RESEARCH ARTICLE

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Effect of Exercise Training on Functional Capacity Head and Neck Cancer Patients Receiving Various Anticancer Therapies: An Interventional Study

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Abstract

Background: Anticancer therapies causes decreased respiratory function, quality of life and functional capacity in head and neck cancer patients. Patients receiving these cancer therapies suffer from fatigue which causes decrease in functional capacity and quality of life. The objective of this present study was to determine and compare the effect of exercise training on fatigue, functional capacity and quality of life in head and neck cancer patients receiving various anticancer therapies. **Method:** A total of 45 subjects were included based on inclusion and exclusion criteria. 6-minute walk test, brief fatigue inventory (BFI) and functional assessment of cancer therapy- general (FACT-G) was used to measure the functional capacity, fatigue and quality of life respectively at baseline and post intervention. Participants received exercise intervention for six weeks (three days a week) for 40 min. Exercise intervention is delivered by a qualified physiotherapist from the Department of Physiotherapy. **Results:** The result of this study shows that there was highly significant improvement in six-minute walk distance pre and post intervention in chemotherapy (33.75+21.55, p=0.000), radiation therapy (39.69+25.46, p=0.000) and chemoradiotherapy (32.06+16.49, p=0.000) within the group. Similarly, significant improvement was also seen in quality of life within the groups, chemotherapy (2.92+2.43, p=0.002), radiation therapy (6.06+3.13, p=0.000) and chemo radiotherapy (5.65+6.93, p=0.004). There was significant reduction in fatigue in chemotherapy (6.92+11.07, p=0.045), radiation therapy (12.38+7.28, p=0.000) and chemo radiotherapy (11.47+8.89, p=0.000). No significant improvement was noted between the groups for six- minute walk distance (p=0.784), quality of life (p= 0.058) and reduction in fatigue (p=0.065). **Conclusion:** This study concluded that exercise training is effective in improving functional capacity, quality of life and reducing fatigue in head and neck cancer patients receiving various anticancer therapies.

Keywords: Head and neck cancer- functional capacity- exercise training- fatigue- quality of life

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Introduction

Head and Neck Cancers (HNC) are rising as major health problems and around 30-35 % occur in India (Kulkarni, 2013) and 57.5% of global HNC occur in Asia (Chauhan et al., 2022). HNC is common in the region where tobacco and alcohol use are more and the effect of alcohol with smoking further increases the risk (Samuel et al., 2013; Grote et al., 2018). Chemotherapy, radiation therapy and chemoradiation in head and neck cancer patients affect speech, swallowing, trismus (Brook 2020), respiratory functions and causes dryness of mouth, mucositis, and damaged skin (Samuel et al., 2013). Psychosocial distress, depression and fatigue leading to physical inactivity and resulting in reduced quality of life (Grote et al., 2018) and impaired functional capacity.

Quality of life (QoL) known as the main outcome parameter and one of the key parts of health-related quality of life is functional capacity. In head and neck cancer, quality of life predicts the prognosis and survival of patients via changes in pre- and post-intervention (Chen et al., 2008) and aims to capture the well- being of patient at a time (Mhesin D et al., 2022). This is the primary outcome measure intended for all cancer patients whereas cancer-related fatigue is a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning. A most common side effect of cancer and cancer treatment is CRF (Floyd and Moyer, 2009). Throughout cancer treatment, the causative factors of fatigue and time course vary and associated with

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lymphocyte count (Chen LM et al., 2021). This affects the patient's life, interfering with daily activities, and disturbing their social and economic well- being.

Exercise after surgical intervention and chemoradiotherapy improves QoL, strength, endurance, fitness, and functional capacity (Su et al., 2017) and also has a positive effect on the cardiovascular system, immune system dysfunction, toxicity to heart, lymphoedema (D'Ascenzi et al., 2021) and reduce the risk of metabolic disorders. Multiple quality of life dimensions encompassing physical, psychosocial, and social domains are all considered important so exercise intervention which includes aerobic exercise and resistance training is effective in improving fatigue, aerobic capacity, flexibility, and quality of life (Fang et al., 2004; Floyd and Moyer, 2009).

Head and neck cancer treatment causes long term effect on the quality of life and functional capacity of the patient. It has severe impact on patients' speech, ability to eat, physical and emotional well-being which leads to inadequate nutritional level and weight loss (Zhao et al., 2015). Prescribing exercise to head and neck cancer patient positively affects functional capacity and quality of life as it significantly improves patients emotional and physical well-being. The aerobic exercise help improving cardiovascular efficiency whereas resistance exercise improves adaptation of neuromuscular system (Schneider et al., 2007; Zhao et al., 2015; Grote et al., 2018). Thus, doing exercise in head and neck cancer is also important.

Several studies have been reported on the effect of exercise in cancer patients improving fatigue and quality of life. Few studies determined the effect of exercise in cancer patients receiving only chemotherapy, radiation therapy, or chemoradiation therapy. There is no retrievable data to evaluate the effect of exercise training in head and neck cancer patients receiving various anticancer therapies. The aim of this study was to determine the effect of exercise training on fatigue, functional capacity, and quality of life in head and neck cancer patients receiving various anticancer therapies. The hypothesis of this study was that exercise training is effective in head and neck cancer patients receiving various anticancer therapies.

Materials and Methods

Study design

This observational study was conducted with 52 patients with HNC receiving various anticancer therapies. Ethical clearance was obtained from the institutional ethics committee.

Setting

This study was conducted at inpatient oncology department in Father Muller Medical College Hospital from March 2019 to February 2020.

Participants

Patients included in this study were diagnosed with head and neck cancer, I, II, &III stages of cancer, were above 18, have undergone surgery for head and neck cancer (1 month after surgery), patients with recurrent head and neck cancer and receiving various anticancer therapies before and after surgery. The patients were excluded who had cardiovascular conditions such as coronary artery disease, uncontrolled angina, ischemic heart disease, neurological conditions such as stroke, Parkinson's disease, Guillain Barre Syndrome, musculoskeletal conditions such as dislocation, osteoarthritis, sprain/ strain, adhesive capsulitis and, recent fracture.

Study size

Sample size was calculated based on the parameters of Schneider et al., (2007). The power of the study was kept at 80 percent with confidence interval of 95%. 52 subjects were be included in the study using a purposive sampling technique. 52 Patients were recruited for this study and they were distributed into chemotherapy (n=17), radiation therapy (n=18) and chemoradiation therapy (n=17) groups.

Variables

Brief fatigue inventory

BFI questionnaire consists of 9 items rated on a 0-10 numeric rating scale where 0 is no fatigue and 10 is severe fatigue and it is a patient report instrument and allows for rapid assessment of fatigue in cancer patients. The global score for the BFI was calculated as the mean value of 9 items ranging from 0 - 10. An internal consistency coefficient of BFI is 0.96 (Floyd and Moyer, 2009).

Functional assessment of cancer therapy- general

The functional assessment of cancer therapy- general (FACT-G) is a patient-reported outcome measure used to assess health-related quality of life in patients undergoing cancer therapy. This assesses the impacts of cancer therapy in four domains: physical, social/family, emotional, and functional. It has 27 questions, each of which is answered using a 5-point ranging from 0 (not at all) to 4 (very much). Test-retest reliability for each subscale and global scale had been observed to range from 0.82- 0.92 (Karthikeyan et al., 2012).

Functional capacity

Functional capacity is estimated using the 6-minute walk test (6MWT). The six-minute walk test was performed using the standard ATS guideline. The coefficient of variations for the 6- minute walk test ranged from 0.24- 0.25 (Floyd and Moyer, 2009).

Data sources/ measurement

Subjects who fulfilled the norms of the inclusion criteria and who agreed to participate in the study by giving their consent were recruited. On day 1, the baseline assessment was conducted. They were asked to fill the Brief Fatigue Inventory questionnaire and Functional Assessment of Cancer Therapy- General questionnaire.

After filling the questionnaires, patients were asked to perform a six-minute walk test. Cones were placed at either end of the 30m stretch as turning points and chairs were set up both side and halfway along the walking stretch. The patient sits on a chair, near the starting point, for at least 10 minutes before the test starts. During this time, pulse and blood pressure was checked. When patient

stand, baseline dyspnea and overall fatigue using the Borg scale was checked. The patient was instructed to walk back and forth for six minutes. If necessary, they can slow down or stop. Upon completion the area distance covered in 6-minute was measured.

Participants received intervention three days a week for 6 weeks as per the American College of sport medicine guidelines. 40 minutes session was conducted by a qualified physiotherapist. All the patients received an exercise intervention program included all the component of strength, endurance and flexibility. This included 5 min warm-up, 15 min aerobic exercise, 15 min strength training exercise followed by 5 min cool down/ flexibility exercise.

Warm-up

Stretching of major muscles
Range of motion exercises
Breathing exercises

Aerobic exercise

Walking briskly on plane ground
Progression to ramp walking

Strength training exercises

Pelvic tilt
Standing push up
Calf raises
Sit to stand
Wall squat

Cool down/ Flexibility exercises

Triceps stretch
Quadriceps stretch
Calf stretches

Post six- weeks intervention fatigue, functional capacity, and quality of life were re-assessed using the same methods. Effect of 6 weeks of an exercise intervention on chemotherapy patients, radiation patients, and chemoradiation therapy patients was determined and compared.

Statistical Analysis

The data were analyzed using the software SPSS version 21. Collected data were represented as the mean and standard deviation for Fatigue, Functional Capacity, and Quality of life. Data for gender and type of anticancer therapies were represented as frequency and percentage distribution. ANOVA test was used for the comparison between the group's homogeneity of chemotherapy, radiation therapy, and chemoradiation therapy. Fisher's exact test was used for gender analysis in the groups. Post hoc analysis done for comparison between the groups using the Kruskal Wallis test done for the brief fatigue inventory, 6-minute walk test, and functional assessment of cancer therapy- general. Comparison within the groups done with the T-test and the p-value was given.

Results

52 Patients were recruited for this study and they were distributed into chemotherapy (n=17), radiation therapy (n=18) and chemoradiation therapy (n=17) groups. Total numbers of participants completed the study were 45, amongst which 35 were males and 10 were females. 12 belonged to chemotherapy, 16 belong to radiation therapy and 17 belonged to the chemoradiation therapy group (Table 1).

As shown in Table 2, baseline data of the patients with respect to parameters there was no significant difference between the groups. As shown in Table 3, there was a highly significant difference seen within the group in the 6-minute walk distance. In the chemotherapy group

Table 1. Frequency Distribution

Gender	Chemotherapy	Radiation therapy	Chemoradiation therapy	Total
Male	10 83.30%	13 81.30%	12 70.60%	35 77.80%
Female	2 16.70%	3 18.80%	5 29.40%	10 22.20%
Total	12 100.00%	16 100.00%	17 100.00%	45 100.00%

Table 2. Baseline Data of Patients

Parameter	Groups	N	Mean + Std.	ANOVA test p-
6 Minute Walk Test	Chemotherapy	12	217.50 + 34.74	0.275
	Radiation therapy	16	211.88 + 31.51	
	Chemoradiation	17	196.47 + 42.01	
Brief Fatigue Inventory	Chemotherapy	12	45.75 + 7.42	0.016
	Radiation therapy	16	47.00 + 8.12	
	Chemoradiation	17	54.29 + 9.53	
Functional Assessment of Cancer Therapy-General	Chemotherapy	12	60.58 + 3.94	0.638
	Radiation therapy	16	62.00 + 3.22	
	Chemoradiation	17	61.88 + 5.17	

Table 3. Comparison within and between the Groups for 6-Minute Walk test, bBrief Fatigue Inventory and Fatigue

Parameter	Groups		N	Mean + S.D.	Mean difference + S.D of difference	Change (%)	T-test p-value	Kruskal Wallis test p value
6MWT	CT	Pre	12	217.50 + 34.74	33.75 + 21.55	15.52	0	
		Post	12	251.25 + 26.81				
	RT	Pre	16	211.88 + 31.51	39.69 + 25.46	18.73	0	0.784
		Post	16	251.56 + 36.64				
	CRT	Pre	17	196.47 + 42.01	32.06 + 16.49	16.32	0	
		Post	17	228.53 + 41.30				
		Pre	12	45.75 + 7.42	6.92 + 11.07			
BFI	CT	Post	12	38.83 + 4.82		15.12	0.045	
		Pre	16	47.00 + 8.12	12.38 + 7.28			
	RT	Post	16	34.63 + 7.51		26.33	0	0.065
		Pre	17	54.29 + 9.53	11.47 + 8.89			
	CRT	Post	17	42.82 + 11.12		21.13	0	
		Pre	12	60.58 + 3.94	2.92 + 2.43			
FACT-G	CT	Post	12	57.67 + 4.64		4.81	0.002	
		Pre	16	62.00 + 3.22	6.06 + 3.13			
	RT	Post	16	55.94 + 4.49		9.78	0	
		Pre	17	61.88 + 5.17	5.65 + 6.93			0.058
	CRT	Post	17	56.24 + 5.27		9.13	0.004	

6MWT, 6-minute walk test, BFI, brief fatigue inventory, FACT-G, functional assessment of cancer therapy- general; CT, chemotherapy; RT, radiation therapy; CRT, chemoradiation therapy; S.D, standard deviation.

pre- and post-intervention, the mean difference was 33.75+21.55; p= 0.000, in the radiation therapy group was 39.69+25.46; p= 0.000 and in chemoradiation therapy group was 32.06+16.49; p= 0.000. But there was no significant difference found between the groups (p=0.784).

The analysis of the brief fatigue inventory showed that there was a significant difference within the chemotherapy group pre- and post-intervention with a mean difference of 6.92+11.07; p= 0.045 whereas it was noted that there was a highly significant difference in radiation therapy and chemoradiation therapy with a mean difference of 12.38+7.28; p= 0.000 and 11.47+8.89; p= 0.000 respectively. In between the group showed that there was no significant difference (p=0.065) as shown in the Table 3.

The pre- and post-intervention analysis for functional assessment of cancer therapy- general showed that there is a highly significant difference within the groups. The mean difference of the chemotherapy group was 2.92+2.43; p=0.002, for the radiation therapy group was 6.06+3.13; p=0.000, and for chemoradiation therapy group was 5.65+6.93; p=0.004. As shown in the Table 3, there was no significant difference between the groups (p=0.058).

Discussion

The objective of this study was to determine the effect of exercise training on fatigue, functional capacity, and quality of life in head and neck cancer patients receiving chemotherapy, radiation therapy, and chemoradiation therapy. There are several studies that evaluated the effect of exercise training in various cancers such as cancer of breast, prostate and colon. This study shows that exercise training help in reducing fatigue, improve functional capacity and quality of life.

In chemoradiation therapy group (n=17), it was seen that within the group pre- and post-intervention, there was a remarkable improvement in six-minute walk distance (p<0.000), quality of life (p<0.000) and fatigue significantly decreased (p<0.000) thereby causing a sense of well-being. This is in a line with the study done by Samuel et al., (2019) with six weeks supervised, individually tailored exercise training in head and neck cancer patients on active chemoradiation therapy. They found in their study that there was a great improvement in the functional capacity, quality of life, and prevention of worsening of fatigue in the exercise group. As this study involved aerobic and resistance exercise programs as intervention, aerobic exercise improved patient's cardiovascular efficiency, and ventilation. It also increased cardiac output, stroke volume, and oxygen transport to the cell. Whereas resistance training increased the cross-sectional area of muscle fiber type and adaptation of the neuromuscular system (Schneider et al., 2007; Grote et al., 2018).

Post intervention, in the chemotherapy group (n=12), showed a highly significant improvement in functional capacity (p<0.00) and quality of life (p<0.00) and there was a significant reduction of fatigue score (p<0.045). Although five patients dropped out of the chemotherapy group as three of them got discharged earlier and two didn't want to be a part of the study anymore. On the other hand, in the radiation therapy group (n=16), following

two dropouts there was a highly significant improvement in the reduction of fatigue ($p<0.00$), functional capacity ($p<0.00$), and quality of life ($p<0.00$) post-treatment was seen. The result of this study is in line with the study was done by Mustian et al., (2009) to demonstrated the feasibility and initial efficacy of aerobic and progressive resistance exercise intervention for aerobic capacity, strength, muscle mass, cancer-related fatigue, and quality of life. Their study showed that exercise during radiation therapy is beneficial for fatigue and aerobic capacity. The improvement in this study can be attributed to the exercise training that has a great impact on the muscle properties, it changes the increase in the fiber type area, the oxidative capacity which causes a gain in muscle weight (Grote et al., 2018) and is an effective strategy for reducing cancer-related fatigue, by maintaining or restoring functional capacity, improving depression and anxiety, as well as enhancing the quality of life in individuals with cancer (Porock and Fu, 2004). There were 7 dropouts in this study, five patients dropped out of the chemotherapy group as three of them got discharged earlier and two didn't want to be a part of the study anymore whereas there were two dropouts in radiation therapy group as both the patient got discharged.

This study found that when comparing the outcome measures between the groups there was no significant improvement in the reduction of fatigue ($p>0.065$), functional capacity ($p>0.784$), and quality of life ($p>0.058$) was seen. These finding is in agreement with the result of an observational study executed by Holmes et al., (2005). Their study reported that women with stages I to III breast cancer who walked the equivalent of 3 to 5 hours per week following their breast cancer diagnosis experienced the greatest reduction in risk of mortality. This suggests a possible hormonal mechanism, through acute and chronic improvements in insulin resistance and reduction in hyperinsulinemia for improved survival among physically active women (Holmes et al., 2005; Palesh et al., 2018; Goodwin et al., 2002). Physical activity was found to improve functional capacity and quality of life of patients undergoing chemotherapy, radiotherapy, or combination therapy (Holmes et al., 2005).

The result of this study shows that there was a reduction in fatigue and improvement in functional capacity and quality of life in head and neck cancer patients receiving chemotherapy, radiation therapy, and chemoradiation therapy post-6-week intervention program. This shows that exercise training had a positive effect on fatigue, functional capacity, and quality of life when receiving active chemotherapy, radiation therapy, and chemoradiation therapy. Although there was significant improvement within the groups there was no significant difference found between the groups. Hence, exercise training is equally effective in reducing fatigue, improving functional capacity, and quality of life.

One of the limitations of this study was unequal ratio of male and female participants. The fraction of radiation was unequal in radiation therapy and chemoradiation therapy groups in this study. The numbers of cycles for chemotherapy were unequal in individuals. The sample size was small hence the distribution of the sample was not equal.

Further studies should be done with a larger sample size to determine the effect of exercise training in between the anticancer therapies and to determine the effect of exercise training on different types of cancer receiving various anticancer therapies. The number of cycles and fractions of radiation should be similar.

This study concluded that exercise training is effective in decreasing fatigue, improving functional capacity, and quality of life in head and neck cancer patients receiving various anticancer therapies.

Author Contribution Statement

Sameeksha Sidhpuria: Formulating research plan, study design, data collection, follow up, collecting outcomes, data analysis; Cherishma D'silva: Formulating research plan, Overall supervision of project, data analysis; Nishitha Shetty: Patient referral, follow up; Leah Mohandas: Supervision of project and manuscript writing.

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This study was approved by the Institutional Ethical Committee of Father Muller Charitable Institutions (Approval number 62/19) and is a part of an approved post graduate thesis.

Conflict of Interest

There is no conflict of interest

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