KETOMY: trail, Safety, efficacy and feasibility of ketogenic diet in mitochondrial myopathy,

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Objective: Our proposed pilot study explores the safety, feasibility and efficacy of ketogenic diet in adults with mitochondrial myopathy to improve exercise intolerence and look for biomarkers that might predict patient response to the MAD...

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

Summary

ID

NL-OMON55294

Source
ToetsingOnline

Brief title
KETOMY

Condition

- Metabolic and nutritional disorders congenital
- Inborn errors of metabolism

Synonym
OXPOS deffects, resporatoirychain deffects

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Danone Vitapole,grant gewonnen van

Danone research

Intervention

Keyword: ketogenic diet, mitochondrial disease

Outcome measures

Primary outcome

- Safety

Adverse events

- Feasibility

Number of patients who complete the 12-week intervention

- Efficacy

VO2max/peak during maximal incremental cycle exercise test

Biomarkers

by using metabolomic profiling in plasma.

Secondary outcome

Secondary outcomes safety:

blood test for:

* glucose (for occurrence hypoglycaemia),

* lipid profile: (triglycerides, high-density lipoprotein (HDL), low-density

lipoprotein (LDL), total cholesterol),

* Uric acid

* ALAT

* blood gas (including Bi-carbonate, lactate, glucose, natrium and potassium)

Secondary outcomes:Feasibility

* Number of patients who manage to reach ketone body levels of *2

* Reason of drop out

* Carbohydrate intake in food record as a variable for diet adherence

* Questions on the feasibility of the diet.

Secondary outcomes:Efficacy

* Muscle contractile function

* Fatigue: CIS fatigue

* Quality of life: SF 12

* Headache: diary

* Questions on the benefits of the diet.

* Activity and energy expendure: Actometer (METS)

Study description

Background summary

Mitochondrial myopathy is a common presentation of mitochondrial disease, for which there is no curative therapy. Diet could be an important disease modifier in these patients, since it provides the essential nutrients for mitochondria to produce energy. Ketogenic diet has been proven effective to treat intractable epilepsy in children with or without a mitochondrial disease. In cell studies and mice models for mitochondrial myopathy, ketone bodies or ketogenic diets significantly improve mitochondrial function and delay disease progression. The hypothesis is that because of heterogenicity in MD not al MD patients will respond in the same way to the MAD intervention.
Ketogenic diets can cause side effects, such as headaches, fatigue, weight loss, nausea, and gastro-intestinal symptoms. More recently, a study in five patients with a mitochondrial myopathy showed muscle damage and increased

muscle pain after two weeks modified Atkins diet (mAD) as a potential additional serious adverse event.

Study objective

Objective: Our proposed pilot study explores the safety, feasibility and efficacy of ketogenic diet in adults with mitochondrial myopathy to improve exercise intolerence and look for biomarkers that might predict patient response to the MAD intervention..

Study design

Study design: controlled trial, one armed intervention, pilot study healthy controls just voor metabolomics

Intervention

Modified Atkins diet

Study burden and risks

During the complete study period, patients are asked for a hospital visit six times, of which three will include a maximal incremental cycling test, muscle strength test and physical examination including body composition measurements. The questionnaires and body composition test are non-invasive but the cycling test can be burdensome for patients with a mitochondrial disease who experience exercise intolerance in daily life. Blood sampling: a venous blood sample will be drawn an screening and at every hospital visit (seven times in total). At home, fingerprick blood sampling to control glucose level will be performed by the participant 25 times. At home, a three-day food diary has to be filled in eight times during the study course. An accelerometer, as an activity tracker, has to be worn four times during the study duration and a headache diary has to be filled in whenever such an event occurs. Side effects are scored at every visit or if such an event occurs in between. The diet itself can be a burden because patients are very much restricted in carbohydrates (e.g. the patients cannot eat comfort food or sweets) for 12 weeks. This is difficult for most patients especially in social situations but they also have to cook and shop different products from their normal eating pattern. Last burden for the participants is that the diet might have side effects. Mild side effects especially in the beginning of the diet are known like gastro- intestinal discomfort (constipation and nausea), fatigue, headage and flu-like symptoms (*keto-flu*). These symptoms are usually mild and can be treated with fine tuning of the diet. A more severe possible side effect is muscle pain that is rare in our experience and will be monitored closely in this study.
Blood test for lipids glucose and body composition measurements are preferably

done in a fasting state in the morning. So 3 out of 6 hospital visit need to be in de morning after an overnight fast.

Patient on a ketogenic diet usually lose weight and this can be both a risk as a benefit for patients depending on their nutritional status. The study can give them other benefits as well: it might give them more energy, and improve their exercise intolerance. Ketogenic diet might also improve their migraine, if present. The diet gives participants an opportunity to help find possible new treatment options for this progressive disease wherefor until now treatment options are scarce. It also gives them the means to possible help themselves. Ketogenic diet is commonly discussed and advised in lay-literature and social platforms and we get plenty of questions from patients who want to try it. This study gives them to opportunity to do so in a safe and controlled manner. Because of the weight loss, the lipid profile and cardiovascular risk can improve but on the other hand hyperlipemia as a side effect of ketogenic diet has also been reported.

healthy controls minor risk only midl side effects are espected like gastro intestinal burden

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

1. Genetically proven mitochondrial disease
2. Age * 18 years
3. Myopathy: this can be muscle weakness or exercise intolerance. The NMDAS sub score for muscle weakness(NMDAS part III question 5) and/or exercise intolerance (NMDAS part I question 9) of 1 or higher.
4. Good understanding of the Dutch language
5. Able to adhere to the diet for 12 weeks, considering their cognition level and cooking skill
6. Signed informed consent

for the healthy controls 1 and 6 + healthy no medication and

Exclusion criteria

1. Elevated CK levels > 1000 u/l
2. Malnutrition: BMI < 20 kg/m2
3. Heart failure / patients with pacemaker
4. Diagnosis of familial hypercholesterolemia (because of risk for hyperlipidaemia)
5. Diagnosis of Diabetes Mellitus (because of risk of hypoglycaemia)
6. Unable to conduct the maximal incremental cycle exercise test

Study design

Design

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

Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-10-2020
Enrollment:	35
Type:	Actual

Ethics review

Approved WMO Date:	26-08-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-05-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL74312.091.20