Carbohydrate induced resilience of the gut microbiome after antibiotics use

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal conditions NEC
Study type	Interventional

Summary

ID

NL-OMON55342

Source
ToetsingOnline

Brief title
The CARMA study

Condition

- Gastrointestinal conditions NEC
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Gut microbiome dysbiosis

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: NWO,Avebe,FrieslandCampina,Nutrition Sciences,Private partners in het consortium (CCC Carbobiotics),TKI Agri&Food,Wageningen Universiteit

Intervention

Keyword: Antibiotics, Microbiome, Prebiotics, Resilience

Outcome measures

Primary outcome

The main outcome parameter will be microbiome resilience, which will be described as the change in gut microbiome composition and activity between baseline, after antibiotics use and during/after 2'-FL/placebo supplementation. This parameter will be investigated at six different timepoints throughout the study.

Secondary outcome

The secondary outcome parameters of the study are BMI, waist-to-hip ratio, body composition, glucose tolerance, fat metabolism, adipose tissue gene and protein expression and levels of short-chain fatty acids, inflammatory markers and satiety hormones in the blood. These parameters will be investigated on three different timepoints during the study: at baseline, after antibiotics use and after the supplementation period.

Study description

Background summary

The gut microbiome is a complex ecosystem with a wide range of functions, and it is thought that it can influence multiple processes in the human body. In turn, the composition and activity of the gut microbiome is affected by many factors as well. Two of these factors are antibiotics and prebiotics, and they are central in this study.

Antibiotics can be very effective in treating bacterial infections, but they are also associated with detrimental health effects. Previous studies have

already shown that antibiotics disturb the human gut microbiome composition by destroying commensal bacteria. As it is well known that the microbiome influences host metabolism, perturbation of the healthy microbiome (dysbiosis) is thought to be disease causing.

Prebiotics, on the other hand, are beneficial for the gut microbiome. These so-called indigestible fibers are naturally present in our foods, but cannot be metabolised by the human body. Many bacteria in the human gut are able to ferment these fibers and they subsequently produce beneficial products for the rest of the body. Besides this, fiber intake stimulates growth of commensal bacteria in the human gut.

Although it has become increasingly clear that prebiotics have a beneficial effect on the gut microbiome and general health, it is still unclear to which extent the beneficial effects of prebiotics supplementation occur after the gut microbiome is disturbed by antibiotics. We hypothesize that prebiotics supplementation after antibiotics use will improve restoration of the gut microbiome to a healthy state compared to placebo.

Study objective

The objective of this study is to investigate the potential of a dietary fiber, 2'-fucosyllactose (2'-FL), to improve gut microbiome resilience after antibiotics use.
Furthermore it will also be investigated whether there is a link between restoration of the gut microbiome and changes in metabolic parameters such as glucose or fat metabolism, and if this is affected by 2'-FL supplementation.

Study design

The proposed study is a double-blind, randomized placebo-controlled study. Here, 40 healthy adults will first receive the antibiotic vancomycin for 7 days to disturb the gut microbiome, after which they will receive either 2'-FL supplementation or placebo (maltodextrin) for 8 weeks.
All study parameters will be assessed in two parallel groups, to which subjects will be assigned using minimization.

Intervention

During the first 7 da7s of the study period, all participants will be provided with the antibiotic vancomycin. Participants will be asked to take two capsules of 250 mg three times per day for 7 days, leading to a total dose of 1500 mg per day.

After this period the group will be randomized into two groups using minimization. One group will receive the 2'-FL supplementation for 8 weeks,

which consists of three portions of 4 g 2'-FL per day, for a total of 12 g 2'-FL daily. The other group will receive a placebo (maltodextrin) supplementation during this period, which consists of three portions of 2 g maltodextrin per day for a total of 6 g maltodextrin daily. The two supplementations are isocaloric.

Study burden and risks

The total study period, from screening until the last clinical investigation day, will take approximately 11 weeks. During this period participants will be asked to visit the university a total of 8 times for both clinical investigation days and supplementation days. The investigation days will take 4 hours, while the supplementation days will take at the most 30 minutes. Although 11 weeks is quite a long period of time, the number of hours participants are asked to be present at university is limited.
Participants will be asked to take the antibiotic vancomycin for 7 days and subsequently, for a period of 8 weeks, to take either the 2*-FL supplementation or placebo. During this period participants will be asked to keep to their habitual diet and physical activity. This will be checked at six timepoints via food diaries and a physical activity questionnaire. At these timepoints, participants will also be asked to collect feces and fill in a questionnaire regarding gastrointestinal symptoms. These actions will take approximately 2 hours per timepoint.

There are no risks associated with 2'-FL or maltodextrin. 2'-FL has been shown to be safe in the dose used here, with side-effects being limited to gastrointestinal discomfort.
The main risk for participants in this study is associated with the 7 days of antibiotics use. Although side-effects of vancomycin are mainly limited to mild gastrointestinal discomfort, permanent hearing loss and kidney insufficiency have been reported in some cases. Furthermore, participants might be allergic to vancomycin without knowing this.

Furthermore, during the clinical investigation days certain measurements will be performed which may be causing some discomfort for participants. One example of such a measurement is the placement of a peripheral intravenous cannula, which will be used to draw blood multiple times during the investigation days. Besides this, an abdominal subcutaneous adipose tissue biopsy will be taken at the investigation days. During this, the discomfort may be higher. As participants can experience these measurements as unpleasant, they will be performed by well-trained and exprienced professionals. Furthermore the amount of blood-drawings and biopsies is kept to a minimum, to limit participant discomfort.

During the screening prior to the start of the study, potential participants will be screened for health risks. If these are present, invidividuals will be excluded from participation. All clinical investigation days will take place in

the Metabolic Research Unit Maastricht and the responsible medical doctor will be aware of all investigation days. Furthermore participants are able to contact the researchers and an independent expert at all times in case of complications or questions.

Given the duration of the study period of 11 weeks, the time-investment is considerable. The amount of time participants have to be present at the university is limited however. Besides this, possible risks for the participants with regards to study products and measurements are limited as much as possible. There are also suffiicient safety measures in place and sufficient professionals on site to minimize potential risks. Given these burden and risks, we feel that is justifiable to conduct the study.

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 overweight/obese (BMI: 25-40 kg/m^2) Caucasian adults (age: 20-65 years), male and female, with a stable body weight (< 3 kg change) for the last 3 months.

Exclusion criteria

- Known allergic reaction to vancomycin or other glycopeptide antibiotics;
- Pre-diabetes, diabetes mellitus, cardiovascular disease, kidney disease, hearing disorders, cancer, asthma or bronchitis, liver malfunciton, diseases affecting glucose tolerance, major illness with a life expectancy < 5 years, gastrointestinal disease or abdominal surgery,
- Abuse of products; alcohol and drugs, excessive nicotine use defined as > 20 cigarettes per day;
- Regular use of laxation products;
- Use of antibiotics in the past 3 months;
- Regular supplementation of pre- or probiotics products, use of pre- or probiotics 3 months prior to the start of the study;
- Plans to lose weight or currently following a hypocaloric diet;
- Following a vegan diet;
- Participation in organized sports activities for > 3 hours per week.
- Suffering from hearing loss or other hearing problems.
- Currently pregnant, planning to become pregnant or currently breastfeeding.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-11-2020
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	07-07-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-01-2021
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	NL73140.068.20