Reassessment of the biological variation of the lactulose mannitol test in healthy volunteers and in patients one year after bariatric surgery

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The study aims to determine the biological variation of the lactulose mannitol ratio. The variation (Cv) in the lactulose mannitol ratio of 0-2 hours urine will be compared to the Cv of the lactulose mannitol ratio of 2-5 hours urine and 0-5 hours...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON53298

Source
ToetsingOnline

Brief title
LacMan

Condition

- Other condition

Synonym
Intestinal permeability disorder

Health condition

Test van de darmdoorlaatbaarheid in gezonde vrijwilligers en patiënten na bariatrische chirurgie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Intestinal, Markers, Permeability, Variation

Outcome measures

Primary outcome

The primary outcome of the study is the lactulose/mannitol ratio of 0-2, 2-5 and 0-5 hours-urine and the coefficient of variation of the lactulose mannitol ratios. The results of different healthy volunteers will be compared to each other (inter-individual variation) as well as the results of one healthy volunteer on a different day (intra-individual variation)

Secondary outcome

A possible outcome is the implementation of the lactulose mannitol test as a standard test in the UMCG. Therefore, participants are asked to fill in a questionnaire about how they experienced the collection of urine and fasting. The questionnaire only has to be filled in after the first measurement.

Study description

Background summary

The intestinal permeability is interesting to investigate because the intestinal barrier plays an essential role in major physiological processes. A non-invasive test like the lactulose mannitol test can be used to determine intestinal permeability. This test is based on orally administering two sugars

and quantifying these in urine samples. Lactulose and mannitol are excreted unmetabolized in urine, so the amount measured in the urine provides information about the intestine's absorption. Lactulose is a sugar that leaks through pores in between the enterocytes and usually is not absorbed. Mannitol is absorbed by enterocytes. Increased intestinal permeability is shown as a higher lactulose/mannitol ratio in the collected urine. The lactulose/mannitol test is the most popular intestinal permeability test which has been used for decades. At this very moment the lactulose/mannitol test is used in various hospitals in the Netherlands, as well as in clinical studies all over the world. The biological variation of the lactulose/mannitol ratio has been assessed once in 1993 using gas-liquid chromatography. Information on the biological variation of the lactulose/mannitol ratio is helpful for the interpretation of results of studies and if population-based reference intervals will be used for the lactulose/mannitol test. Nowadays the lactulose mannitol test is performed by collecting urine for five hours after ingestion of the sugars. However, more studies are performing the lactulose/mannitol test by collecting urine for two hours. Scientific research has shown that the lactulose/mannitol ratio of the urine of the first two hours specifically reflects small intestinal permeability, while the lactulose/mannitol ratio of urine after two hours also partly reflects colonic permeability.

Because more studies are performing the lactulose/mannitol test by collecting urine for a shorter period of time, and because the biological variation has been established long ago and with a different quantification technique, we want to reassess the biological variation with the use of liquid chromatography-mass spectrometry. We want to assess the biological variation in urine collected for two hours, the total five hours and the last three hours.

We expect that the lactulose/mannitol ratio of 0-5 hour collected urine will show more variation than 0-2 hour collected urine and 2-5 hour collected urine because 0-5 hour collected urine shows both small intestinal as colonic permeability. The permeability of the small intestine and colon is different because both have different epithelial cells present, and because of differences in anatomy.

Study objective

The study aims to determine the biological variation of the lactulose mannitol ratio. The variation (Cv) in the lactulose mannitol ratio of 0-2 hours urine will be compared to the Cv of the lactulose mannitol ratio of 2-5 hours urine and 0-5 hours urine.

The inter-individual variation will be assessed by comparing the results of different individuals. The intra-individual variation will be assessed by comparing the results of a single individual on different days.

Study design

Written valid informed consent for fasting will be obtained from all participants before starting the study. Participants will also fill in their bank account information for the incentive. After a minimum of eight hours or overnight fast participants are asked to collect a baseline urine sample when waking up in a plastic urine container. Then, the participants will ingest the sugar solution and drink 200 ml of water to prevent dehydration. After ingestion, the participants will collect urine in the "0-2 hour" container. At the end of the first two hours, participants will void all urine left in the bladder in the 0-2 hours-container to collect all urine of the first two hours. Participants will drink another 200 ml of water to prevent dehydration. After the first two hours, urine will be collected in a different urine container labeled as *2-5 hours*. Right before the end of the five hour collection, participants will void all urine left in the bladder in the 2-5 hours container to collect all urine. Participants will deliver the urine containers at the UMCG. The deadline is two days after the measurement. After one week the second measurement takes place, and one week after the second measurement the third can take place.

Study burden and risks

Ingestion of the sugar solution has no risks. Fasting could be uncomfortable for participants, but also here there are no risks involved. Fasting will not damage the body. Urinating in containers could be a burden, but since urinating is a natural occasion the burden is expected to be negligible.

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 volunteers:
- Provide written informed consent
- Age >= 18 years old
- BMI < 30 kg/m2

Patients after bariatric surgery:Provide written informed consent
- Age >= 18 years old
- One year after OAGB or RYGB

Exclusion criteria

The usage of NSAIDs (e.g. ibuprofen, naproxen, diclofenac, acetylsalicylic acid) within the prior week or during the study.

Chronic use of diuretics

Chronic use of antibiotics

Pregnancy

Alcohol consumption of >8 units/week

The use of tobacco products within the prior week

The presence of gastrointestinal diseases (e.g., Crohn*s disease, ulcerative colitis, irritable bowel disease, gastric cancer) including stomach and intestinal complaints

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2024
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO Date:	31-08-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-06-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL83799.056.23