Glucotoxity and Endothelial Function

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The main purpose of this study is to evaluate the effect of glycemic control on microvascular endothelial function in type 2 diabetes mellitus.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON31935

Source
ToetsingOnline

Brief title
Glucotoxity and Endothelial Function

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: diabetes mellitus, endothelium, glycoHb, vascular function

Outcome measures

Primary outcome

To assess the relationship between glycemic control and endothelial function on

the microvascular level in diabetes mellitus type 2 (NO, ET-1, Ang II).

Secondary outcome

To assess underlying mechanisms involved in microvascular endothelial

dysfunction and possibly its improvement

Study description

Background summary

Diabetes-associated atherosclerosis is a major clinical problem. Diabetic patients have a two- to fourfold increased incidence of coronary artery disease and stroke and a tenfold increased incidence of lower extremity vascular disease (1,2). Not only macrovascular, but also microvascular dysfunction is a considerable cause of morbidity and mortality in diabetic subjects. Microvascular dysfunction, besides leading to nephropathy and retinopathy, also affects the microcirculation of the myocardium (3,4). Diabetes mellitus is associated with a diminished coronary flow reserve and impaired cardiac ischemic preconditioning (3,4). Intervention studies have shown that improved glycemic control reduces the risk of especially microvascular complications in diabetes (5,6).

With regard to the pathogenesis of vascular disease in diabetes endothelial dysfunction is considered to be a critical initial event (7,8). This endothelial dysfunction might be caused by an adverse effect of hyperglycemia (glucotoxicity) on endothelial vascular function. However, elevated blood pressure and dyslipidemia may be involved as well.

Study objective

The main purpose of this study is to evaluate the effect of glycemic control on microvascular endothelial function in type 2 diabetes mellitus.

Study design

This is a prospective, non-randomized, single-center study which will evaluate the ability of glycemic control to reverse or improve endothelium-dependent and endothelium-independent microvascular function in patients with poorly controlled diabetes mellitus type 2.

Study burden and risks

to undergo two skin biopsies: one at baseline and the second after 12 weeks improved glycemic control. At the same time-points serum will be collected. The biopsies will be used for isolation of microvascular resistance vessels. The isolated vessels will be used in a standard microvascular functional assay to study NO-dependent and -independent vasodilatation and endothelin-1 (ET-1) and angiotensin II (Ang II)-induced vasoconstriction. The collected serum will be used for experiments with cultured endothelial cells.

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 or female type 2 diabetic patients; Documented GlycoHb > 8.5% for at least 6 weeks; Age 30-60 years; BMI 25-35 kg/m2; LDL-cholesterol concentration < 3.0 mmol/l; Blood pressure < 140/90 mmHg

Exclusion criteria

(Clinical or laboratory) evidence of atherosclerosis or cardiovascular disease; Other systemic disorder with likelihood of (micro)vascular involvement; diabetic nephropathy (albuminuria > 300 mg per day); Kidney disease other than diabetes (serum creatinine > 120 µmol/l); Alcohol abuse; Unwillingness to give written informed consent; Condition that precludes follow-up; Oral anticoagulant therapy or bleeding diathesis

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	04-07-2008
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL22134.078.08