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ORIGINAL ARTICLE

Anaerobic Exercise Capacity in Patients With Juvenile-Onset Idiopathic Inflammatory Myopathies

TIM TAKKEN, JANJAAP VAN DER NET, AND PAUL J. M. HELDERS

Objective. **To 1) report the feasibility of an "all-out" 30-second cycling exercise test (Wingate Anaerobic Exercise Test [WAnT]) in juvenile-onset idiopathic inflammatory myopathy (JIIM) patients, 2) describe the anaerobic exercise capacity in juvenile dermatomyositis patients, and 3) determine if the anaerobic exercise capacity could be related to disease duration or disease phase.**

Methods. **Twenty patients (age 14.13 ± 5.4 years) with JIIM participated in this study. All patients were able to perform the WAnT without adverse events.**

Results. **Comparison with healthy controls revealed a –29.3 ± 26.58% ($P = 0.001$) and –27.6 ± 25.7% ($P = 0.002$) impairment in mean power and peak power on the WAnT, respectively. The WAnT correlated with disease phase and with knee extensor muscle strength.**

Conclusion. **The WAnT might be a valuable adjunct next to other assessment tools in the followup of JIIM patients.**

KEY WORDS. Short-term muscle power; Exercise tolerance; Exercise test; Children; Adolescents; Juvenile dermatomyositis; Juvenile polymyositis.

INTRODUCTION

The juvenile-onset idiopathic inflammatory myopathies (JIIM) include juvenile dermatomyositis (DM) and juvenile polymyositis (PM) and are a group of autoimmune diseases in which the immune system targets the vascularization of both the skin and muscle. Patients with JIIM often experience strong exercise intolerance. In 1931, Steinitz and Steinfeld reported abnormal muscle creatine levels and glucose metabolism in the muscle of a patient with DM (1). Since then, several authors reported abnormal levels of energy-rich phosphates (adenosine triphosphate, phosphocreatine, inorganic phosphate) and metabolites (e.g., magnesium) in patients with JIIM and IIM. These findings have been reported in both rest and during exercise as measured using ^{31}P magnetic resonance imaging and ^{31}P magnetic resonance spectroscopy (^{31}P MRS) (2–4). Moreover, a defect in the purine nucleotide cycle (adenosine monophosphate deaminase deficiency) in patients with IIM has been found (5). Additionally, during active disease periods, a large loss of muscle bulk occurs in patients with JIIM and IIM (6). These changes in the muscle have a major impact on energy regulation and metabolism. The physical actions (leg raising) studied in these ^{31}P MRS investigations miss a clear relationship with daily activities. Besides, they are very costly.

Exercise testing could be a cheaper and a more function-related alternative, because, at least in Europe, most children and adolescents use a bicycle for transportation purposes (e.g., riding to school). In a previous study, we described the aerobic exercise capacity during treadmill exercise in a sample of patients with juvenile DM and found a relationship with disease phase (7). In the current study, we investigated the anaerobic exercise capacity of patients with JIIM using the Wingate Anaerobic Exercise Test (WAnT), which is a 30-second all-out sprint on a cycle ergometer (8).

Our aims were first to describe the feasibility of the WAnT in patients with JIIM, second to determine whether short-term anaerobic exercise capacity is impaired in patients with JIIM, and third to determine whether the an-

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Tim Takken, MSc, PhD, Janjaap van der Net, PhD, Paul J. M. Helders, PhD: University Hospital for Children and Youth "Het Wilhelmina Kinderziekenhuis," University Medical Center Utrecht, Utrecht, The Netherlands.

Address correspondence to Tim Takken, MSc, PhD, Department of Pediatric Physical Therapy & Exercise Physiology, University Hospital for Children and Youth "Het Wilhelmina Kinderziekenhuis," University Medical Center Utrecht, Room KB.02.056. P.O. Box 85090, 3508 AB Utrecht, The Netherlands. E-mail: t.takken@wkz.azu.nl.

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aerobic exercise capacity could be related to disease duration or disease phase.

PATIENTS AND METHODS

Patients. Nineteen patients with juvenile DM and 1 patient with juvenile PM participated in this study (6 males, 14 females). The patients were recruited from the pediatric rheumatology outpatient clinic of the Wilhelmina Children's Hospital and fulfilled the criteria for the diagnosis of juvenile DM or PM (9). Each patient was classified as having either a monocyclic, polycyclic, or continuous disease course as proposed by Spencer et al (10). Monocyclic is defined as full recovery within 2 years without relapse. Polycyclic is a prolonged, relapsing course with at least 1 relapse occurring while not receiving any medication. A continuous disease course is defined as persistent disease for >2 years despite daily glucocorticoid therapy with all the initial relapses occurring during therapy. In addition, the patients were classified as having active disease, being in clinical remission (remission while taking medication), or being in remission without taking medication. Parents and patients gave their informed consent for participating in the study. The local ethics committee approved all procedures.

Anthropometry. The patients' weight and height were determined using an electronic scale and a measuring stick. Subcutaneous adiposity was measured from skinfold thickness using Harpenden skinfold calipers. Measurements were taken in triplicate at 7 sites (at the right side of the body); triceps, biceps, subscapular, suprailiac, midabdominal, medial calf, and thigh by the test leader conforming to the American College of Sports Medicine guidelines (11). The mean values of the 7 sites were summed (Σ7SF) according Pollack et al (12) and used as an index of subcutaneous adiposity.

Functional ability. Functional ability was measured using the Dutch version of the Childhood Health Assessment Questionnaire (CHAQ) (13) for patients <18 years old and the Dutch version of the Health Assessment Questionnaire (HAQ) (14) for patients >18 years old. Knee extension muscle strength was determined using a Citec handheld myometer (Citex, Groningen, the Netherlands). Published reference values for children (15) and adults (16) were used to compute Z-scores.

Exercise capacity. The WAnT was performed as described by Bar-Or (8) on a recently calibrated electromagnetic braked cycle ergometer (Lode Examiner, Lode BV, Groningen, the Netherlands). The ergometer was upgraded and calibrated by the manufacturer to a maximal resistance of 800 W instead of the standard 400 W. The external resistance was controlled and the power output was measured using the Lode Wingate software package (17). The seat height was adjusted to the patient's leg length (comfortable cycling height).

The external load (torque; in N-m) was determined using bodyweight (at 0.53 × bodyweight and 0.55 × bodyweight for girls and boys <14 years of age and 0.67 × bodyweight and 0.7 × bodyweight for older girls and boys, respectively), according to the user's manual.

The patient's feet were put in the Velcro toe straps and the exercise protocol was explained. The patients were instructed to exercise for 1 minute at the cycle ergometer with an external load of 15 W at 50 revolutions per minute. Thereafter the sprint protocol started. The patients were instructed to cycle all-out for 30 seconds. Measured variables were mean power and peak power and were recorded with a frequency of 5 Hz. Mean power represents the average power output over the 30-second sprint. Peak power is the highest recorded power output achieved during the 30-second sprint. Power output during the WAnT was corrected for the inertia of the mass of the flywheel (23.11 kg/m^2).

The anaerobic exercise capacity of the patients with JIIM was compared with age-, weight-, and sex-matched reference values obtained from 50 healthy Dutch children and adolescents. Control subjects consisted of a sample of 50 healthy children and adolescents in the same age range (23 females, 27 males) matched for weight and sex. The subjects were recruited from family members of staff of our hospital or were living in the neighborhood of our hospital. All controls were tested following the same protocol as the patients.

Statistics. Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (Version 10.0, SPSS Inc., Chicago, IL). Variables were expressed as mean ± SD and range; statistical comparisons between measurements were made by using the Student's *t*-test. The data were also expressed as the percent of impairment compared with reference values. Spearman's correlations and Pearson's correlations were used where appropriate. The level of statistical significance was set at $P = 0.05$.

RESULTS

The mean age of the patients was 14.13 ± 5.4 years (range 8–27), age at disease onset was 7.3 ± 3.4 years, time since diagnosis was 6.8 ± 4.8 years, and the male:female ratio was 6:14. Twelve patients had a monocyclic disease course, 6 patients had a polycyclic disease course, and 2 patients had a continuous disease course. Twelve patients were in remission, 2 patients were in clinical remission, and 5 patients had active disease. The weight of the patients was 49.2 ± 15 kg, the mean height was 1.55 ± 0.12 meters, and body mass index (BMI) was 20.0 ± 4.16 kg/m^2. There was a large range in BMI from 13.1 to 29.4, indicating that our sample consisted of both lipodistrophic and Cushingoid patients. This is also reflected in the sum of the 7 skinfolds, which was 140 ± 71 mm with a range of 35–287 mm. Normal values for our laboratory for the sum of the 7 skinfolds are 100.7 ± 36 mm for girls and 72 ± 28 mm for boys. In the current sample, 6 patients (2 males, 4 females) had a sum of the 7 skinfolds that was 2 standard deviations above healthy children, confirming the Cushin-

Table 1. Anaerobic exercise capacity of JIIM patients*

	JIIM (mean ± SD)	Controls (mean ± SD)	% difference	*P*
Mean power (watt)	256.25 ± 98.95	407.2 ± 188.9	−29.3 ± 26.58	0.001
Peak power (watt)	464.85 ± 216.3	703.02 ± 339.9	−27.6 ± 25.7	0.002

* JIIM = juvenile-onset idiopathic inflammatory myopathy.

goid appearance. Seven patients were taking prednisone, with a mean dosage of 30 ± 28.6 mg/day (range 3.5–90). Mean CHAQ/HAQ score of the patients was 0.65 ± 0.79 (range 0.0–2.63) and mean Z-score for knee extension muscle strength was –1.46 ± 1.56 (range –3.8 to +2.9) standard deviations lower than reference values.

All patients were able to complete the 30-second bicycle sprint. No adverse events were reported after the tests. The results of anaerobic exercise tests are depicted in Table 1, as are comparisons with the healthy controls. The results indicate that the anaerobic exercise capacity is indeed reduced in patients with JIIM and was almost 30% lower for both peak power and mean power compared with the healthy controls.

In Figure 1, the percentage impairment of anaerobic exercise capacity of patients with JIIM can be appreciated. This figure shows a large variability in anaerobic capacity. Some patients performed average or just above, whereas others scored almost 80% lower than predicted. It is noteworthy to mention that 3 of the 4 adult patients (>18 years) still had an impaired anaerobic exercise capacity, although their disease was considered in remission for many years. These 3 patients were also partly unfit for labor.

Table 2 displays the correlation coefficients of the percentage impairment in anaerobic exercise capacity with selected physical variables. There was a significant negative correlation with subcutaneous adiposity and with disease phase. Percentage of predicted anaerobic exercise capacity did not correlate with age. Anaerobic exercise capacity was only borderline significantly positively associated ($P = 0.05–0.1$) with disease duration.

DISCUSSION

The JIIM are a group of significant illnesses leading to exercise intolerance, disability, and physical inactivity. Since the introduction of new therapies, the attention of outcome measures has shifted from mortality toward morbidity, functional ability, and exercise capacity (18). The aim of this study was to describe the feasibility of the WAnT in patients with JIIM, to compare their anaerobic exercise capacity with that of healthy controls, and to relate the anaerobic exercise capacity to disease duration or activity.

Aerobic exercise tests are performed in patients with juvenile (7,19) and adult DM/PM (20,21), but this is the

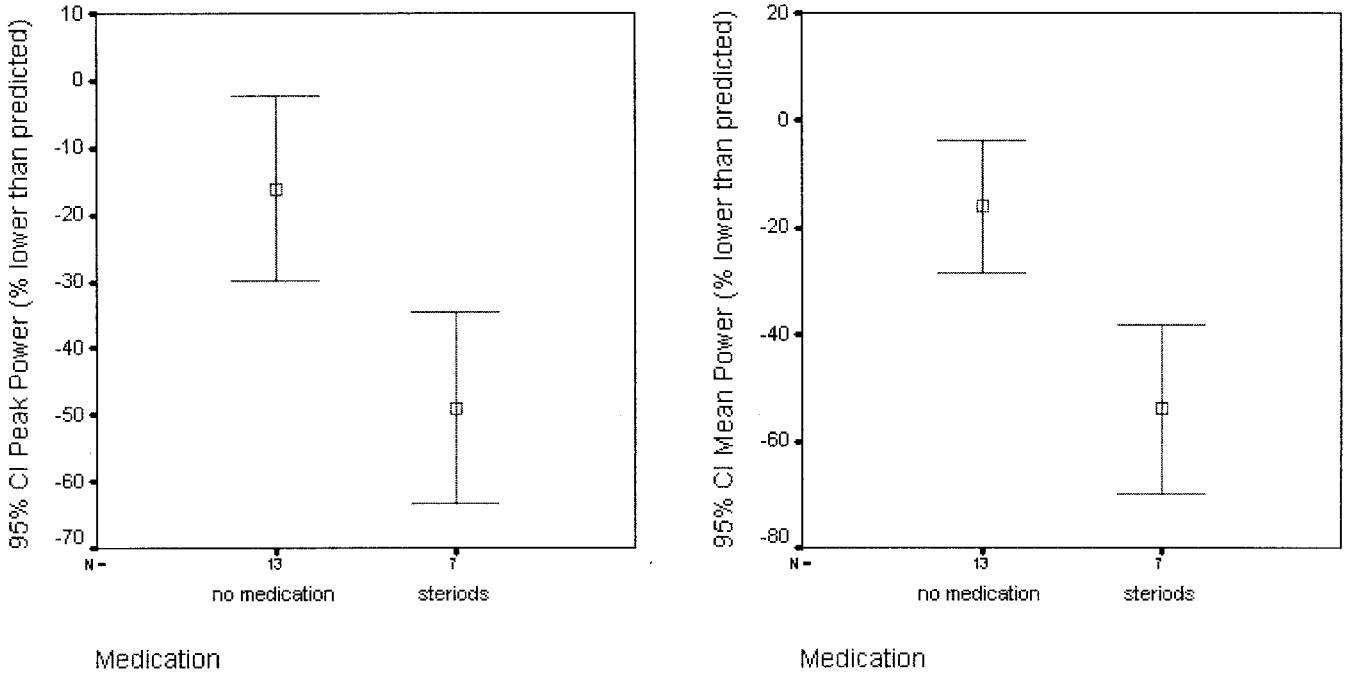

Figure 1. Percentage impairment in anaerobic capacity of patients with juvenile-onset idiopathic inflammatory myopathies. Values are expressed as a percentage difference compared with healthy subjects. A positive value indicates a value above predicted, a negative value indicates a lower value compared with healthy controls. The left panel depicts the 95% confidence interval (95% CI) of peak power, the right panel depicts the 95% CI of mean power.

Table 2. Correlation coefficients of percentage impairment in anaerobic exercise capacity with selected physical variables

	Age	Disease duration	Disease phase	Subcutaneous adiposity	Z-score strength knee extension
Mean power	−0.1	0.38	−0.76*	−0.79*	−0.43†
Peak power	−0.09	0.41	0.7*	−0.75*	−0.49‡

* $P < 0.0001$.
† $P = 0.05–0.1$.
‡ $P < 0.05$.

first study exploring the anaerobic exercise capacity in patients with JIIM. We found an almost 30% decrease in anaerobic exercise capacity in patients with JIIM. This decrease might be explained by the lower adenosine triphosphate and phosphocreatine levels found in muscles of patients with juvenile DM in a previous study using MRS in rest, during exercise, and during recovery (2). These 2 energy-rich phosphates are the major fuel source during short-term, high-intensity exercises. The decrease in anaerobic exercise capacity might also be explained by the fact that during high-intensity exercise, such as in WAnT, type II muscle fibers are recruited predominantly. Corticosteroid therapy causes a more pronounced atrophy of these type II muscle fibers compared with type I muscle fibers (22), which might account for the decreased anaerobic exercise capacity. The limited cycle exercise may be influenced by leg muscle weakness. Hilario et al (6) found the greatest muscular atrophy in the gluteus maximus and the quadriceps muscle of patients with juvenile DM, 2 muscles used in cycling exercise. The significant correlation between peak power and knee extensor muscle strength in this study confirms this; however, it explained only 24% of the variance in peak power. This confirms that anaerobic exercise capacity is dependent on multiple factors. Other contributing factors of the decreased anaerobic exercise capacity might be a reduced motor unit activation, and muscle atrophy due to hypoactivity (23).

The significantly negative correlation between disease phase and percent of the predicted anaerobic exercise capacity indicated that the decline in anaerobic exercise capacity was not only related to physical inactivity, but also to disease activity. Moreover, there was a significant negative correlation between subcutaneous adiposity and percentage of predicted anaerobic capacity. This might be explained, at least in part, by the relationship between disease phase and subcutaneous adiposity ($r = 0.49$, $P = 0.03$), illustrating the effects of corticosteroid therapy on subcutaneous adiposity. Moreover, myopathic obesity, similar to rheumatic obesity (24), might also account for the increased body fat levels and the reduced exercise capacity. In several diseases, a significant relationship has been found between plasma levels of inflammatory parameters (in particular tumor necrosis factor α) and protein breakdown (25). In addition, during the restoration phase, the damaged muscle tissue might be in part replaced by adipose tissue, altering the body composition of these patients (24,26).

One of the limitations of this cross-sectional study is the small sample size. However, juvenile DM is a very rare disease. Previous studies on exercise testing in juvenile DM patients had only sample sizes of 12 (27), 14 (19), and 15 patients (7). To improve sample size, a multicenter approach should be initiated. With a larger patient sample, physical and physiological factors contributing to the anaerobic exercise capacity could be found. In the present study, we found a wide range in anaerobic capacity in JIIM patients. It is our clinical experience that anaerobic capacity alters with changes in disease activity (T. Takken, unpublished observations). This indicates that the anaerobic capacity of JIIM patients is not a fixed variable. As can be appreciated from Figure 1, patients in disease remission (no medication group) do have better anaerobic capacities than the patients with an active JIIM or who are in clinical remission (steroids group). This indicates that there could be a regeneration of muscle function after a period of active disease.

The impairment in anaerobic exercise capacity might have a strong clinical implication because a lot of activities of daily living, such as play, leisure, and sports activities, are short term and high intensity (anaerobic) in nature (28). Impairment in anaerobic exercise capacity makes these activities difficult to perform or they cannot be performed at all. In a previous study of patients with juvenile idiopathic arthritis, we found a significant relationship between anaerobic exercise capacity and functional ability (29). This shows the importance of anaerobic exercise capacity for the performance of activities of daily living in pediatric rheumatology patients.

The above findings support the notion of improving anaerobic exercise capacity in patients with JIIM. Supplementation of creatine monohydrate in patients with JIIM might improve anaerobic exercise capacity. In a supplementation study with a group of patients with various neuromuscular disorders, including adult DM and PM, a significant improvement in muscle strength was observed (30). In addition to supplementation of performance-enhancing substances, exercise training could be a way to increase the anaerobic exercise capacity in patients with JIIM. In patients with DM and PM (31–34) and inclusion body myositis (35), physical training studies have shown improvement in exercise capacity. One of these studies observed an increase in percentage of type I muscle fibers and an increase in cross-sectional area of type II muscle fibers in PM and DM patients after a dynamic strength training program (36). Therefore, it would be very interesting and clinically relevant to start a study exploring the effects of a physical training program in patients with JIIM.

In summary, the WAnT is a feasible exercise test in patients with JIIM, and it showed an almost 30% decrease in the anaerobic exercise capacity of patients with JIIM.

The WAnT might be a valuable adjunct next to other assessment tools, such as the CHAQ, Childhood Myositis Assessment Scale, myometry, and aerobic exercise tests. However, the reliability of the WAnT has not been established within this patient population. Since the reliability of an exercise test is very important for evaluative purposes, a future study should address this issue.

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REFERENCES

1. Steinitz H, Steinfeld F. Untersuchungen zum Kreatinstoffwechsel bei Dermatomyositis. Zeitschrift fuer die Gesamte Experimentelle Medizin 1931;79:319–28.
2. Park JH, Niermann KJ, Ryder NM, Nelson AE, Das A, Lawton AR, et al. Muscle abnormalities in juvenile dermatomyositis patients: P-31 magnetic resonance spectroscopy studies. Arthritis Rheum 2000;43:2359–67.
3. Niermann KJ, Olsen NJ, Park JH. Magnesium abnormalities of skeletal muscle in dermatomyositis and juvenile dermatomyositis. Arthritis Rheum 2002;46:475–88.
4. Newman ED, Kurland RJ. P-31 magnetic resonance spectroscopy in polymyositis and dermatomyositis: altered energy utilization during exercise. Arthritis Rheum 1992;35:199–203.
5. Sabina RL, Sulaiman AR, Wortmann RL. Molecular analysis of acquired myoadenylate deaminase deficiency in polymyositis (idiopathic inflammatory myopathy). Adv Exp Med Biol 1991;309B:203–5.
6. Hilario MO, Yamashita H, Lutti D, Len C, Terreri MT, Lederman H. Juvenile idiopathic inflammatory myopathies: the value of magnetic resonance imaging in the detection of muscle involvement. Sao Paulo Med J 2000;118:35–40.
7. Takken T, Spermon N, Helders PJ, Prakken AB, van der Net J. Aerobic exercise capacity in patients with juvenile dermatomyositis. J Rheumatol 2003;30:1075–80.
8. Bar-Or O. The Wingate anaerobic test: an update on methodology, reliability and validity. Sports Med 1987;4:381–94.
9. Bohan A, Peter JB. Polymyositis and dermatomyositis (second of two parts). N Engl J Med 1975;292:403–7.
10. Spencer CH, Hanson V, Singsen BH, Bernstein BH, Kornreich HK, King KK. Course of treated juvenile dermatomyositis. J Pediatr 1984;105:399–408.
11. Latin RW. Surface anatomy. In: Roitman JL, editor. ACSM's resource manual for guidelines for exercise testing and prescription. 3rd ed. Baltimore: Williams and Wilkins; 1998. p. 89–100.
12. Pollack ML, Schmidt DH, Jackson AS. Measurement of cardio-respiratory fitness and body composition in the clinical setting. Compr Ther 1980;6:12–27.
13. Wulffraat N, van der Net JJ, Ruperto N, Kamphuis S, Prakken BJ, Ten Cate R, et al. The Dutch version of the Childhood Health Assessment Questionnaire (CHAQ) and the Child Health Questionnaire (CHQ). Clin Exp Rheumatol 2001;19 Suppl 23:S111–5.
14. Bijlsma JWJ, Oude Heuvel CHB, Zaalberg A. Development and validation of the Dutch questionnaire capacities of daily life (VDF) for patients with rheumatoid arthritis. J Rehabil Sci 1990;3:71–4.
15. Beenakker EA, van der Hoeven JH, Fock JM, Maurits NM. Reference values of maximum isometric muscle force obtained in 270 children aged 4–16 years by hand-held dynamometry. Neuromuscul Disord 2001;11:441–6.
16. Bohannon RW. Reference values for extremity muscle strength obtained by hand-held dynamometry from adults aged 20 to 79 years. Arch Phys Med Rehabil 1997;78:26–32.
17. Lode. Wingate software. In. Version 1.09 for DOS ed. Groningen, the Netherlands: Lode B.V.; 1999.
18. Takken T, Elst E, Spermon N, Helders PJ, Prakken AB, van der Net J. The physiological and physical determinants of functional ability measures in children with juvenile dermatomyositis. Rheumatology (Oxford) 2003;42:591–5.
19. Hicks JE, Drinkard B, Summers RM, Rider LG. Decreased aerobic capacity in children with juvenile dermatomyositis. Arthritis Rheum 2002;47:118–23.
20. Wiesinger GF, Quittan M, Nuhr M, Volc-Platzer B, Ebenbichler G, Zehetgruber M, et al. Aerobic capacity in adult dermatomyositis/polymyositis patients and healthy controls. Arch Phys Med Rehabil 2000;81:1–5.
21. Hebert CA, Byrnes TJ, Baethge BA, Wolf RE, Kinasewitz GT. Exercise limitation in patients with polymyositis. Chest 1990;98:352–7.
22. Plotz PH, Dalakas M, Leff RL, Love LA, Miller FW, Cronin ME. Current concepts in the idiopathic inflammatory myopathies: polymyositis, dermatomyositis, and related disorders. Ann Intern Med 1989;111:143–57.
23. McComas AJ, Belanger AY, Garner S, McCartney N. Muscle performance in neuromuscular disorders. In: Jones NL, editor. Human muscle power. Champaign (IL): Human Kinetics; 1986. p. 309–24.
24. Walsmith J, Roubenoff R. Cachexia in rheumatoid arthritis. Int J Cardiol 2002;85:89–99.
25. Roubenoff R, Roubenoff RA, Cannon JG, Kehayias JJ, Zhuang H, Dawson-Hughes B, et al. Rheumatoid cachexia: cytokine-driven hypermetabolism accompanying reduced body cell mass in chronic inflammation. J Clin Invest 1994;93:2379–86.
26. Sharma R, Anker S. Cytokines, apoptosis and cachexia: the potential for TNF antagonism. Int J Cardiol 2002;85:161–71.
27. Drinkard BE, Hicks J, Danoff J, Rider LG. Fitness as a determinant of the oxygen uptake/work rate slope in healthy children and children with inflammatory myopathy. Can J Appl Physiol 2003;28:888–97.
28. Bailey RC, Olson J, Pepper SL, Porszasz J, Barstow TJ, Cooper DM. The level and tempo of children's physical activities: an observational study. Med Sci Sports Exerc 1995;27:1033–41.
29. Takken T, van der Net J, Helders PJ. Relationship between functional ability and physical fitness in juvenile idiopathic arthritis patients. Scand J Rheumatol 2003;32:174–8.
30. Tarnopolsky M, Martin J. Creatine monohydrate increases strength in patients with neuromuscular disease. Neurology 1999;52:854–7.
31. Wiesinger GF, Quittan M, Aringer M, Seeber A, Volc-Platzer B, Smolen J, et al. Improvement of physical fitness and muscle strength in polymyositis/dermatomyositis patients by a training programme. Br J Rheumatol 1998;37:196–200.
32. Wiesinger GF, Quittan M, Graninger M, Seeber A, Ebenbichler G, Sturm B, et al. Benefit of 6 months long-term physical training in polymyositis/dermatomyositis patients. Br J Rheumatol 1998;37:1338–42.
33. Alexanderson H, Stenstrom CH, Jenner G, Lundberg I. The safety of a resistive home exercise program in patients with recent onset active polymyositis or dermatomyositis. Scand J Rheumatol 2000;29:295–301.
34. Varju C, Petho E, Kutas R, Czirjak L. The effect of physical exercise following acute disease exacerbation in patients with dermato/polymyositis. Clin Rehabil 2003;17:83–7.
35. Arnardottir S, Alexanderson H, Lundberg IE, Borg K. Sporadic inclusion body myositis: pilot study on the effects of a home exercise program on muscle function, histopathology and inflammatory reaction. J Rehabil Med 2002;35:31–5.
36. Esbjornsson-Liljedahl M, Dasmalchi M, Alexanderson H, Stahlberg M, Lundberg IE. Changed muscle morphology in myositis patients following a home exercise program. In: Klarlund Petersen B, Febbraio M, Fleshner M, editors. 6th International Society of Exercise Immunology Symposium; 2003; Copenhagen, Danmark; 2003. p. 47.