Stepwise assessment of the relation between glycocalyx dimensions, oxidative stress and level of glycaemia

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To assess at which level of glycemia the process of endothelial damage, represented by ROS formation and glycocalyx damage begins and to determine whether there is a glycemic threshold value for oxidative stress formation and glycocalyx damage. To...

Ethical review	Approved WMO
Status	Pending
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON32609

Source
ToetsingOnline

Brief title
STARDOM

Condition

- Diabetic complications

Synonym
Diabetes mellitus, hyperglycaemia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Stichting Asklepios

Intervention

Keyword: Endothelial glycocalyx, Oxidative stress, Stepwise hyperglycaemic clamp

Outcome measures

Primary outcome

Relation between level of glycemia and glycocalyx thickness, relation between

level of glycemia and ROS formation.

Secondary outcome

Relation between glycocalyx thickness and ROS formation, relation between level

of glycemia and activation of coagulation parameters.

Study description

Background summary

Endothelial dysfunction is a hallmark of diabetic vascular complications. Hyperglycemia induced formation of reactive oxygen species (ROS) is thought to induce endothelial dysfunction by enhancing four mechanisms of tissue damage. Also, oxidative stress may have a direct effect on the glycocalyx, a network of membrane-bound proteoglycans and glycoproteins exerting vasoprotective effects. It has been shown that patients with diabetes mellitus have higher levels of oxidative stress and a diminished glycocalyx volume compared to healthy controls. However, little is known about the degree of glycemia at which these changes occur and whether damage is influenced by glycemic swings.

Study objective

To assess at which level of glycemia the process of endothelial damage, represented by ROS formation and glycocalyx damage begins and to determine whether there is a glycemic threshold value for oxidative stress formation and glycocalyx damage. To assess whether there is a direct relationship between increased ROS formation and loss of glycocalyx. To investigate the relation between level of glycemia and activation of coagulation parameters.

Study design

After a screening visit the actual study consists of a stepwise hyperglycemic

clamp at glucose levels of fasting, 6, 8 and 10 mmol/l. Each plasma glucose concentration will be held constant for 120 minutes. At each glucose level glycocalyx thickness and will be measured every 30 minutes by OPS recordings and shedding of glycocalyx components and ROS formation by determination of plasma malondialdehyde and nitrotyrosine. After this, glucose infusion will be increased to reach the next level of glycemia. In total, the clamp will take 420 minutes. The day after the clamp, the participants will come to the AMC for visit 3 for evaluation of glycocalyx restoration and ROS formation.

Intervention

Hyperglycaemic clamp. The plasma glucose concentration will be elevated in a stepwise manner by administration of somatostatin, glucose and insulin (fasting, 6 mmol/l, 8 mmol/l and 10 mmol/l).

Study burden and risks

Included subjects will visit the AMC hospital three times:
Visit 1 (Screening visit): informed consent, medical history, vital signs, vena puncture (7.5 ml in total).
Visit 2: stepwise hyperglycemic clamp with a total duration of 420 minutes: Placement of two intravenous catheters; venous blood sampling for glucose measurement every 5 minutes and venous blood sampling for determination of ROS formation and coagulation activation at 14 time points (294 ml in total); somatostatin, insulin and glucose infusion; OPS recordings every 30 minutes (14 in total);
Visit 3: OPS recording and vena puncture (9 ml in total)
Burden for the subjects consists of coming to the hospital in a fasting state on three different occasions, a period of lying down during the clamp and two venapunctures as well as the placement of two intravenous catheters. The infusion of somatostatin may cause nausea. The overall risk of this study is minimal.

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
Caucasian race
Age 18-30 years

Exclusion criteria

Diabetes mellitus or fasting glucose >5.5 mmol/l
Smoking
BMI > 25 kg/m2
Blood pressure >= 130 mmHg systolic; >= 90 mmHg diastolic
Total cholesterol >= 5 mmol/l, LDL-cholesterol >= 3 mmol/l or triglycerides >= 1.7 mmol/l
Use of lipid lowering or antihypertensive drugs
Use of antioxidants in the two weeks before the hyperglycemic clamp
Acute illness within 3 months before the study
Any other illness that inhibits participation in the study according to the study physician

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2009
Enrollment:	10
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	NL30031.018.09