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Efficacy of Aerobic Training on Maximal Oxygen Consumption and Total Leukocytes Count after Chemotherapy in Breast Cancer Patients

Zakaria Mowafy Emam Mowafy[1]*, Ibrahim Mohamed Ibrahim Zoheiry[2], Mohamed Gamil Abd Elmonem[3] and Dalia Katter[1]

[1]Physical Therapy Department for Surgery, Faculty of Physical Therapy, Cairo University, Egypt.
[2]Physical Therapy Department for Surgery, Faculty of Physical Therapy, 6 October University, Egypt.
[3]National Cancer Institute, Cairo University, Egypt

Abstract: Purpose: to evaluate the efficacy of aerobic training on maximal oxygen consumption and total leukocytes count after chemotherapy in breast cancer patients. **Methods of evaluation** (Measurement of the maximal oxygen consumption (VO2Max) and the total leukocytes count (TLC). **Methods:-** Forty breast cancer patients undergoing chemotherapy with ages ranging from 35 to 55 years and suffering from cancer related fatigue, they were selected from the National Cancer Institute. They were divided into two groups. Group (A) composed of 20 patients received the aerobic exercises and cycling (25 minutes session day after day for four successive months) in the form of walking 5 minutes at lowest speed on treadmill as warming up, active phase in the form of 15 minutes cycling and walking another 5 minutes at lowest speed on treadmill for the cooling down. Group (B) received only chemotherapy. Measurements were conducted before starting the treatment as a first record and at the end of the fourth month of treatment as a second (final) record. **Results and conclusion:-** Results showed that application of the aerobic training had a valuable improving effects in breast cancer patients after chemotherapy as evidenced by the highly significant increases in maximal oxygen consumption (VO2Max) and total leukocytes count (TLC).
Key words (Aerobic training, Maximal oxygen consumption, Total leukocytes count, Chemotherapy and Breast cancer).

1.Introduction

Chemotherapy can damage bone marrow and therefore impair the production of white blood cells, platelets and red blood cells. The resulting anemia decreases the oxygen transport capacity of blood and hence the oxygen supply to the cells. Cardio toxic cytostatic agents like anthracyclines and bleomyzcim can cause reduction in cardiac output and hence impairment in the blood supply to the muscles[2,3,8].

In the general population, low exercise capacity is an independent predictor of all-cause mortality and specifically death from cardiovascular disease**.** Age-adjusted all-cause mortality rates decline across physical fitness (exercise capacity) quintiles. These trends remain after adjustment for age, smoking status, cholesterol levels, systolic blood pressure, fasting glucose levels, and family history of heart disease. The higher fitness categories also show lower mortality rates for cancer and cardiovascular disease. Furthermore, the Surgeon

General's Report on Physical Activity and Health cites research documenting an inverse association of physical inactivity with morbidity and mortality from several chronic diseases. It is reasonable to expect that similar relationships also exist in cancer patients undergoing chemotherapy [4,5,9].

Impairment of physical performance figure among the most important etiological factors of chemotherapy related fatigue. Cardiorespiratory and muscular deconditioning as well as chemotherapy induced anemia can reduce work capacity; therefore patients require a higher degree of effort to perform their usual activities. The resulting increments in metabolic rate and energy consumption produce tiredness and fatigue even with normal daily activities. The resulting physical inactivity induces muscular wasting and produces further loss of performance. Lowering endurance thus creates a self-perpetuating condition; diminished activity leads to easy fatigability and vice versa. About 70% of people with cancer report feelings of fatigue during radiotherapy or chemotherapy, or after surgery. This form of fatigue is generally much disruptive than that associated with other diseases as depression, multiple sclerosis or arthritis. Irrespective the type of cancer related fatigue influences all parts of patient's quality of life and aggravates other distressing symptoms as pain, nausea and dyspnea [1,6,7,10,21].

There are clinical and experimental evidence at tests to the neurological and psychological benefits of physical exercise. Prescribing exercise for children after cancer treatment has the potential to facilitate recovery, performance and development with the consequent improvement in quality of life and long-term outcome. After rehabilitation of cancer patients and 6 months postoperatively, the average VO2max (in liters per minute) had increased 43% compared with preoperatively, an increase approximately three times greater than that found in sedentary people going through a similar period of training three times weekly at 50% of VO2max.[15,16,19.]

Aerobic exercise has increased work capacity, improved cardio respiratory fitness, improved ventilatory muscle endurance, enhanced the immune function and brings favourable changes in body mass and body composition, even without dietary restriction. The aerobic conditioning phase of the exercise sessions utilized several modalities; treadmills, lower-extremity ergometers, arm ergometers, combined upper and lower ergometers, were used. Aerobic exercise therapy consisting of a track or treadmill walking, upright or recumbent cycling, rowing, stair-stepping, elliptical trainer exercise, and arm-ergometer training. The advantages of the treadmill are to be independent as the speed and grade can be varied and the work load can be measured accurately. [11,12,18,21.]

The combined effect of cancer treatment and reduced physical activity often decreases your capacity for physical performance. Thus, you must use greater effort and more energy to do your usual activities. This leads to fatigue. Physical exercise builds up your energy levels, leading to reduced effort in doing your usual activities and less fatigue. A careful work-up by a physical therapist can help plan the right exercise program for you. Any chemotherapy drug might cause fatigue, but it might be a more common side effect of drugs such as vincristine, vinblastine, and cisplatin. Patients frequently experience fatigue after several weeks of chemotherapy, but this varies among patients. In some patients, fatigue lasts a few days, while others report fatigue persisting throughout the course of treatment and continuing after the treatment is complete[1,13,14].

There is strong epidemiological evidence for reduced risk of some cancers with increasing physical activity. The strongest evidence exists for colorectal and postmenopausal breast cancer, with possible associations for prostate, endometrial and lung cancer. However, an understanding of the amount, type and intensity of the activity needed has not been fully elucidated. In addition, these associations are based on cohort and case-control studies of self-reported physical activity. The impact of physical activity on reducing cancer risk in previously sedentary individuals is not known. To date randomized clinical trials of physical activity with primary cancer prevention has not been undertaken, but only 2 published randomized clinical trials examined the effect of physical activity on biomarkers of cancer risk. Aerobic exercise has increased work capacity, improved cardio respiratory fitness, improved ventilatory muscle endurance, enhanced the immune function and brings favourable changes in body mass and body composition, even without dietary restriction, [1,17,21.]

Material and Methods

Subjects:

This study was carried out on Forty breast cancer patients undergoing chemotherapy with ages ranging from 35 to 55 years and suffering from cancer related fatigue, they were selected from the National Cancer Institute. They were divided into two groups. Group (A) composed of 20 patients received the aerobic exercises and cycling (25 minutes session day after day for four successive months) in the form of walking 5 minutes at lowest speed on treadmill as warming up, active phase in the form of 15 minutes cycling and walking another 5 minutes at lowest speed on treadmill for the cooling down. Group (B) received only chemotherapy. Measurements were conducted before starting the treatment as a first record and at the end of the fourth month of treatment as a second (final).

Instrumentation:

In this study the measuring equipment were the cardiopulmonary exercise testing unit (CPETU) to measure VO2 Max and the coulter hematology analyzer (Coulter Electronics, USA) to measure the total leukocytes count (TLC), while the therapeutic equipment were the Bicycle Ergometer for the active phase of the aerobic training (Stationary bicycle ergometer manufactured by Enraf – Nonious International, made in the Netherland) and Electric treadmill for the warming up and cooling down phases of aerobic training (an electronic treadmill Kettler- marathon model No 7899-800, made in Germany)[3,15,19].

Procedures:

Evaluation:

1- Cardiopulmonary exercise testing unit (CPETU) to measure VO2 Max:

Oxy com. Pro (Jaeger; Germany), it consisted of breath gas O2 and CO2 analyzer, electric break ergonomic bicycle (Erg-900); 12 channels electrocardiogram (ECG). The breath gases were measured using breath-by-breath technique and circuit method. The workload pattern of bicycle was controlled by pre-selected software. The apparatus provided vacuum suction units to fix the metal electrodes of ECG on the subjects' chest. The results of the test were displayed on two panels, on for O2 and Co2 analysis curves and the other panel display ECG traces. VO2 Max is considered as an excellent indicator for the functional capacity. Measurement of the VO2 were done before starting the treatment as a first record and at the end of the fourth month of treatment as a second (final) record. [6,9,18,19.]

2- Coulter hematology analyzer (Coulter Electronics, USA) to measure the total leukocytes count (TLC):

An electronic counting instrument called the coulter counter analyzer, fine needle, sterile syringe and sterile glass**.** Measurements of the total leukocytes count (TLC) were done before starting the treatment as a first record and at the end of the fourth month of treatment as a second (final) record. A venous anticoagulated blood sample of 5 mL was taken in the morning, the specimen placed in a biohazard bag, and then blood processed in the lab automatically via an electronic counting instrument called the coulter counter analyzer. [1,15,18.]

1- Treatment procedures in the study group:

Bicycle ergometer and electronic treadmill treatment protocol:

Exercises were applied three times weekly for a total period of treatment for 4 months with a special protocol of 25 minutes for every session, these exercises were divided into 3 components as follow: A- **Warm up Phase of the aerobic training exercise:** Simple stretching exercises for all muscle groups, then walking for 5 minutes on the treadmill at lowest speed. B-**Active Phase of the aerobic training exercise:** When patients attended for treatment, they received full explanation about the purpose of the treatment, the therapeutic and physiological benefits of this method of treatment. Before starting the treatment, the height of the seat was modified according to the patient's comfort, then the patient's data were entered and the workload protocol was modified according to the individual ability of each patient. Then patient sit on the stationary bicycle ergometer with his back in relaxed position, before exercise the limit of subject tolerance was assessed by exercise test which is comprised a 3 minute control period of unloaded pedaling, followed by an incremental ramp on a cycle ergometer at a rate of 10 W per minute to the limit of subject tolerance (intensity corresponding to the individually recommended heart rates; individual heart rate was determined as that corresponding to 50% of their VO_2 Max as determined during the maximum exercise test. Then the intensity was increased every 60 seconds by 15 W until exhaustion and the duration of the active phase of treatment was 15 minutes in the form of cycling. C- **Cool down Phase of the aerobic training exercise:** Simple stretching exercises for all muscle groups then walking for 5 minutes on the treadmill at lowest speed, [4,5,6,11,21].

Data analysis:

VO2 Max and the total leukocytes count (TLC), were measured pre-treatment as a first record and after four months as a second final record in both groups. Collected data were fed into computer for the statistical analysis; descriptive statistics as mean, standard deviation, minimum and maximum were calculated for each group. The t-test was done to compare the mean difference of the two groups before and after application and within each group. Alpha point of 0.05 was used as a level of significance,[20.]

Results:

As shown in table (1) and figure (1), the mean value of the VO2 Max before treatment was (21.0000 ± 2.5330) ml/kg/min in the study group, while after treatment was (30.8600 ± 3.5560) ml/kg/min. These results revealed a highly significant increase in VO2 Max ($P < 0.0001$). While in the control group, the mean value of the VO2 Max before treatment was (21.1500 ± 2.5808) ml/kg/min, while after treatment was (21.0500 ± 2.4165) ml/kg/min. These results revealed non-significant difference in the VO2 Max ($P > 0.05$).

Table (1): Comparison of the mean values of the VO2 Max values in ml/kg/min before and after treatment in the study and control groups

	Before treatment		After treatment		Mean difference	T-value	P.value	Level of significance
	Mean	SD	Mean	SD				
Study group	21.0000	2.5330	30.8600	3.5560	-9.86000	-10.10	0.0001	Highly significant increase
Control group	21.1500	2.5808	21.0500	2.4165	0.100000	0.13	0.900	Non-significant

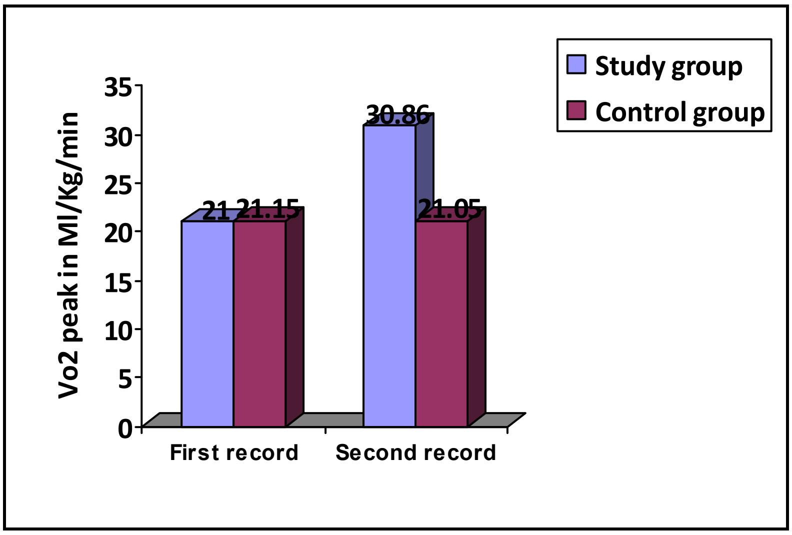

Fig (1): Mean values of the mean values of the VO2 Max values in ml/kg/min before and after treatment in the study and control groups

As shown in table (2) and figure (2), the mean value of the total leukocytes count (TLC), before treatment was (3620.0 ± 181.4) mm^3 in the study group, while after treatment was (4950.0 ± 324.0) mm^3. These results revealed a highly significant increase in the total leukocytes count, ($P < 0.0001$), while in the control group, the mean value of the total leukocytes count before treatment was (3620.2 ± 185.9) mm^3, while after treatment was (3622.3 ± 186.2) mm^3, these results revealed non-significant difference in the total leukocytes count ($P > 0.05$).

Table (2): Comparison of the mean values of the total leukocytes count (TLC) in mm^3 before and after treatment in the two groups

	Before treatment		After treatment		Mean difference	T-value	P.value	Level of significance
	Mean	SD	Mean	SD				
Study group	3620.0	181.4	4950.0	324.0	-1330.00	-16.02	0.0001	Highly significant increase
Control group	3620.2	185.9	3622.3	186.2	-2.10000	-0.04	0.972	Non-significant

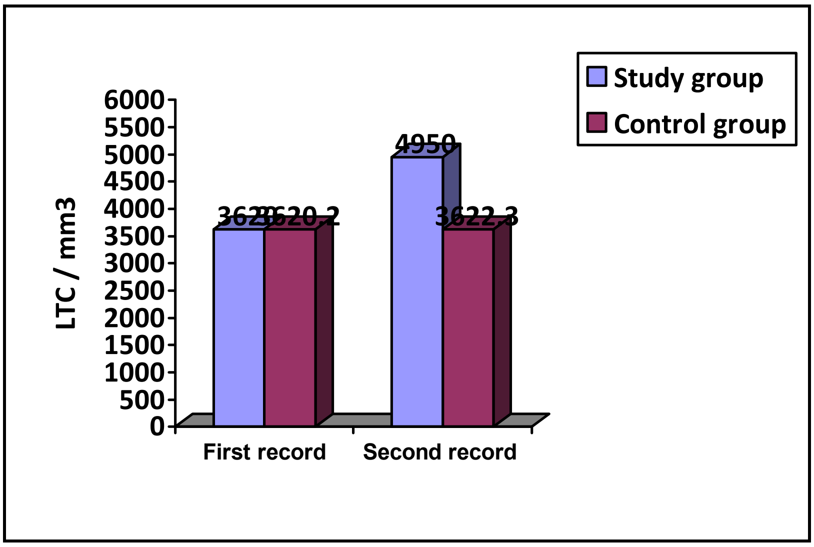

Fig (2): Mean values of the total leukocytes count (TLC) in mm^3 before and after treatment in the two groups.

Discussion:

Everyone has experienced normal fatigue, which improves with rest, however there is a difference between the fatigue patients feel after a long day and the fatigue patients may experience while undergoing treatment for cancer. Chronic fatigue associated with a disease or treatment of a disease does not improve with rest and can seriously affect a person's ability to function and his/her quality of life. Fatigue can impact quality of life in many different ways physically, emotionally, socially, and spiritually. In the acute Fatigue; symptoms begin quickly, symptoms are intense, of short duration, less than 7 days, relieved by a rest or a good night's sleep and usually related to excessive physical activity, lack of exercise, poor diet, dehydration, increase in activity, or other environmental factor. While in the chronic Fatigue; symptoms are unusual, excessive and constant, of long duration, two weeks or more, can interfere with normal life activities and symptoms do not get better with rest,[3, 4,7,17.]

Fatigue for people having treatment for cancer is different from the fatigue some people feel long after finishing their treatment. Things that can cause long term fatigue include; bone marrow transplants in some cases, these can cause fatigue for many years after the transplant, cancer treatment in childhood, especially for brain tumors, taking tamoxifen for a long period. Fatigue is the feeling of being tired physically, mentally, and emotionally. It means having less energy to do the things you normally do or want to do. Cancer-related fatigue is defined as a persistent and subjective sense of tiredness or exhaustion that can occur with cancer or cancer treatment. It can persist over time and can interfere with usual activities,[7, 12, 13,18.]

Cancer-related fatigue is the most common side effect of cancer and its treatment. Research suggests that about 90% of cancer patients receiving treatments such as radiation therapy, chemotherapy, immunotherapy, or bone marrow transplants have fatigue. Thirty percent to 75% of cancer survivors have reported fatigue that continues for months or years after completing active treatment. Cancer survivors or patients who are no longer actively being treated must still be watched for fatigue because it can exist after treatment. Even though fatigue is a very distressing symptom, doctors and nurses seldom focus on it, and patients and caregivers rarely report it. Although it may be difficult to talk about, fatigue is a normal and common occurrence for people with cancer. There are things that can be done to help if the health care team knows about the symptom[, 8,11,21.]

Aerobic exercise has increased work capacity, improved cardio respiratory fitness, improved ventilatory muscle endurance, enhanced the immune function and brings favourable changes in body mass and body composition, even without dietary restriction**.** The aerobic conditioning phase of the exercise sessions utilized several modalities; treadmills, lower-extremity ergometers, arm ergometers, combined upper and lower ergometers, were used. Aerobic exercise therapy consisting of a track or treadmill walking, upright or recumbent cycling, rowing, stair-stepping, elliptical trainer exercise, and arm-ergometer training, [4, 6,9,15, 18.]

The findings of the present study showed non-significant differences in the pre-treatment records of both VO2 Max and TLC between the mean values of the study and control groups.

Results of the study group revealed a highly significant increase in the mean values of VO2 Max and TLC, after application of the aerobic training, when compared against the pre-application results.

Significant differences showed in the study and control groups were consistent with those observed and recorded by Beer et al, 2004; Burnham and Wilcox, 2002; Cade et al., 2004; Courneya et al., 2003; Demetri et al., 2008; Dimeo et al., 2007; Jennen and Uhlenbruck, 2004; Kerstin et al., 2009; Lucia et al., 2003; Mock et al., 2004; Muller et al., 2007 and Schneider et al., 2008.

Results of this study support the expectation that application of the aerobic training had a valuable improving effects in breast cancer patients after chemotherapy as evidenced by the highly significant increases in maximal oxygen consumption (VO2Max) and total leukocytes count (TLC).

Conclusion:

Application of the aerobic training had a valuable improving effects in breast cancer patients after chemotherapy as evidenced by the highly significant increases in maximal oxygen consumption (VO2Max) and total leukocytes count (TLC).

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