Intestinal imidazole propioNaTE productioN after histiDinE supplementation in healthy and type 2 Diabetes mellitus subjects: role of the gut microbiota; INTENDED-study

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Evaluate pharmacokinetic levels of imidazole propionate (ImP) as a result of orally administrated histidine and assess the role of the gut microbiota in this respect, in Type 2 diabetes (T2D) from Dutch and South Asian Surinamese descent as compared…

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

Summary

ID

NL-OMON54977

Source
ToetsingOnline

Brief title
INTENDED

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Diabetic complications

Synonym
diabetes mellitus, sugar disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Beurs vanuit het Joint Programme Initiative van de EU en subsidie van de Nederlandse Hartstichting

Intervention

Keyword: Diabetes, Histidine, Microbiota

Outcome measures

Primary outcome

Primary objective will be determination of ImP levels after histidine intake

and other degradation products such as urocanate and glutamate before and after

oral antibiotics.

Secondary outcome

Secondary objectives will be differences in histidine uptake effect upon oral

histidine supplementation on PBMC inflammatory status, influence of gut

microbiome on ImP production, continuous (freestyle libre) as well as

postprandial (after a mixed meal test) glucose levels between healthy and T2D

subjects on stable dose of oral metformin. Furthermore, we will evalualte if

the kinetics and other mentioned parameters are affected differently between

ethnicities by histidine intake.

Study description

Background summary

The gut microbiota plays a pivotal role in the pathophysiology of cardio-metabolic diseases (CMD), such as T2D, obesity and atherosclerosis. The diet shapes the gut microbiota which can further transform dietary food items into circulating metabolites, which acts on the host. Among them, Imidazole

propionate (ImP) has recently been discovered. In vitro and mouse experiments demonstrated that ImP originate from histidine metabolization by the gut microbiota. Furthermore, ImP is increased in T2D individuals as compared to healthy controls and induces glucose intolerance in mice. In this study we aim to confirm in humans that ImP indeed derives from gut microbiota processing of oral histidine intake. In addition to this, the composition of the mircobiome has been shown to be different between ethnicities, particularly between individuals from Dutch or South Asian Surinamese descent. Therefore, we also want to evaluate of histidine kineticsc and other relevant parameters are different between these two ethnicities. Furthermore, we aim to evaluate ImP concentrations after an oral challenge and demonstrate that it differs between T2D and controls.

Study objective

Evaluate pharmacokinetic levels of imidazole propionate (ImP) as a result of orally administrated histidine and assess the role of the gut microbiota in this respect, in Type 2 diabetes (T2D) from Dutch and South Asian Surinamese descent as compared to healthy controls from the same ethnicities.

Study design

Interventional controlled single centre study

Intervention

We will orally administrate 4g of the food supplement histidine (Vital Cell Life L-Histidine 500 MG Capsules 100CP) once a day for 7 weeks, after the first 2 weeks, one week of antibiotics will be added to suppress the gut microbiome followed by a four weeks recovery period. Plasma and urinary ImP, histidine, urocanate and glutamate levels will be measured as well as, peripheral blood monocyte cells (PBMC) for inflammatory status will be measured at specific time points.

Study burden and risks

Subjects will visit the AMC for the screening and then eight times. They will orally take the food supplement histidine for 7 weeks and antibiotics (for 7 days). Blood samples will be taken at different time points, with a total amount of 464 ml in total over 7 weeks. Also 24h urine and 24h feces will be collected at four visits and subjects are asked to monitor their dietary intake during the study days. Two days after starting with antibiotics, individuals will be asked to freeze their feces at home and bring it to the next study visit. In a previous study higher dosages of the food supplement histidine were given without any adverse effecte, therefore, in this study we do not expect

any adverse effect of histidine use.

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

Healthy subjects: (n=11 Caucasian and n=11 from South Asian Surinamese descent)
- Healthy subjects 40-70 years,
- BMI 19-25
T2D subjects:(n=11 Caucasian and n=11 from South Asian Surinamese descent)
- T2D patients
- Caucasian / South Asian Surinamese
- 40-70 years
- BMI 25-35
- Stable anti-diabetic drugs for 3 months (metformin is obligatory)

- Statin use
- Stable medication use past 3 months
- Able to give informed consent

Exclusion criteria

All participants:
- Previous major cardiovascular event (e.g. AMI/stroke/TIA)
- Proton-pomp inhibitor use
- GLP1 or insulin
- Antibiotics use for the past 3 months
- Probiotic of symbiotic usage
- 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
- Vegetarian diet
- >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:	Recruitment stopped
Start date (anticipated):	28-05-2020
Enrollment:	44

Type:	Actual

Ethics review

Approved WMO Date:	07-02-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-12-2020
Application type:	Amendment
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	NL71957.018.19