CASE REPORT

Exercise capacity in a 78 year old patient with McArdle's disease: it is never too late to start exercising

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Br J Sports Med 2006;**40**:725–726. doi: 10.1136/bjsm.2006.026666

The case is reported of a 78 year old man with McArdle's disease and a history of treated coronary heart disease. Despite the pre-exercise administration of sucrose allowing the patient to exercise with normal physiological responses, and without typical McArdle's symptoms or biochemical evidence of muscle damage, his exercise capacity was very low ($\dot{V}O_2PEAK$ = 10.7 ml/min/kg), probably attributable to his lifetime of sedentary living. The data suggest that, with pre-exercise sucrose administration, such patients may be candidates for systematic reconditioning, which may improve functional capacity and quality of life.

Human muscle glycogen phosphorylase deficiency (McArdle's disease) is a metabolic disorder characterised by considerable exercise intolerance—that is, premature fatigue, myalgia, and cramps during exertion.[1 2] These patients are typically advised to adopt a sedentary lifestyle to prevent episodes of severe and potentially life threatening rhabdomyolysis. However, this sedentary behaviour may compound the exercise intolerance and reduce quality of life. Sedentary habits induce muscle catabolism and contribute to a further decrease in functional capacity and the development of cardiovascular disease.

The deleterious effects of lifelong sedentary habits may be especially important in older patients, in that ageing per se affects functional capacity through reductions in skeletal muscle energy metabolism and contractile function.[3] No study has assessed the exercise capacity of elderly patients with McArdle's disease, particularly those with concomitant cardiovascular disease. One reason for this lack of data may be the risk of discomfort and rhabdomyolysis.

It was the purpose of this study to assess the exercise capacity of a patient with a primary diagnosis of McArdle's disease and a secondary diagnosis of cardiovascular disease.

CASE REPORT

The patient was a 78 year old man (height 161 cm, body weight 75.5 kg). He provided written informed consent before performing the tests. The study was approved by the local institutional ethics committee.

He reported having experienced muscle weakness, easy fatigability, and intolerance to physical activity since childhood. He had been sedentary since these early years and was not diagnosed with McArdle's disease until 2001 with molecular analysis. Sequencing of the *PYGM* gene evidenced that he was homozygous for the most common R49X mutation.[4] In 1999 he presented with unstable angina, which was successfully treated with angioplasty of the left anterior descending coronary artery. Since then, cardiological check ups have shown no evidence of exertional ischaemia and normal ventricular function. The electrocardiogram was within normal limits. Resting blood and urine analyses evidenced no abnormality except consistently raised creatine kinase activity (~1000 units/l) indicative of muscle injury, a common finding in patients with McArdle's disease. Physical examination showed no abnormality except appreciable muscle atrophy.

The patient reported to our laboratory at 9 am after an overnight fast and performed a graded cycle ergometer test to fatigue (workload increases of 10 W/min, starting at 10 W). To prevent muscle cramps and exercise induced rhabdomyolysis, the exercise test was preceded by the ingestion (30 minutes before exercise) of 660 ml solution containing 75 g sucrose[5] and a 10 minute warm up period (freewheel pedalling). Gas exchange data were collected breath by breath to determine peak oxygen uptake ($\dot{V}O_2PEAK$). Heart rate (beats/min) was monitored from the electrocardiogram.

Capillary blood samples for the measurement of lactate, glucose, and ammonia concentrations were obtained from a fingertip during the graded test. Total creatine kinase activity and cardiac troponin I concentration were measured in venous blood before and one hour after testing to detect skeletal muscle or myocardial damage induced by exercise.

The subject tolerated the exercise task relatively well and did not report muscle cramps, but did experience local fatigue in the quadriceps muscle by the end of the graded test. Concentrations of cardiac troponin I before and after the exercise were within normal limits (<0.01 ng/ml), ruling out myocardial damage caused by the exercise, and creatine kinase activity was unchanged after exertion (921 and 891 units/l before and after exercise). Glucose concentrations were consistently above 100 mg/dl during exercise.

$\dot{V}O_2PEAK$ and peak power output were 10.7 ml/kg/min and 55 W respectively. Heart rate increased to 140 beats/min—that is, ~99% of age predicted maximal heart rate. Lactate concentration at baseline (before sucrose administration) was 0.9 mmol/l—that is, typical of values reported for patients with McArdle's disease,[5] and increased to a peak value of 4.0 mmol/l.

DISCUSSION

Despite the fact that sucrose administered to the patient before exercise allowed exercise to be performed with minimal symptoms, the $\dot{V}O_2PEAK$ (~11 ml/kg/min) was very low—that is, below levels (13 ml/kg/min) considered necessary for independent living and at least 50% lower than values previously reported in younger patients with McArdle's disease (men and women, <50 years) and in carriers of the most common R49X and/or G204S mutations (after sucrose administration).[6] $\dot{V}O_2PEAK$ was also lower than values (~15 ml/kg/min) reported for patients with McArdle's disease not receiving sucrose administration and thus with blocked glycolysis.[7] Thus our results suggest that the most likely outcome in patients with McArdle's disease during the last decades of their life is a considerable decrease in $\dot{V}O_2PEAK$,

What is already known in the topic

- McArdle's disease is a genetic disorder characterised by considerable exercise intolerance—that is, premature fatigue, myalgia, and cramps during exertion
- Patients are typically advised to adopt a sedentary lifestyle to prevent episodes of severe and potentially life threatening rhabdomyolysis

What this study adds

- The exercise capacity of a 78 year old man with McArdle's disease and a history of treated coronary heart disease was very low ($\dot{V}O_2PEAK$ = 10.7 ml/min/kg), probably attributable to a lifetime of sedentary living
- The data suggest that even elderly patients with McArdle's disease may be candidates for systematic reconditioning, which may improve functional capacity and quality of life

which is at least partially attributable to their very sedentary lifestyle. This is an important consideration as $\dot{V}O_2PEAK$ is an excellent indicator of health status and one of the most powerful independent predictors of mortality in both healthy and diseased humans.[8]

In the past, exercise has generally been considered inappropriate for frail or very aged people because of both low expectations of benefit and exaggerated fears of exercise related injury. Fortunately, extensive research provides reassurance of the safety of exercise in even the oldest adults (including those suffering from various types of chronic diseases), and shows that subjects such as the one studied here should be encouraged to participate in regular exercise as an effective intervention to attenuate the functional decline that accompanies ageing.[9 10]

ACKNOWLEDGEMENTS

This work was supported by grants from FIS numbers PI040487, PI041157, and PI040362.

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Competing interests: none declared

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Accepted 20 March 2006

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COMMENTARY

Over the last few decades, physical activity has become recognised as having a major role in combating many disease states. Physical inactivity is a primary risk factor for cardiovascular disease because of its positive effects on the other primary cardiovascular risk factors of hypertension, blood lipid profile, and obesity. Physical activity is now also recognised as having a preventive role for some types of cancer. This article addresses a new disease state, McArdle's disease, where physical activity may be beneficial. It is hoped that it will be a starting point for the examination of possible positive benefits on the overall health status, as well as improving the quality of life, of patients with McArdle's disease.

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