ORIGINAL RESEARCH

The impact of upper limb exercise on function, daily activities and quality of life in systemic lupus erythematosus: a pilot randomised controlled trial

Kyriaki Keramiotou, Christos Anagnostou, Evangelia Kataxaki, Antonios Galanos, Petros P Sfikakis, Maria G Tektonidou

ABSTRACT

Objective To assess the effect of upper limb exercise on hand function, daily activities performance and quality of life of patients with systemic lupus erythematosus (SLE).

Methods We performed a pilot randomised, 24-week follow-up, unmasked controlled trial. Inclusion criteria were upper limb arthralgias, a Disabilities of Arm, Shoulder and Hand (DASH) questionnaire score >10 and a stable treatment over the past 3 months. Patients were randomly allocated in the routine care (control) or exercise group that received an individually tailored 30-min daily upper-limb exercise programme by a hand therapist for 12 weeks.

Results From 293 consecutive SLE patients, data from 32 patients allocated to the exercise group and 30 to the control group were analysed. There was a significant difference between the two groups in percentage changes of DASH, HAQ, grip strength, pinch strength, LupusQoL-physical health and fatigue, and VAS scores from baseline to 6, 12 and 24 weeks, and from baseline to 12 weeks for dexterity test (p<0.001). No interaction was observed between exercise and disease activity or medication use at baseline and during the observation period.

Conclusion Upper-limb exercise significantly improves hand function, pain, daily activity performance and quality of life in SLE.

Trial registration number NCT03802578.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with a significant impact on function, activities of daily living, work ability and patients’ quality of life. It has been well documented that upper limb exercise is beneficial to patients with rheumatic disorders such as rheumatoid arthritis, psoriatic arthritis and osteoarthritis. A recent meta-analysis showed that full body exercise was well tolerated and improved physical fitness in patients with SLE. No studies have examined the effect of upper limb exercise on hand function and performance of daily activities in SLE patients.

The aim of this study was to evaluate the impact of an individually tailored upper limb exercise programme on hand strength, dexterity and performance of daily activities, and the quality of life of SLE patients, in addition to best practice usual care.

It was hypothesised that upper limb exercise programme would improve the earlier parameters.

PATIENTS AND METHODS

Study design and participants

A randomised, parallel-group, 24-week follow-up, unmasked controlled trial was designed. Inclusion criteria were the 2012...
Standards of Reporting Trials statement was followed. 

It was calculated that a sample size of 32 patients per group was required for a 80% probability of demonstrating a difference of 15% between comparison groups (exercise: -25%±20 vs control: -10%±20) in percentage change of DASH score from baseline to 12 weeks with a significance of <5% (two-tailed test). The patients of the pilot study were included in the final sample. The estimation of sample size was performed using G*Power V.3.1.9.2 programme.

Allocation was unmasked to participants and therapists delivering the exercise programme. The Consolidated Standards of Reporting Trials statement was followed.

Assessment tools

A hand therapist (KK) assessed all patients at baseline, 6, 12 and 24 weeks. Rheumatologists working in the two hospitals evaluated all participants and were masked to group allocation. Clinical evaluation included tender and swollen joint count.

Performance of daily activities was evaluated with the DASH questionnaire and the Health Assessment Questionnaire (HAQ). The DASH questionnaire is an assessment tool of symptoms and function of the entire upper extremity. It has 30 items regarding symptoms (pain, tingling/numbness, weakness, stiffness) and function (physical function, social/role function). Items are scored on a scale from 1 (no difficulty) to 5 (extreme difficulty/unable to do). The HAQ is an assessment tool measuring the difficulty of coping with everyday activities such as dressing, walking, arising, reach, eating, grip, hygiene and outside activity. Both questionnaires are self-administered, reliable, valid and responsive to change. High score in both questionnaires indicates a decreased ability in performance of daily activities. Participants completed all questionnaires independently.

The grip and pinch strength of dominant hand were evaluated with the Jamar dynamometer and Jamar pinch gauge tools, respectively. For both grip and pinch strength assessment participants were seated, with the shoulder joint adducted and in neutral position, forearm in neutral position, elbow flexed to 90°, wrist slightly extended. Three trials were attempted, and the mean score was recorded.

Dexterity of dominant hand was evaluated with the Purdue Pegboard Test. The participants were required to take as many pins as possible within a 30-s period out of a cup and place each one into a hole in a board.

The quality of life was evaluated with Lupus Quality of Life (LupusQoL), a questionnaire with good construct, face, discriminative and concurrent validity, and internal and test-retest reliability. LupusQoL evaluates eight domains including physical health, pain, planning, intimate relationships, a burden to others, emotional health, body image and fatigue. Each domain of the LupusQoL is scored separately, on 0–100 scale, with greater values indicating better quality of life. All participants were evaluated for physical health and fatigue domain.

SLE activity and cumulative organ damage were evaluated with the SLE disease activity index 2000 (SLEDAI-2K) and Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index (SLICC/ACR-DI), respectively, at baseline, 12 and 24 weeks. The lupus low disease activity state (LLDAS) was also evaluated. Pain intensity was evaluated with pain visual analogue scale (VAS). Participants completed the pain VAS independently. Fibromyalgia was evaluated with the fibromyalgia rapid screening tool (FIRST), a simple and rapid self-administered questionnaire with excellent discriminative value.

Primary and secondary outcomes

The primary outcome was the percentage change of DASH score from baseline to 12 weeks. Secondary outcomes were the percentage change of HAQ score, grip and pinch strength, Purdue test and LupusQoL from baseline to 12 weeks.

Exercise program

A team of hand therapists examined a variety of exercises described in the literature or proposed by experts and selected the most appropriate ones to include in a programme designed for SLE, taking into consideration the clinical relevance and home application. Participants were provided with a booklet including pictures and instructions for the exercise programme and a kit of equipment including a stick, two resistance bands and a plastic container of 4oz, with therapeutic putty of medium soft or medium resistance depending on their strength. In order to enhance adherence, participants were provided with an exercise diary to record completion of the daily exercise programme. Patients were encouraged to use as little analgesic medication as possible and advised to try topical substances. Use of nonsteroidal anti-inflammatory drugs (NSAIDs) was not allowed. Clinicians recorded participants’ medication in every session.

Participants had an initial assessment to tailor the exercise programme to their strength, pain level and flexibility. The initial intensity of exercise was set at a moderate level and the programme was reassessed, using a modified Borg Scale, to maintain the same intensity, in every face to face session with the hand therapist at 0, 3, 6 and 9 weeks.

Patients in the exercise group received by the hand therapist a 30-min daily programme at home of...
strengthening and stretching upper limb exercises for 12 weeks, in addition to routine care. The programme included 9 strengthening and stretching exercises for the upper extremities with a stick (figure 1A), 10 strengthening and stretching exercises for the fingers (figure 1B) and 11 strengthening exercises against resistance with therapeutic putty (figure 1C). In addition to the exercise group, participants in the control group had four sessions of training in alternative methods of performing daily activities, use of aids, joint protection and energy conservation, additionally to assessment at baseline, 6, 12 and 24 weeks, in order to keep them also committed and motivated. All participants received the same training in alternative methods of performing daily activities, use of aids, joint protection and energy conservation.

Statistical analysis
Data were expressed as mean±SD or median (in case of violation of normality) for continuous variables and as percentages for categorical data. The Kolmogorov-Smirnov test was utilised for normality analysis of the parameters.

The comparison of variables at each time point between interventions was performed using the independent samples t-test or non-parametric Mann-Whitney test.

One factor repeated measures analysis of variance (ANOVA) model was used for the comparison of different time measurements (0 vs 6 vs 12 vs 24 weeks) of variables for each intervention. Pairwise multiple comparisons were performed using the Bonferroni test. The median percentage changes from baseline after 6, 12 and 24 weeks, respectively, were calculated in order to examine the two interventions adjusted for any baseline difference. Comparison of percentage changes from baseline of parameters during the observation period showed a statistically significant change between 0 and 12, 0 and 24 weeks (p<0.001). Pairwise comparisons between 0, 6 and 12 weeks showed a statistically significant difference for all test parameters in the exercise group (p<0.001), while no significant differences were detected at baseline or between the two groups at 12 and 24 weeks (p=0.840).

Comparison of absolute values of tested parameters during the observation period for each group
Comparisons of the absolute values of tested parameters during the observation period showed a statistically significant difference from baseline to 12 and 24 weeks for all test parameters in the exercise group (p<0.001) (table 2). More specifically, the DASH and HAQ scores improved more than double from baseline to 12 and 24 weeks (p<0.001). Pairwise comparisons between 0, 6 and 12 weeks showed a statistically significant difference for all variables, but not between 12 and 24 weeks (table 2). In the control group, only the Purdue score showed statistically significant change between 0 and 12, 0 and 24, 6 and 24 weeks (p=0.001).
Figure 1  The exercise programme of participants in exercise group. (A) Strengthening and stretching exercises with a stick. (B) Strengthening and stretching finger exercises. (C) Strengthening and stretching exercises with therapeutic putty.
Comparison of the absolute changes of the HAQ sub-items, related to the upper limb functionality, ‘dress yourself, including shoelaces and buttons’ and ‘cut your own meat’, during the observation period, showed a statistically significant difference from baseline to 12 and 24 weeks, in the exercise group (p<0.001).

**Comparison of percent changes of tested parameters from baseline between compared groups**

There was statistically significant difference between the comparison groups (exercise vs control) in relation to percentage change of DASH variable from baseline to 6 weeks (−33.72% vs −1.25%, p<0.001), 12 weeks (−43.41% vs −11.23%, p<0.001) and 24 weeks (−51.86% vs −7.10%, p<0.001) (figure 3A). Similarly, there was significant difference between the two groups in relation to percentage change of HAQ variable from baseline to 6 weeks (−20.00% vs 0.00%, p<0.05), 12 weeks (−55.00% vs −9.72%, p<0.001) and 24 weeks (−69.75% vs −9.13%, p<0.001) (figure 3B). Moreover, all percent changes of grip strength, pinch strength and LupusQoL (physical health and fatigue domains) were significantly higher in the exercise group compared with control group at all-time points (figure 3C, D, F and G). Moreover, the percentage change of purdue was significantly higher in the exercise group compared with control group from baseline to 12 weeks (p<0.001) (figure 3E). Finally, the percent change of pain VAS was significantly higher in the exercise group compared with control group at all-time points (p<0.001) (figure 3H).

There was no interaction between intervention and disease duration, disease activity, corticosteroid and immunosuppressive use at baseline (table 3). Prednisolone dosage remained stable at 12 weeks in 80% of 30 remaining patients in both groups, was decreased in 16.7% of patients in both groups and was increased in 3.3% of patients in both groups (p=1.000). The use of immunosuppressive agents remained stable during the whole observation period.

No harms and adverse reactions occurred in the exercise group related to the exercise programme during
Table 1  Baseline characteristics

| Demographics | Exercise group n=32 | Control group n=30 | P value |
|--------------|----------------------|---------------------|---------|
| Age (years), mean (SD) | 43.34 (8.90) | 48.77 (12.38) | 0.062 |
| Female, n (%) | 31 (96.9) | 27 (90) | 0.346 |
| Marital status n (%) | 10 (31.3)/19 (59.4) | 6 (20)/20 (66.7) | 0.580 |
| Education n (%) | 30 (93.8)/2 (6.3) | 28 (93.3)/2 (6.7) | 1.000 |

| Disease-related characteristics | Exercise group n=32 | Control group n=30 | P value |
|---------------------------------|----------------------|---------------------|---------|
| Disease duration, median (IQR) | 6 (10) | 11 (15) | 0.065 |
| SLEDAI-2K, mean (SD) | 4.25 (3.24) | 4.20 (3.58) | 0.937 |
| LLDAS (%) | 18 (56.3) | 13 (43.3) | 0.446 |
| SLICC mean (SD) | 0.34 (0.60) | 0.63 (0.93) | 0.242 |
| Symptomatic joint count, median (IQR) | 10 (11) | 11 (7) | 0.587 |
| Swollen joint count, mean (SD) | 1.39 (3.05) | 1.43 (2.53) | 0.509 |
| Arthritis n (%) | 5 (15.62) | 6 (20) | 0.652 |
| Fibromyalgia n(%) | 4 (12.5) | 3 (10) | 0.756 |
| VAS score, mean (SD) | 5.81 (1.67) | 6.03 (1.77) | 0.616 |
| Corticosteroid use (%) | 20 (54.1) | 17 (46.0) | 0.640 |
| Prednisolone dosage (mg) mean (SD) | 4.63 (5.55) | 4.97 (5.80) | 0.884 |
| Hydroxychloroquine use (%) | 26 (81.3) | 25 (83.3) | 0.985 |
| Immunosuppressive agents use (%) | 15 (46.9) | 15 (50.0) | 0.806 |
| Biologic agents use (%) | 1 (3.1) | 3 (10) | 0.271 |

| Procedure parameters | Exercise group n=32 | Control group n=30 | P value |
|-----------------------|----------------------|---------------------|---------|
| DASH score, mean (SD) | 39.02 (16.10) | 43.08 (16.39) | 0.330 |
| HAQ score, mean (SD) | 0.81 (0.45) | 1.10 (0.55) | 0.029 |
| Grip strength DH mean (SD) | 22.86 (8.77) | 21.42 (9.75) | 0.542 |
| Pinch strength Jaws DH, mean (SD) | 4.27 (2.01) | 3.91 (2.19) | 0.509 |
| Perdue DH, mean (SD) | 13.25 (2.05) | 12.27 (2.36) | 0.084 |
| LupusQoL PH, mean (SD) | 56.44 (22.62) | 51.25 (20.62) | 0.346 |
| LupusQoL fatigue, mean (SD) | 56.63 (23.74) | 49.44 (21.03) | 0.213 |

DASH, Disabilities of Arm, Shoulder and Hand; DH, dominant hand; HAQ, Health Assessment Questionnaire; Jaws, three point pinch; LLDAS, lupus low disease activity state; LupusQoL, Lupus Quality of Life; PH, physical health; SLEDAI-2K, systemic lupus erythematosus disease activity index 2000; SLICC, Systemic Lupus International Collaborating Clinics; VAS, Visual Analogue Scale.

the intervention period. Two patients reported adverse events not related to the study intervention. There was one hospital admission in the control group for cholecystectomy and one patient in the exercise group was diagnosed with influenza and treated with oseltamivir.

DISCUSSION

Based on the results of this study, we confirmed the hypothesis that upper limb exercise programme, in patients with SLE, would result in improvements in hand strength, dexterity, performance of daily activities and quality of life, as adjunct to ongoing routine care. This study demonstrates for the first time that an individualised upper limb exercise programme significantly improved hand function, daily performance, pain and quality of life of patients with SLE, independently of SLE activity and medication use or dosage at baseline and during the observation period.

Previous studies have shown that SLE patients face hand or general health problems causing disability in a wide range of daily life activities, including household tasks, work, studies and childcare with consequent effect in their quality of life.1 3 5 18 19 A small number of studies examined the effects of exercise on different aspects of the patient daily life, and the majority reported beneficial responses. Almost all studies involved general or full body programmes focusing on...
and pain in RA. Similarly, Roger-cise programmes improve hand function, grip strength. Hammond and Prior24 concluded that home hand exercise programmes improved hand function, dexterity, grip and pinch strength, duration for longer than exercise programme leading in better performance of activities of daily living. These findings were in accordance with the results of Lamb et al for RA patients.6 Another important finding was that the exercise group presented a significant decrease of pain in all time points compared with control group, in accordance with the results of other studies in SLE patients.36 or RA patients.37–39 However, some studies failed to present post-exercise decrease in pain in SLE patients30 and RA patients,31 32 likely due to different types of the exercise programme. Our results are consistent with other studies showing that exercise in SLE patients is safe and well tolerated30 and half of them were on LLDAS.

In our study, DASH and HAQ scores, reflecting the performance of everyday activities, improved more than double in the exercise group. Significant improvement was also detected in grip strength, pinch strength, dexterity and quality of life at 6, 12 and 24 weeks compared with baseline in the exercise group. Interestingly, at 24-week reevaluation, the scores were better than or equal to scores at 12 weeks, when the exercise programme was completed, probably due to improved grip and pinch strength and dexterity duration for longer than exercise programme leading in better performance of activities of daily living. These findings were in accordance with the results of Lamb et al for RA patients.6 Another important finding was that the exercise group presented a significant decrease of pain in all time points compared with control group, in accordance with the results of other studies in SLE patients.36 or RA patients.37–39 However, some studies failed to present post-exercise decrease in pain in SLE patients30 and RA patients,31 32 likely due to different types of the exercise programme. Our results are consistent with other studies showing that exercise in SLE patients is safe and well tolerated30 and results in improved function and quality of life.

A wide range of studies has evaluated the effectiveness of hand exercise on other rheumatic disorders. Lamb et al6 studied the efficacy of a home hand exercise programme in 246 patients with RA compared with 244 patients in usual care. They showed significant improvement in hand function, dexterity, grip and pinch strength, pain and ROM. Subsequently, a systematic review of Hammond and Prior24 concluded that home hand exercise programmes improve hand function, grip strength and pain in RA. Similarly, Roger-Sylva et al3 studied the efficacy of resistance exercise in 20 patients with psoriatic arthritis compared with 21 patients of usual care. They concluded that resistance exercises are effective in improving functional capacity, disease activity and the general quality of life of patients with psoriatic arthritis. A Cochrane systematic review concluded that exercise may reduce hand pain and finger joint stiffness and may improve hand function in patients with hand OA.25

To our knowledge, this is the first study that evaluated the impact of upper limb exercise on function and quality of life in patients with SLE. We recruited patients who were stable on a drug regimen and thus in symptoms control, before the initiation of exercise programme, in order to achieve better adherence to the programme. Moreover, their disease activity was mild to moderate; their mean SLEDAI-2K score was 4.25, and half of them were on LLDAS.

| Variables | Group | Baseline | 6 weeks | 12 weeks | 24 weeks | P value within group |
|-----------|-------|----------|---------|----------|----------|---------------------|
| DASH      | Exercise | 39.02 (16.10) | 27.82 (14.18)* | 21.49 (16.19)† | 19.09 (14.52)‡ | <0.001 |
|           | Control  | 43.08 (16.39) | 43.45 (19.36) | 38.38 (16.29) | 38.85 (18.90) | 0.058 |
| HAQ       | Exercise | 0.81 (0.45) | 0.65 (0.48) | 0.45 (0.45)† | 0.34 (0.34)‡ | <0.001 |
|           | Control  | 1.10 (0.55) | 1.14 (0.55) | 1.04 (0.49) | 1.09 (0.56) | 0.420 |
| Grip strength DH | Exercise | 22.86 (8.77) | 26.84 (8.92)* | 29.09 (8.52)† | 29.47 (9.65)‡ | <0.001 |
|           | Control  | 21.42 (9.75) | 22.16 (10.88) | 22.54 (10.78) | 22.83 (11.54) | 0.435 |
| Pinch strength Jaws DH | Exercise | 4.27 (2.01) | 5.16 (1.93)* | 5.66 (1.99)† | 5.65 (1.86)‡ | <0.001 |
|           | Control  | 3.91 (2.19) | 3.99 (1.96) | 3.92 (1.95) | 3.80 (2.26) | 0.583 |
| Purdue DH | Exercise | 13.25 (2.05) | 14.34 (2.31)* | 15.38 (2.20)† | 15.09 (2.39)‡ | <0.001 |
|           | Control  | 12.27 (2.36) | 12.63 (2.47) | 13.07 (2.20)§ | 13.50 (2.13)§† | 0.001 |
| LupusQoL PH | Exercise | 56.44 (22.62) | 67.18 (23.03)* | 72.95 (21.54)† | 73.44 (22.77)§ | <0.001 |
|           | Control  | 51.25 (20.62) | 50.83 (22.23) | 53.33 (22.12) | 52.18 (22.88) | 0.527 |
| LupusQoL fatigue | Exercise | 56.63 (23.74) | 66.21 (23.59)§ | 69.34 (22.36)§ | 70.18 (26.96)* | <0.001 |
|           | Control  | 49.44 (21.03) | 51.67 (22.68) | 51.67 (22.12) | 52.18 (22.88) | 0.527 |
| Pain VAS  | Exercise | 5.81 (1.67) | 4.22 (1.52) | 2.97 (1.45)† | 2.71 (1.38)‡ | <0.001 |
|           | Control  | 6.03 (1.77) | 5.60 (1.54) | 4.87 (1.56)† | 4.93 (1.61) | <0.001 |

All values are presented as mean (SD).
*<p<0.005 6, 12, 24 weeks vs baseline.
†<p<0.05 12, 24 weeks vs 6 weeks.
‡<p<0.005 12, 24 weeks vs 6 weeks.
§<p<0.05, 6, 12, 24 weeks vs baseline.
DASH, Disabilities of Arm, Shoulder and Hand; DH, dominant hand; HAQ, Health Assessment Questionnaire; Jaws, three point pinch; LupusQoL, Lupus Quality of Life; PH, physical health; VAS, Visual Analogue Scale.
Figure 3  Median percentage change from baseline of (A) DASH, (B) HAQ, (C) grip strength DH, (D) pinch strength DH, (E) purdue (Jaws) DH, (F) LupusQoL physical health, (G) LupusQoL fatigue and (H) pain VAS. DASH, Disabilities of Arm, Shoulder and Hand; DH: dominant hand; HAQ, Health Assessment Questionnaire; Jaws: three point pinch; LupusQoL, Lupus quality of life.
Interestingly, small, not statistically significant improvement in all parameters (except for purdue test) was also observed in the control group, due to the initiation of patient training in alternative methods of performing daily activities, use of aids, joint protection, and energy conservation.

One of the strengths of our study is that it is the first RCT that evaluated the impact of upper limb exercise in a number of parameters in SLE patients. In addition, the exercise programme was individually tailored to each patient, and the exercise programme is easy enough to be adopted in all outpatient rheumatology clinics. This study had some limitations. First, participants and therapists were unmasked as in most intervention studies, but the independent completion of questionnaires limited the risk for bias. The study had mild to moderate disease activity. The results may not apply to patients with severe disease activity.

Although the HAQ score was lower in the exercise group compared with the control group at baseline, this difference could not bias the results because there were no significant differences in all other baseline demographic, disease-related characteristics and all procedure parameters (except HAQ score) between the two groups. Furthermore, the median percentage changes from baseline after 6, 12 and 24 weeks, respectively, were calculated in order to examine the two interventions adjusted for any baseline difference. Finally, the difference was due to sub-items unrelated to upper limb function such as ‘climb up five stairs’, ‘walk outdoors on flat ground’, ‘bend down to pick up clothing from the floor’ and ‘get in and out of a car’.

An application with videos demonstrating exercises, with monitoring of frequency of performing the exercise programme and with goals setting is being developed to achieve better adherence and help patients with SLE to continue performing exercise long term, as has been suggested for RA patients.24

In conclusion, the introduction of a 30-min session of therapeutic exercise for the upper limbs, as an adjunct to routine care, can improve hand function, dexterity, performance of activities of daily life and quality of life in patients with SLE.

Table 3 No interaction between intervention and disease duration, disease activity and medications

| Treatment effect, 95% CI | P interaction |
|------------------------|--------------|
| Time since diagnosis   |              |
| <5 years               | −48.96% (−74.2% to −23.7%) 0.322 |
| >5 years               | −30.79% (−54.2% to −7.4%) |
| SLEDAI-2K              |              |
| ≤4                    | −39.66% (−54.0% to −25.3%) 0.501 |
| >4                    | −28.13% (−68.1% to 11.9%) |
| Corticosteroid use     |              |
| No                    | −40.37% (−57.6% to −23.1%) 0.722 |
| Yes                   | −35.46% (−61.1% to −9.8%) |
| Immunosuppressive agents use |         |
| No                    | −25.16% (−40.2% to 10.1%) 0.150 |
| Yes                   | −48.3% (−77.7% to 18.9%) |

SLEDAI-2K, systemic lupus erythematosus disease activity index 2000; VAS, Visual Analogue Scale.

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