Comparing the effect of a high SFA diet and high fructose diet on hepatic insulin sensitivity

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Primairy objective:To determine the effect of a 4-week high SFA diet compared to a 4-week high fructose diet on hepatic insulin sensitivity (determined by insulin-stimulated suppression of endogenous glucose production).Secondary objectives: - To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON54415

Source
ToetsingOnline

Brief title
SFA and fructose study

Condition

- Hepatic and hepatobiliary disorders
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
decreased insulin sensitivity, Insulin resistance

Research involving
Human

Sponsors and support

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

Intervention

Keyword: De novo lipogenesis, Fructose, Insulin sensitivity, Saturated fat

Outcome measures

Primary outcome

The primary outcome is hepatic insulin sensitivity (suppression of EGP during

clamp) upon a 4-week high SFA diet versus a 4-week fructose diet.

Secondary outcome

Secondary outcomes are:

- de novo lipogenesis upon 4-week high SFA versus 4-week high fructose diet

- change in (baseline-end intervention) hepatic SFA fraction upon 4-week high

SFA versus 4-week high fructose.

Study description

Background summary

The liver is an important organ in our body and, among other things, plays an important role in fat and sugar metabolism in the body. A disturbance of fat and sugar metabolism in the liver leads to accumulation of fat in the liver and lowers insulin sensitivity. The more sensitive the body is to insulin, the better it can regulate blood sugar. Thus, low insulin sensitivity results in poorer blood sugar regulation. However, little is known about how accumulation of fat in the liver contributes to poorer insulin sensitivity in humans.

Previous research conducted by us has shown that specifically the accumulation of saturated fat in the liver is associated with poorer insulin sensitivity. In addition, we know that the production of new fats in the liver from sugars specifically increases saturated fat in the liver. This fat production in the liver is additionally associated with poorer insulin sensitivity. Until now it is unknown whether the saturated fat in the liver or specifically the process of new fat production (de novo lipogenesis) is the main culprit for insulin sensitivity. We want to investigate this by using two different diets.

Diet can influence the new production of fat from sugars and the amount of

saturated fat in the liver. A diet high in saturated fat can directly increase the amount of saturated fat in the liver. Examples of products with relatively high saturated fat are: meatballs, steak, snacks, butter, full-fat cheese, butter cookies, milk chocolate. A diet high in fructose increases the process of production of new (saturated) fats in the liver. Thus, this diet may indirectly increase saturated fat in the liver and decrease insulin sensitivity. It is possible that there are other negative effects of the production of newly synthesized fat on insulin sensitivity. Examples of products relatively high in fructose are: Fruit juices, soft drinks, candy, jam, syrup, sweetened breakfast cereals.

Study objective

Primairy objective:
To determine the effect of a 4-week high SFA diet compared to a 4-week high fructose diet on hepatic insulin sensitivity (determined by insulin-stimulated suppression of endogenous glucose production).

Secondary objectives:
- To determine the effect of a 4-week high SFA diet compared to a 4-week high fructose diet on hepatic saturated fatty acid fraction
- To determine the effect of a 4-week high SFA diet compared to a 4-week high fructose diet on de novo lipogenesis

Exploratory objective:
- To determine the effect of a 4-week high SFA diet compared to a 4-week high fructose diet on sleeping metabolic rate (SMR) and nocturnal substrate metabolism (RER, fat and carbohydrate oxidation).

Study design

This is a randomized intervention study comparing the effects of a 4-week high SFA diet compared to a 4-week high fructose diet on hepatic insulin sensitivity in 14 overweight/obese males and females.
Volunteers who are included will visit the University for 14 visits:
- one general screening visit incl. MRI scan,
- for each of the two study periods four short visits to determine body weight and discuss dietary compliance.
- For each of the two periods an MRI scan at the beginning and at the end during which liver fat composition and content are measured.
- For each of the two periods, an overnight visit where de novo lipogenesis and nocturnal substrate oxidation are measured.
- for each of the two periods a 24-hour visit during which insulin sensitivity is measured
- one follow-up visit 4 weeks after the end of the last diet.
The 4-week SFA diet and the 4-week fructose diet will be followed randomly,

alternating with (at least) a 6-week wash-out period.

Intervention

Participants follow a 4-week high SFA diet and a 4-week high fructose diet. Examples of products included in the high SFA diet include: Red meat, mature 48+ cheese, butter, all-butter biscuits, full-fat dairy products, milk chocolate. Examples of products included in the high fructose diet include: Fruit juices, soda drinks, candy, jam, syrup, sweetened cereals, cookies. The saturated fat diet will be high in fats (40-50 En% vs. 20-30 En% in the fructose diet) and will consist of about 20En% saturated fat (vs. 5En% in the fructose diet). The fructose diet will be high in carbohydrates (60-70 En% vs. 35-45 En% in the SFA diet) and will consist of about 20En% fructose (vs. 5En% in the SFA diet).

Study burden and risks

The risks of the performed measurements and the physical discomfort are low; risks related to the measurements are low because of clear exclusion criteria aimed at reducing risks and the well-experienced researchers performing these tests and isotopically-labelled water ingestion is entirely safe and non-toxic with body water enrichment up to 20 mol%. The prescribed diets will consist of only commercially available food products and the intake of these products is therefore considered safe. Furthermore, the effects of the diet in humans are quickly reversible and after the subjects have completed the two diets, they will receive tips and recipes to return to a healthier diet. After two weeks, they will be contacted by phone to discuss progress and after 4 weeks, a final visit will take place to check that blood values are within normal ranges, weight has not increased and subjects adhere to a healthier diet. In the case of a persistent unhealthy diet, we will discuss other support options with the participant

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

- Participants are able to provide signed and dated written informed consent prior to any study specific procedures
- Participants should have suitable veins for cannulation or repeated venipuncture
- Women are post-menopausal (defined as at least 1 year post cessation of menses)
- Aged >= 45 and <= 75 years
- Body mass index (BMI) 27 - 38 kg/m2
- Stable dietary habits (no weight loss or gain >5kg in the past 3 months)
- Sedentary lifestyle (not more than 2 hours of sports per week)
- No signs of active cardiovascular disease, liver or kidney malfunction
- Liver fat content >= 2% weight/weight.

Exclusion criteria

- Type 2 diabetes
- Previous enrolment in a clinical study with an investigational product during the last 3 months or as judged by the Investigator
- Patients with congestive heart failure and and/or severe renal and or liver insufficiency or another condition that may interfere with outcomes measured in this study
- Any contra-indication MRI scanning
- Alcohol consumption of >2 servings per day for men and >1 servings per day for woman

- Smoking in the past 6 months
- Men: Hb <8.4 mmol/L, Women: Hb <7.8 mmol/l
- Vegetarian, vegan, food intolerant to common foods (e.g. gluten intolerant, lactose intolerant)
- Medication use that may influence outcome parameters

A medical doctor will judge participation eligibility based on the medical history questionnaire, medication use and fasting blood parameters. If the medical doctor advises that a volunteer cannot participate, the volunteer will be excluded from enrollment.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-11-2021
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	13-10-2021
Application type:	First submission
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	NL78281.068.21