Effects of ABCA1 Mutations on Glucose Tolerance

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Aim of this study is to address the role of pancreatic ABCA1 dysfunction in humans. We hypothesize that beta cell capacity (insulin production) is reduced in subjects with loss-of-function-mutations in ABCA1.

Ethical review	Approved WMO
Status	Pending
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON30208

Source
ToetsingOnline

Brief title
EAT

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
familial hypoalphalipoproteinemia, laag HDL

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: ABCA1, beta cell, glucose tolerance, insulin

Outcome measures

Primary outcome

Glucose tolerance as measured by OGTT

Secondary outcome

n/a

Study description

Background summary

The ATP Binding Cassette A1 (ABCA1) has been shown to play a pivotal role in high-density lipoprotein (HDL) metabolism, by its capacity to transport intracellular free cholesterol to nascent HDL. Individuals with ABCA1 dysfunction due to hetero- or homozygosity for mutations in the gene encoding for ABCA1 are at increased risk for coronary artery disease. (van Dam et al. Lancet 2002;359:37-42) ABCA1 is widely expressed throughout the body (Wellington et al. Lab Invest 2002;82:273-83), but the contributions of ABCA1 in specific tissues is currently unknown.
Based on its function as a trans-membrane transporter, ABCA1, however, could conceptually be crucial in non-lipoprotein related processes as well.
Recently, Brunham and co-workers have been able to generate a mouse-model, in which ABCA1 is selectively knocked out in specific tissues and organs (J Clin Invest. 2006 Apr;116(4):1052-62). In mice in which ABCA1 was solely knocked out in the pancreas, cholesterol accumulation in beta cells was noticed (unpublished, confidential data). Of special interest was the finding that insulin secretion was significantly reduced in these mice, compared to the wild type controls.
This finding suggests that cholesterol accumulation in beta cells due to ABCA1 dysfunction could be important in the pathophysiology of diabetes.

Study objective

Aim of this study is to address the role of pancreatic ABCA1 dysfunction in humans. We hypothesize that beta cell capacity (insulin production) is reduced in subjects with loss-of-function-mutations in ABCA1.

Study design

Subjects with different degrees of ABCA1 dysfunction and controls will be subjected to a standard oral glucose tolerance test.

Intervention

75 grams of glucose, dissolved in water, for oral use (standard for OGTT)

Study burden and risks

Burden and risks are minimal

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
Nederland
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

Seven subjects, age * 18 years
Body Mass Index 20-35 kg/m2
Able to communicate well with the investigator and to comply with the requirements of the study.
Written informed consent.

Exclusion criteria

No participation in other medical intervention studies in the last three months
No diabetes mellitus

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:	Pending
Start date (anticipated):	15-09-2006
Enrollment:	7
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission

Review commission: METC Amsterdam UMC

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	NL14140.018.06