Acute microbial switch study

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In this project we aim to investigate whether we can precisely measure the changes in fermentation gas patterns after supplementation of a complex fibre mixture over a 36-hour period in both lean normoglycemic and insulin resistant and/or...

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

Summary

ID

NL-OMON56140

Source
ToetsingOnline

Brief title
Acute microbial switch

Condition

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

Synonym
insulin resistance, overweight

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: NWO Domain Applied and Engineering Sciences (AES)

Intervention

Keyword: dietary fibers, gut microbiota, microbial gas, substrate metabolism

Outcome measures

Primary outcome

The difference in the 36h pattern of expired gut fermentation gases (H2S, H2 and CH4) after supplementation of a complex fibre mixture compared with placebo treatment in lean normoglycemic and overweight/obese prediabetic individuals. Furthermore we will compare the responses of the two different study populations.

Secondary outcome

- Energy expenditure and substrate oxidation over a 36h period (indirect calorimetry)
- Faecal and circulating microbially derived metabolites
- Circulating hormones insulin, PYY (peptide YY) and GLP-1 (glucagon like peptide-1)
- Circulating metabolites (glucose, FFA, and triacylglycerols).
- Faecal microbiota composition
- Fecal and blood SCFAs acids and BCFAs
- Urinary markers of proteolytic and saccharolytic fermentation
- Three-day food record. A three-day food record will be completed three days prior to each CID.
- Appetite (Visual Analog Scales (VAS)-scoring system for hunger and satiety).
- Gastrointestinal Symptom Rating Scale (GSRS) questionnaire. The GSRS will be completed the day before and during the clinical investigation

days.

- Expired 13CO2

- Cortisol from saliva when waking up

- Cognitive testing (CANTAB)

The variables will be compared between ingestion of the fiber supplement versus the placebo. Additionally we will compare the responses between the two research populations included in the study.

Study description

Background summary

The gut contains trillions of microbes that produce a large variety of products that impact host metabolism, immunity and brain health. Recent evidence indicating that fermentation products from indigestible food compounds, like dietary fibres or proteins, may impact metabolism and immune status has led to the awareness that microbial fermentation is instrumental for maintaining health in humans. More information on the response and interaction of our gut microbiota to diet and environmental factors, such as physical activity and medication use, may lead to more effective and targeted approaches in prevention and management of chronic diseases like obesity, non-alcoholic fatty liver disease, diabetes, cardiovascular disease and mental disorders. We will develop a novel methodology that enables the development and evaluation of ground-breaking interventions targeted on the modulation of the gut microbiome. To achieve the novel gut-microbial methodology, a whole-body room calorimetry installation will be redesigned to achieve a *non-invasive real-time in vivo microbial fermentation chamber*. The system will measure human-expired gut microbial relevant gases such as methane (CH4), hydrogen (H2) and hydrogen sulphide (H2S) combined with host energy expenditure and substrate utilization. It will provide the unique opportunity to measure real-time microbial fermentation combined with host substrate energy metabolism. This allows the screening of dynamic gut-microbial response to the impact of amongst others foods, medication and exercise. Therefore, this system will deliver fundamental data to better understand the interplay between diet, other environmental factors and the gut microbial fermentation. Through this, it will be possible to steer the production of beneficial fermentation products in the intestine

with food products or lifestyle intervention strategies to support gut, metabolic, immune and brain health. This study is an important part of NWO Human Measurement Models 2.0 with the aim is to facilitate the development of new, more efficient human measurement models for health research to ensure that research results can be applied better and faster in humans. With this methodology, researchers can test and develop nutritional compounds and intervention strategies aimed to improve gut microbial health underlying human health. This will be the first study on real-time, non-invasive gut microbial fermentation in humans. We will investigate with this study whether we can determine the switch from proteolytic to saccharolytic fermentation following ingestion of a dietary fibre mixture in healthy lean and overweight/obese insulin resistant and/or prediabetic individuals.

Study objective

In this project we aim to investigate whether we can precisely measure the changes in fermentation gas patterns after supplementation of a complex fibre mixture over a 36-hour period in both lean normoglycemic and insulin resistant and/or prediabetic individuals with overweight/when compared with a placebo. Additionally, we will investigate whether changes in fermentation patterns will be directly related to changes in substrate metabolism and metabolites/hormones in expired air, blood, faeces, and urine.

Study design

Double blind, controlled, randomized, crossover design.

Intervention

Starting from CID1, participants will start a two-day daily consumption of either a complex dietary fibre mixture: 12 g (3 × 4 g) of long-chain inulin (Frutafit TEX! Sensus B.V., Roosendaal, The Netherlands) in combination with 9.39 g (3 × 3.13 g (80% resistant starch RS2 (3 × 2.5 g)) granular potato starch (Avebe, Veendam, The Netherlands) or 11.43 g (3 × 3.81 g) maltodextrin Glucidex IT 12 (Roquette Freres, Lestrem, France) maltodextrin as a placebo treatment for two consecutive days.

At the first breakfast in the respiration chamber during the fiber supplementation period, 500 mg of inulin will be replaced with 500 mg inulin that is naturally enriched with 13C (DP 3-60, IsoLife, Wageningen, The netherlands).

Study burden and risks

all participants will be screened prior to participation and will thereby gain information about their health status. In the future there can be general

benefits for the public, but the volunteers will have no personal benefit of participating in the study. The general interest in this study is that there is currently no methodology to study the kinetics of fermentation in real-time faithfully. The amounts of long-chain inulin and resistant starch have been used in previously performed human trials and have been proven safe. In this study participants may experience the following as a burden. After initial screening, subjects will have to invest approximately 72 hours in the study (See table 1). During the study participants will remain in a respiration chamber. The participant may consider staying in a predefined space for a prolonged period of time as a burden. Blood will be collected via a venous catheter. Venepunctures can occasionally cause a local hematoma or bruise to occur. Some participants report pain during venepuncture. Also the collection of stool and urine samples can be seen as a burden. Receiving a standardized diet and having to perform a stepping workout at specific timepoints can be considered as a burden. Lastly having to ingest the fiber supplemen may be considered as a burden.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Fourteen lean (BMI >= 18.5kg/m2 and <= 24.9kg/m2) normoglycemic individuals (fasting glucose < 5.6 mol/L and HOMA-IR < 2.2) aged 30 - 75 years and fourteen individuals with overweight/obesity (BMI >= 28kg/m2 and <= 40 kg/m2) with insulin resistance (HOMA-IR>2.2) and/or impaired fasting glucose (IFG: plasma glucose >= 5.6 mmol/l) aged between 30 - 75 years will be included.

Exclusion criteria

- diabetes mellitus
- gastroenterological diseases or major abdominal surgery (allowed i.e.: appendectomy, cholecystectomy)
- lactose intolerance and other digestive disorders
- cardiovascular disease, cancer, liver or kidney malfunction (determined based on ALAT and creatinine levels,
respectively)
- disease with a life expectancy shorter than 5 years
- abuse of products (alcohol consumption > 15 units/week, or any drugs)
- excessive nicotine use defined as >20 cigarettes per day
- plans to lose weight or follow a hypocaloric diet
- regular supplement of pre- or probiotic products
- intensive exercise more than three hours a week
- use of any medication that influences glucose or fat metabolism and inflammation, like i.e. lipid
lowering-drugs (e.g. PPAR γ or PPARα (fibrates) agonists), glucose-lowering agents (including all
sulfonylureas, biguanides, α-glucosidase inhibitors, thiazolidinediones, repaglinide, nateglinide and insulin),
anti-oxidants or chronic corticosteroids treatment.
- use of laxation products in the last three months or during the study period
-pregant or breastfeeding

Study design

Design

Study type: Interventional

Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-01-2024
Enrollment:	56
Type:	Actual

Ethics review

Approved WMO Date:	13-06-2023
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-10-2023
Application type:	Amendment
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	NL82078.068.22