



**ORIGINAL RESEARCH PAPER**

**Oncology**

**IMPACT OF A MODERATE INTENSITY INTERMITTENT AEROBIC EXERCISE TRAINING WITH PROGRESSIVE RELAXATION TECHNIQUE ON PHYSIOLOGICAL AND PSYCHOLOGICAL VARIABLES IN INDIAN CANCER PATIENTS- AN EXPERIMENTAL STUDY**

**KEY WORDS:** Cancer, fatigue, peak expiratory flow rate, Brief Fatigue Inventory, aerobic training, progressive relaxation technique

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**ABSTRACT**

**Background & Objective:** Cancer is characterized by the uncontrolled growth and spread of abnormal cells. It causes multiple impairments, activity limitations, participation restrictions, depression, and an overall decrease in the quality of life. Fatigue is a common problem experienced by cancer patients during chemotherapy and radiotherapy. Fatigue and other psychological problems like anxiety and depression follow the diagnosis of cancer and its subsequent treatment. This study aimed to find out the effect of moderate intensity intermittent aerobic training along with progressive relaxation technique on physiological and psychological variables in the Indian cancer patients.

**Methods:**

The present experimental study was conducted in thirty (30) adult cancer subjects including both males and females between the age group of 18-65years undergoing chemotherapy and radiation therapy. All the subjects received moderate intensity intermittent aerobic training along with progressive relaxation technique. Baseline scores of physiological and psychological variables were noted on the 1st day and at the end 4th week. Post values obtained were compared with the baseline values.

**Results:**

Statistical analysis of outcome variables at pre and post intervention demonstrated statistically significant improvements ( $p \leq 0.05$ ) in the physiological variables like systolic blood pressure, diastolic blood pressure, mean arterial pressure, rate pressure product, peak expiratory flow rate, six minute walk distance and calories expenditure and psychological variables like fatigue, depression, anxiety and quality of life.

**Conclusion:** The study demonstrated a positive effect on the physiological variables like hemodynamic responses, six-minute walk distance and also on the psychological variables like fatigue, pain, anxiety, depression and QOL.

**Introduction:**

Cancer is defined as a group of diseases which is characterized by the uncontrolled growth and spread of abnormal cells and if not controlled can result in death.<sup>1</sup>In aging population, cancer is largely associated with age more than 65years.<sup>2</sup>Age-adjusted incidence rates for cancer are still quite low in the demographically young country. Slightly more than 1 million new cases of cancer are diagnosed every year in a population of 1.2 billion. An estimated 600 000–700 000 deaths in India were caused by cancer in 2012.<sup>3</sup>About 1,658,370 new cancer cases have been diagnosed in 2015. Cancer is caused by external factors, such as tobacco use, infectious organisms such as human papillomavirus (HPV), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and Helicobacter pylori (H. pylori), and an unhealthy diet and internal factors, such as inherited genetic mutations, hormones, and immune conditions. Cancers are divided into groups according to the type of cell they start from and they include carcinomas, brain tumors, lymphomas, sarcomas and leukaemias. Treatments include surgery, radiation, chemotherapy, hormone therapy, immune therapy, and targeted therapy (drugs that specifically interfere with cancer cell growth).<sup>1</sup>

Cancer-related fatigue as defined by the National Comprehensive Cancer Network (NCCN) is a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning.<sup>4,5</sup>Physical inactivity, induces muscular catabolism, causing deconditioning which will even more cause fatigue. Even years after the treatment, fatigue still poses as a problem for up to 30% of cancer survivors and has a great impact on the patient's quality of life. Psychological factors also play an important role in the commencement of cancer fatigue.<sup>6</sup>Psychosocial problems follow the diagnosis of cancer and subsequent treatment with chemotherapy.

Physical exercise has shown to enhance the functional dimension of QOL by decreasing the incidence of nausea, weight gain, muscle wasting, and fatigue which are often the symptoms experienced by the cancer patients undergoing chemotherapy.<sup>7-12</sup> Depression is considered to be a contributing factor to fatigue in cancer patients. Exercise is an effective intervention for improving side effects such as CRF, cognitive impairment, sleep problems,

depression, pain, anxiety and physical dysfunction including impaired muscular function, cardiopulmonary function and bone density. Aerobic exercise which utilizes large muscle groups has been suggested for rehabilitation of cancer patients affected by the problem of "energy loss".<sup>13</sup>Relaxation training is the most commonly investigated and clinically used intervention in cancer population. It is generally easy to learn and readily accepted by any patient.

Although exercise in the form of aerobics, resistance training and relaxation technique appears to have a positive effect on physiological and psychological function in people rehabilitating from cancer treatment, however there is dearth in literature regarding effect on moderate intensity intermittent aerobic training and progressive relaxation technique on physiological and psychological variables in the Indian cancer patients. Hence, the present study was taken up to evaluate and assess the same in cancer patients.

**Methodology:**

The primary data was collected which targeted all adult male and female cancer subjects receiving chemotherapy and radiation therapy from tertiary care hospital, India. The study period ranged from March 2015 to February 2016. This Experimental study design (pre-post clinical trial) with a Non-probability sampling technique with Convenience sampling method included all adult male and female cancer subjects receiving chemotherapy and radiation therapy in an age group ranging from 18-65 years, who received at least one series of chemotherapy treatment and also willing to participate in the study were included. Subjects with documented metastases, anticoagulation treatment, and symptomatic cardiac disease including clinical congestive heart disease, treatment for arrhythmia or myocardial infarction within the last 3 months, dementia and mentally unstable subjects were excluded

Ethical clearance was obtained from Institutional Ethical Committee prior to the commencement of the study. Informed consent was obtained only those subjects willing to take intervention of minimum 4 weeks intervention. A total of 80 participants were screened for the study out of which 40

participants were excluded as they did not meet the inclusion criteria. Forty (40) subjects were selected for the study out of which thirty (30) participants completed the study. Demographic data and physiological parameters like heart rate (HR), respiratory rate (RR), blood pressure (BP), pulse pressure (PP), mean arterial pressure (MAP), peak expiratory flow rate (PEFR) and rate pressure product (RPP) were measured along with the initial score of BFI, Mood scale and Visual Analogue Scale-Quality of life (VAS-QOL). Subjects were then made to perform moderate intensity intermittent aerobic exercise training in the form of brisk walking as tolerated by the subject on the basis of RPE Borg's scale followed by progressive relaxation exercises.

#### Procedure:

##### Moderate intensity intermittent aerobic exercise training protocol:

**Warm –up exercises** included upper and lower body stretches (Triceps, biceps, quadriceps, hamstrings, calf stretches) with moderate intensity intermittent aerobic training in the form of brisk-walking with the exercise intensity of 40-60% heart rate reserve (HRR) along with progressive relaxation technique for 15 minutes for 5days/week. This was same for all the 04 weeks.

##### 1<sup>st</sup> week:

The duration of the aerobic exercise for 1<sup>st</sup> week was 15 minutes along with intermittent rest periods for 01 minute every 05 mins or as tolerated by subject with 12-15 on RPE scale of 6-20 followed by 15 minutes of progressive relaxation technique for 5days/week. The total duration for the 1st week session was 30 minutes.

##### 2<sup>nd</sup> week:

The duration of the aerobic exercise for 2<sup>nd</sup> week was 20 minutes along with intermittent rest periods for 01 minute every 05minutes or as tolerated by subject with 12-16 on RPE scale of 6-20 followed by 15 minutes of progressive relaxation technique for 5days/week. The total duration for the 2nd week session was 35 minutes.

##### 3<sup>rd</sup> week:

The duration of the aerobic exercise for 3<sup>rd</sup> week was 25 minutes along with intermittent rest periods for 01 minute every 05 minutes or as tolerated by subject with 12-16 on RPE scale of 6-20 followed by 15 minutes of progressive relaxation technique for 5days/week. The total duration for the 3<sup>rd</sup> week session was 40 minutes.

##### 4<sup>th</sup> week:

The duration of the aerobic exercise for 4<sup>th</sup> week was 30 minutes along with intermittent rest periods for 01 minute every 05 minutes or as tolerated by subject with 12-16 on RPE scale of 6-20 followed by 15minutes of progressive relaxation technique for 5days/week. The total duration for the 4<sup>th</sup> week session was 45 minutes.

During exercise sessions, Caltrac accelerometer was tied to the waist of all the subjects to record the amount of energy expended during the aerobic exercise training in each exercise session. Peak expiratory flow rate (PEFR) was measured using portable Wright's peak flowmeter. Heart rate and SpO<sub>2</sub> was monitored using a digital pulse oximetry. After 04weeks of intervention, the pre (baseline) and post-test values of physiological and psychological variables were noted and then the results were analyzed.

#### Outcome measures:

##### Brief Fatigue Inventory (BFI):

This is a 6 items scale which is used to rapidly assess the severity and impact of cancer related fatigue which correlates with the quality of life. Each of the items have a 10 point scale drawn where 0 indicates no interference or no fatigue and 10 indicates completely interferes or fatigue as bad as one can imagine at the time or past 24 hours when fatigue is being assessed. A global fatigue score can be obtained by averaging all the items. It takes 5 minutes to administer and the method of administration is via self-report or an interview.

#### Visual Analogue Scale – Quality of Life (VAS-QOL):

It is a scale used for the assessment of pain. A VAS scale of 10cms was used where 0 indicated no pain and 10 indicated maximum pain.

#### Statistical analysis:

Statistical analysis was done manually as well as using statistical package of social sciences (SPSS) version .21 so as to verify the results obtained. Nominal data of all subjects including demographic data i.e. age, gender, BMI, height, weight distribution were analyzed using mean and standard deviation and percentage distribution. Percentage of distribution of males and females, diagnosis of cancer, type of cancer, and stages of cancer and status of chemotherapy and radiation therapy was noted. Physiological variables of all the four weeks were compared with the baseline values using students 't' test. Comparison of the pre intervention and post intervention outcome measures such as psychological variables like Brief Fatigue Inventory, VAS-QOL was compared using Wilcoxon matched test. Probability values of  $p \leq 0.05$  were considered statistically significant.

#### Results:

##### Demographic profile:

A total of thirty 30 subjects participated in the study out of which 15 were males and 15 were females with mean duration of diagnosis in both the gender were  $9.52 \pm 7.25$  months. Among all the subjects 40% (12) of them were diagnosed with cervix cancer followed by 13.33% (4) with esophageal cancer followed by 10% (3) each with buccal mucosa cancer and tongue cancer. One subject each is diagnosed with cricoid cancer, cancer of hard palate, cancer of upper esophagus, rectosigmoid colon cancer, rectoperitoneal tumor and sinonasal carcinoma. Among 30 subjects, 20 subjects were suffering from I<sup>st</sup> and II<sup>nd</sup> stage of cancer followed by 10 subjects who were suffering from stage III cancer. Only 1 subject was diagnosed with Iva cancer. The mean cycles of chemotherapy/radiation therapy were  $4.90 \pm 3.10$  cycles.

#### Outcome measures

##### Physiological variables

The comparison between the baseline physiological values like respiratory rate (RR), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) with all the 4 weeks demonstrated statistical significant difference when compared with mean baseline values. Though clinically respiratory rate did not show much change from the mean baseline values compared to 1<sup>st</sup> week, 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week. There was neither clinical significance nor statistical differences in heart rate values when compared with the baseline mean with the values of all the 4 weeks. Systolic blood pressure and diastolic blood pressure demonstrated statistically significant differences when compared with the baseline mean values with the values obtained in 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week. However there were no changes seen in the 1<sup>st</sup> week. Mean Arterial Pressure showed statistically significant differences during the end of 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week when compared to the baseline values. However, there were no significant differences in the values obtained of the Pulse pressure. Values of Peak Expiratory Flow Rate demonstrated statistically significance when compared with the baseline values. Rate Pressure Product also demonstrated significant differences in the values obtained in the 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week when compared to the baseline mean values. Six-minute walk distance also demonstrated significant improvements at the end of the 4th week when compared to the baseline values. Calories expended during the exercise performance on subjects have also demonstrated significant improvements.

##### Psychological variables

The BFI scores obtained demonstrated statistical significant differences when compared with the baseline scores and at the end of intervention suggesting the fatigue levels at the end of exercise intervention has decreased.

VAS-QOL improved in all subjects under study by the end of 4th week as compared to the baseline values.

#### Discussion:

The present study was conducted to examine the effect of a moderate intensity intermittent aerobic exercise training in the form of brisk walking along with progressive relaxation technique on physiological variables like respiratory rate (RR), heart rate (HR), blood pressure (BP), pulse pressure (PP), Rate pressure product (RPP), peak expiratory flow rate (PEFR), 6 minute walk distance (6MWD) and on psychological variables like Brief fatigue inventory (BFI), mood scale, visual analogue scale- Quality of life (VAS-QOL).

In the present study the average age of males and females was 54.33±7.85 and 50.86±8.83 years respectively. Raina V et. al. suggested that the age specific incidence rates were higher in females as compared to males in the age group between 25 to 54 years. At older age group of 55 to 75 and above the incidence rates are higher in males when compared to females.<sup>14</sup>

Cancer of cervix uteri is the second susceptible site for women. India has higher incidence rates of cancers of oral cavity, pharynx and cervix. One-third of cancers are caused due to tobacco chewing. The most common cancer among men is lung and bronchus which has shown to be more evident in Mumbai, Delhi and Bhopal whereas the other important sites among men are the oral cavity, pharynx, larynx and rectum. Among women, cervical cancer followed by breast cancer is seen to be common in places like Barshi, Bangalore, Bhopal and Chennai.<sup>15</sup> However, majority of them in the present study demonstrated that is 40% (12) of subjects were diagnosed with cervix cancer followed by 13.33% (4) with esophageal cancer followed by 10% (3) each with buccal mucosa cancer and tongue cancer.

The TNM staging system determines the extent and progression of cancer. The higher the stage the further the cancer has progressed. The TNM system meets the criteria which is developed by the American Joint Committee on Cancer and thus is the recommended classification system.<sup>16</sup> In the present study 33.33% were in stage II b, 20% were in stage II and III, 10% in stage I a and III b and 3.33% in stage I and IV a according to TNM staging. Majority of the subjects were in stage II, which suggests that as the stage advances the severity also increases. Evidences also suggested that as stage advances the dosage increases that crosses the blood brain barrier and induces neurotoxicities, which further causes increase in the fatigue levels.<sup>17</sup>

Baines CL. et.al also demonstrated significant changes in both systolic blood pressure and diastolic blood pressure after 12 weeks of low-intensity exercise conditioning program.<sup>18</sup> However, in the present study systolic blood pressure and diastolic blood pressure demonstrated statistically significant differences when compared with the baseline mean values with the values obtained in the 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week.

Mean arterial pressure (MAP) is strongly associated with increased cardiovascular disease risk in younger men (<60 years).<sup>19</sup> However, the present study demonstrated statistical significant differences during the end of 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week when compared to the baseline values.

Rate pressure product (RPP) is a valuable marker of oxygen requirement and reflects the internal myocardial work performed by the beating heart. Nagpal S et al. suggested that normal individuals developed a RPP of 20-35mmHgxb/min which is an indicative of normal ventricular function. Low RPP value suggests the restricted coronary blood supply with inadequate ventricular function.<sup>20</sup> However, in the present study RPP demonstrated significant differences in the values obtained in 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week when compared to the baseline values.

Peak expiratory flow rate (PEFR) is used to assess the ventilatory capacity of an individual. In a study, peak expiratory flow rate was used as it is easy to administer and a quick assessment to show improvement in overall pulmonary function over a period of 10 weeks which suggests that physical activity in the form of aerobic exercises enhances the cardio-respiratory and pulmonary functions and have shown improvement in peak expiratory flow rate (PEFR). The cause of improvement in PEFR values can be

because of aerobic exercises, which are known to enhance the breathing efficiency and decrease pulmonary resistance.<sup>21</sup> However, in the present study it has also shown to have an improvement in the pulmonary function capacity of the study subject by comparing the values of all the 4 weeks with the baseline values.

Caltrac accelerometer is used to record the amount of energy (calories) expended, during the 6-minute walk and has strong correlations with maximum oxygen uptake and doubly labelled water. Reliability and validity have been demonstrated for exercise modes like walking, running, and cycling. Calories expended during exercise were measured by the Caltrac accelerometer which gives the information about the type and duration of the exercise.<sup>22</sup> In the present study, subjects were subjected to perform moderate intensity intermittent aerobic exercise training using the Caltrac accelerometer which was tied at the waist to record the energy expended in terms of kcal during exercise. The exercise intensity was continuously monitored by using the Borg scale 6-20.

Fatigue is one of the most common problems experienced by 70% of cancer patients during chemotherapy and radiotherapy. In the present study the BFI was used to measure fatigue based on the activities that were done daily which demonstrated significant reduction in fatigue levels in all study subjects which could be attributed to improvement in the physical activity level in subsequent weeks. It has shown that cancer patients receiving high dose of chemotherapy/radiotherapy must increase their physical activity rather than rest after treatment showing improvement in fatigue, measured in terms of hemoglobin concentration.<sup>23</sup>

The QOL of cancer patients can be improved by implementing walking programs, as this present study demonstrated that aerobic training in the form of brisk walking has improved patients functional capacity thereby, reducing the fatigue levels and improving the quality of life. Increase in 6MW distance was moderately to strongly associated with higher maximum exercise capacity (VO 2peak) and perceived physical function. The six (6) Minute Walk Distance seems to be as valid for assessing physical function in cancer patients as in healthy elderly and patients and also seem to be safe and clinically feasible in cancer patients. Similarly the present study also demonstrated improvements in the walking distance at the end of the intervention.<sup>24</sup>

**Conclusion:**

The present study concludes to have a positive effect on the physiological variables like hemodynamic responses, six-minute walk distance and also on the psychological variables like fatigue, pain, anxiety, depression and QOL.

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**Table 1: Demographic characteristics of all subjects in study**

Characteristics	No of samples	% of samples	Mean & SD
Gender			
Male	15	50	-
Female	15	50	-
Age	-	-	52.60 ± 8.40
Male	-	-	54.33±7.85
Female	-	-	50.86±8.83
Height	-	-	155.97±7.81
Male	-	-	160.2±8.04
Female	-	-	151.73±4.81
Weight	-	-	49.57±7.78
Male	-	-	52.13±6.35
Female	-	-	47±8.41
BMI	-	-	20.32±2.66
Male	-	-	20.20±1.40

Female	-	-	20.43±3.45
Diagnosis of cancer	-	-	9.52±7.25
Type of cancer			
Ca Buccal Mucosa	3	10	-
Ca Cricoid	1	3.33	-
Ca Hard palate	1	3.33	-
Ca Oesophagus	4	13.33	-
Ca Tongue	3	10	-
Ca rectum	2	6.67	-
Ca upper oesophagus	1	3.33	-
Recto sigmoid colon	1	3.33	-
Retroperitoneal	1	3.33	-
Sinonasal Carcinoma	1	3.33	-

**Table 1: Demographic characteristics of all subjects in study (Contd)**

Characteristics	No of cycles	% of subjects	Mean & SD
Stage of cancer			
I	1	3.33	-
II	6	20.00	-
II a	3	10.00	-
II b	10	33.33	-
III	6	20.00	-
III b	3	10.00	-
IV a	1	3.33	-
	-	-	4.90±3.10

**Table 2: Comparison of Physiological variables of all 4 weeks with baseline values**

Physiological variables	Baseline	1st week	2nd week	3rd week	4th week
	Mean	Mean	Mean	Mean	Mean
Respiratory rate	18.73±1.46	21.40±1.99	21.90±2.35	22.27±1.96	22.47±1.68
% of change	-	-14.23	-16.9	-18.86	-19.93
Paired t-test	-	-9.4919	-10.5646	-11.9968	-14.7326
p-value	-	0.0001*	0.0001*	0.0001*	0.0001*
Heart rate	84.63±12.64	86.33±10.17	84.80±7.21	85.37±9.21	84.17±10.08
% of change	-	-2.01	-0.2	-0.87	0.55
Paired t-test	-	-1.4296	-0.1068	-0.3021	0.1745
p-value	-	0.1635	0.9157	0.7647	0.8627
Systolic BP	111.80±5.88	113.73±8.96	118.67±6.22	122.20±4.88	122.60±5.76
% of change	-	-1.73	-6.14	-9.3	-9.66
Paired t-test	-	-1.3367	-5.119	-7.4417	-9.2391
p-value	-	0.1917	0.0001*	0.0001*	0.0001*
Diastolic BP	71.20±3.18	73.33±5.47	78.00±4.07	79.47±1.74	79.53±2.81
% of change	-	-3	-9.55	-11.61	-11.7
Paired t-test	-	-1.7592	-5.7217	-13.1875	-11.1192
p-value	-	0.0891	0.0001*	0.0001*	0.0001*

\*Level of significance p ≤ 0.05

**Table 2: Comparison of Physiological variables of all 4 weeks with baseline**

Physiological variables	Baseline	1st week	2nd week	3rd week	4th week
	Mean & SD	Mean & SD	Mean & SD	Mean & SD	Mean & SD

Mean arterial BP(MAP)	84.47±4.10	86.44±5.83	91.74±3.56	93.67±2.21	93.96±3.43
p-value	-	0.1287	0.0001*	0.0001*	0.0001*
Pulse pressure	40.60±3.37	39.40±9.08	41.67±5.85	42.73±4.77	43.40±4.76
p-value	-	0.3967	0.2113	0.0588	0.0029
Peak expiratory flow rate(PEFR)	235.33±45.08	262.33±51.24	289.00±53.39	309.33±50.03	335.33±48.26
p-value	-	0.0001*	0.0001*	0.0001*	0.0001*
Rate pressure product	9107.4±2202.8	9726.5±1549.9	10091.7±1074.9	10418.8±1054.1	10364.6±1518.4
p-value	-	0.1283	0.007	0.0041	0.0079
Six minute walk distance	276.00±46.21	313.00±47.50	346.33±52.16	369.33±48.13	404.67±59.00
p-value	-	0.0001*	0.0001*	0.0001*	0.0001*
Calorie expended during exercise	42.60 ± 3.29	46.03 ± 3.50	50.03 ± 4.19	52.63 ± 4.29	56.43 ± 5.10
p-value	-	0.0001*	0.0001*	0.0001*	0.0001*

\*Level of significance p ≤ 0.05

**Table 3: Comparison of baseline and post intervention scores of BriefFatigue Inventory (BFI), and Visual Analogue Scale-Quality of Life (VAS-QOL) in all subjects under the study.**

	BFI score		VAS-QOL	
	Pre	Post	Pre	Post
Mean & SD	3.11 ± 1.67	1.49 ± 1.22	4.47 ± 1.03	7.67 ± 1.15
p-value	0.0001*	0.0001*		

\*Level of significance p ≤ 0.05

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