Labelled-butyrate and labelled-glucose breath testing to detect mesenteric ischemia, a proof of principle study in healthy volunteers

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To explore the possibility of detecting mesenteric ischemia by 13C-butyrate, 13C-glucose, and 13C-glucose and D-butyrate breath testing by comparing the timing and concentration of the peak of expired 13CO2 and DHO.

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal vascular conditions
Study type	Interventional

Summary

ID

NL-OMON50079

Source
ToetsingOnline

Brief title
CMI breath test

Condition

- Gastrointestinal vascular conditions

Synonym
Chronic mesenteric ischemia, intestinal oxygen shortage

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 13C-butyrate, 13C-glucose, breath test, Mesenteric ischemia

Outcome measures

Primary outcome

The possibility of detecting mesenteric ischemia by 13C-butyrate, 13C-glucose, and 13C-glucose and D-butyrate breath testing by differences in timing and concentration of the peak of expired 13CO2 and DHO between control and intervention group.

Secondary outcome

To determine the optimal oral dose of D-butyrate for the measurement of D-butyrate metabolism in enterocytes by performing a DHO breath test

Study description

Background summary

Chronic mesenteric ischemia (CMI) is an incapacitating disease that can progress to potentially fatal acute mesenteric ischemia. The yearly incidence of CMI is 9.2 per 100.000 and will increase due to the aging population and the rising prevalence of cardiovascular risk factors. A gold standard diagnostic test to diagnose CMI is currently lacking, causing both undertreatment and overtreatment of patients and thereby superfluous healthcare expenses. Since oxygen is needed to absorb and metabolize butyrate and glucose in the enterocyte, a 13C-butyrate, 13C-glucose, or 13C-glucose and D-butyrate breath test could theoretically quantify mucosal oxygen content and thereby identify patients with CMI.

Study objective

To explore the possibility of detecting mesenteric ischemia by 13C-butyrate, 13C-glucose, and 13C-glucose and D-butyrate breath testing by comparing the

timing and concentration of the peak of expired 13CO2 and DHO.

Study design

This study is a multi-center randomized interventional proof of principle study, exploring the possibility of quantifying mucosal oxygen content by 13C-butyrate, 13C-glucose, and 13C-glucose and D-butyrate breath testing.

Intervention

Three control groups consisting of 5 volunteers will be used during the study. The first group will receive an oral dose of 0.03 µmol 13C-butyrate, the second group 3.5 gr D-glucose-1-13C, and the third group 3.5 gr D-glucose-1-13C and a dose of D7-butyrate. The D7-butyrate dose is set by performing dose-finding experiments, before the start of inclusion. The control groups will perform breath tests without performing any physical exercise. Three intervention groups both consisting of 5 volunteers will receive similar dosages of 13C-butyrate, 13C-glucose, and 13C-glucose and D7-butyrate as the control group. All intervention groups will be performing a standardized bicycle ergometer exercise test with a total duration of 30 minutes(10). The exercise test has been proven to provoke mesenteric ischemia in athletes(11).
All volunteers will perform two breath tests at the following time points baseline, 0.5, 1, 1.25 1.5, 1.75, 2, 2.25, 2.5, 3, 3.5, and 4 hours after ingestion of 13C-butyrate, 13C-glucose, or 13C-glucose and D7-butyrate. The decision to perform breath testing for a total of 4 hours was based on a study that determined 14CO2 elimination after administering 14C-butyrate (7, 12). A peak in expired 14CO2 was measured after 2 hours. Since we are interested in the peak of expired 13CO2 and DHO, a measurement period of 4 hours seems sufficient, even in the intervention group, in whom a delayed or lower peak is expected. The frequency of breath testing is intensified between 1 and 2.5 hours after ingestion, to detect the timing of the 13CO2 and DHO peak more precisely. Samples will be analyzed using mass spectrometry.

Description of intervention: The exercise test consists of 3 phases. Phase 1: The first 10 minutes of exercise are used to gradually increase the workload until submaximal exercise intensity is reached. Submaximal exercise is defined as lactate between 3 and 5.5 mmol/L, obtained from a peripheral intravenous catheter. Lactate measurements are performed every 2 minutes, using a rapid lactate measurement kit. Phase 2: From minute 10 until 20 submaximal exercise intensity is maintained by adjusting the workload based on lactate measurements. The lactate measurements are performed every 3 minutes. Phase 3: Minute 20 until 30 are used to reach maximal exercise intensity. Every 3 minutes the workload is increased by 10% of the submaximal workload until exhaustion. Lactate measurements will be continued with 3-minute intervals.

Study burden and risks

All participating volunteers will perform 2 breath tests at baseline, 0.5, 1, 1.25 1.5, 1.75, 2, 2.25, 2.5, 3, 3.5, and 4 hours after ingestion of 13C-butyrate, 13C-glucose, and 13C-glucose and D-butyrate. A peripheral intravenous cannula will be inserted in patients in the intervention group, to obtain a serum blood sample at baseline and after the exercise test. The cannula will also be used to obtain blood for the lactate measurements during the exercise test. Participating volunteers will not experience any benefits of participation. No adverse events are expected and risks associated with participation are deemed very low to non-existent. Insertion of the peripheral intravenous cannula can result in a hematoma.

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

* *18 years of age
* Experience with cycling
* Signed informed consent
* Unremarkable medical history (no gastrointestinal diseases, no cardiac or pulmonary diseases)
* No gastrointestinal complaints

Exclusion criteria

* Unable to sign informed consent
* Pregnancy

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2020
Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO

Date:	29-04-2020

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-01-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL72878.078.20