CASE REPORT

Can patients with McArdle's disease run?

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Patients with McArdle's disease commonly adopt a sedentary lifestyle. This sedentary behaviour, however, usually worsens the limited exercise capacity of these patients. Although eccentric muscle work can be associated with rhabdomyolysis, supervised eccentric training with gradually increasing loads has important advantages compared with conventional concentric work, particularly for patients with a poor cardiorespiratory system. We report the beneficial effects (particularly, increased $\text{VO}_{2\text{peak}}$ (from 14.6 to 30.8 ml/kg/min) and increased gross muscle efficiency (from 13.8% to 17.2%)) induced by a supervised aerobic training programme of 7 months duration including 3–4 running sessions (≤ 60 min/session) per week in a 38-year-old patient. These preliminary data suggest the potential therapeutic value of this type of exercise in these patients.

Muscle glycogen phosphorylase deficiency (glycogenosis type V or McArdle's disease) is a disorder characterised by marked exercise intolerance—that is, premature fatigue and cramps during exertion, with frequent episodes of rhabdomyolysis.¹ Clinicians caring for these patients commonly recommend that they avoid vigorous physical activity to prevent rhabdomyolysis. Unfortunately, sedentary behaviour may worsen exercise intolerance by further reducing the limited oxidative capacity caused by blocked glycogenolysis. A recent preliminary report has shown the beneficial effects of an approximately 3-month aerobic exercise training programme involving concentric muscle contractions (leg pedalling) on the functional capacity of patients with McArdle's disease.²

Rhabdomyolysis is usually associated with eccentric muscle contractions. In severe cases, marked proteinuria could also occur, with increased risk of acute renal failure. Thus, this type of exercise would seem especially contraindicated in patients with McArdle's disease. However, eccentric muscle work (eg of the quadriceps) is an important part of our everyday activity—that is, in breaking or preventing falls.³ Supervised eccentric training with gradually increasing loads induces important structural and functional adaptations in skeletal muscles: increased hypertrophy and strength, and improved efficiency.³ Compared with conventional concentric work, another advantage of eccentric training, particularly for patients with poor cardiorespiratory systems, is the low energetic cost for a given level of muscle force.⁴

The purpose of this study was to assess the effects of aerobic exercise training involving eccentric muscle work in a patient with McArdle's disease.

CASE REPORT

The patient was a 38-year-old man (170 cm, 53 kg). Informed consent was obtained from the patient and the study was approved by the institutional ethics committee.

He reported muscle weakness and marked exercise intolerance since childhood. He had been sedentary since then and was diagnosed with McArdle's disease at the age of 18 years

with muscle biopsy and genetic analysis.⁵ Resting blood and urine analyses carried out in the past years showed no abnormality except consistently increased serum creatine kinase activity (1000–5000 U/l), indicating an ongoing process of rhabdomyolysis (or increased susceptibility to rhabdomyolysis) even while following a sedentary lifestyle.

In late October 2005, he reported to our laboratory after an overnight fast and underwent both a graded cycle ergometer test for fatigue and a 12-min constant-load test.⁶ To prevent the occurrence of muscle cramps and exercise-induced rhabdomyolysis, the first exercise test was preceded by the ingestion of a 660-ml solution containing 75 g of sucrose.⁷ Gas exchange data and heart rate were collected continuously during the tests. Venous blood samples were obtained for determination of plasma lactate and glucose, and serum creatine kinase. The mean gross mechanical efficiency⁸ was assessed during the constant-load tests.

The patient underwent 3–4 supervised training sessions per week, building up from 10 to 60 min of aerobic exercise involving eccentric muscle work (running) at an intensity of ≤ 80 –85% maximum heart rate.⁸ He underwent heart rate monitoring during each session, which was performed within 1 h after ingesting approximately 100 g of complex carbohydrates (pasta, rice and bread). Additionally, he ingested a commercialised sports drink (330 ml solution containing approximately 30 g of simple carbohydrates (glucose and fructose)) during the warm-up period.

We monitored serum levels of creatine kinase every 2 weeks to ensure that they stayed within the usual limits for this patient (< 5000 U/l). The duration of each session was gradually increased (combining both running and walking bouts) until he was able to complete 60 min of continuous running (approximately 10 km) after 4 months of training. However, when trying to run for longer periods (up to 90 min), he reported marked myalgia, and creatine kinase levels were > 5000 U/l. Accordingly, we instructed the patient to limit the duration of running sessions to ≤ 60 min. He returned to our laboratory after the training period (early June 2006) to repeat the exercise testing protocol.

RESULTS AND DISCUSSION

Table 1 shows the data before training. Glucose-based energy production was evidenced by an increase in blood lactate concentration from 0.8 mmol/l at baseline (before sucrose ingestion) to 1.7 mmol/l at the end of the graded test. The patient experienced acute myalgia in the quadriceps shortly after the beginning of exercise, and his peak oxygen uptake ($\text{VO}_{2\text{peak}}$, the most widely accepted measure of exertional capacity) was very low, slightly above levels (13 ml/kg/min) considered necessary for independent living.

His functional capacity improved with training (table 1). The approximately 53% increase in $\text{VO}_{2\text{peak}}$ and his ability to reach the higher peak heart rate and peak power output were especially remarkable, indicating an improved ability to stress his cardiorespiratory system before the onset of myalgia. Muscle gross efficiency also increased after training and approached the low limits ($\geq 18\%$) of healthy people. He

Table 1 Main laboratory data of the patient before and after the 7-month training programme

	Before training	After training
Blood glucose (mg/dl)		
Before sucrose	82	87
After sucrose (before exercise)	133	135
Blood lactate (mmol/l)		
Before sucrose	0.8	0.8
Serum CK (U/l)		
Before exercise	5682	2641
After exercise	5700	2805
Results of graded tests		
VO _{2peak} (ml/kg/min)	14.6	30.8
Peak power output (watts)	59	120
Peak blood lactate (mmol/l)	1.7	1.8
Peak HR (beats/min)	140	166
Results of 12-min constant-load tests		
Gross muscle efficiency (%)	13.8	17.2
HR (beats/min)	113	95

CK, creatine kinase; HR, heart rate; VO_{2peak}, peak oxygen uptake.

reported an improved sense of well-being and improved ability to perform activities of daily living. He also indicated that he planned to continue systematic exercise training. Interestingly, creatine kinase levels at baseline and after exercise were lower (–51–53%) than before training. This finding is consistent with published data on these patients¹⁰ and suggests that the stimulus for muscle growth prompted by supervised exercise training can to some extent counterbalance the increased susceptibility to muscle injury commonly observed in McArdle's disease.

In summary, carefully supervised running training can be used as a therapeutic tool in patients with McArdle's disease.

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What is already known on this topic

- McArdle's disease (glycogenosis type V) is a genetic disorder (deficiency of muscle glycogen phosphorylase) characterised by marked exercise intolerance and increased risk of exertional rhabdomyolysis.
- Clinicians caring for these patients typically recommend that they adopt a sedentary lifestyle to prevent episodes of severe rhabdomyolysis.

What this study adds

- We report for the first time the beneficial effects of a carefully supervised aerobic training programme involving eccentric muscle work (ie running) on the functional capacity and overall health status of a patient with McArdle's disease.
- Although more research is needed, these preliminary findings suggest the potential therapeutic value of this type of training in patients with McArdle's disease.

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COMMENTARY

This is an interesting case report showing that paradoxically some controlled exercise may benefit patients with McArdle's syndrome, although it has been previously suggested that exercise may be harmful and that patients should abstain from exercise. Although the findings of a case report should be viewed with caution, this paper will hopefully stimulate further research in this field, as it has great potential benefits to those with the disease.

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