Original article

Poor muscle strength and function in physically inactive childhood-onset systemic lupus erythematosus despite very mild disease

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ABSTRACT

Objective: To compare muscle strength (i.e. lower- and upper-body strength) and function between physically inactive childhood-onset systemic lupus erythematosus patients (C-SLE) and healthy controls (CTRL).

Methods: This was a cross-sectional study and the sample consisted of 19 C-SLE (age between 9 and 18 years) and 15 CTRL matched by age, sex, body mass index (BMI), and physical activity levels (assessed by accelerometry). Lower- and upper-body strength was assessed by the one-repetition-maximum (1-RM) test. Isometric strength was assessed through a handgrip dynamometer. Muscle function was evaluated by the timed-stands test (TST) and the timed-up-and-go test (TUG).

Results: When compared with CTRL, C-SLE showed lower leg-press and bench-press 1-RM ($p = 0.026$ and $p = 0.008$, respectively), and a tendency toward lower handgrip strength ($p = 0.052$). C-SLE showed lower TST scores ($p = 0.036$) and a tendency toward higher TUG scores ($p = 0.070$) when compared with CTRL.

Conclusion: Physically inactive C-SLE patients with very mild disease showed reduced muscle strength and functionality when compared with healthy controls matched by physical activity levels. These findings suggest C-SLE patients may greatly suffer from a physically inactive lifestyle than healthy controls do. Moreover, some sub-clinical "residual" effect of the disease or its pharmacological treatment seems to affect C-SLE patients even with a well-controlled disease.

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Redução na força muscular e capacidade funcional em pacientes fisicamente inativos com lúpus eritematoso sistêmico de início juvenil, apesar de doença muito leve

RESUMO

Palavras-chave:
Força muscular
Capacidade funcional
Doença reumática
Nível de atividade física

Objetivo: Comparar a força muscular (ou seja, a força muscular dos membros inferiores e superiores) e a capacidade funcional de pacientes fisicamente inativos com lúpus eritematoso sistêmico de início juvenil LESJ com controles saudáveis (CTRL).

Métodos: Trata-se de um estudo transversal cuja amostra foi composta por 19 pacientes com LESJ (idades entre 9 a 18 anos) e 15 CTRL pareados por idade, sexo, índice de massa corporal (IMC) e nível de atividade física (avaliada através do uso de acelerômetros). A força de membros inferiores e superiores foi avaliada pelo teste de uma repetição máxima (1-RM). A força isométrica foi avaliada com o uso de um dinamômetro. A capacidade funcional foi avaliada pelo Timed-stands test (TST) e Timed-up-and-go test (TUG).

Resultados: Quando comparados aos CTRL, os pacientes com LESJ apresentaram menor força em 1-RM no leg press e supino (p = 0,026 e p = 0,008, respectivamente), e uma tendência a menor força de preensão manual (p = 0,052). Os pacientes com LESJ apresentaram menores escores no TST (p = 0,036) e uma tendência a maior tempo de execução no TUG (p = 0,070), quando comparados ao grupo CTRL.

Conclusão: Pacientes com LESJ, fisicamente inativos, com doença muito leve mostraram redução na força muscular e capacidade funcional quando comparados a controles saudáveis pareados por níveis de atividade física. Estes achados sugerem que pacientes com LESJ podem apresentar mais efeitos deletérios por manter um estilo de vida fisicamente inativo do que controles saudáveis. Além disso, alguns efeitos "residuais" subclínicos da doença ou o tratamento farmacológico parecem afetar pacientes com LESJ, mesmo com uma doença bem controlada.

Introduction

Childhood-onset systemic lupus erythematosus (C-SLE) is an autoimmune disease characterized by B and T cells hyperactivity, formation and deposition of antibodies throughout the body, which results in chronic systemic inflammation and multi-organ involvement (e.g. skin, kidney, muscle, cardiovascular system, etc.).[1–4] C-SLE has a prevalence of 3–24 cases per 100,000 inhabitants[5] and has been associated with a more severe disease than adult-SLE.[6]

Disease itself (e.g. systemic inflammation) and drug regimen (e.g. prolonged corticoid use) may contribute to a multitude of clinical manifestations (e.g. musculoskeletal disorders, physical dysfunction and fatigue),[7–9] which may, ultimately, predispose patients to a sedentary lifestyle. A sedentary lifestyle, in turn, may negatively affect physical capacity, function, and health-related quality of life, in a vicious circle of physical inactivity and poor clinical outcomes.[10] A few studies have shown that pediatric rheumatic populations are not engaged in sufficient levels of physical activity compared to healthy children and adolescents.[11–13] However, although it is plausible to assume that a sedentary behavior may affect physical capacity, this remains to be determined.

The aim of this study was to compare muscle strength (i.e. lower- and upper-body strength) and function between physically inactive C-SLE and healthy controls (CTRL). We hypothesized that physically inactive patients with low disease activity and low cumulative damage would show similar muscle strength and function when compared to healthy controls matched for physical activity levels.

Patients and methods

Study design and patients

This was a cross-sectional study conducted in Sao Paulo, Brazil (Clinical Hospital, School of Medicine, University of Sao Paulo). The sample consisted of 19 C-SLE patients (age between 9 and 18 years) and 15 healthy controls (CTRL) matched for age, sex, body mass index (BMI), and physical activity levels (assessed by accelerometer). Aerobic capacity, health-related quality of life, and physical activity level data from part of this sample has been reported elsewhere.[14] Disease activity was determined by means of Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI) scores,[15] and cumulative damage by Systemic Lupus International Collaborating Clinics/ACR Damage Index (SLICC) scores.[16] All patients fulfilled the revised American College of Rheumatology criteria for the diagnosis of C-SLE.[17] Healthy subjects, recruited by local advertising at University of Sao Paulo, were free of any current or past chronic diseases, and were not engaged in any exercise training programs.

Exclusion criteria were as follows: (1) physically active patients (according to general physical activity recommendations)[18]; (2) cardiovascular and musculoskeletal disorders; (3) kidney and pulmonary involvement; (4) peripheral neuropathy, (5) secondary rheumatic disease (e.g. Sjögren syndrome, fibromyalgia, and antiphospholipid syndrome).

The Committee of Ethics in Research of the General Hospital of the School of Medicine, University of Sao Paulo, Brazil (CAPPesq) approved the study and all legal guardians provided written informed consent.

Physical activity level assessment

Physical activity was objectively measured using Actigraph GT3X® accelerometers (ActiGraph, Pensacola, FL). All participants were instructed to wear the accelerometer during waking hours, except when bathing or swimming, for seven consecutive days. All participants accumulated at least ten hours of valid activity recordings per day for at least five days. Data were exported from the device in 15-s epochs for children and adolescents, using ActiLife 6 software (ActiGraph, Pensacola, FL). Everson cut-points were used to define epochs for children and adolescents as follows: sedentary time (<100 counts/min), light-intensity physical activity ($\geq$101 to <2295 counts/min), and MVPA (moderate-to-vigorous physical activity) ($\geq$2296 counts/min).[19] Physical activity guidelines recommend a minimum of 60 min/day of MVPA for children and adolescents.[18] Thus, participants were considered physically active if they met this recommendation.

Muscle strength and function

Participants performed two preliminary sessions, separated by at least 72 hours, to familiarize themselves to the main exercise tests. These consisted of one-repetition-maximum (1-RM) tests to determine both upper- and lower-body muscular strength, as assessed by bench-press and leg-press exercise, respectively. Prior to the 1-RM test, two light warm-up sets interspersed by two-minute intervals were performed. Subsequently, participants achieved 1-RM for each exercise in 1–5 attempts interspersed by 3-min intervals.[20] 1-RM tests were conducted by two experienced researchers and verbal encouragement was provided during testing sessions.

Isometric strength was assessed through a handgrip dynamometer (Takei A5001 Hand Grip Dynamometer, Takei Scientific Instruments Co., Ltd., Tokyo, Japan). The protocol consisted of three maximal isometric contractions of 5 s interspersed with 60-s recovery periods. The test was performed on the participant's dominant hand.[21]

Muscle function was evaluated by the timed-stands test (TST) and the timed-up-and-go test (TUG). TST assesses the maximum number of stand-ups that a subject can perform from a standard armless chair within 30 s,[22] whereas TUG assesses the time required for the subject to rise from a standard arm chair, walk toward a 3-meters line drawn on the floor, turn, return to the chair, and sit down again.[23]

Statistical analysis

Data normality was tested using the Shapiro–Wilk W-test. Independent samples were compared using either the unpaired T-test for normally distributed variables or the Mann–Whitney U-test for non-normally distributed variables. Data analysis was performed using the SPSS (17.0) for Windows. The level of significance was set at $p \leq 0.05$. Data are presented as mean $\pm$ standard deviation (SD), 95% confidence interval of the difference (CI) were also calculated.

Results

Table 1 shows demographic data, current clinical treatment, disease activity and damage parameters in C-SLE and CTRL. Groups were comparable regarding age, sex, BMI and physical activity levels ($p > 0.05$).

Muscle strength and function

Muscle strength and function data are presented in Table 2. When compared with CTRL, C-SLE showed lower leg-press and bench-press 1-RM ($p = 0.026$ and $p = 0.008$, respectively), and a tendency toward lower handgrip strength ($p = 0.052$).

Additionally, C-SLE showed lower TST scores ($p = 0.036$) and a tendency toward higher TUG scores ($p = 0.070$) when compared with CTRL.

Discussion

The main finding of this study was that physically inactive C-SLE patients with very mild and well-controlled disease had impaired muscle strength and function when compared with healthy controls matched by physical activity levels.

Disease-related symptoms and clinical manifestations may predispose the pediatric rheumatic patient to a physically inactive lifestyle.[10,24,25] Physical inactivity in childhood may track into adulthood and senescence, and has been associated with a higher risk of developing chronic diseases (e.g. obesity, type 2 diabetes, hypertension), and all-cause mortality.[26–28] Moreover, physical inactivity may result in weakness and muscle dysfunction, ultimately leading to poor health-related quality of life.[10,26] In this study, we expected that C-SLE patients with very mild disease (i.e. low cumulative damage and low disease activity) would show similar levels of muscle strength and function when compared with controls matched by physical inactivity. Based on our findings, nonetheless, one may assume that insufficient physical activity level may impose a greater "cost" to C-SLE than to healthy controls in relation to weakness and muscle dysfunction.

It is not clear why muscle strength and function highly differ physically inactive well-controlled C-SLE patients and healthy controls. To avoid any apparent disease-related symptoms that could potentially account for differences in physical capacity, we selected only patients with low disease activity (mean SLEDAI = 2), low cumulative damage (mean SLICC = 0.4), and free of musculoskeletal involvement. Yet, remarkable differences in muscle strength and function were noted, suggesting that other factors may have adversely affected C-SLE. Drug regimen is one of the potential factor to explain these findings. Long-term corticoid therapy, for instance, has been associated with many adverse effects and damages in pediatric populations (e.g. growth suppression, weight gain, bone mass loss, myopathy, ocular complications),[6,7,9,29] which may

Table 1 – Demographic, current clinical and treatment data in C-SLE and CTRL.

	C-SLE (n = 19)	CTRL (n = 15)	p
Age (years)	14.5 ± 2.5	14.7 ± 4.0	0.901
Weight (kg)	52.4 ± 17.2	56.4 ± 19.3	0.532
Height (cm)	154.8 ± 0.2	161.4 ± 0.2	0.221
BMI (kg/m^2)	21.4 ± 4.3	21.0 ± 4.1	0.777
Disease parameters			
SLEDAI	2.3 ± 2.2	–	–
SLICC	0.4 ± 0.6	–	–
Disease duration (years)	3.5 ± 2.7	–	–
Drugs			
Current use of prednisone (mg/kg)	5.4 ± 7.6	–	–
Cumulative use of prednisone (g/kg)	13.6 ± 8.0	–	–
Hydroxychloroquine [n°(%)]	16 (84.2%)	–	–
Metotrexate [n°(%)]	3 (15.8%)	–	–
Azathioprine [n°(%)]	9 (47.4%)	–	–
Physical activity level			
Sedentary time (min/day)	592.3 ± 72.4	566.9 ± 92.1	0.375
Light PA (min/day)	230.8 ± 63.2	256.2 ± 68.8	0.271
MVPA (min/day)	36.3 ± 16.1	30.0 ± 15.6	0.258

BMI, body mass index; MVPA, moderate-to-vigorous; PA, physical activity; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLICC, Systemic Lupus International Collaborating Clinics/ACR Damage Index.
Data are expressed as means ± SD.

Table 2 – Muscle strength and function in C-SLE and CTRL groups.

	C-SLE (n = 19)	CTRL (n = 15)	p	95% CI Lower	95% CI Upper
Leg press (kg)	96.9 ± 39.3	135.9 ± 50.9	0.026[a]	−72.93	−4.99
Bench press (kg)	17.7 ± 5.7	24.6 ± 8.3	0.008[a]	−11.85	−1.93
Hand grip (kg)	21.3 ± 6.7	26.0 ± 6.3	0.052	−9.36	0.04
Timed stands test (reps)	18.1 ± 1.6	19.6 ± 2.2	0.036[a]	−2.83	−0.11
Timed up & go test (s)	5.5 ± 0.5	5.2 ± 0.3	0.070	−0.04	0.62

Data are expressed as means ± SD.
CI, confidence intervals.
[a] Significant difference when compared to healthy control groups.

explain, at least partially, the reduction in physical capacity experienced by C-SLE patients. Moreover, studies have shown that C-SLE patients may have selective atrophy of type-II muscle fiber, impaired excitation–contraction coupling, and microcirculatory lesions,[30,31] which could directly affect muscle strength and function in this disease. The influence of potential abnormal muscle morphology upon muscle dysfunction in C-SLE remains unclear, as we were unable to measure muscle mass or any other muscle physiological parameters in this study.

Adult-SLE populations appear to have reduced physical capacity (e.g. aerobic conditioning, muscle strength and function), higher fatigue and disability when compared with their health counterparts.[32–34] To the best of our knowledge, only one study showed lower aerobic capacity, higher fatigue, and poorer health-related quality of life in a C-SLE cohort,[35] although physical activity level was not well-controlled in this investigation. From our findings, it is possible to infer that physical inactivity can contribute to aggravate muscle

function deficits seen in C-SLE patients to a greater extent than in healthy controls. Further studies involving only physically active patients and controls may provide novel insights on the impact of a broader range of physical activity levels on strength and function, allowing testing whether increased physical activity may overcome muscle dysfunction in C-SLE.

Increased activity levels through exercise training programs have been proven to be effective on counteracting disease-related symptoms and improve physical capacity in several rheumatic populations.[10,25,36–38] To the best of our knowledge, however, a single case report and a single randomized controlled trial have been conducted to test the efficacy of aerobic training in C-SLE patients,[36,39] with both of them showing positive findings in relation to improvements in physical capacity, disease symptoms, and health-related quality of life. Further studies are clearly necessary to investigate the efficacy and safety of more complex interventions in C-SLE (e.g. structured and non-structured activities aimed at improving both aerobic and muscle function, enjoyable

children-oriented physical activities, programs focused on reducing sedentary time, individual and collective sports).

In conclusion, physically inactive C-SLE patients with very mild disease showed reduced muscle strength and functionality when compared with healthy controls matched by physical activity levels. These findings suggest C-SLE patients may greatly suffer from a physically inactive lifestyle than healthy controls do. Moreover, some sub-clinical "residual" effect of the disease or its pharmacological treatment seems to affect C-SLE patients even with a well-controlled disease.

Conflict of interests

The authors declare no conflict of interests.

Acknowledgements

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