Aerobic Capacity in Adult Dermatomyositis/Polymyositis Patients and Healthy Controls

Guenther F. Wiesinger, MD, Michael Quittan, MD, Martin Nuhr, MD, Beatrix Voll-Platzer, MD, Gerold Ebenbichler, MD, Manfred Zehetgruber, MD, Winfried Graninger, MD


Objective: Assessment of myositis patients has relied on symptoms, strength testing, and serum muscle enzyme activity. Recently, functional assessments and evaluation of strength by dynamometry and of disease activity by magnetic resonance imaging have also been added. Aerobic testing in selected patients has been considered useful.

Design: Case-control study.

Setting: University Hospital, Vienna, Austria.

Patients: Twenty-two subjects (8 outpatients with chronic dermatomyositis and 3 outpatients with chronic polymyositis, and 11 healthy controls) participated, allowing the identification of 11 case-control pairs matched by age (±3 years) and gender (mean age, 48 ± 14yrs; ratio of women to men, 18/4).

Main Outcome Measures: Target parameters were peak oxygen uptake (peak VO₂) to estimate aerobic exercise capacity and peak isometric torque for muscle strength. Creatine phosphokinase (CPK) was measured to assess elevation of muscle enzymes.

Results: The mean peak VO₂ in patients with dermatomyositis/polymyositis was 13.5mL/min/kg (SD = 5.8) and in the healthy controls 28.7mL/min/kg (SD = 7.8). Cardiorespiratory capacity expressed as peak VO₂ was thus significantly reduced at 53% (p = .0001) of the control value. Muscle strength expressed as peak isometric torque was significantly lower (p = .01) in patients (mean 148 ± 73Nm) when compared to the control group (mean 261 ± 99Nm). In myositis patients peak VO₂ and peak isometric torque correlate well with each other (r = .7631; p = .0001), but not at all with serum CPK levels (r = .056; p = .869).

Conclusion: Peak VO₂ is significantly diminished in patients with dermatomyositis/polymyositis, compared with age- and sex-matched controls. Serum CPK did not significantly correlate with VO₂. Aerobic exercise testing may be a useful assessment parameter in selected patients with dermatomyositis/polymyositis.

Key Words: Exercise, aerobic; Dermatomyositis; Polymyositis; Rehabilitation.

© 2000 by the American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation

In recent years, outcome assessments of physical strength, endurance, range of motion (ROM), and activities of daily living (ADL) have become important elements of clinical trials and the evaluation of children and adults with various rheumatic diseases. Physical fitness, as an outcome measure, has been less routinely used.

Aerobic exercise is frequently recommended for the comprehensive management of rheumatic disease and physical fitness, including aerobic fitness, has been suggested as an important outcome measure in arthritis. Both isometric and isokinetic strengthening programs increased strength without sustained elevation of serum enzymes in dermatomyositis/polymyositis (DM/PM) patients. Aerobic testing also did not elevate enzymes in these patients. Aerobic testing in children with juvenile DM showed decreased VO₂. A physical training program in DM/PM patients increased muscle strength and cardiorespiratory fitness without any significant change of serum muscle enzymes.

DM/PM are inflammatory myopathies of unknown etiology. Muscle weakness, myalgias, and generalized fatigue lead to decreased use of striated muscles. Direct involvement of cardiac muscle and lung by the disease can reduce cardiopulmonary fitness. Decreased muscle activity leads to further atrophy of muscle fibers and decrease of cardiorespiratory training status. In a healthy population, general health benefits are clearly associated with regular exercise that promotes even a minimal level of fitness.

A diagnosis of PM must include three of the four following criteria: symmetrical muscle weakness by manual muscle testing; muscle inflammation by biopsy and by electromyography; and elevated serum muscle enzymes (creatine phosphokinase [CPK]/aldolase). To have DM, an additional criterion of skin rash must be present. However, there is a poor correlation between inflammatory changes on biopsy and the progression of disease in many patients. Although electromyography is useful in establishing disease diagnosis, its usefulness in determining degree of disease activity has not been established. Muscle enzymes are released from the muscle fiber when it degenerates or its membrane becomes defective. Albeit, studies have suggested that CPK assay is the most sensitive laboratory index of muscle disease. Muscle enzyme levels are limited in their usefulness because they do not consistently reflect disease activity. Nevertheless, laboratory tests are often used for therapeutic monitoring. Assessment of muscle strength is one of the most relevant clinical variables.

The purpose of this study was (1) to determine cardiorespiratory fitness and muscle strength in patients with DM/PM, compared with matched healthy controls; (2) to evaluate the usefulness of exercise testing in these patients; and (3) to relate target parameters of exercise testing to muscle strength and to serum CPK level.
METHODS

Fourteen patients with a diagnosis of primary inflammatory muscle disease as defined by the criteria of Bohan and Peter were enrolled in this study. In all patients with DM/PM muscle biopsies, electromyograms, muscle strength testing, and laboratory studies had been performed to establish the diagnosis. Eight patients were treated with prednisone (up to 15mg/d); four patients received high-dose intravenous immunoglobulins: two patients were additionally on azathioprine, 100 mg/d, and two patients were on cyclosporine A; one patient was treated with a nonsteroidal anti-inflammatory drug only. Patients had inactive or mildly active but stable chronic myositis for at least the 3 months before the observation. Elevation of serum muscle enzyme values at three or more consecutive observations during the preceding 3-month period had to be stable. Inclusion required normal transthoracic routine 12-lead electrocardiogram, hemoglobin/hematocrit above 12/35, normal echocardiogram (DM/PM only), normal spirometry, and inconspicuous clinical cardiopulmonary examination findings. Pretest manual muscle test result of the knee extensors and hip flexors had to be 3+ or greater.

Exclusion criteria included: inclusion body myositis, DM/PM with neoplasms or arthritis, physical inability of patients to pedal an ergometer, increase of muscle destruction during the 3 months before the start of the training program, as indicated by at least a 50% increase of CPK levels over the baseline value, or manifest pulmonary disease secondary to myositis, evidence of parenchymal lung disease, atelectasis) and manifest cardiogenic disorders (eg, cardiomyopathy secondary to myositis, pericardial effusions due to myositis, congestive heart failure, arrhythmias, valvular lesions, or arteriosclerotic heart disease).

Of the 14 patients with DM/PM, 3 were excluded. One man had a myocardial infarction 6 months earlier and a pathologic echocardiogram; one woman had signs of a restrictive lung disease in the spirometry; and another woman had a hemoglobin/hematocrit of <12/35.

Twenty-two subjects (8 patients with chronic DM, 3 patients with chronic PM, and 11 healthy controls) participated, allowing the identification of 11 case-control pairs matched by age (±3 years) and gender (mean age, 48 ± 14 years; ratio of women to men, 18/4). The characteristics of patients with DM and PM were similar.

Healthy controls were between 26 and 72 years of age and had a sedentary lifestyle (no regular physical training program). Before testing, a clinical history, transthoracic routine 12-lead electrocardiogram, blood pressure measurement, and physical examination were performed. Informed consent was obtained from all subjects. The study was conducted at the University Hospital, Vienna.

Each subject performed a subjective maximal graded exercise tolerance test on a cycle ergometer and isometric peak torque measurement of the thigh. All patients had their CPK and aldolase levels measured once before evaluation.

Method of Exercise Testing

Exercise studies were performed in all subjects using a symptom-limited, incremental cycle ergometer protocol. Pedalling at 50 to 60rpm, the work rate was increased every 2 minutes by 25 watts from an initial load of 25 watts. The heart rate was recorded continuously at rest and throughout exercise with a 12-lead electrocardiogram. After each increment, blood pressure was measured. Ventilatory parameters were collected breath by breath using a computer-based device (Sensor Medics 2900 System), and 10-second averages for each parameter were registered. Patients breathed through a mouthpiece connected to a mass flowmeter. Minute ventilation was measured by the thermal conductivity technique. Oxygen uptake (VO₂) was measured with a fast response zirconium-oxide analysers. Anaerobic threshold was determined by using the V-slope technique. Samples of whole blood were taken at rest from the hyperemic earlobe and at maximal exercise with a 20-µL capillary to assess lactate concentration. Peak oxygen uptake (peak VO₂) was defined as the highest O₂ consumption obtained during the symptom-limited exercise test.

Measurement of Muscle Strength

Pretest mean manual muscle test scores for the hip flexors and knee extensors in subjects with DM/PM were observed. The muscle strength of the knee extensors on both the right and left sides was measured by a computerized isokinetic system that measures the peak isometric torque (PIT). This system has been used extensively to measure muscle strength in healthy and in some diseased populations and has been reported to give valid and reliable measurements. The method has been outlined and its utility in assessment of strength in patients with inflammatory muscle disease has been described.

Testing began by positioning the subject in a sitting position with the hips in 90° of flexion. Stabilization straps were positioned across the subject’s chest, pelvis, and anterior thigh of the leg to be tested. The input shaft of the dynamometer was aligned with the axis of the knee joint. The lever arm shin pad was placed just proximal to the malleoli. Isometric strength was tested at −45° knee extension as adjusted by the dynamometer. Measurement of subject’s muscle strength was always done by the same person. During these measurements, the best of three attempts by the individual subject was recorded. Pretest manual muscle test strength of the knee extensors and hip flexors had to be 3+ or greater.

Data Analysis

To assess exercise performance, we chose to analyze maximal heart rate, oxygen uptake (peak VO₂), and exercise duration. We determined ventilatory anaerobic threshold from VO₂ and VCO₂ data using conventional criteria. The measurements of the PIT (in Newton-meters [Nm]) are expressed as the sum of values obtained for the muscle groups. Normal values for CPK in our laboratory are ≤70U/L.

Statistical Analysis

Descriptive statistics (means, standard deviation) were performed on all dependent variables. The exact Mann-Whitney U test served to compare the patients with healthy controls, as implemented in the Statistics Package for Social Sciences. The Pearson correlation coefficient was determined to estimate the correlation (r) between CPK level and target parameters of cardiorespiratory fitness and muscle strength. A p < .05 was considered statistically significant.

RESULTS

The characteristics of the study groups are reported in table 1. Demographic results in the pairs matched for age and gender showed that average body surface area (DM/PM group, 1.828 ± .19m² vs controls, 1.776 ± .17m²) was similar and not statistically different. There were 18 women and 4 men. In patients with DM/PM disease duration was 115 ± 75 months, and their mean CPK level was 205 ± 192 U/L. All patients had a hemoglobin/hematocrit ratio above 12/35 (mean, 13.6 ± 1/40 ± 3). None of the controls had elevated serum levels of CPK.
Exercise Testing

The mean exercise duration for patients with DM/PM was 314sec (range, 130 to 790) and was significantly (p < .0006) shorter than in the controls (mean, 706sec; range, 360 to 1,160). Exercise was terminated in all patients with DM/PM because of peripheral lower extremity muscle fatigue. The mean resting heart rate was 77beats/min (SD = 8) and increased throughout exercise in patients with DM/PM to a mean peak heart rate of 131beats/min (SD = 19). The mean resting heart rate of the controls was not significantly lower, 76beats/min (SD = 7), whereas the mean peak heart rate was higher, 166beats/min (SD = 22; p = .0014). Sinus rhythm was present in all subjects at rest and during exercise. No serious arrhythmias were seen and no test was terminated because of arrhythmia. None of the patients experienced a blood pressure decrease during the test.

At ventilatory anaerobic threshold, mean VO2 for the patients with DM/PM (8.82mL/min/kg; SD = 2.1) was statistically significantly lower than it was in the matched controls (15.92mL/min/kg; SD = 4.76; p = .0001). Thus, ventilatory anaerobic threshold VO2 in patients with DM/PM was only 55% of the value found in the healthy control subjects.

The mean peak VO2 in patients with DM/PM was 15.28mL/min/kg (SD = 5.8); in the controls, it was 28.74mL/min/kg (SD = 7.8). This means that patients with DM/PM achieved only 53% peak VO2 of their matched controls (p = .0001).

No statistically significant correlation (r = −.0566; p = .869) was found in patients with DM/PM between elevation of CPK level and peak VO2.

Muscle Strength

Pretest manual muscle test scores for the hip flexors and knee extensors in subjects with DM/PM were 7.3/10 (range, 7 to 9) and 8.7/10 (range, 8 to 10), respectively. Muscle strength when measured with PIT of knee extensors was significantly lower (p = .0104) in patients (mean, 148 ± 73Nm) than in healthy controls (mean, 261 ± 99Nm). Overall, patients with DM/PM achieved only 57% of the control group’s mean level. There was no statistically significant correlation (r = −.2292; p = .498) of muscle strength and CPK level in DM/PM patients (fig 1). A significant correlation was found between PIT and peak VO2 (r = .7631; p = .0001) or maximal exercise time (r = .8318; p = .001), respectively (fig 2).

DISCUSSION

Our data show that patients with DM/PM are highly impaired in their aerobic exercise capacity when compared with healthy matched controls. Muscle strength, when measured with the PIT of the thigh, significantly correlated with target parameters of exercise testing. There was no serious complication related to the exercise testing. Sinus rhythm was present in all subjects at rest and during exercise. No serious arrhythmias were seen and no test was terminated because of arrhythmia. None of the patients experienced a blood pressure decrease during the test.

The results of this study demonstrate that oxygen uptake at anaerobic threshold in DM/PM patients was significant lower than in their matched controls. This shows that patients with DM/PM have an anaerobic muscle metabolism at low workload. The anaerobic threshold is defined as the maximum exercise intensity at which exercise can be maintained without...
increasing the accumulation of lactate. Exercise above the anaerobic threshold induces a rapid accumulation of lactate and an increase in anaerobic metabolism and increases the secretion of catecholamines and adrenocorticotropic hormone. This low VO2 at anaerobic threshold in patients with DM/PM in comparison to their matched controls could contribute to limited functional capacity in daily activities.

Peak VO2 as our main parameter has traditionally been considered as the “golden standard” of aerobic exercise performance. We preferred to use the term “peak VO2” rather than “VO2 max” because true VO2 max may not have been reached by these sedentary patients, eg, because of fatigue in lower extremity muscles most involved in cycling.

The amount of skeletal muscle is another important determinant of exercise capacity. In younger populations, muscle mass correlates with peak VO2. In women, the reduced peak VO2 compared to men is in part attributable to smaller muscle mass. In elderly or deconditioned populations, loss of muscle mass appears to limit peak VO2. We found a significant correlation between FIT and peak VO2 or maximal exercise time, respectively (fig 2).

The reasons why patients with DM/PM demonstrate impaired exercise capacity remain to be clarified. Nevertheless, the main hypotheses can be considered as (1) sedentary lifestyle because of subjective muscle symptoms or physician’s recommendations, (2) cardiac involvement (myositis of cardiac muscle), (3) pulmonary involvement by myositis, and (4) inflammation of muscle or muscle atrophy from steroids and/or disuse. Glucocorticoids are known to induce muscle atrophy. Patients on prednisone exhibit both a decreased capillary number and a decreased mass of myofibers. It might be that glucocorticoids diminish the myofibers by inhibiting protein synthesis and the capillary number is diminished as a consequence of a reduced mass of myofibers. Alternatively, therapy with glucocorticoids reduces the capillary number and as a consequence the myofibrillar mass shrinks. However, it might be that glucocorticoids affect capillaries and myofibers to a different extent and override mutual adaptive mechanisms between myofibers and capillaries. Cyclosporine has been shown to impair mitochondrial respiration both in vitro and in vivo.

Steroid therapy causes a rather selective atrophy of type II muscle fibers. However, type II muscle fiber atrophy, and hence increased muscle weakness, can also occur in patients with idiopathic inflammatory myopathy because of poor mobility or disuse resulting from active disease or “burn-out” myopathy. Such muscle fiber atrophy can even coexist with features of active myopathy and inflammation. Rather than performing serial muscle biopsies, clinical judgment must distinguish steroid myopathy from inflammatory disease activity. For this purpose, functional assessment is therefore considered to be useful.

We found no statistically significant correlation between elevation of the serum CPK level and target parameters of cardiorespiratory fitness or muscle strength in these patients. These findings are in line with previous observations of no correlation or inconsistent correlation between muscle strength assessment or ADL assessment and elevation of muscle enzymes. Our results confirm the limitation of laboratory values as indicators of activity and severity of disease in these patients. The therapeutic aim for many patients is to achieve a more “effective” lifestyle and to preserve their functioning and well-being. A common practice is the habit of “chasing” or “treating” the creatine kinase level instead of the muscle weakness in patients with inflammatory myopathies.

CONCLUSION

Incremental graded exercise testing with respiratory gas exchange analysis can be safely used in stable inactive or mildly active myositis patients without cardiac involvement to quantitatively assess aerobic capacity. Further studies are needed to clarify the cause of the demonstrated decreased aerobic capacity in DM/PM patients and the clinical value of this testing.

Acknowledgment: We thank Prof. R. Knobler for his cooperation.

References

45. Tarlov AR. Shattuck lecture: the increasing supply of physicians, the changing structure of the health services system and the future practice of medicine. N Engl J Med 1983;308:1235-44.

**“Key Words” Publication Reinstated**

Effective with this issue, the *Archives of Physical Medicine and Rehabilitation* resumes publishing “key words” at the end of article abstracts. The purpose is to assist indexers in cross-indexing articles and to facilitate their retrieval by researchers and other interested readers. Authors submitting manuscripts to the *Archives* should include on the cover page of their manuscripts from three to five key words or phrases taken from the National Library of Medicine publication “Permuted Medical Subject Headings (2000).” Key words or phrases may also be found at the NLM’s website. The address is: www.nlm.nih.gov/mesh.