Understand and prevent the production of microbially-produced pro-diabetic metabolites in different ethnic groups: impact of protein dietary changes (MICRODIET)

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To investigate the effects of a short term (3 months) high protein (HP) diet compared to a low protein (LP) diet in T2D patients of Caribbean and Caucasian ethnic background with regards to gut microbiota composition and production of pro-diabetic...

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

Summary

ID

NL-OMON48642

Source
ToetsingOnline

Brief title
MICRODIET

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Diabetic complications

Synonym
diabetes mellitus, suger disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Beurs vanuit het Joint Programme Initiative van de EU

Intervention

Keyword: Diabetes, Microbiota, Protein

Outcome measures

Primary outcome

Primary objective:

- Does a short term (3 months) LP diet favorably affect glucose levels after a

mixed-meal test (MMT) in T2D patients of both Dutch and Caribbean descent?

Secondary outcome

Secundary objective:

- Does a HP diet increase pro-diabetic metabolites, such as ImP, in T2D

patients?

- Do T2D patients from Dutch or Caribbean ethnicity respond differently to a HP

vs LP diet intervention in terms of glucose levels after a MMT and the

production of pro-diabetic metabolites, such as ImP?

- Does baseline gut microbiota diversity in Caribbean subjects affect (post)

prandial glucose response upon (high or low) protein diet?

-Will a HP diet alter oral microbiota composition?

-Will a LP diet favorably influence body weight and body composition (as

measured via body impedance)?

- Will a protein diet affect leukocyte methylation profiles and is this related

to glucose metabolism?

Study description

Background summary

The prevalence of obesity and type 2 diabetes (T2D) is increasing worldwide at an allarming pace. A relatively new recognized player involved in the pathophysiology of type 2 diabetes (T2D) is the gut microbiota .The gut microbiota can be seen as an environmental factor that promotes cardio-metabolic diseases (CMD) including diabetes, obesity and atherosclerosis. The gut microbiota itself is strongly influenced by diet, ethnicity and medication use.

Preleminary results has shown a diverse gut microbiota richness between subjects from different ethnicities, with subjects of Surinamese/Caribbean descens having the lowest gut microbiota diversity compared to Dutch Caucasians. Other preleminary results from our group has identified the Imidazole Propionate (ImP), a degredation product of the essential aminoacid histidine, as a potential metabomolite which plays a role in insulineresistance. We also found that the gut microbiota of T2D subjects drive histidine degradation into ImP production and urocanate.

In the MICRODIET study we would like to investigate the effects of a short term (3 months) high protein (HP) VS a low protein (LP) diet on gut microbiota composition and production of pro-diabetic metabolites in T2D patients from Caucasian and Carribean ethnicity.

We hypothesize that increased protein intake in T2D subjects will lead to an increased production of pro-diabetic metabolites, such as ImP, and higher plasma glucose levels. We also hypothesize that in some ethnic groups this effect is larger due to a reduced microbial diversity

Study objective

To investigate the effects of a short term (3 months) high protein (HP) diet

compared to a low protein (LP) diet in T2D patients of Caribbean and Caucasian ethnic background with regards to gut microbiota composition and production of pro-diabetic metabolites.

Furthermore, we will also investigate the oral microbiota compositation as this is also linked with cardio-metabolic diseases (CMD), such as T2D.

Study design

This is a randomized controlled three months dietary intervention study comparing the effects of a high vs low protein diet in T2D subjects of Caucasian or Caribbean ethnicity.

Intervention

Patients will be randomized to either a high protein or a low protein diet for three months. They will have weekly contact with an AMC dietician and will also record 3 day food diaries per week. Subjects are required to collect 24hours urine and feces 3 times during the intervention.

Study burden and risks

The total duration of the study is three months and participants will visit the AMC four times. All participants are required to fill out food diaries three days per week and have weekly contact with the dietician. Subjects are required to collect 24h urine and feces at baseline, week 6 and week 12 of the study. Furthermore, subjects will undergo multiple blood sampling after a mixed meal test (MMT). The proposed diet is safe and no immediate harm is likely to occur. However, glycemic control of DM2 can theoretically worsen and we therefore measure HbA1c again at 6 weeks. Subjects will be discontinued from the study if HbA1c >9% (75mmol/mol). In total subjects will spent 5 hours in the AMC (2x 4h for the MMT plus REE/BIA/questionnaires at baseline and 12 weeks, as well as 1 hour during time point 6 weeks) and we will collect 300ml blood (at baseline, week 6 and week 12) in total.

The placing of the intravenous cannula in our study can be an unpleasant experience for the subjects. There is a low risk of phlebitis at the intravenous injection sites, this is unpleasant, but not harmful, of temporary nature and self-limiting.

A potential benefit for participating in this study can be weight loss and with that better glycemic control and reduced risk for major vascular events. Futhermore, data from this project will increase our knowledge regarding the production of pro-diabetic metabolites by the gut microbiota and potentially

give rise to new pathways which can be intervened.

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

- Age between 40-70 years
- Presence of T2D
- BMI* 25kg/m2
- Use of metformin on a stable dose (i.e. no changes in the last three months)
- Adequate knowledge of the Dutch language to comprehend the provided study information

Exclusion criteria

- Use of insulin
- Use of a proton-pump inhibitor
- Use of antibiotics 3 months before inclusion
- Vegetarian diet
- Presence of inflammatory bowel disease or other chronic inflammatory disease
- More than 5 units of alcohol consumption per week
- Active malignancy
- bariatric or other weight loss surgery in the history
- patients diagnosed with eating disorders (such as bulimia nervosa, anorexia nervosa or binge-eating disorder)
- HbA1c >9% (75mmol/mol)
- Unmotivated or not able to adhere to a specific diet.
- Estimated glomerular filtration (eGFR) < 50ml/min/1.73m2
- The subject is already involved in a clinical trial

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-09-2018
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	27-07-2018

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-03-2019
Application type:	Amendment
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

ID: 27966
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL65782.018.18
OMON	NL-OMON27966