Original Article

JHSMR Journal of Health Science and Medical Research

Effect of Aerobic Training on Quality of Life in the Elderly with Idiopathic Chronic Fatigue

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Received 10 May 2024 ● Revised 23 May 2024 ● Accepted 23 May 2024 ● Published online 4 December 2024

Abstract:

Objective: Idiopathic chronic fatigue (ICF) is described as clinically diagnosed physical and/or psychological chronic fatigue of more than 6 months, with no known/detected underlying pathologies/disorders. As no study has discussed the effect of scheduled, regular, and supervised aerobic exercise on fatigue severity, physical performance, and quality of life (QoL) in ICF elderly, this study was applied to achieve this aim.

Material and Methods: Forty ICF elderly (from both genders) were divided evenly into the study group that received 8-week aerobic exercises plus traditional physical therapy balance and stretching exercises (n=20) and the control group (n=20) who received traditional physical therapy balance and stretching exercises only. The fatigue severity assessment scale (FSAS), The elderly's Brief-Version Quality-of-Life Questionnaire (EBVQOLQ), six-minute walking distance (6MWD), and serum glutathione (as an anti-oxidative substance) were assessed.

Results: Only the study group's outcomes (EBVQOLQ, six minute walk distance (SMWD), serum glutathione, and FSAS) showed significant improvements.

Conclusion: Eight-week aerobic exercises in ICF elderly can improve fatigue perception, physical performance/capacity, QoL, and anti-oxidative defense.

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J Health Sci Med Res
doi: 10.31584/jhsmr.20241127
www.jhsmr.org

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Keywords: elderly, exercise, idiopathic chronic fatigue, quality of life

Introduction

Fatigue is highly prevalent in 70% of the elderly. It is a disabling/distressing by-patient reported/perceived symptom while executing common or usual mental and/or physical daily activities. Physical fatigue is a highly prevalent complaint in the older population that usually produces negative health-related outcomes[1]. Chronic fatigue perception (CFP) medically non-justified, more-than 6-month fatigue perception, is classified into two common types/forms according to its severity and/or accompanying symptoms/manifestations. The first type of CFP is idiopathic chronic fatigue (ICF) and the second type of CFP is chronic fatigue syndrome (CFS)[2].

CFS is a form of idiopathic fatigue perception disorder whose symptoms/manifestations involve at least four criteria from the following: presence of less than three manifestations/signs of the following: generalized muscular weakness, sleep disturbance issues and/or insomnia, generalized headaches, throat soreness/pain, muscular pain/tenderness, migratory arthralgias, pain/soreness of cervical/axillary lymph nodes, and perception of fatigue for >24 hours after finishing any activity/exertion[3].

In the complete/perfect absence of any associated medical conditions[4], with a preponderance of women over men[3], ICF is described as clinically diagnosed physical, psychological, and/or physiological CFP with no known/detected underlying pathologies/disorders, and does not need to meet four of above-mentioned diagnostic criteria of CFS[5,6].

Although, no documented cause/mechanism exists for ICF, it has been suggested to originate from skeletal muscles' metabolic, size, and function abnormalities. Aging-related abnormalities in mitochondrial regulation/function in skeletal muscle tissue are also suggested as a potential connection or cause for ICF disorder. Aging-associated deterioration in energy production from dysfunctioning mitochondria, overproduction of free radicals and reactive oxygen specimens, aberrations in mitochondrial function/regulation, inhibition of mitochondrial autophagy, and inactivation of by-mitochondria mediated apoptosis are suggested mitochondrial abnormalities that cause ICF[7].

Also, different pathways, such as inflammatory, immune, nitrosative/oxidative[8], lipid peroxidative[9] and stress-activated signaling pathways, are potential pathways/causes suggested to evoke a series of immunological/biological consequences/complications that further explain or decline ICF-associated physical, social, and psychological dysfunctions[8].

Since there is no available approved/documented pharmacological treatment for ICF or CFS[10], the functional impact of untreated CFS and/or ICF rapidly deteriorates, because it massively reduces ICF and CFS patients' ability to execute normal and simple daily tasks/activities[11]. Patients with CFS and ICF are usually inactive and spend more hours/days resting compared with healthy people[12]. These prolonged times of rest and/or inactivity increase the deconditioning of ICF and CFS patients. Deconditioning of ICF/CFS patients decreases their ability to perform basic activities of daily living, reduces their cardiorespiratory/muscular fitness[13], lowers their exercise tolerance and quadriceps strength[12], and decreases their body functionality and quality of life[13].

Nowadays, exercise training/rehabilitation is the most widely appreciated researched non-pharmacological therapy to manage/decrease older adults' fatigue perception in cases of multi-morbidities. Selecting moderate or low-intensity aerobic/endurance exercises may better decrease CFP than resistance exercises. Aerobic/endurance exercise is very gentle on the elderly's joints and muscles. This gentle nature of aerobic exercise appears to produce greater patient adherence and more hopeful CFP-combating effects in more lethargic/apathetic older patients, who have low levels of energy[14].

Studies suggest that engaging older adults in aerobic exercise sessions may reduce/lessen aging-associated immobility, skeletal muscle weakness, imbalance, and dependence. Also, this increases the elders' level of cardiorespiratory/muscular fitness, exercise tolerance, quadriceps strength, body functionality and quality of life. Aerobic exercises also increase elders' independent performance of basic/simple activities of daily living; hence, their psychological status and moods improve[13,15].

This study aimed to investigate the effects of scheduled, regular, and supervised aerobic exercise on fatigue severity, physical performance, and quality of life in ICF elderly.

Material and Methods

Design

Older patients with ICF (n=40) participated in this randomized controlled aerobic exercise trial.

Settings

Outpatient clinic of Pharos University, Alexandria, Egypt.

Ethical criteria of this ICF research

Local Unit of Research Ethics Affiliated to Pharos University, Alexandria, Egypt, approved this ICF trial (Approval ID: PUA0320239243132). Helsinki recommendations were followed.

Inclusion criteria

Patients (n=20 ICF elderly) that reported ages from 60-70 years old, having a body mass index (BMI) of 25-29.9 kg/m^2, and achieved the standard following three diagnostic criteria of ICF were included: 1) new perception/onset of severe fatigue that has lasted at least 6 months, which has reduced/restricted their performance/execution of elderly daily activities to <50% of elderly's normal activity level before ICF diagnosis; 2) presence of less than three manifestations/signs of the following: generalized muscular weakness, sleep disturbance issues and/or insomnia, generalized headaches, throat soreness/pain, muscular pain/tenderness, migratory arthralgias, pain/soreness of cervical/axillary lymph nodes, and perception of fatigue for >24 hours after finishing any activity/exertion; 3) discarding any medical condition that evokes fatigue perception[2]. Older ICF patients that walk without assistance by others or assistive walking devices were included in this ICF 8-week interventional study.

Exclusion criteria

Patients having a body mass index (BMI) >30 kg/m^2, a history of medical care for ICF within the previous 6 months, history intake of antidepressants or antipsychotics, history of abnormal findings in laboratory or screening tests/studies (e.g. neurological tests, neurophysiological studies, complete blood picture, serum hormones of thyroid glands, electrocardiography, electroencephalography, urine/stool test, liver and kidney function test, blood glucose test, blood pressure measurement, pulmonary function tests and X-ray on upper and lower limbs), history of autoimmune/malignant disorders, history of articular arthritis, history intake of sleeping pills, and history intake for-fatigue complementary medicines (exercise, foods, acupuncture, herbs, yoga, etc..) history were excluded.

Randomization

A professional statistician used a computer-based randomized block method to randomly assign ICF elderly (from both genders) to the study group, which consisted of 20 elderly who received aerobic exercise plus traditional physical therapy exercises, and the control group (n=20), which received traditional physical therapy exercises only (Figure 1).

Aerobic exercise (treadmill walking)

Aerobic training for ICF elderly in the study group was supervised during the performance of its three phases, three times weekly. The authors of this study utilized the popular exercise equation, the Karvonen formula, to detect patients' target heart rate limit (an indicator of exercise intensity) during every phase of exercise. For example, 30-40% of ICF patients' Karvonen-formula results were the upper limit reached by the ICF patients during the opening (warming up performed as walking on a treadmill for 5-10 minutes) or finishing (cooling up performed as walking on the treadmill for 5-10 minutes) phases of exercise. Also, 60-75% of ICF patients' Karvonen-formula results were the upper limit reached by the ICF patients during the main (35-minute intermediate phase; between opening and finishing phases of 8 weeks of exercise)[16,17].

Traditional physical therapy exercises (3 times per week)

In the first session, inactive (passive) stretching (flexibility) exercises were explained, supervised, and taught by the authors for both groups of ICF patients, which were to be applied by ICF patients in their homes. Bilateral ankle plantar flexors, hip flexors, hamstring, and hip adductors were the selected muscle groups for inactive

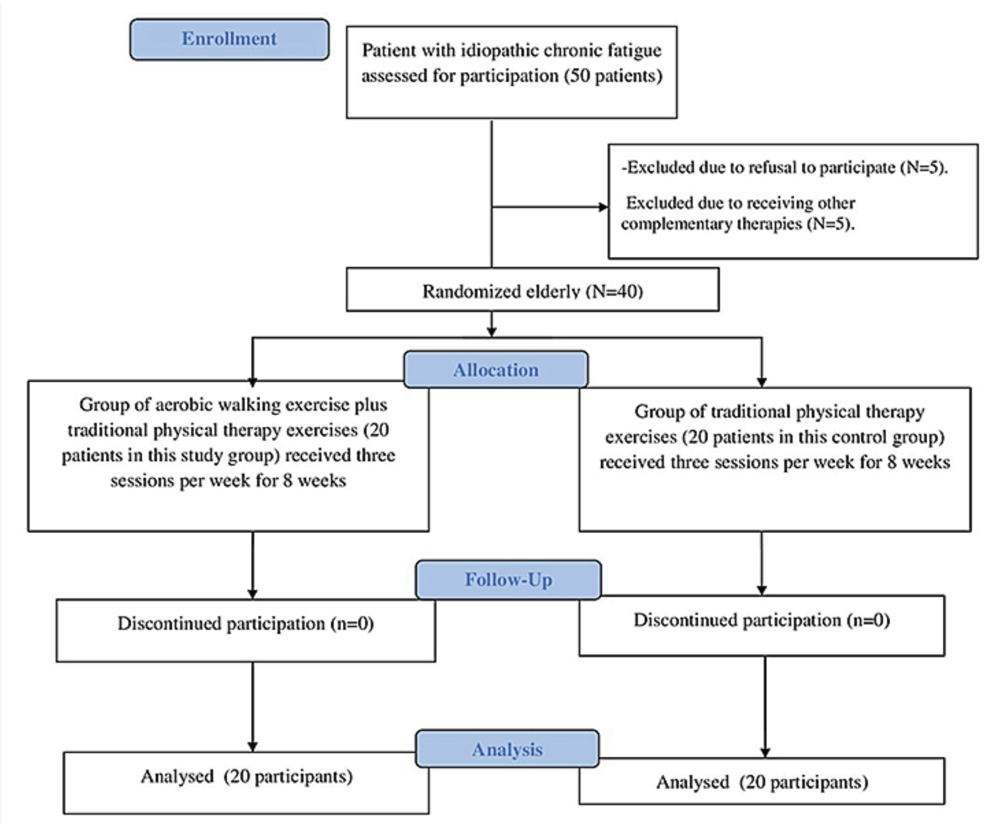

Figure 1 Idiopathic chronic fatigue patients' participation chart

stretching exercises. Each muscle group was stretched for five repetitions (each repetition was maintained for 20-30 seconds, then the ICF patient was allowed to take a 60-second rest before applying the next repetition). All selected muscles of the right lower limb were stretched, followed by the left lower limb selected muscles.

After ending the inactive stretching exercises, both groups of ICF patients were involved in the designed balance-exercise program. The sequence of applied exercises within this program were as follows: 5-minute tandem standing, 30-repetition forward reaching training/exercises, 5-minute single-right-leg support/standing, and 5-minute single-left-leg support/standing.

At the end of the supervised first session of the traditional physical therapy session in both groups, a booklet containing procedures and pictures of balance and stretching exercises was given to every ICF patient (or his/her family relative), to be with him/her during the application of home balance and stretching exercises. Besides being given a home booklet, the ICF patient or his/her relative was contacted by a telephone call or WhatsApp message 3 times weekly to ensure their adherence to the application of home-based traditional physical therapy exercises.

Outcomes

Fatigue severity assessment scale

A simple valid, and reliable 10-item scale was utilized for assessing both ICF groups' physical/mental fatigue perception levels after the 2-week rehabilitation period. Each item within the fatigue severity assessment scale (FSAS) was evaluated via 5-category Likert responses; starting from no perception of fatigue (which equals 1) to severe constant perception of fatigue (which equals 5)[18].

ICF Elderly's Brief-Version Quality-of-Life Questionnaire (EBVQOLQ)

Different aspects (such as physical, psychological, and social well-being) of ICF patients' quality of life (QoL) in this study were assessed via a valid, simple, and understandable EBVQOLQ. Items/questions of EBVQOLQ-related topics; such as ICF patients' overall life satisfaction, ICF patients' social support, ICF patients' emotional wellness as well as ICF patients' physical and mental health, were asked. ICF patients responded to the items/questions with 5-category Likert responses; starting from strongly agree (equal=1), agree (equal=2), neither (equal=3), disagree (equal=4), and strongly disagree (equal=5). After adding all EBVQOLQ-related items/questions to obtain the ICF patient's overall EBVQOLQ score, positive items of EBVQOLQ were reverse-coded to indicate the patient's QoL with a higher score[19].

Six-minute walking distance (6MWD)

ICF patients' functional capacity was assessed by asking ICF patients to cover the 6MWD test's 30-meter corridor through a back-and-forth walking as fast as she/he could; the result of this test was recorded in meters[20].

Glutathione blood test

Glutathione is an anti-oxidative substance which prevents/repairs cellular damage and augments the immune system[21]. Fasting serum levels of glutathione were analyzed/assessed using tandem-mass spectroscopy.

Blinding

The examiners of the outcomes of this ICF trial did not know the details of the performed exercise.

Statistical analysis

Shapiro-Wilk test (the most popular statistical test/analysis for data-normality evaluation) affirmed basic and outcome parameters. A chi-squared test (the most popular statistical test/analysis for gender differences between clinical trial groups) was used. Paired and unpaired statistical tests/analyses examined within and between

ICF groups' significance of parameters, respectively. The applied p-value for any test's significance was <0.05, using SPSS version 27.

Results

Between-group pre-treatment comparison of ICF patients' age, gender, BMI (as presented in pre-treatment ICF patients' basic data in Table 1), glutathione, EBVQOLQ, 6MWD, and FSAS (Table 2) did not show a significant difference.

After ending/achieving the designed ICF therapies, table-2 comparison of ICF patients' glutathione, EBVQOLQ, 6MWD, and FSAS within the study group showed significant improvement; however, within the other group (control one), no significant differences occurred.

After ending/achieving the designed ICF therapies, Table-2 shows a comparison of ICF patients' post-values of glutathione, EBVQOLQ, 6MWD, and FSAS between ICF groups, the study group was shown to best improve ICF patients' glutathione, EBVQOLQ, 6MWD, and FSAS.

Discussion

The role of aerobic exercise in improving physical performance, anti-oxidative status, fatigue severity perception, and QoL in ICF elderly has not been well studied, According to the results of this clinical trial, confirm the expected and hoped-for role of aerobic exercise in improving ICF elderly's glutathione, EBVQOLQ, 6MWD, and FSAS. The mechanism of outcomes' improvement in this ICF clinical trial is difficult to justify due to the small number of ICF-related aerobic-exercise publications.

The selection of for-ICF-patient moderate-intensity exercise in this clinical trial was supported by McCully et al.[22], who did not recommend the use/selection of high-intensity exercises that may aggravate/exacerbate symptoms in CFS cases. According to McCully et al.[22], low-intensity exercise not only maintains fatigued patients' muscle tone/endurance but also counteracts the effects of inactivity tendency associated with CFS in addition to providing a sense of control of CFS patients' conditions.

Compared to usual care or passive therapies, one promising therapy for ICF or CFS patients that complain of feelings of fatigue and low bodily energy is chronic, structured, and regular exercises[23]. Chronic exercise is a type of exercise rehabilitation/training that uses cumulative/repeated and planned/structured bouts of physical activity to maintain components of patients' physical fitness, including muscle strength/endurance, cardiorespiratory/aerobic capacity, body flexibility and body composition[24]. Improved components of physical fitness after regular chronic exercise in CSF patients may improve fatigue perception in addition to their QoL[25].

Exercise-induced improved CFP may be justified by the increase in patients' core body temperature, which

Table 1 ICF elderly's basic data

Items	Study group (aerobic exercise plus traditional physiotherapy)	Control group (traditional physiotherapy)	p-value
Age of ICF elderly (years)	64.6±2.99	64.85±2.80	0.786
Body mass index of ICF elderly (kg/m^2)	26.65±1.96	27.34±1.73	0.245
Gender of ICF patients (number of males/females)	10/10	10/10	1.000

ICF=Idiopathic chronic fatigue, ICF patients' p-value was >0.05; hence, significance in this structured Table 1 is not achieved, All ICF patients' data are expressed in the form of mean±S.D. (tested by unpaired test), except gender of the ICP elderly (this is expressed as number, and was tested by chi-squared test)

Table 2 ICF elderly's randomized-controlled results

ICF elderly's parameters	Study group (aerobic exercise plus traditional physiotherapy)	control group (traditional physiotherapy)	p-value (between ICF groups)
Fatigue severity assessment scale	Mean±S.D.	Mean±S.D.	
Before ICF elderly's training	33.1±3.32	33.15±3.25	0.961
After ICF elderly's training	24.5±4.23	32.75±2.97	0.001*
p-value (within ICF older patients' groups)	<0.001 *	0.866	
EBVQOLQ	Mean±S.D.	Mean±S.D.	
Before ICF elderly's training	7.45±1.88	7.5±1.87	0.933
After ICF elderly's training	10.05±1.57	7.4±1.85	0.0001*
p-value (within ICF older patients' groups)	<0.001 *	0.722	
Six-minute walking distance (m)	Mean±S.D.	Mean±S.D.	
Before ICF elderly's training	397.3±25.84	397.45±25.82	0.985
After ICF elderly's training	419.05±25.67	397.75±25.84	0.012*
p-value (within ICF older patients' groups)	<0.001*	0.894	
Glutathione in serum (Ug/ml)	Mean±S.D.	Mean±S.D.	
Before ICF elderly's training	205.55±13.14	205.65±13.1	0.980
After ICF elderly's training	218.8±12.01	205.85±12.99	0.002*
p-value (within ICF older patients' groups)	<0.001 *	0.289	

*ICF patients' p-value was <0.05; hence, significance in this structured table 2 is achieved
S.D.=standard deviation, ICF=idiopathic chronic fatigue, EBVQOLQ=elderly's brief-version quality-of-life questionnaire

reduces the perception of abnormal levels of stress and muscle tension, lowers complaints of interrupted sleep, and improves psychological/mental fatigue. Reduced depression or mental fatigue after chronic exercise may inhibit afferent feedback to CFS patients' motor cortex; hence, the sensation of effort of fatigue reduces[25].

Contrary to what is common among CFP patients, which is the fear of performing exercises because it increases the feeling of fatigue, a recent study has shown that the feeling of this fatigue is subjective. Scientifically, aerobic exercise in CFS patients did not change neurotransmission-involved pathways or genetic expression of leucocytes, metabolite-sensing compounds or immune-sensing substances[26]; hence, it may be a safe intervention in those patients.

Exercise-induced modification of peak oxygen consumption is associated with improvements in chronic disease patients' peripheral contents (glycogen/myoglobin content, mitochondrial density/volume, capillarization and oxidative/antioxidative enzyme activity), and central contents (oxygen diffusion to lungs, output of cardiac muscle and oxygen-hemoglobin affinity). Exercise-induced improvements in peripheral and central contents lower pain perception, decreases fatigue, increases physical performance and improves QoL[27].

Our results support the graded application of exercise training for 12 weeks as more effective than stretching training in improving CFS patients' perception of fatigue severity. Additionally, the study's aerobic capacity/fitness, conducted in 1997, supports our results[28]. Also, compared to flexibility training, graded exercise training for 12 weeks in CFS patients improved patients' depression, cognition, cardiorespiratory fitness, heart rate, blood pressure, oxygen uptake, respiratory exchange ratio, and physical capacity[25].

Low-intensity exercise (Qigong exercise, a regular program of body movement combined with breathing exercises) was found to improve CFS patients' pain/sleeping, vitality, body/physical functioning, general mobility, and mental attitude[29]. The 4-month choice of low-intensity exercise training improvements in physical and mental fatigue symptoms in CFP and CFS patients may be due to the significant improvement in telomerase activity (a substance involved in cell longevity and vitality in humans)[8]. Again, low-intensity exercises; such as the Qigong exercise, can reduce CFS patients' CFP[30].

Aerobic training of 4 weeks of bicycle and treadmill rehabilitation significantly improved CFS adolescents' quality of life, depression, onset time of fatigue perception, fatigue severity, and physical performance (assessed by a number of push-ups and sit-to-stand repetitions)[31]. Also, the selection of a short duration (8 weeks) and low-intensity aerobic exercise in our study was the recommended safe choice for applying exercise intervention in eleven CFS women, because this selection significantly improved CFS women's physical capacity (assessed by 6MWD), rate of perceived exertion, and fatigue perception[32].

Regarding the antioxidative effect of the applied exercise in this study, exercise induces adaptive responses/changes within different cells/tissues; including skeletal muscular, hepatic and cardiac cells. One of these adaptive responses is an exercise-induced increase in the production of glutathione, one of the main antioxidant enzymes in skeletal muscular, hepatic, and cardiac cells[33]. Exercise triggers glutathione, reeducates and releases glutathione from glutathione disulfide in the presence of NADPH[34]. Using glutathione peroxidase, increased production of glutathione after exercise enhances the removal of many oxidative stress substances, such as peroxides, and therefore, the imbalance between the overproduction of oxidative stress and low efficacy of anti-oxidative defense is corrected[35]. Corrected/inhibited oxidative stress may lower CFP and other clinical symptoms in CFS patients[9].

The results of ICF patients' blood glutathione were in line with a study published in 2004, confirming the importance of exercise in improving antioxidant enzymes and combating side effects of oxidative stress in eccentrically trained women[35]. Also, the amount of swimmers' blood glutathione, in a study conducted in 2001, showed a significant increase after participation in 100-meter swim (this 100-swim is considered an aerobic exercise according to the proposal of this study)[36]. Furthermore, blood glutathione was significantly increased after a single-bout (acute) exercise in bodybuilders[37]. Opposite to our ICF patients' after-exercise glutathione levels, long-distance runners' in-serum glutathione lowered by 30% in the trained group after applying on-bicycle acute exercise[38].

Limitations

Besides tracking the presented results, further ICF research is necessary to fully understand and investigate the impact of aerobic training on other ICF-related outcomes, such as skeletal muscle metabolites and cognitive skills in older adults. Comparing the effect of continuous versus interval training on the tested outcomes is another limitation that may be further investigated in future ICF trials.

Conclusion

Aerobic exercise (in its moderate-intensity form for 8 weeks) is a promising therapeutic rehabilitation modality for improving the glutathione, EBVQOLQ, 6MWD, and FSAS of ICF elderly patients.

Acknowledgement

We thank all the participants who participated in this study.

Funding sources

This ICF study received no funding.

Conflict of interest

The authors of this ICF trial report no conflicts of interest.

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