Effects of fructose on glucose and lactate excursions during an oral glucose tolerance test

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

Summary

ID

NL-OMON49169

Source
ToetsingOnline

Brief title
Effects of fructose added to OGTT

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Sugar tolerance

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Diabetes Fonds

Intervention

Keyword: Fructose, OGTT, Sugar metabolism

Outcome measures

Primary outcome

The area under the curve (AUC) for plasma glucose and lactate excursions during an OGTT will be calculated.

The glucose and lactate AUC*s for the OGTT without fructose will be compared to the glucose and lactate AUC*s for the OGTT(s) with fructose.

Secondary outcome

Secondary parameters:

Serum fructose, insulin, triglycerides, urate and beta-hydroxybutyrate levels will be measured at baseline and the end of each OGTT and compared with the OGTT without fructose.

Urinary fructose will be measured at the end of each OGTT and compared with the OGTT without fructose.

Furthermore, plasma will be stored future analyses.

Other study parameters include:

• Age

• Sex

• BMI

• Waist and hip circumference

• Fasting plasma glucose

• Fasting serum insulin

• Fasting serum lipids (total cholesterol, HDL cholesterol, LDL cholesterol,

triglycerides)

• Systolic and diastolic blood pressure

Study description

Background summary

Despite the consensus that added sugars - i.e. all sugars that are added during food manufacturing and preparation - play an important role in the current epidemic of obesity and consequently type 2 diabetes mellitus (T2DM), dyslipidaemia and cardiovascular disease (CVD), there is an ongoing discussion whether the type of sugar, i.e. fructose or glucose, matters. Previous animal studies have suggested that hepatic fructose and glucose metabolism are linked through the action of glucokinase regulatory protein (GKRP).

Study objective

The aim of the present study is to examine the interaction (and underlying mechanisms) between hepatic fructose and glucose metabolism in humans. The first objective is to determine the dose-effect relationship between oral fructose and the plasma glucose and lactate excursions during an oral glucose tolerance test (OGTT).
The second objective is to elucidate the role of GKRP in the fructose-induced change in plasma glucose and lactate excursions during an OGTT.

Study design

This study consists of:
Substudy I) A single-blind, dose response study in healthy individuals (objective 1);
Substudy II) A single-blind, cross-over intervention study in carriers of aldolase B mutation, carriers of glucokinase mutation and healthy controls (objective 2).

Intervention

For substudy I, all participants will undergo eight OGTTs in total, including one standard OGTT, five standard OGTTs with addition of different dosages of fructose, one standard OGTT with addition of glucose (iscaloric control), and oral test with fructose only (*isofructose* control), after an overnight fasting in a random sequence (with at least 4 days interval between each OGTT)

on different occasions.

For substudy I protocol amendment, the 10 additional participants will undergo four OGTTs in total, including one standard OGTT and three standard OGTTs with addition of different dosages of fructose, after an overnight fasting in a random sequence on different occasions.

For substudy II, all participants will undergo one standard OGTT without fructose and one standard OGTT with fructose, after an overnight fasting in a random sequence on different occasions.

Study burden and risks

For substudy I, all participants will undergo eight OGTTs in total.

For substudy I protocol amendment, the 10 additional participants will undergo four OGTTs in total.

For substudy II, all participants will undergo two OGTTs in total.

In total, 85 ml blood will be collected per OGTT (Substudy I: ~680 ml total blood; Substudy I protocol amendement: ~340 ml total blood; Substudy II: ~170 ml total blood).
Administration of an oral glucose load may cause faintness, nausea and vomiting.
Venous blood withdrawal using the cannula technique can occasionally cause a local haematoma.

All participants will undergo a general health check regarding cardiovascular risk factors which may be of potential benefit.

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

Substudy I:
Healthy men, age 18-75 years, blood Hb >= 8,2 mmol/L.
Healthy women, age 18-75 years, blood Hb >= 7,3 mmol/L, either postmenopausal women or premenopausal using an oral contraceptive without a *stop week*,

Substudy I protocol amendment for the 10 additional study participants:
Healthy men, age 18-75 years.
Healthy women, age 18-75 years, either postmenopausal women or premenopausal using an oral contraceptive without a *stop week*,

Substudy II:
a) Genetic diagnosis (i.e. heterozygous carrier) of aldolase B mutation, age 18-75 years.
b) Genetic diagnosis of Maturity-Onset Diabetes of the Young Type 2 (MODY-2), i.e. carrier of glucokinase mutation, age 18-75 years.
c) Healthy individuals, age 18-75 years.

Exclusion criteria

• Fasting blood glucose >11 mmol/L;
• Clinical diagnosis of diabetes including type 1 and type 2;
• Use of medications known to interfere with glucose homeostasis (i.e. corticosteroids);
• Medical conditions that can interfere with the study outcome (i.e.

gastrointestinal disease);
• Cancer, end-stage liver, kidney, cardiac or lung disease;
• Unstable weight for 3 months prior to inclusion (i.e. 5% change in bodyweight (13));
• Abuse of drugs and/or alcohol;
• Pregnancy;
• Physical stress one month prior to inclusion (i.e. post-surgery, trauma or infection or extreme psychological stress);
• Periodic hypokalemic paralysis;
• Inability to give inform consent.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-05-2019
Enrollment:	74
Type:	Actual

Ethics review

Approved WMO

Date:	17-04-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	01-12-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL68189.068.18

Study results

Date completed:	24-05-2023
Actual enrolment:	13

Summary results
Trial ended prematurely