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Research Article

Evaluation of aerobic capacity and muscle function in a case series of patients with relapsing polychondritis

Diego Sales de Oliveira, Alexandre Moura dos Santos, Rafael Giovani Misse, Jean Marcos de Souza, Fernanda Rodrigues Lima, Rosa Maria Rodrigues Pereira, and Samuel Katsuyuki Shinjo*

Division of Rheumatology, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, SP, Brazil (BR)

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***Corresponding author:** Samuel Katsuyuki Shinjo, Division of Rheumatology, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, Brazil (BR). Tel: 55 11 3061-7176; Fax: 55 11 3061-8595; E-mail: samuel.shinjo@gmail.com

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Abstract

Background: To evaluate aerobic capacity and muscle function in patients with Relapsing Polychondritis (RP).

Methods: A cross-sectional single center study evaluated seven women with RP (McAdam criteria) that were compared to seven healthy control individuals matched for age, gender, and body mass index. Both groups performed a treadmill-graded maximal exercise. Aerobic capacity was assessed by peak oxygen uptake (VO_2 peak), time at anaerobic Ventilatory Threshold (VAT) and Respiratory Compensation Point (RCP) and time-to-exhaustion. Muscle function was evaluated through the sit-to-stand and the timed up-and-go test.

Results: RP patients had an average age of 52.7 years. Disease was stable with at least one immunosuppressive drug and without glucocorticoid. Patients showed an impaired aerobic capacity characterized by lower VO_2 peak (relative and absolute), and lower time-to-exhaustion. Furthermore, patients had also a tendency to impairment in lower extremities muscle function, when compared with control group.

Main findings: In the present study, patients with RP show a tendency to impaired aerobic capacity and lower extremities muscle function when compared with healthy individuals. Further studies should confirm the present findings.

Introduction

Relapsing Polychondritis (RP) is a rare systemic immune-mediated disease characterized by recurrent episodes of inflammation of cartilaginous and proteoglycan-rich tissues, resulting in progressive anatomical deformation and functional impairment of the involved structures [1]. Typical features include recurrent episodes of nasal and auricular chondritis, ocular inflammation, and tracheobronchial tree involvement [2-5], which have high proteoglycan-rich structures [3].

The annual incidence of RP is 3.5 cases per million, and the disease affects predominantly female and white individuals [2-5]. Moreover, the RP onset occurs mainly in the fourth and fifth decades [2-5].

RP has been scarcely described in the literature, leading to considerable delay in establishing a diagnosis and poses a significant management challenge in practical [6]. The challenges remain, both in the understanding of its pathophysiology and diagnosis, evaluation of its activity, prognosis, and its treatment [5].

The precise pathogenesis of RP is not yet clearly defined, and there is no specific test for RP. Moreover, laboratory changes are nonspecific and generally reflect only an inflammatory state [5]. A biopsy of the atrial chondritis can be performed that shows the presence of mononuclear.

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It is estimated that the 5-year survival rate is 74% of the patients, and the infectious and respiratory involvement contributes to the survival reduction [4] and occasional polymorphonuclear cells, with fibrosis at the fibrochondral junction.

To date, only one population-based study has evaluated mortality in patients with RP [7]. In United Kingdom population with RP, respiratory disease, cardiac conditions and cancer were the most frequent causes of death in these patients [7]. However, high incidence of respiratory diseases and cardiovascular involvement were demonstrated in Brazil, China, and other oriental population [8-10], suggesting that these outcomes may be the main cause of death in these patients.

Impaired aerobic capacity and muscle dysfunction are present in several autoimmune rheumatic diseases [11-14]. However, no study has evaluated these outcomes in patients with RP. Impairment in these physical capacities has been associated with higher risk for pulmonary dysfunction, cardiovascular diseases, and higher mortality [15-17], which could worst the clinical prognosis in patients with RP. Therefore, the aim of the present study was to evaluate aerobic capacity and muscle function in patients with RP.

Methods

This study was approved by the local ethics committee (Ethics Committee for Analysis of Research Projects, number 62111316.1.0000.0068) and was registered at ClinicalTrials (NCT03092141).

This single center cross-sectional study that initially included 30 patients with RP diagnosis, according to McAdam criteria [18]. Twenty-three out of 30 patients were excluded due to: tracheostomy (n = 6), medical release or we could not get in touch (n = 6), and personal problems (n = 11), resulting in seven patients who were age-, sex- and Body Mass Index (BMI)-matched to the seven health individuals (Table 1).

Inclusion criteria for patients were fulfill the classification criteria of McAdam et al [18], age ≥ 18 years, using more than 0.5 mg/kg/day of prednisone in the last three months, and not engaged in exercise programs in the last six months.

Exclusion criteria were patients with disease activity or relapsing, other associated-systemic autoimmune diseases, acute or chronic infections, diabetes, and smoking.

The following data were collected from the participants:

- Current age, gender, weight, height, Body Mass Index (BMI) and disease duration;
- Current age (%) according to World Health Organization (WHO) world standard [19];
- Current laboratory parameters: C-protein reactive - reference value < 5.0 mg/L, by immunoturbidimetric methods; Erythrocyte Sedimentation Rate (ESR) - reference value < 10 mm/1st hour, by automated Westergren method;

Table 1: General data of 7 patients with relapsing polychondritis and control group.

	RP patients (n=7)	Control group (n=7)	*P value*
General data			
Age (years)	52.7±8.1	48.4±3.7	0.224
Weight (kg)	69.8±7.5	72.1±8.0	0.600
Height (cm)	157.6±0.5	160.9±0.5	0.250
Body mass index (kg/m^2)	28.1±3.0	27.8±2.0	0.791
Disease duration (years)	6.5±6.7	-	-
Laboratory data			
C-protein reactive (g/dL)	3.5±1.2	1.4±1.1	0.543
Erythrocyte sedimentation rate (mm/1st h)	6.1±3.3	4.2±2.7	0.654
Treament			
Glucocorticoid	0	-	-
Immunosuppressive drugs	6 (85.7)	-	-
Azathioprine	3 (42.9)	-	-
Methotrexate	3 (42.9)	-	-
Disease status			
Remission	7 (100)	-	-

Data are expressed as mean ± standard deviation, or frequency (%).
RP: relapsing polychondritis.

- Current drug treatment: Glucocorticoids and immunosuppressive drugs (e.g., azathioprine, methotrexate, etc).
- Disease status: disease remission (basing on clinical and laboratory parameters).

All subjects completed a maximal graded treadmill cardiopulmonary exercise test to determine peak oxygen uptake (VO_2 peak). The cardiopulmonary exercise test was considered to be maximal when one of the following criteria was met: VO_2 plateau (e.g., less than 150 mL/min increase between two consecutive stages), heart rate no less than 10 beats below age-predicted maximal heart rate and respiratory exchange ratio value above 1.10. VO_2 peak was considered as the average of the final 30 seconds of the test [13]. Ventilatory Anaerobic Threshold (VAT) and Respiratory Compensation Point (RCP) were determined as described previously [13]. VAT was determined when ventilatory equivalent for VO_2 (VE/VO2) increased without a concomitant increase in ventilatory equivalent for carbon dioxide (VE/VCO2). RCP was determined when VE/VO2 and VE/VCO2 increased simultaneously.

Lower extremities muscle function was assessed by the Sit-to-Stand Test [20] and Timed Up-and-Go Test [21]. To avoid learning effects, the patients underwent two familiarization sessions, at least 48 hours apart, for all strength and functional tests. The coefficients of variation for these tests were ≤ 0.5%. All tests were supervised by a seasoned rheumatologist to report adverse events.

The Kolmogorov-Smirnov test was used to evaluate the distribution of continuous variables, which were expressed as mean ± standard deviation or median (interquartile 25th - 75th). Categorical variables were expressed as percentages (%). Data

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normally-distributed were analyzed by a paired *t*-Student test, and data with a non-normal distribution were analyzed by Wilcoxon's test. Categorical variables were analyzed by Fisher's exact test. *P* values ≤ 0.05 were considered to be statistically significant. The Effect Size (ES), a measure of the magnitude of change, was also calculated using Cohen's *d* for aerobic capacity and strength variables. All statistical analyses were performed using the software SPSS, version 15.0 (Chicago, IL, USA).

Results

As outlined in Table 1, patients and control individuals had comparable aged: 52.7 ± 8.1 years (WHO world standard: 5.370%) and 48.4 ± 3.7 years (WHO world standard: 6.040%), respectively.

The patients with RP had disease duration of 6.5 years. All patients were female and had disease remission, using at least one immunosuppressive drug (azathioprine or methotrexate), and without glucocorticoids.

The Table 2 shows the aerobic capacity and muscle function data. Patients with RP showed an impaired aerobic capacity characterized by lower VO_2 peak relative (P = 0.05) and lower time-to-exhaustion (P = 0.03).

For lower extremities muscle function, RP patients shows a tendency to be worst in Sit-to-Stand Test (P = 0.05) and tendency to be worst in Timed Up-and-Go Test (P = 0.05), when compared with their healthy peers.

Discussion

To the best of our knowledge, this is the first study to evaluate aerobic capacity and lower extremities muscle function in cases series of patients with RP, who showed an impairment in aerobic capacity and a tendency to worst lower extremities muscle function when compared with their healthy peers.

Impaired aerobic capacity and lower extremities muscle dysfunction have been reported in several autoimmune rheumatic diseases, such as rheumatoid arthritis [12], systemic lupus erythematosus [22], systemic autoimmune myopathies [14] and vasculitis [13]. Patients with RP have recurrent inflammatory episodes of cartilaginous and proteoglycan-rich tissues, which can lead to progressive anatomical deformation and functional impairment of the involved structures [4]. Polyarthritis and airway compromise, that are two clinical manifestations that are recurrent finding in these patients, could contribute to the findings of the present study. Besides the clinical manifestations of RP, physical inactivity and sedentary behaviour have been demonstrated to be overlooked risk factors in autoimmune rheumatic diseases [23]. As we not select patients that were engaged in exercise programs and according to BMI, patients in the present study show overweight, we believe that these patients had an important sedentary behavior. Therefore, these two outcomes could contribute to the findings of the present study, once that a higher prevalence of these behaviors have been documented in autoimmune rheumatic diseases [24,25].

To date, therapy of RP is still empiric, due to the lack of standardized guidelines on treatment, and is defined based on disease activity and severity of organ involvement [1]. Mortality in patients with RP is more than twice that of the general population [7]. Impaired aerobic capacity and lower extremities muscle function are two important factors associated with mortality in general population and chronic diseases [15-17]. Thus, strategies that could contribute to reverse these impairments should be applied in patients with RP.

Exercise training programs, which was once neglected in patients with autoimmune rheumatic diseases [23], has been shown to be an important coadjuvant therapy, capable of increase aerobic capacity and reestablish muscle function in these diseases [13,26,27]. In a recent case report, a supervised 12-weeks exercise training program showed to be effective in increase aerobic capacity, muscle strength and function in a patient with RP, without causing disease relapsing [28]. Even though it was a case study, this preliminary findings suggest, that, like other autoimmune rheumatic diseases, exercise training can be a safe and well-tolerable tool capable of improve aerobic capacity and muscle function in patients with RP. However, more studies with more patients are necessary to confirm these findings.

The present study has some limitations. The samples are small. Second, only woman patients with stable disease were assessed, not allowing us to extrapolate these findings for more severe disease. Thus, additional studies will help to corroborate the findings of the present studies.

In conclusion, our patients with RP show impairment in aerobic capacity and a tendency to worst lower extremities muscle function. Strategies that can attenuate or reverse these impairments must be applied in these patients.

Table 2: Aerobic capacity and muscle function in the patients with relapsing polychondritis and control group.

	RP patients (n=7)	Control group (n=7)	*P*
Aerobic capacity			
VO_2 peak (L/min)	21.6±1.7	25.0±3.7	0.047
VO_2 peak (mL/kg/min)	1.5±0.1	1.8±0.3	0.052
Peak heart rate (bpm)	158.9±19.5	167.6±11.7	0.330
Peak respiratory exchange rate	1.0±0.1	1.2±0.1	0.052
Ventilatory anaerobic threshold (min)	4.9±1.3	5.3±1.0	0.544
Respiratory compensation point (min)	8.8±2.3	11.4±2.1	0.053
Time-to-exhaustion (min)	11.1±2.4	13.6±1.3	0.032
Muscle function			
Sit-to-Stand Test (reps)	13.5±1.6	16.0±1.8	0.053
Timed Up-and-Go Test (s)	7.1±0.9	6.1±0.8	0.055

RP: relapsing polychondritis; VO_2 peak: peak oxygen uptake.

Declaration of interest

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