and $P = 0.589$).

However on the 15th day, comparison of fatigue scores of case (M = 37.93 and SD = 9.54) and control ($M = 28.40$ and SD = 5.12) showed statistical significance ($t = 3.40$ and $P = 0.002$). These results suggest that fatigue score improved better in patients who underwent exercise intervention.

DISCUSSION

Fatigue is one of the most common symptoms reported by patients diagnosed with cancer and undergoing treatment for it. In recent years, several researches have been conducted to show efficacy of exercise in diminishing fatigue.

The results of this investigation show that an exercise regimen of limited duration has substantially reduced fatigue reported by patients on chemotherapy. CRF has been related to decrease in physical performance brought on by the disease and its therapy.[7] However, physical fatigue and impairment of physical activities is just one aspect of the difficulties that fatigue causes. A form of this is mental fatigue resulting in lack of will to begin a new activity, socialize or even carry on normal household tasks. At the end of this research, it was seen that there was considerable improvement in both physical as well as mental fatigue in the patients who underwent exercise intervention. Several other investigations that were also conducted with the aim of studying the effect of exercise on CRF have produced the same result where there was significant improvement in fatigue scores of case as compared with control.[7-10] A meta-analysis conducted by the Cochrane review comparing 28 randomized controlled trials studying effect of exercise on fatigue associated with cancer concluded that exercise can be regarded as beneficial for individuals with cancer-related fatigue during and post cancer-therapy.[5]

Patients with fatigue require a higher effort to carry out even their usual household activities. There is increased energy requirement and metabolic distress that not only leads to fatigue, but also other physical symptoms such as tachycardia, dyspnea, and muscle pain. Psychological distress due to these symptoms can lead to mental fatigue. The third symptom of fatigue that is, cognitive impairment leading to decrease concentration was not studied in this research. Hence, it is not known if exercise can lead to an improvement in cognitive fatigue as well.

The effects of physical activity are not only seen in improvement in cardiovascular function, but can also lead to a feeling of liberation, control, and better self-esteem leading to improvement in social interaction. Thus, improved

physical performance has several secondary benefits including improvement of mood and reduction in stress. These changes have also led to an improvement in fatigue.[11]

This study has some limitations. It cannot be ruled out that the improvement in fatigue scores were as a result of increased social contact or motivation or expectations from being a participant in a study, especially since studies have shown that psycho-stimulants have a placebo effect in CRF.[12]

A further limitation of this study was that it did not evaluate cognitive fatigue. The questionnaire used did allow a differentiation between physical and mental fatigue, but questions for assessment of cognitive fatigue was not included. The period over which assessment of fatigue was done was short and the sample size was relatively small. A long-term follow-up to check the efficacy of exercise on fatigue was not possible. Perhaps if the research was carried out on a larger number of patients over a longer duration the long-term effect of exercise on CRF could be studied better.

The result of this study does show that exercise is an effective therapeutic approach to relieving CRF. Further research should be conducted to study the type of exercise and optimum duration that would lead to maximum improvement in fatigue. Role of psychological stimulants needs to be further studied in improving fatigue. Other factors associated with fatigue such as quality of life, emotional distress such as depression and anxiety, aerobic capacity may also be considered.

CONCLUSION

According to the guidelines provided by NCCN,[11] non pharmacological interventions are to be incorporated into cancer patient care to reduce CRF. Several such interventions have been identified and carried out such as physical exercise, yoga, acupuncture, psychosocial therapy, and anticipatory guidance. Of these, physical exercise is the intervention type that has received maximum scientific approval and research based evidence in being able to reduce fatigue in patients. The type of exercise that is the most effective in reducing CRF however is not yet been recognized.

Fatigue being a persistent and debilitating effect of cancer and chemotherapy; measurement of fatigue and its management should be incorporated into the routine care of cancer patients. Every possible reversible cause of fatigue should be identified and cared for such as anemia, hypothyroidism and other several co-morbidities. More research has to be conducted in this area by the scientific community in order to aid in the clinical management of patients suffering from this condition.

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Cite this article as: Jose S, Diwan SK. Effect of standardized exercise program on reported fatigue in patients of cancer receiving chemotherapy. Clin Cancer Investig J 2014;3:373-6.
Source of Support: Short term studentship Program, Indian Council of Medical Research, **Conflict of Interest:** None declared.