The effect of dietary interventions on endothelial glycocalyx dimensions and barrier function in South Asian patients with diabetic nephropathy.

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

Summary

ID

NL-OMON50642

Source
ToetsingOnline

Brief title
Dietary interventions on glycocalyx dimensions in diabetic nephropathy.

Condition

- Diabetic complications
- Nephropathies

Synonym
diabetic kidney damage, diabetic nephropathy

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: de nierstichting,Glycocheck,Health Holland;Microvascular Health Solutions;Glycocheck;L-Nutra,L-Nutra,Microvascular Health Solutions

Intervention

Keyword: Diabetic nephropathy, Dietary interventions, Glycocalyx, South Asian

Outcome measures

Primary outcome

The primary endpoint is an improvement of the Microvascular Health index in the diet group compared to the placebo group, and in the food supplement group compared to the placebo group, after 3 months of the intervention.

Secondary outcome

Secondary endpoints: reduce albuminuria, decrease inflammation (urinary heparanase and MCP-1 expression, serum CRP and MCP-1 levels), reduce occurrence of specific urinary HS domains, improve metabolic parameters; fasting glucose, HbA1c, C-peptide, IGF-1, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides serum levels, waist circumference, waist-to-hip ratio, body weight and systolic blood pressure after 3 months of the fasting mimicking diet and after 3 months of the food supplement. The legacy effect of the interventions is also determined, 3 months after stopping with the intervention.

Study description

Background summary

Micro- and macrovascular complications are the pathological hallmarks of diabetes mellitus, with diabetic nephropathy as one of the most serious microvascular complications. South Asians have a high incidence of type 2 diabetes and a higher change to progress to end-stage renal disease than West European patients, which may be due to a higher sustained systemic and glomerular inflammation. The endothelial glycocalyx, covering endothelial cells, is essential for maintaining vascular homeostasis. In the diabetic environment, impairment of the glycocalyx can be induced by invading macrophages which excrete the glycocalyx degrading enzyme heparanase and its activator cathepsin L. In the glomerulus, impairment of the glycocalyx results in increased permeability for albumin alongside renal and vascular inflammation. SDF-imaging is a non-invasive technique to visualize the endothelial glycocalyx and obtains parameters that reflect the microvascular endothelial status, combined in the Microvascular Health Index (MHI). Here we investigate if dietary interventions, which either provide the nutritional building blocks to support and maintain the endothelial glycocalyx or reduce the overall inflammatory burden, can aid in restoration of the glomerular endothelial glycocalyx and in turn result in a reduction of albuminuria and further delay, or prevent renal damage.

Study objective

The primary aim of the study is to improve microvascular endothelial health after 3 months expressed by the Microvascular Healt Index, using a non-invasive imaging technique, upon two different dietary interventions compared to the placebo. The secondary objective is to monitor the dietary effects after 3 months on systemic inflammation, metabolic parameters and albuminuria. Finally, we aim to determine new urinary heparan sulphate fragment biomarkers which can be related to specific glomerular extracellular heparanase activity, a possible central player in local glomerular damage and renal inflammation.

Study design

A randomized, placebo controlled, 3-arm intervention field study for 3 months with additional 3 month follow up measurements.

Intervention

One group receives a monthly 5-day fasting mimicking diet for 3 consecutive months, one group receives daily 4 capsules of a food supplement and one group receives daily 4 placebo capsules, all for 3 consecutive months.

Study burden and risks

Eligible patients are randomly assigned to the fasting mimicking diet, food supplement or placebo arm. At baseline, after 3 months and at 6 months, the MHI

is measured by non-invasive SDF imaging of the microcirculation under the tongue, and blood and urine samples are collected. In the FMD arm, dosages of the hypoglycaemic drugs are adapted during the 5 days of the diet prevent hypoglycaemia. Glucose monitoring is done during the diet and at the end of each month in all intervention arms through a finger prick blood sample.

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

1. South Asian patient with diabetes mellitus type 2.
2. Female or male, aged between 18 and 75 years.
3. Body Mass Index *18.5.
4. CKD-EPI >45 ml/min/1.73m² at baseline.
5. Proven microalbuminuria defined as albumin/creatinine ratio *0.3 and <30

mg/mmol (single portion) or 3-300 mg albumin per day (24 hours urine collection) in the last twelve months.
6. Blood pressure of *180 mmHg with standard antihypertensive care.
7. Treatment with hypoglycaemic drugs: metformin, sulphonylureas and/or insulin.
8. Subject is willing to participate in the study, must be able to give informed consent and the consent must be obtained prior to any study procedure.
9. Patients must be able to adhere to the study visit schedule and protocol requirements.
10. If female and of child-bearing age, patients must be non-pregnant, non-breastfeeding, and use adequate contraception.

Exclusion criteria

1. Any concurrent illness, disability or clinically significant abnormality that may, as judged by the investigator, affect the interpretation of clinical efficacy or safety data or prevent the subject from safely completing the assessments required by the protocol.
2. Non-diabetic renal disease e.g. known polycystic kidney disease.
3. Use of LMW heparin and/or immunosuppressive drugs.
4. Significant food allergies for galactose, nuts, soy, tomato, corn, grape, melon and artichoke, which would make the subject unable to consume the food provided.
5. Signs of active infection or autoimmune disease, requiring systemic treatment.
6. A psychiatric, addictive or any disorder that compromises ability to give truly informed consent for participation in this study.
7. Malignancy (including lymphoproliferative disease) within the past 2-5 years (except for squamous or basal cell carcinoma of the skin that has been treated with no evidence of recurrence).
8. Use of any other investigational drug.
9. Patient has enrolled another clinical trial within last 4 weeks.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Control:	Placebo
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-05-2018
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO

Date:	07-03-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	08-05-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	06-02-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	25-09-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	20-08-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	15-10-2108
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL63186.058.17