Acute Nutritional Ketosis and Exercise in Glycogen Storage Disease type IIIa.

Published: 05-01-2017
Last updated: 14-04-2024

To investigate the potential of a novel dietary substrate preparation to enhance muscle mitochondrial function in GSD IIIa via acute nutritional ketosis. Secondary objectives are to further investigate in vivo exercise tolerance and intramuscular...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON43152

Source
ToetsingOnline

Brief title
Acute Nutritional Ketosis in GSD IIIa

Condition

- Metabolic and nutritional disorders congenital
- Inborn errors of metabolism

Synonym
Cori Disease, glycogen storage disease type IIIa

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Stichting Stofwisselkracht en Stichting Metakids

Intervention

Keyword: exercise, glycogen storage disease type IIIa, ketone esters, magnetic resonance spectroscopy

Outcome measures

Primary outcome

- physical performance during bicycle exercise bout 1

- VO2, VCO2 dynamics during bicycling exercise bout 1.

- steady-state in vivo intramuscular levels of glycogen, Pi, PCr, and pH during exercise bout 2 versus rest.

- kinetic rate constants of metabolic recovery post-exercise bout 2

Secondary outcome

- time of individual desired workload upright bicycling bout (#minutes)

- completion of 10 min supine bicycling bout at desired workload in scanner (yes/no; if no, #minutes)

- subjective fatigue and muscle ache score after each exercise bout (scale 0-10) and 24 hours after exercise

- International Physical Activity Questionnaire

- Muscle ultrasound density of the biceps, quadriceps, calf (gastrocnemius and/or soleus) and tibialis anterior muscles.

- Muscle force unilateral (left) with a hand-held dynamometer (Type CT 3001, C.I.T. Technics, Groningen, The Netherlands).

- Blood levels of glucose, *-hydroxybutyrate, acetoacetate, free fatty acids, insulin, creatine kinase, ammonia, lactate, NT-proBNP and pH prior to and post-exercise.

- Urine levels of myoglobin, ketones, tetraglucoside

- Structural muscle parameters: fat infiltration.

- optional: muscle metabolic profile (according to Cox et. al. 2016 [9]) prior

to and immediately post-exercise (on a patient-voluntary basis).

- optional: individual phenotypic muscle properties (fiber type, mitochondrial

density, capillary density prior to and immediately post-exercise (on a

patient-voluntary basis).

Study description

Background summary

Glycogen Storage Disease type IIIa (GSD IIIa) is an inborn error of carbohydrate metabolism caused by impaired glycogen debranching enzyme (GDE) activity. The ageing GSD IIIa cohort shows that muscle involvement -despite dietary management- is a common disabling phenotype in adulthood. Currently, no specific therapy has been established for muscle problems in adult GSD IIIa patients. However, it could be hypothesized that nutritional ketosis (NK) will be highly beneficial to patients. Amongst others, ketone bodies could take on the role of primary energy source in exercising muscle. Collaborator Kieran Clarke in Oxford and her team have recently produced an edible ketone ester that can achieve acute NK in human subjects via oral ingestion without any undesired side-effects. It was found that the ketone ester produced significant physical performance enhancement in human athletes (Cox et al., 2016. Cell Metabolism). The effect has been attributed to enhanced muscle mitochondrial function in addition to glycogen sparing. Here, we will investigate if acute NK in adult GSD IIIa patients can boost muscle mitochondrial function in vivo.

Study objective

To investigate the potential of a novel dietary substrate preparation to enhance muscle mitochondrial function in GSD IIIa via acute nutritional ketosis. Secondary objectives are to further investigate in vivo exercise tolerance and intramuscular energy balance dynamics during exercise in GSD IIIa patients and to identify phenotypic muscle properties (fiber type, mitochondrial density, capillary density) in GSD IIIa patients before and after exercise.

Study design

This is a randomised, blinded, comparator-controlled, 2-way cross over trial.

Intervention

oral intake of nutritional drinks; moderate-intensity exercise on bicycle ergometer; in vivo Magnetic Resonance Spectroscopy; muscle ultrasound; dynamometry;(optional) muscle microbiopsy; venipuncture.

Study burden and risks

For the nature and extent of the burden and risks associated with participation, benefit and group relatedness we woulde like to refer to point E4, E6 and E9 of this ABR form, and section 11c of the research protocol (C1. Onderzoeksprotocol).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-GSD III confirmed with enzyme assay and/or AGL mutation analysis and GSD IIIa further specified as deficient debranching enzyme activity in muscle or clinical and/or biochemical signs of cardiac and/or skeletal muscular involvement.
-age 18-65

Exclusion criteria

-contraindications for MRI studies (assessed by standardised questionnaire as previously used in METC 08-267/K; see UMCG section F METC documents)
-inability to perform bicycle exercise.
-intercurrent illness which may influence exercise tolerance (anemia, musculoskeletal injury, or other undiagnosed illness under investigation).
-known coronary artery disease, positive history for angina or cardiomyopathy.
-insulin-dependent diabetes mellitus.
-loss of, or an inability to give informed consent.
-pregnancy or current breastfeeding.
-any other cause which in the opinion of the investigators, may affect the participant's ability to participate in the study

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	07-04-2017
Enrollment:	3
Type:	Actual

Ethics review

Approved WMO Date:	05-01-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL59081.042.16