

## Research

## Effect of Exercises Training on Fatigue, Depression and Physical Activity in Patients with Systemic Lupus Erythematosus

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### ABSTRACT

**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune disease associated with widespread inflammation and tissue damage. It is more common and severe among Blacks, Hispanics, and Asians; with higher incidence in women. While the goals of medical treatment are to prevent flares and reduce organ damage, up to 50% of patients perceive their health to be suboptimal with unaddressed needs including fatigue and pain. Recent SLE treatment guidelines focus on improving quality of life. Fatigue in SLE is associated with lower fitness levels, reduced exercise capacity, reduced muscle strength, and greater disability when compared to sedentary healthy subjects.

**Aim:** To compare the effect of aerobic exercise versus stretching and strengthening exercise on fatigue and physical activity in patients with SLE.

**Subject and method:** 40 females patients with SLE from department of internal medicine, Cairo university hospitals were included in this study divided into 2 groups. Group 1 treated by aerobic exercises and group 2 treated by stretching and strengthening exercises. Self-rating Depression Scale (SDS), Sf- 36, Fatigue Severity Scale (FSS). 6 Minutes' Walk Test (6MWT), 2 minutes (Min) step test, functional performance battery consists of 30 seconds (S) chair stand test and 30 s arm curl test. All parameters measured pre-treatment and after 3 months of treatment.

**Results:** analysis of results showed significant difference in both groups post treatment than pre-treatment  $p < 0.001$ . Comparing the results of both groups showed that no significant difference in 30 s chair up and 30 s arm curl  $p > 0.05$ , there is significant difference in SDS, SF-36, FSS  $p < 0.05$ , and highly significant difference in 6 MWT and 2 Min step test  $p < 0.001$ .

**Conclusion:** Both aerobic exercises, stretching and strengthening are effective non-pharmacological method to increase physical activity and decrease severity of fatigue and depression.

**Keywords:** Systemic Lupus Erythematosus, Fatigue, Exercises, Quality of live, Physical Activity, Depression.

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### INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease in which immune system dysregulation leads to widespread inflammation and tissue damage. Lupus is a chronic disease that causes inflammation affecting the skin, joints, kidneys, lungs, nervous system and/or other organs of the body [1-6].

The risk for SLE development has a genetic component that is often associated with environmental factors and lifestyle choices, such as solar radiation exposure, stress, sedentary behavior, and the use of certain medications that tend to trigger disease manifestation [7].

Lupus occurs ten times more often in women than men [4,5,8].

The peak SLE incidence occurs at age 20–29 years, followed by 30–39 years old for females, but in 70–74 years old for males [9].

While the goals of medical treatment are to prevent flares and reduce organ damage, up to 50% of patients perceive their health to be suboptimal with unaddressed needs including fatigue and pain. Recent SLE treatment guidelines focus on improving quality of life (QOL) [10].

Fatigue is one of the most disturbing symptoms, and it is reported in 50-92% of SLE patients [11].

Fatigue in chronic conditions is described as both central and peripheral. Peripheral fatigue results from neuromuscular dysfunction and relates to impaired neuro transmission in peripheral nerves and/or defects in muscular contraction. Central fatigue is described as abnormalities in

neurotransmitter pathways within the central nervous system [12].

The etiology of fatigue remains unclear. Many factors associated with fatigue have been reported such as physical activity, obesity, sleep quality, depression, anxiety, mood, cognitive dysfunction, vitamin D deficiency, and other comorbidities [13].

Fatigue manifests itself as an overwhelming sense of tiredness and lack of energy that can result in significant impairment of a person's participation in activities of daily living and work and is related to sleep disorders, pain, depression, and QOL [14-18].

Those with SLE tended to be younger, were more often employed, and offered more complaints of fatigue but reported less joint pain. As mentioned in the literature [19-21].

Specifically, fatigue in SLE is associated with lower fitness levels, reduced exercise capacity, reduced muscle strength, and greater disability when compared to sedentary controls [22].

Participation in aerobic exercise has been reported to improve cardiorespiratory fitness, increase physical activity levels, and diminish the severity of fatigue in patients with severe illnesses [23].

## MATERIALS

Forty females' subjects with SLE age between 16 and 45 years were included in this study from department of internal medicine, Cairo university hospitals, Egypt. Subjects were divided into 2 groups: group 1 were treated by aerobic exercise for 12 weeks and group 2 were treated by stretching and strengthening for 12 weeks.

### *Inclusion criteria*

- Female  $\geq$  16 years of age.
- Ambulatory.
- Experience fatigue for the last 3 months or longer.
- Sedentary (exercise < 3 times per week for 30 min in the past 6 months).
- Had permission from their physician to participate in the study.

### *The exclusion criteria were*

- Control of metabolic diseases; or other concurrent systemic health problems (e.g., infections, malnutrition), which are known to contribute to increased fatigue levels; known electrolyte abnormalities.
- Severe visual and/or hearing impairment that cannot be corrected using assistive devices.
- Significant functional impairments due to heart disease, arrhythmias, chronic pulmonary disease.
- Conditions such as avascular necrosis of the hip or knee, or severe arthritis of 3 or more weight-bearing joints that prevent exercising.
- Systolic blood pressure > 200 mm Hg or diastolic blood pressure > 115 mm Hg [24].
- Patients were excluded if they had evidence of active severe myositis, nephritis, neurological involvement.

- Pregnant patients and patients under 16 or over 55 years were also excluded [25].

## METHODS

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients for being included in the study.

### *Group 1*

Patients were instructed to exercise to 70%-80% of their maximum heart rate.

Each exercise session began with a 5-10 minute warm-up, was followed by 20-30 minutes of aerobic activity, and concluded with a 5-10 minute cool-down period.

### *Group 2*

Range of motion/muscle strengthening. In phase I of the ROM/MS, exercise group,

An exercise program limited to isolated upper and lower extremity joint range of motion as well as to limb movement patterns. Care was taken to include several rest periods so as not to influence cardiovascular fitness. The exercises were done 3 times a week for 50-minute sessions. Duration of the program was 3 months. Muscle strengthening was added to the range of motion exercise. The program began with stretching exercises, preceded to the isometric and progressive resistive exercises, and ended with gentle stretching. A typical strengthening program included 2 to 3 sets of 10 repetitive isotonic contractions per muscle group using increasing weights from 1 to 2 pounds depending on subject tolerance [26].

## ASSESSMENT

The following was measured pre-treatment and after 12 weeks of treatment.

### *Self-rating Depression Scale (SDS)*

SDS was used to assess the depression of patients. It has 20 items, and all items are scored from 1 to 4 to specify the occurrence frequency. Score over 70 means severe depression, score between 60 and 69 indicating moderate to marked depressive symptoms, score between 50 and 59 meaning minimal to mild depression, and score less than 50 indicates no depression [27].

### *Sf- 36*

SF- 36 was used to measure patient's QOL. It has 8 subscales: Physical Functioning (10 items), Role-Physical (4 items), Bodily Pain (2 items), General Health (5 items), Vitality (4 items), Social Functioning (2 items), Role-Emotional (3 items), and Mental Health (5 items). Item scores were coded, summed, and transformed. Total score ranges from 0 to 100, with higher score indicating better health status [27].

**Fatigue Severity Scale (FSS)**

For English-speaking SLE patients, the FSS has been validated and found reliable [28]. The FSS consists of a form with nine items concerning fatigue symptoms; each item is rated from one to seven. A higher score indicates a higher level of fatigue. The FSS has been translated and validated in several languages [29-31].

**6 Minutes' Walk Test (6MWT)**

It evaluates the functional capacity. Patients were instructed to walk as far as possible, for 6 min in a 30 meters level corridor, and the distance was recorded in meters. The patients were encouraged verbally, minute by minute, using standardized phrases [32].

**The 2 min step test**

Number of steps covered in 2 min [33].

**Functional performance tests**

Physical function was assessed through the following battery of tests. The 30 S. chair stand test evaluated the number of

times that a subject was able to stand from a standard chair and sit down again in 30 s [24]. The 30 s arm curl test assessed upper-body muscle function by the number of arm curl repetitions performed with 2 kg dumbbell for 30 s [34].

**STATISTICAL ANALYSIS**

Data were statistically described in terms of mean ± SD; the collected data were fed into computer for statistical analysis and the statistical significance at a confidence level of 95%. All statistical calculations were carried out using computer programs, Microsoft Excel 2010 (Microsoft Corporation, New York, USA) and Minitab version 19.

**RESULTS**

Pre and post treatment measures of group 1 and group 2 are given in **Tables 1 and 2**. Post treatment measures of both groups are given in **Table 3**.

**Table 1:** Pre and post treatment measures group 1.

Item	Group 1 pre	Group 1 Post	T value	P value
	Mean ± SD	Mean ± SD		
SDS	61.65 ± 4.44	41.15 ± 4.404	16.99	0.000
SF-36	36.10 ± 2.2	60.6 ± 4.68	23.06	0.000
FSS	57.35 ± 3.67	33.35 ± 3.689	19.63	0.000
6MWT	131.5 ± 16.31	202.5 ± 19.7	10.95	0.000
2 min step test	9.45 ± 1.356	17.1 ± 1.917	13.36	0.000
The 30-s chair stand test	5.3 ± 1.129	11.95 ± 1.905	11.62	0.000
The 30-s arm curl test	5.65 ± 1.226	10.55 ± 1.191	12.79	0.000

**Table 2:** Pre and post treatment measures of group 2.

Item	Group 2 pre	Group 2 post	T value	p value
	Mean ± SD	Mean ± SD		
SDS	63 ± 4.84	39.85 ± 3.87	21.12	0.000
SF-36	40 ± 4.54	59.05 ± 6.61	10.40	0.000
FSS	55.4 ± 4.95	37.4 ± 4.76	10.02	0.000
6MWT	115 ± 11.47	212.5 ± 32.42	12.59	0.000
2 min step test	6.4 ± 1.095	11.5 ± 1.469	11.73	0.000
The 30-s chair stand test	5.85 ± 0.813	11.9 ± 2.972	9.73	0.000
The 30-s arm curl test	5.95 ± 0.686	10.75 ± 1.118	15.77	0.000

**Table 3:** Post treatment measures of both groups.

Item	Group 1 post	Group 2 post	T value	p value
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	Mean ± SD	Mean ± SD		
SDS	41.15 ± 4.404	39.85 ± 3.87	1.09	0.289
SF-36	60.6 ± 4.68	59.05 ± 6.61	1.17	0.256
FSS	33.35 ± 3.69	37.4 ± 4.76	3.73	0.001
6MWT	202.5 ± 19.7	212.5 ± 32.42	1.17	0.257
2 min step test	17.1 ± 1.917	11.5 ± 1.469	11.1	0.000
The 30-s chair stand test	11.95 ± 1.905	11.9 ± 2.972	0.06	0.954
The 30-s arm curl test	10.55 ± 1.191	10.75 ± 1.118	0.58	0.569
p<0.001: Highly significant; p<0.05: Significant				

## DISCUSSION

This study was conducted to compare the effect of aerobic exercises versus stretching and strengthening exercises on fatigue, depression and physical activity in SLE patients.

In most cases of SLE the cause of fatigue is not known, although it is likely to result from a number of contributing factors, such as disease activity [35-38], mood disorder [35,39], poor sleep patterns and associated fibromyalgia [40,41]. Other important contributing factors might include inferior physical conditioning and muscle strength, possibly as a result of reduced levels of physical activity.

Fatigue may contribute to a reduction in physical fitness (i.e., muscle weakness and low cardiovascular capacity), which, in turn, leads to an impairment in the performance of activities of daily living and consequently, in the overall QOL [42].

However, decrements in muscle strength have also been strongly associated with a greater number of cardiovascular events and early mortality [43-46].

Gualano et al. proposed a vicious cycle to explain the mechanism of fatigue and multiple physical dysfunction symptoms. A lack of physical exercise may aggravate these symptoms. Later, accumulative symptoms (e.g., fatigue and muscle weakness) drive patients toward a physically inactive lifestyle. Gualano et al., study believe that physical exercise could be a treatment to break this vicious cycle [47].

SLE patients were found to be less fit with reduced levels of aerobic fitness and reduced exercise capacity including reduced muscle strength, reduced resting lung function, depressed mood, poor sleep quality and functional incapacity, and this physical disability correlated with increased levels of fatigue by a linear regression model [48].

In a study of women with SLE, that measured aerobic capacity (maximal oxygen uptake/VO<sub>2</sub> max) with a bicycle ergometer exercise test during low-to-moderate activity, VO<sub>2</sub> max was significantly lower in SLE females than levels predicted for sedentary women [49].

Another study looking at SLE women and aerobic capacity supported the previous study's findings that aerobic capacity measured by peak oxygen consumption during the treadmill tests was decreased in SLE women compared to controls, was lower than expected for physiologic deconditioning and that

this aerobic insufficiency was highly correlated with the perception of severe, activity limiting fatigue in this population [50].

The American College of Sports Medicine (ACSM) proposed that exercise is a vital medication and should be prescribed to every patient as necessary [51].

Aerobic exercise appears to be an effective, appropriate and feasible non-pharmacological intervention for reducing fatigue in people with Multiple Sclerosis (MS), rheumatoid arthritis (RA) and SLE, which is consistent with recommendations for cancer-related fatigue and chronic fatigue syndrome. Low-cost, low to moderate impact exercise programs gradually progressing in duration and frequency may be acceptable to most people, but they should also take into account individual fluctuations in fatigue intensity [52].

Physical exercise has been shown to have multiple benefits including significant reduction in fatigue levels, weight loss, and improvement in sleep quality, physical fitness, and QOL for people with SLE [53,54].

Rongen van et al. showed that aerobic exercise was effective in reducing fatigue among patients with RA after 12 weeks, but not after 24 weeks [55].

McMillan and Newhouse found that exercise programs completed in a supervised setting were more effective for reducing fatigue among cancer patients and survivors than unsupervised exercise programs [56]. A meta-analysis showed that the two-mode delivery of interventions had similar effects on older adults' health [57].

Meta-analysis of chronic fatigue syndrome research also showed that exercise reduced fatigue significantly after 12 weeks [58].

Tench et al. followed up the participants' fatigue severity 3 months after the exercise training and found that the participants who continued with regular exercise were more energetic than those who stopped exercising. Maintaining exercise is important for physically inactive patients to extend the effects of training. In this study there are significant difference in FSS after three months of aerobic, stretching and strengthening exercises and this agree with the present study [25].

Previous studies of patients with SLE have shown the impact of aerobic or muscle strengthening or supervised exercise strategies on improved health outcomes including fatigue [59,60], improved exercise tolerance [61,62] and QOL [25,62]. And in this study, there are significant differences in FSS, physical performance and QOL.

A graded exercise tolerance test preceded all aerobic exercise interventions, during which participants were instructed to exercise at heart rates equivalent to 60–80% of maximum aerobic capacity. Group interventions involved supervised exercise classes, including warm up, low impact aerobic activity, and strengthening or stretching before cool down. Homebased programmes made use of exercise bicycles, walking, cycling, jogging or swimming. The duration of effective aerobic exercise programmes averaged 12 weeks, with most interventions occurring three times weekly for 30–60 minutes. Three studies that reported reduced fatigue followed participants' progress after the intervention ended [63-65] and this agrees with the present study. In this study there are improvements in FSS and physical performance.

Ayan and Martin suggest that physical exercise can improve cardiovascular fitness, reduce metabolic abnormalities or fatigue and consequently contribute to an improved QOL for individuals with SLE and this agrees with the present study [53].

The study performed by Carvalho et al. reinforces this hypothesis because it reported a significant improvement in exercise tolerance, aerobic capacity, QOL and depression symptoms after the completion of a supervised cardiovascular training program for patients with SLE [61]. The results of these two studies agree with the results of the present study there are significant differences in physical performance, 6MWT, 2Min step test, SDS, and QOL.

In another study using two groups of volunteers with SLE, one performing aerobic training and the other performing strength training with 70-80% of the maximum load with 2–3 sets of 10 repetitions at three weekly 50-minute sessions, the exercises performed by both groups were considered safe and did not aggravate the symptoms of SLE over a period of eight months. Individuals from both groups showed improvements in fatigue, functional capacity, cardiovascular fitness, and muscle strength [26].

In the present study aerobic group, have highly significant differences in SDS, Sf- 36, and FSS. 6MWT test, functional performance battery consists of 30 S. Chair stand test and 30 S. Arm curl test. In the group of stretching and strengthening, there are also significant differences in SDS, Sf- 36, and FSS. 6MWT test, functional performance battery consists of 30S. chair stand test and 30 S. arm curl test. And the present study agrees with the results of these studies.

Rosalind's et al. study showed that aerobic, range of motion, and muscle strengthening exercise in SLE patients is safe and results in improved fatigue and functional status. And this agrees with the present study.

In this study, comparing the results of both groups showed that no significant difference in 30 S. chair up and 30 S. arm

curl, there is significant difference in SDS, SF-36, FSS, and highly significant difference in 6MWT.

Bearing in mind the characteristics and symptoms of SLE patients, aerobic exercise can be a useful tool, not only for patients' low aerobic capacity, but also for the low difficulty level of the exercises themselves. For instance, walking at an intensity of 70% of the patient's maximum heart rate, three times a week, starting from 25 minutes per session in the first week to 40 minutes from the third week onwards, is an easy way to improve aerobic capacity and reduce fatigue, with no aggravation of the illness [66].

Other activities, such as swimming or stationary cycling at an intensity between 70–80% of the maximum heart rate, for 30-50 minutes, three times a week, can be just as effective [25,60].

A suitable strength training programme could consist of isometric and progressive resistance exercises, performed three times a week, for instance, weightlifting programmes of two to three sets of 10 repetitive isotonic contractions per muscle group using increasing weights from one to two pounds, and resting three minutes between sets [53].

In the present study the group of stretching and strengthening 50 min three times/week for three months were enough to make significant differences in SDS, Sf- 36, and FSS. 6MWT test, functional performance battery consists of 30 S. chair stand test and 30 S arm curl test.

Maintenance of improvements in fatigue due to exercise was difficult to assess in most studies due to lack of follow-up. In three studies vitality increased significantly as a result of aerobic exercise [60,63,66].

An increasing number of non-pharmacologic therapies are available for patients with fatigue, including relaxation, programmed exercise, education, counselling, rehabilitation, and energy conservation [52,67], but their actual effect on SLE patients is not well known. Although some systematic reviews [13,42,52] and 1 meta-analysis reported on the effectiveness of no pharmacologic interventions for fatigue [67].

Therefore, routine assessment of physical fitness in clinical practice might be useful to identify and monitor patients with SLE who would benefit from aerobic exercise training programs to improve exercise tolerance and fatigue [25].

## CONCLUSION

Fatigue in SLE is associated with lower fitness levels, reduced exercise capacity, reduced muscle strength, and greater disability when compared to sedentary controls. Studies examining the functional status of patients with SLE report a reduction in functional status measures. Non-pharmacological treatment as exercises is a vital part of treatment of patients with SLE. Both aerobic, stretching and strengthening exercises were effective in reducing FSS, SDS, 6MWT, 2 Min step test, physical performance and QOL.

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