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

Gepubliceerd: 11-02-2020 Laatst bijgewerkt: 13-12-2022

Histidine supplementation will lead to higher plasma ImP levels in T2D patients, but not in healthy controls and this effect is mediated by the gut microbiota.

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20133

Bron
NTR

Verkorte titel
INTENDED

Aandoening

Type 2 diabetes

Ondersteuning

Primaire sponsor: N/A
Overige ondersteuning: N/A

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Evaluate ImP, urocanate, glutamate and histamine plasma level excursions upon 4 grams of histidine supplementation before, during and after a short course of oral antibiotics in T2D and healthy controls of Caucasian and Surinamese ethnicity.

Toelichting onderzoek

Achtergrond van het onderzoek

Background:
In-vivo and in-vitro studies have suggested that histidine could drive metabolic alterations in obese type 2 DM (T2D) humans via the production of imidazole proprionate (ImP), the production of which might be driven via an altered gut microbiota composition. Since there are currently no data on direct oral histidine supplementation on several markers of cardiometabolism in obese T2D humans nor on its related metabolite production ImP by the gut microbiota in humans, we therefore propopose the following study.

Objective:
Evaluate pharmacokinetic levels of imidazole propionate as a result of orally administrated histidine and assess the role of the gut microbiome in this respect, T2D as compared to healthy controls.

Rationale:
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, ImP has recently been discovered. In- vitro and animal 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 can induce glucose intolerance in mice. In this study we aim to confirm in humans that ImP indeed derive from gut microbiota processing of oral histidine intake. Furthermore, we aim to evaluate ImP concentrations after an oral challenge and demonstrate that it differs between T2D and controls. We also aim to see if these processes differ by ethnicity, as the gut micorbiota has been shown to also differ per ethnic group.

Study design:
Interventional controlled single centre study

Study Population:
44 subjects: 22 healthy controls, 22 type 2 diabetes mellitus (T2D) on stable metformin use. 11/22 subjects of both groups will be of Caucasian descent and the other 11 of Surinamese

descent.

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.

Outcome measures:
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 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.

Sample Size: 44

Doel van het onderzoek

Histidine supplementation will lead to higher plasma ImP levels in T2D patients, but not in healthy controls and this effect is mediated by the gut microbiota.

Onderzoeksopzet

total intervention will be 2 months per subject and the subjects will visit the center for 7 times in total during the 2 months

Onderzoeksproduct en/of interventie

Histidine supplemenation 4g/day for 7 weeks.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Healthy controls:
- 22 healthy controls 40-70 years, BMI <30kg/m2
- 11 controls of Caucasian descent and 11 of Surinamese descent

Type 2 Diabetes (T2D) subjects:
- 22 T2D patients (11 of Caucasian descent and 11 of Surinamese descent)
- 40-70 years
- BMI 25-35
- Stable anti diabetic drugs for 3 months (metformin is obligatory)
- All on statin
- Stable medication uses past 3 months
- Able to give informed consent

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Previous major cardiovascular event (e.g. AMI/stroke/TIA)
- PPI
- GLP1 nor insulin
- antibiotic use in the past 3 months
- Probiotic or 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 (can also influence microbiota)
- Vegetarian diet (since they have different microbiota)
- >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

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	11-02-2020
Aantal proefpersonen:	44
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	11-02-2020
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8372
Ander register	METC AMC : METC 2019_261

Resultaten