Lifestyle program in treatment of Pompe disease. Combining exercise training and dietary intervention.

Published: 04-05-2021
Last updated: 19-08-2024

To determine the effect of a personalized lifestyle program on endurance, muscle strength, muscle function, core stability, quality of life, bone mineral density, body composition, energy expenditure, physical activity, muscle morphology,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolism disorders NEC
Study type	Interventional

Summary

ID

NL-OMON50978

Source
ToetsingOnline

Brief title
Lifestyle in Pompe disease.

Condition

- Metabolism disorders NEC
- Muscle disorders

Synonym
Pompe's disease; Glycogen storage disease type II (GSD II); Acid maltase deficiency.

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Prinses Beatrix Spierfonds

Intervention

Keyword: Diet, Exercise, Lifestyle, Pompe

Outcome measures

Primary outcome

Endurance: highest volume of oxygen uptake during maximal effort performing a cardiopulmonary incremental exercise test (VO2peak in millilitres/kilogram/minute).

Secondary outcome

* Functional endurance: highest workload (Wmax) in Watts during a maximal incremental cardiopulmonary exercise test; 6 minutes walking test in meters. *Muscle strength: hand held dynamometer in Newton; manual muscle testing according to medical research council 0-5* Muscle function: Quick Motor Function Test (QMFT), scores 0-64; timed tests in seconds.* Quality of life: SF-36 questionnaire, scores 0-100; Fatigue Severity Scale, scores 9-63.*Core stability: balancing times in seconds. *Bone mineral density and body composition: by dual energy X-ray absorptiometry: total body mineral, lean, fat and fat-free body mass in kilograms and percentages; Bone mineral density in grams/square foot centimetres. Abdominal, waist, arm and leg circumference and skinfold measurements in centimeters * Energy expenditure: by indirect calorimetry in kilocalories/day.*Muscle morphology: by histologic examination of muscle biopsies; magnetic resonance imaging of muscles (optional). *Physical activity: by ActiGraph activity monitor in activity counts and daily activity percentages.*Respiratory function: by spirometry: forced expiratory volume in one second, forced vital capacity (while sitting and supine) and total lung

capacity in litres; mean inspiratory and expiratory pressures in kilo Pascal.

*Metabolic state: blood samples on creatine kinase in units/litre, aspartate amino transferase in units/litre, alanine amino transferase in units/litre, creatine in micromole/litre, alkaline phosphatase in units/liter, gamma-glutamyltransferase in units/liter, triglycerides, cholesterol, HDL cholesterol, LDL cholesterol in millimole/litre, glucose in millimole/litre, HbA1c in millimole/mol and insulin in milliunits/litre.

Study description

Background summary

Glycogen storage disease type II is also known as Pompe disease. This is a rare autosomal recessive disorder with a deficiency of lysosomal enzyme acid α-1,4-glucosidase.This results in accumulation of glycogen mostly in cardiac, skeletal and smooth muscle cells. Pompe disease displays a broad clinical spectrum. Patients with the classic infantile subtype are severely affected with hypotonia and cardiomyopathy from the first months of life. Without treatment patients die within the first year of life due to cardiorespiratory failure. Late onset Pompe disease varies in onset from early childhood to the 6th decade of life, if this is under the age of 18, it is also classified as juvenile onset. Severity of the phenotype varies but all patients show progressive muscle weakness with a limb-girdle distribution, and weakness of respiratory muscles. Eventually, these patients become wheelchair and/or ventilator dependent. Pompe disease is the first myopathy to be treated with enzyme replacement therapy (ERT), which is implemented in 2006. This therapy improves muscle strength, muscle function, and stabilizes respiratory function. However, there is individual variation in response to ERT, targeting the enzyme to skeletal muscles remains difficult and not all muscle damage is reversed. Furthermore, other disease related factors influence the condition of Pompe patients: first, at least in part related to physical inactivity and a decreased resting metabolism, patients are often overweight. Fifty percent of the Dutch Pompe patient population has a BMI >= 25.This overweight further inclines mobility of the patients and negatively influences respiratory function. Second, reduced mechanical forces on the skeleton, lowers the patients* bone mineral density, predisposing to development of osteoporosis. Third we found a higher incidence of hypertension and signs of increased aortal stiffness in our patients. All these factors predispose patients to

cardiovascular disease and diabetes and all these factors may benefit from a life style intervention. However, unaccompanied dieting or training by patients with a myopathy may lead to increased loss of muscle mass. Therefore we think personalized lifestyle programs, developed by a team specialized in Pompe disease and lifestyle, comprising exercise training and dietary intervention are strongly needed to complement enzyme replacement therapy.
Our team has already demonstrated improvement of cardiorespiratory fitness, muscle strength and physical functioning from a feasible and safe training program of 12 weeks in mildly affected Pompe patients. However, data on efficacy and safety of a complete life style intervention are limited. Only two previously published studies concern a lifestyle intervention comprising dietary intervention and exercise, but both studies have major limitations including a very small amount of patients and do not provide psychological guidance. Our aim is to implement a personalized lifestyle program combining exercise and dietary intervention, with psychological support, in the largest population of late onset Pompe patients so far.

Study objective

To determine the effect of a personalized lifestyle program on endurance, muscle strength, muscle function, core stability, quality of life, bone mineral density, body composition, energy expenditure, physical activity, muscle morphology, respiratory function and metabolic state.

Study design

Interventional cohort study. First 12 weeks patients will maintain their usual daily activities and intake. In the second 12 weeks patients start following a personalized lifestyle program. Measurements are performed at the start, 12 and 24 weeks. When not on ERT, patients can start the lifestyle program without a resting phase. When not on ERT the duration of the lifestyle program is 12 weeks.

Intervention

Based on patients* energy requirement and physical ability to perform exercise, a personalized lifestyle program will be made. Program duration is 12 weeks. A combination of endurance, resistance and core stability training will be implemented. Patients will exercise at a maximum of three times a week for 60 to 90 minutes per session at their local physiotherapy practices The dietary intervention will be based on patients* BMI (underweight <18,5, normal 18,5-24.9 and high >=25) giving rise to respectively a hypercaloric, isocaloric or hypocaloric feeding, which always consists of high-protein, low-carbohydrate and normal fat content diet. A lifestyle coach will help the patients to adjust their lifestyle to the proposed interventions.

Study burden and risks

The study requires a time investment of 24 weeks. Patients visit our outpatient clinic for measurements at the start ,12 and 24 weeks (only at the start and 12 weeks when not on ERT). These measurements are distributed over two days, meaning patients will visit our outpatient clinic on a total of 6 days (4 days when not on ERT) during the program. Two of these days will coincide with their regular outpatient clinic visits. Because an incremental exercise test could affect another test outcome, two measurement days are required. The following measurements are performed at our outpatient clinic: height, weight, abdominal and hip circumference, skinfold thickness measurement; blood pressure measurements; blood sampling; incremental cardiopulmonary exercise testing (CPET) with measurement of gas exchange variables, 12-lead electrocardiography, pulse oximetry, heart rate, and intermittent non-invasive blood pressure during exercise, using a cycle; submaximal incremental exercise test with measurement of gas exchange variables, 12-lead electrocardiography, heart rate, and intermittent non-invasive blood pressure during exercise ; respiratory function tests; muscle strength MRC and HHD; muscle function: timed tests and QMFT; core stability tests; muscle biopsy (optional); MRI-scan of muscles (optional); total Body DEXA-scanning; medical interview and physical examination by sports doctor; nutritional assessment by a dietician with indirect calorimetry. Furthermore, a psychologic assessment and guidance by a psychologist (optional) will be implemented. In the weeks between measurements patients fill out questionnaires, record their daily intake and wear an activity monitor at home for 10 hours a day

Invasive procedures comprise blood sampling (3 samples at the start, 12 and 24 weeks (only 2 samples when not on ERT: at start and 12 weeks). and muscle biopsy which is optional (needle biopsy of the quadriceps muscle, before and after lifestyle intervention). These procedures could lead to pain, hematoma or infection. However these interventions will be performed by trained personnel following hospital protocols. Maximal incremental exercise tests could provoke cardiac arrhythmias, these tests are secured by monitoring with continuous electrocardiograms and frequent bloodpressures. Exercise training is performed 3 times a week, during 60-90 minutes. Training consists of endurance training (tread mill or cycling at submaximal workload), resistance training (consisting of repetitive exercises for arm and leg muscles, with or without weights, during a maximum of three sets of 15-20 repetitions) and core stability training with various planking exercises in accordance of patients* abilities. Exercise could lead to muscle soreness and sports injuries. To prevent these, patients are seen by a sports physician in advance of the program and guided by physiotherapists at each training session. After each training session patients will record their experience in a diary. Patients will follow a dietary intervention (daily, during 12 weeks).The investigator will contact patients weekly. Biweekly blood tests (1 sample) will be performed for safety monitoring. This sampling will be combined with their regular biweekly

treatment through intravenous application of enzyme therapy. Dieticians and psychologist will contact patients during the program to evaluate the adherence and give guidance where needed.

Based on our previous experience in training mildly affected Pompe patients, which was feasible and safe, we expect no major complications. We expect all patients to benefit from a lifestyle program. Patients will be able to continue training, dietary therapy, guidance by a dietician and a psychologist after this study.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewatwrplein 40
Rotterdam 3015 GD
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewatwrplein 40
Rotterdam 3015 GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Confirmed diagnosis of late onset Pompe disease measured by decreased acid α-glucosidase activity in leukocytes or fibroblasts and also by mutation analysis.

- Diagnosis is made at the age of >= 1 years.
- Patients are >= 18 years of age.
- Patients sign an informed consent prior to participation.

Exclusion criteria

- Any concurrent medical condition interfering with participation in a lifestyle program.
- Participation in studies on alternative enzyme replacement therapy.
- Treatment with usual care enzyme replacement therapy, (Myozyme ®, Genzyme) for >1 and <52 weeks.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2021
Enrollment:	43
Type:	Actual

Ethics review

Approved WMO

Date:	04-05-2021
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL75553.078.21