Peripheral Insulin Uptake in Type 2 Diabetes Mellitus and in Non-Diabetic Individuals

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We hypothesize that impaired insulin uptake into skeletal muscle interstitium (thus decreased transendothelial transport of insulin) is impaired in patients with type 2 diabetes mellitus. This hypothesis will be addressed in the present study.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON38749

Source
ToetsingOnline

Brief title
Peripheral Insulin Uptake Study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes, type 2 diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Kennemer Gasthuis
Source(s) of monetary or material Support: via een beurs van het Posthumus Meyjesfonds

Intervention

Keyword: Glucose metabolism, Insulin uptake, Type 2 Diabetes

Outcome measures

Primary outcome

Primary objective: Is insulin uptake impaired in T2DM patients as compared to non-diabetic individuals, both in the fasted state and during postprandial hyperinsulinemia? (Specific parameters that will be calculated are explained in the study protocol page 7).

Secondary outcome

Secondary objectives: what are determinants of insulin uptake in T2DM patients and in non-diabetic controls (i.e. metabolic parameters known to affect insulin sensitivity, and hemodynamic parameters)? Are glucose uptake and insulin uptake differentially related in T2DM patients as compared to non-diabetics? Does insulin uptake associate with measures of glycemic control such as fasting or postprandial glucose levels and A1C?

Study description

Background summary

Background: Impaired glucose uptake by skeletal muscle is a hallmark of type 2 diabetes mellitus (T2DM) and a significant contributor of postprandial hyperglycemia. Glucose uptake is facilitated by insulin, which promotes glucose transport into skeletal muscle following binding to its insulin receptor on skeletal muscle membrane. However, insulin affects endothelial cells resulting in increased blood flow and recruitment of capillaries, thereby increasing surface for nutrient exchange. There is evidence that insulin uptake into skeletal muscle interstitium is of physiological relevance, however, it is unclear whether this process is impaired in T2DM. We hypothesize that impaired insulin uptake into skeletal muscle interstitium (thus decreased

transendothelial transport of insulin) is impaired in patients with type 2 diabetes mellitus.

Study objective

We hypothesize that impaired insulin uptake into skeletal muscle interstitium (thus decreased transendothelial transport of insulin) is impaired in patients with type 2 diabetes mellitus. This hypothesis will be addressed in the present study.

Study design

Methodology: A prospective, single center study in T2DM patients (n=50) and non-diabetic individuals (n=50) will be performed. During elective coronary angiography (CAG), arteriovenous (AV) balances of glucose and insulin will be measured using the forearm balance method. In each group, 25 patients will be measured in the fasting state, whereas 25 patients will be measured in the postprandial state, i.e. 1 hour following ingestion of an oral glucose tolerance test. Hormones and metabolites of interest will be obtained from blood sampling. Hemodynamic parameters will be derived from doppler/ultra sound measurements (limb blood flow), applanation tonometry (arterial stiffness), continuous non-invasive arterial blood pressure measurements (cardiac index, peripheral resistance, cardiac output and stroke volume) and heart rate variability (autonomic nervous system balance).

Study burden and risks

There are no risks to participate in this study (see above)

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

Inclusion criteria for all participants:
- written informed consent
- hemodynamically stable with a systolic blood pressure > 100 mmHg
Inclusion criteria for non-diabetic individuals:
- 30 years * age * 80 years (extremes included)
- fasting glucose level of < 7.0 mmol/L and HbA1C < 6.5% (<= < 48 mmol/mol)
Inclusion criteria for T2DM patients:
- 30 years * age * 80 years (extremes included)
- fasting glucose level of > 7.0 mmol/L, or HbA1C > 6.5 (<= > 48 mmol/mol) or known T2DM

Exclusion criteria

Exclusion criteria for all participants:
- ongoing myocardial infarction as determined from elevated cardiac markers
- participation in an investigational trial within 90 days prior to present study
- donation of blood (> 100 mL) within 90 days prior to present study
- serious mental impairment or language problems i.e. preventing to understand the study protocol/aim
- Use or recent use (within 3 months of study participation) of oral glucocorticoids
Exclusion criteria for non-diabetic individuals:
- known T2DM/use of glucose-lowering medication
Exclusion criteria for T2DM patients:
- treatment with insulin preparations

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-03-2014
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	16-12-2013
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)

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	NL45266.094.13

Study results

Date completed:	13-05-2015
Actual enrolment:	74