Activation of the innate immune system and vascular inflammation in patients with type 1 diabetes mellitus

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Primary Objective: 1. To determine whether there is a difference in arterial wall inflammation between well-controlled and poorly-controlled type 1 diabetes patients2. To determine whether patients with type 1 diabetes have a higher level of...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Diabetic complications
Study type	Observational invasive

Summary

ID

NL-OMON44648

Source
ToetsingOnline

Brief title
Activation innate immune system in type 1 diabetes

Condition

- Diabetic complications
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: European Foundation for the Study of

Diabetes

Intervention

Keyword: Atherosclerosis, Diabetes, Inflammation

Outcome measures

Primary outcome

Vascular wall inflammation in the aorta, left and right carotid artery and left

and right iliac and femoral arteries, as quantified by FDG-PET scanning.

Secondary outcome

FDG uptake in spleen and bone marrow.

Ex vivo determination of the inflammatory/atherogenic phenotype, cellular

metabolism of circulating monocytes and epigenetic signature of monocytes.

Study description

Background summary

Hyperglycemia is a well-known cardiovascular risk factor. It has also been shown that episodes of hyperglycemia increase the risk for cardiovascular diseases despite return to normoglycemia, a phenomenon termed 'glycemic or metabolic memory'. The molecular mechanism underlying this phenomenon remains unclear.
Cardiovascular events, such as myocardial infarction and stroke are caused by atherosclerosis, which is characterized by low grade inflammation of the vascular wall, including accumulation of innate immune cells such as monocytes and macrophages.
We hypothesize that chronic hyperglycemia shifts intracellular metabolism of innate immune cells towards glycolysis and changes the epigenetic state of (progenitors of) innate immune cells (monocytes and macrophages), which reprograms these cells towards a more aggressive, pro-atherogenic phenotype, thereby accelerating atherosclerosis.
In this study, we aim to test this hypothesis. This research will reveal whether the innate immune cells of patients with chronic hyperglycemia show a durable shift in intracellular metabolism and epigenetic changes and whether

this associates with vascular inflammation.

Study objective

Primary Objective:
1. To determine whether there is a difference in arterial wall inflammation between well-controlled and poorly-controlled type 1 diabetes patients
2. To determine whether patients with type 1 diabetes have a higher level of arterial wall inflammation than patients without diabetes.

Secondary Objectives:
3. To determine whether poorly-controlled type 1 diabetes patients have an increased FDG uptake in the bone marrow and spleen as compared to well-controlled patients, and whether type 1 diabetes patients differ from healthy controls with this respect.
4. To investigate whether circulating monocytes of patients with poorly-controlled type 1 diabetes are characterized by a more pro-inflammatory phenotype compared to well-controlled type 1 diabetes patients, and whether there is a difference between type 1 diabetes patients and healthy controls.
5. To study whether there is a shift in intracellular metabolism in monocytes of type 1 diabetes patients (well-controlled versus poorly-controlled patients) compared to healthy controls.
6. To explore epigenetic changes in monocytes of type 1 diabetes patients (well-controlled versus poorly-controlled patients) compared to healthy controls.

Study design

Observational study in patients with type 1 diabetes (well-controlled versus poorly-controlled patients) and healthy controls.

Study burden and risks

The risks associated with participation in this study are low. In total, 100 ml blood will be obtained, which is not associated with relevant side effects. In addition, all patients will undergo an 18FDG-PET/CT. This diagnostic procedure will be performed according to standard state-of-the-art clinical procedures as define by the European association of Nuclear Medicine. Duration of the procedure: 3 hours. Procedure-related exposure to radioactivity: 5.0 mSv. Patients will not have a direct benefit from participation in the study.

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

Group 1: Type 1 diabetes, HbA1c > 64 mmol/mol; Group 2: Type 1 diabetes, HbA1c <64 mmol/l; Group 3: Healthy controls.
Group 1 and 2: type 1 diabetes, diagnosis based on clinical data, duration of diabetes *10 years, age *20 years, * 60 years, written informed consent
Group 3: absence of disease; matched for age,, gender and BMI; HbA1c <42 mmol/mol; written informed consent

Exclusion criteria

- Inability to provide informed consent
- Smoking
- Specific Medication use:
o Use of immunosuppressive drugs
o Use of statins < 2 weeks before performing PET-CT (Those that use statins will be asked to discontinue for two weeks. This can be safely done in the context of primary prevention.)

o Use of acetylsalicylic acid
- Previous cardiovascular events (ischemic stroke/TIA, myocardial infarction, peripheral arterial disease)
- Auto-inflammatory or auto-immune diseases
- Current or recent infection (< 3 months)
- Previous vaccination (< 3 months)
- Renal failure (MDRD <45)
- BMI>30 kg/m2
- Pregnancy
- Claustrophobia
- Severe hypoglycaemia < 1 week before PET-CT

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-01-2018
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	05-09-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL62200.091.17