Effect of diEtaRy fructose on fructose kinetics in type 2 dIabetEs

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Determine the kinetics of fructose metabolism and its role as a metabolic substrate following a high vs low fructose diet in subjects of SAS or Caucasian ethnicity.

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

Summary

ID

NL-OMON51729

Source
ToetsingOnline

Brief title
ERIE

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
sugar disease, Type 2 Diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMW;VICI

Intervention

Keyword: Diet, Fructose, Kinetics, Type 2 diabetes

Outcome measures

Primary outcome

Primary endpoints are changes in oral fructose handling (measured by a fructose tolerance test with 120mg 13C6 -labeled fructose in relation to other metabolic effects (eg on lipids, HOMA and continuous glucose monitoring Freestyle libre) at baseline and after 4 weeks

Secondary outcome

Changes in gutmicrobiota composition between individuals of SAS or Caucasian descent on high versus low fructose diet. Also, effects on body composition (measured via bio impedance analysis) and 24h feces and urine for fructose content and compliance will be studied. Finally, (postprandial) untargeted plasma metabolites including endogenous ethanol at both timepoints will be done to identify involved metabolic pathways.

Study description

Background summary

The prevalence and accompanying morbidity and mortality of obesity and type 2 diabetes (T2D) is increasing on a global scale. Unfortunately the underlying (patho)physiological mechanisms are only partially understood. A key step in the development of negative health effects of metabolic disease might be via dietary fructose metabolism and its accompanying aberrant metabolite production, in which ourgut microbiota plays a crucial role.
By bypassing the normal glucose metabolism pathway, fructose plays a role in the development of metabolic disease such as diabetes en fatty liver disease. The mechanism of this effect is unclear and possibly plays in the observation of ethnic specific metabolic risk factors. That is, subjects of different ethnicities (for instance South-Asian Surinamese (SAS)) have a higher risk and worse trajectory of metabolic diseases then Caucasians. Since gutmicrobiota is altered between these two ethnicities, we propose that aberreant fructose catabolism in patients of South Asian Surinamese (SAS) results in production of

specific (gutmicrobiota derived) metabolites such as ethanol. In this study, fructose metabolism will thus be studied in patients of South Asian Surinamese (SAS) and Caucasian Dutch descent. To this end we will examine (stable isotope based) fructose fluxes before and after randomizing subjects into a four-week high- or low fructose diet, this study aims to elucidate the physiological and microbial catabolism of fructose and possible differences in these two ethnicities.

Study objective

Determine the kinetics of fructose metabolism and its role as a metabolic substrate following a high vs low fructose diet in subjects of SAS or Caucasian ethnicity.

Study design

Isocaloric non-blinded single centre dietary intervention study

Intervention

High (100gr/day) vs Low (30gr/day) fructose diet for 4 weeks. Fructose will be ingested via regular dietary route (food/drink changes) and the process will be monitored by a dietician.

Study burden and risks

The total duration of the study is four weeks and participants will visit the AmsterdamUMC, location 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 2 and week 4 of the study. Furthermore, subjects will undergo multiple blood sampling after a Fructose Challenge Test (FCT). The proposed diet is safe and no immediate harm is likely to occur. However, glycaemic control of T2D can theoretically worsen. Therefore, we measure HbA1c, fasting glucose and perform continuous glucose monitoring throughout the study. Subjects will be discontinued from the study if HbA1c >9% (75mmol/mol). In total subjects will spend 13 hours in Amsterdam UMC, location AMSTERDAM UMC, location AMC :2x 6.25 h for the FCT plus REE/BIA at baseline and 4 weeks, as well as 25 minutes during screening and 25 minutes during test day 2. We will collect 170ml blood (at baseline, week 2 and week 4) in total. Subjects will not undergo invasive procedures, besides venous blood draw through a peripherally placed cannula (therefore only 1 puncture is needed per test day).

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

- 40 T2D patients (20 Caucasian and 20 SAS)
- 40-70 years
- BMI 25-35
- Stable anti diabetic drugs for 3 months (metformin is obligatory)
- Stable medication uses past 3 months
- Able to give informed consent

Exclusion criteria

- Proton-pump inhibitor usage (known to effect gut microbiota)
- GLP1 or insulin use (known to effect gut microbiota)

- Antibiotic for the past 3 months (known to effect gut microbiota)
- Probiotic or symbiotic usage (known to effect gut microbiota)
- Pregnant women
- Chronic illness (including a known history of heart failure, renal failure (eGFR <30 ml/min), pulmonary disease, gastrointestinal disorders, or hematologic diseases), or other inflammatory diseases
- Active infection
- Previous intestinal (e.g., bowel resection/reconstruction) surgery
- Smoking (due to its influence on gut microbiome)
- Vegetarian diet (since they have different microbiota)
- >6 alcohol units per day or >14 alcohol units per week
- Active malignancy
- HbA1c >9% (75mmol/mol)
- 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:	Pending
Start date (anticipated):	01-10-2022
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

Date:	14-10-2022
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	NL82353.018.22