Intestinal production of Imidazole Propionate in healthy and obese subjects with or without DM2; a pilot trial

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To study the pharmacokinetics of non-reactive labelled histidine (L-HISTIDINE:HCL:H2O (D5, 98%; 15N3,98%) and the effect on intestinal imidazole propionate (IP)production in small intestine vs colon in healthy controls, metabolic syndrome and DM2…

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

Summary

ID

NL-OMON44179

Source
ToetsingOnline

Brief title
IP-pilot

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Metabolism disorders NEC

Synonym
diabetes, Diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Diabetes mellitus, Gut microbiota, Histidine, Imidazole propionate

Outcome measures

Primary outcome

Primary objective will be determination of plasma and 24h fecal concentrations of labelled L-histidine and its degradation products, urocanate, IP and glutamate upon either ingestion of gelatin capsules (thus small intestinal release) or colopulse capsules (colonic release).

Secondary outcome

Secondary objective will be differences in uptake and production between subjects with a normal and impaired insulin sensitivity as well as in DM2 subjects on stable dose of oral metformin in relation to fecal microbiota composition.

Study description

Background summary

The prevalence of type 2 diabetes mellitus (DM2) remains alarmingly high. Mounting evidence links the human intestinal microbiota (bacteria) as well as their produced metabolites to the development of cardiometabolic diseases, including DM2. A recent study identified a new microbiota-derived amino acid on glucose metabolism. We found that the microbially upregulated histidine-derived metabolite imidazole propionate (IP) may contribute to the pathogenesis of type 2 diabetes (DM2). But the interventional part of this study was performed in mice and in vitro only. Therefore, in the current pilot study we aim to further unravel the role of this IP in the human metabolism by first studying the

pharmacokinetics of labeled histidine and the pathway leading to IP in different parts of the intestine in subjects with a normal en impaired glucose tolerance (metabolic syndrome and DM2).

Study objective

To study the pharmacokinetics of non-reactive labelled histidine (L-HISTIDINE:HCL:H2O (D5, 98%; 15N3,98%) and the effect on intestinal imidazole propionate (IP)production in small intestine vs colon in healthy controls, metabolic syndrome and DM2 subjects

Study design

Interventional controlled single centre pilot study

Intervention

We will orally administrate labelled histidine twice (either using gelatin capsules that are releasing histidine in the small intestine versus ColoPulse-capsules that release histidine in the colon) and subsequently measure histidine, urocanate, IP levels and glutamate levels until 24h after ingestion.

Study burden and risks

Subjects will visit the AMC for the screening and then four times: for both the capsules they will come on two consecutive days with a week in between. They will orally take labelled histidine and blood samples will be taken at different time points, with an amount of blood taken of 220 ml in total. 24h urine and 24h feces will be collected twice and subjects are asked to monitor their dietary intake during the study days.

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

All subjects: age 18-54 years old, caucasian male, able to give informed consent;- Healthy controls: Subjects do not meet the criteria for metabolic syndrome or diabetes type 2, BMI <25 kg/m2
- Metabolic syndrome subjects: at least 3 out of 5 NCEP metabolic syndrome criteria (fasting plasma glucose * 5.6 mmol/l OR HOMA * 2.5, triglycerides * 1.7 mmol/l, waist-circumference > 102 cm, HDL-cholesterol < 1.04 mmol/l, blood pressure * 130/85 mmHg).
- DM2 subjects: must meet the criteria for DM2: a random blood glucose level of >11.1 mmol/L and/or a fasting blood glucose level of >7.0 mmol/L and/or a blood sugar glucose of >11.1mmol/L two hours after an oral glucose toleralance test and/or an HbA1c of >47mmol/mol. Stable metformin use for at least 1 month (preferably 3dd 500mg)

Exclusion criteria

All subjects:
- Cholecystectomy
- A history of cardiovascular event (MI or pacemaker implantation)
- Use of medication in the last three months with the exception of metformin for DM2 subjects
- (expected) prolonged compromised immunity (due to recent cytotoxic chemotherapy or HIV infection with a CD4 count < 240).
- Smoking, drugs- or alcohol abuse

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-02-2018
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO

Date:	08-09-2017
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	NL61849.018.17