Carbohydrate regulation of lipid metabolism

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON28287

Source
Nationaal Trial Register

Brief title
SODA

Health condition

Metabolic syndrome, Insulin resistance, Dyslipemia, Bariatric surgery

Sponsors and support

Primary sponsor: Academic Medical Center (AMC), Amsterdam
Source(s) of monetary or material Support: Academic Medical Center (AMC), Amsterdam

Intervention

Outcome measures

Primary outcome

Effect of carbohydrates (glucose and fructose) on lipogenic pathways, and the in vivo de novo lipogenesis flux in obese humans with or without hepatic steatosis and insulin resistance.

Secondary outcome

In vivo relationships between fat distribution/ectopic fat accumulation, lipid/carbohydrate fluxes, hepatic/peripheral insulin sensitivity, tissue lipid composition and gene/protein expression profiles.

Study description

Background summary

Rationale: In long-term obesity, de novo lipogenesis (DNL) in adipose tissue is decreased, and lipids accumulate in ectopic sites such as liver and muscie. Altered lipid metabolism and storage is implicated in the development of insulin resistance and the metabolic syndrome. Intake of simple carbohydrates may be linked with altered DNL and ectopic fat accumulation.
Objective: To study the mechanisms underlying ectopic fat accumulation (in liver) by intake of fructose versus glucose in relation to insulin resistance in obese humans
Subjects and methods: In this observational study of obese adults that are scheduled for bariatric surgery (n=36), we will combine gold-standard isotope tracer studies to assess metabolic fluxes in vivo and analyses of human tissue biopsies. Obese subjects will be divided into groups with or without hepatic steatosis (i.e. liver fat content > or <5.56%) by magnetic resonance spectroscopy. Endogenous glucose production, hepatic insulin sensitivity, peripheral insulin sensitivity and adipose tissue lipolysis will be assessed during a two-step euglycemic hyperinsulinemic clamp with infusion of [6,6-2H2]glucose and [1,1,2,3,3-2H5]glycerol. On another visit, subjects will be randomly assigned (1:1) to consume a drink containing either fructose (75 grams in 225 ml water) or glucose (75 grams in 225 ml water), and lipid metabolism will be assessed in response to either fructose or glucose ingestion. Subjects will consume the same drink containing either fructose or glucose two hours before surgery, and biopsies from liver and abdominal fat compartments will be taken during bariatric surgery. Regulation of gene, protein and metabolite expression by intake of fructose or glucose will be assessed in insulin-sensitive tissues.
Main endpoints: Differences in the regulation of carbohydrate response/lipogenesis pathways, and the in vivo DNL flux by fructose versus glucose. Relationships between fat distribution/ectopic fat accumulation, in vivo lipid/carbohydrate fluxes, hepatic/peripheral insulin sensitivity, tissue lipid composition and gene/protein expression profiles.

Study objective

We hypothesize that i) as compared to healthy obese humans, metabolically unhealthy obese humans, characterized by ectopic fat accumulation and insulin resistance, show an enhanced lipogenic response in liver and a lower lipogenic response in adipose tissue after a fructose as compared to glucose challenge, and ii) fructose as compared to glucose has a higher lipogenic potential in liver due to preferential metabolism by the liver.

Study design

- baseline (t = 0)

- study measurements (t = 1 to 3 weeks)

- bariatric surgery (t = 4 weeks)

Intervention

none

Contacts

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Eligibility criteria

Inclusion criteria

- scheduled for bariatric surgery (Roux-en-Y gastric bypass)

- 18-65 years of age

- ability to provide informed consent

- stable weight 3 months prior to inclusion

- willingness to stop lipid lowering medication 4 weeks prior to studymeasurements

Exclusion criteria

- use of exogenous insulin, GLP-1 agonists or DPP-4 inhibitors

- all medica! and psychiatric conditions except for obesity-related diseases

- primary lipid disorders

- childhood onset obesity

- coagulation disorders

- uncontrolled hypertension

- renal insufficiency

- excessive alcohol intake

- contraindication to MRI scanning

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-08-2015
Enrollment:	36
Type:	Actual

Ethics review

Positive opinion

Date:	30-07-2015
Application type:	First submission

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
NTR-new	NL5203
NTR-old	NTR5351
Other	METC AMC : 2014_202

Study results