The effect of lipid lowering by Acipimox on cardiac and skeletal muscle mitochondrial function.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON35239

Source
ToetsingOnline

Brief title
ACP-study

Condition

- Heart failures
- Diabetic complications
- Diabetic complications

Synonym
sugar and heartfailure

Research involving
Human

Sponsors and support

Primary sponsor: Center for Translational Molecular Medicine (CTMM)

Source(s) of monetary or material Support: ZonMW-VICI grant P. Schrauwen,CTMM project ' PREDICCt' en EFSD grant,CTMM; Centre for Translational Molecular Medicine

Intervention

Keyword: Acipimox, heart, mitochondria, skeletal muscle

Outcome measures

Primary outcome

Main study parameters are the changes in mitochondrial function, lipid accumulation and cardiac function after Acipimox treatment, compared to the placebo treatment group. As secondary endpoints in changes insulin sensitivity, oxidative stress markers and the relationship with the tissue parameter lipid accumulation are considered.

Secondary outcome

As secondary endpoints in changes insulin sensitivity, oxidative stress markers and the relationship with the tissue parameter lipid accumulation are considered.

Study description

Background summary

Accumulation of lipid in skeletal and cardiac muscle has been associated with insulin resistance and cardiomyopathy. In skeletal muscle lipotoxicity has been suggested to lead to mitochondrial dysfunction. It remains unknown whether lipotoxicity leads to cardiac mitochondrial dysfunction and due to this also leads to cardiomyopathy. Although it has been shown that antilipolytic agents can improve insulin sensitivity, the effect of lowering free fatty acids on cardiac and skeletal muscle mitochondrial function remains unknown.

Study objective

The major research objective is to investigate 1) whether lowering cardiac and

muscular lipid content will improve mitochondrial and cellular function in type 2 diabetic patients, and 2) whether this lipid lowering effect also improves uncoupling in these subjects and leads to a lowering of ROS production.

Study design

Type 2 diabetic patients and their BMI-matched controls will be included in a randomised and blinded cross-over design. Both groups will perform basaline measurements to compare characteristics. Afterwards, only the type 2 diabetic patients will will receive a lipid lowering agent (Acipimox) or placebo for 2 weeks in random order. During these treatments, diabetes medication will be stopped. Baseline measurements will be performed prior to the study and after each treatment to asses cardiac and muscular lipid accumulation, cardiac function, mitochondrial function and insulin sensitivity.

Intervention

Diabetic ubjects will receive Acipimox or a placebo in random order. Acipimox is a commercially available and registrated drug, that lowers free fatty acids by inhibiting hormone sensitive lipase in the peripheral adipose tissue. No serious side-effects are known other than rare anaphylactic reactions.

Study burden and risks

Before the start of the study subjects will be screened to access eligibility (visit duration: 30 min). Subsequently both groups will receive their baseline measurements, for which they have to visit the University twice. Then the diabetic subjects will receive randomized treatments and will receive the baseline measurements twice more. The diabetic subjects will eventually visit the department 7 times (screening and day -2/-1/14/15/56/57) during the 9-weeks study period. The control subjects only visit the University 3 times (screening/-2/-1) in a 2 week period. During these visits three hyperinsulinemic-euglycemic clamps, including 1 muscle biopsy during each clamp, will be performed and 6 MRS-sessions will take place.

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

- male
- BMI>30kg/m2
- non-insulin dependant type 2 DM or controls
- no cardiovascular or DM related diseases
- Use of only metformin or SU-derivates

Exclusion criteria

- no contra-indications for MRS
- No contra-indications Acipimox
- no weight loss/gain last 3 months

Study design

Design

Study type: Interventional

Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-03-2010
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-10-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-11-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-11-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-01-2011

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-04-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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
EudraCT	EUCTR2009-012341-39-NL
CCMO	NL27953.068.09