Glucagon challenge in patients with type 2 diabetes mellitus

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

Summary

ID

NL-OMON33022

Source
ToetsingOnline

Brief title
Glucagon challenge T2DM

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Ministerie van OC&W,Roche

Intervention

Keyword: Diabetes, Methodology

Outcome measures

Primary outcome

- Hepatic glucose production

- Plasma glucagon, glucose and insulin concentrations

- Subcutaneous glucose concentrations

- Endothelial function

- Ex vivo cytokine responses in whole blood stimulated with LPS & SEB

Secondary outcome

N/A

Study description

Background summary

Patients with type 2 diabetes mellitus exhibit several abnormalities in hormones involved in glucose homeostasis. Elevated glucagon levels play an important role in the maintenance of increased basal hepatic glucose production and fasting hyperglycemia, demonstrating the possibility of the glycogenolytic pathway as therapeutic target.
The glucagon challenge, allowing assessment of hepatic glucose production, can be used as a tool to assess the anti-glucagonaemic effect of a pharmacological or dietary intervention. In a previous study we evaluated the glucagon challenge as a method to investigate the glycogenolytic pathway in healthy volunteers. In this study we will investigate the glucagon challenge in T2D patients. In addition, the influence of use of oral antidiabetics on the response to glucagon challenge will be investigated. This study integrates investigation of glucose metabolism, endothelial function, and inflammatory state, and allows investigation of the effect of therapeutic intervention on these processes.

Study objective

The main objective of this study is to investigate the effects of a glucagon challenge on hepatic glucose production, abdominal subcutaneous glucose levels in type 2 diabetes patients with and without oral antidiabetics. In addition, endothelial function and possible acute effects of hyperglucagonemia on inflammatory response on a variety of stimuli will be investigated.

Study design

Two-way crossover, intervention study in which subjects will continue (Period A) or discontinue (Period B) their oral antidiabetic agents two weeks before the study day.

Study burden and risks

In this study subjects will participate in two occasions of approximately 20 hours. Especially during the glucagon challange the number of measurements is extensive. Subjects will be asked to stay in bed for six hours. There is a possibility that the glucagon challenge will lead to hyperglycemia during the glucagon challenge or a rebound hypoglycemia afterwards. Therefore, glucose levels will be monitored frequently during and after the challenge. Furthermore, during the wash-out period of oral antidiabetics, hyperglycemia may occur. For that reason, subjects will be emphatically instructed about hyperglycemic symptoms. Please note that based on earlier findings in subjects with T2D, withdrawal of oral antidiabetic medication is not expected to induce severe hyperglycaemia, as participating patients are not insulin dependent.

Contacts

Public
Centre for Human Drug Research

Zernikedreef 10
2333 CL Leiden
Nederland
Scientific
Centre for Human Drug Research

Zernikedreef 10
2333 CL Leiden
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Type 2 diabetes mellitus controlled by oral antidiabetics (except for PPAR-gamma agents) for at least one year;
- Age 18 to 65 years;
- Males or females (with regular menstrual cycles if premenopausal);
- Able and willing to provide written informed consent.

Exclusion criteria

- Use of insulin or PPAR-gamma agents;
- Glycated hemoglobin (HbA1c) > 8%;
- BMI <= 22 kg/m2 and >= 35 kg/m2;
- Any evidence of cardiovascular, pulmonary, renal, hepatic or other major organ system disease as determined by history, physical examination, and routine laboratory tests;
- Uncontrolled hypertension (systolic blood pressure >= 150 mm Hg or a diastolic blood pressure >= 95 mm Hg);
- Use of medication known to affect glucose homeostasis (except for biguanides and sulphonylureas), anti-inflammatory drugs, non-selective beta blockers such as propranolol, oral anticoagulants, systemic glucocorticoids or other immunosuppressive drugs;
- Use of prescription or over-the-counter drug(s) to promote weight loss;
- Pregnancy or breastfeeding;
- Not able or willing to use an acceptable contraceptive method for study duration for females (hormonal contraceptives, intra-uterine device or condom/pessary);
- Not able and willing to refrain from smoking and/or xanthine use on study day;
- Positive test result for HIV, hepatitis B virus, and/or hepatitis C virus;
- History of alcohol or drug abuse;
- Undergoing or have undergone treatment with an investigational drug, biologic agent or device within 90 days prior to screening

- Blood donation within three months and plasma donation within two weeks of screening.

Study design

Design

Study type:	Observational invasive
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-10-2009
Enrollment:	16
Type:	Actual

Medical products/devices used

Generic name:	Guardian RT continuous monitoring
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Actrapid
Generic name:	insulin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	GlucaGen
Generic name:	glucagon
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Somatostatine-Eumedica
Generic name:	somatostatine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-08-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-10-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	21-10-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	22-10-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	25-01-2010
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	09-02-2010
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2009-014847-36-NL
CCMO	NL29286.058.09