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Protein gastrointestinal permeability and exercise

Submission date	Recruitment status	[_] Prospectively registered
12/12/2014	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
21/01/2015	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
17/12/2020	Digestive System	

Plain English summary of protocol

Background and study aims
It is commonly assumed that the proteins that we eat in our diet are broken down by the digestive system into organic compounds called amino acids. However, recently the focus has switched towards a view in which small amounts of intact protein and peptides do enter the circulation. What molecules pass from the digestive system to the circulation depends on so-called intestinal permeability, where the intestine allows nutrients pass though the gut wall while acting as a barrier to keep potentially harmful substances, such as bacteria, from passing through to the general circulation. Current research into intestinal permeability to proteins has focussed on its role in a number of different conditions including Crohn's disease, celiac disease and inflammatory bowel disease . Little research has been done with regard to the uptake of proteins and peptides (fragments of proteins) under different degrees of intestinal permeability and their biological relevance in a healthy population. Here, we want to look at the effect of exercise-induced permeability on the amount of casein (a type of protein found in milk) and casein-derived peptides available in the blood (plasma bioavailability). We also want to compare intestinal permeability to simple sugars with intestinal permeability to casein and casein-derived peptides. Lastly, we plan to study the effect of exercise-induced permeability on markers of inflammation, exercise metabolism, and function of the digestive system (gastro-intestinal function).

Who can participate?
Men aged between 18-35 that cycle at least twice a week, with a body mass of 20-25 kg/m2.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 (intervention) drink a multisugar solution just before starting a two day exercise test. Those in group 2 (control) drink the multisugar solution but do not do any exercise.The exercise test consists of two parts. The first part is performed in the evening and involves exercise that is meant to use up the body' s glycogen (energy) stores. The second part is performed after an overnight fast and involves 90min cycling at 50% of the maximal capacity of each participant (calculated using Wmax and VO2max) . The gut barrier function of all participants are measured by collecting urine and blood just before group 1 start the exercise test and then at regular intervals for the next 5 hours after the exercise test. Sugars, casein-derived amino acids and other compounds (related to energy

metabolism, immune system and inflammation) are measured from the collected urine and plasma. One more blood sample is taken from all participants 24 hours after the exercise test is complete for group 1 participants and after an overnight fast. This complete three-day-protocol is repeated one week later with the control and intervention groups swapped around to see whether the results are reproducible.

What are the possible benefits and risks of participating?
There is no direct health-related benefit for the subjects, but for the subjects the measurement of the Wmax and VO2max is of great value, because they can use it to improve and optimize their training program and progress. Subjects completing the study will receive financial compensation of €220. There are minor risks for the subjects during this study. People most at risk of allergic reactions are excluded from participating. The exercise the subjects will have to perform is severe and will result in fatigue, and can give rise to some muscle soreness afterwards, but this intensity is needed to ensure a reaction on intestinal permeability and immunity. The intensity of the exercise will be well-tolerated in the participants chosen i.e. trained athletes. There is a small risk of bruising regarding the blood sampling procedures.

Where is the study run from?
Wageningen University (Netherlands)

When is the study starting and how long is it expected to run for?
June 2013 to December 2013

Who is funding the study?
Wageningen University and Research Centre (Netherlands)

Who is the main contact?
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NL44947.081.13

Study information

Scientific Title
The effect of intense exercise on intestinal permeability and protein and peptide levels in plasma of healthy men

Acronym
Protégé

Study objectives
1. The primary objective is to study the effect of exercise-induced permeability on plasma bioavailability of casein and casein-derived peptides, and to evaluate its reproducibility.
2. The secondary objective is to compare intestinal permeability to simple sugars with intestinal permeability to casein and casein-derived peptides.
3. The tertiary objective is to study the effect of exercise-induced permeability on markers of inflammation, exercise metabolism, and gastro-intestinal function.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wageningen University Medical Ethical Testing Committee (METC-WU), 23/09/2013, ref: 13/10; NL44947.081.13

Study design
This intervention study comprises of an exercise trial with cross-over design

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details below to request a participant information sheet

Health condition(s) or problem(s) studied
Intestinal permeability

Interventions
Each participant is his own control. On the first day participants came in fasted overnight (=resting condition) and ingested a sugar probe solution containing 5 grams lactulose, 1 gram L-rhamnose, and 0.5 gram D-Xylose. Next to this, they ingested a protein solution containing 40 grams of sodium caseinate. Hereafter, urine and blood was sampled at regular intervals over a period of 5 hours. On the evening of the first day (after dinner), the participants came back for the first part of the exercise test consisting of a 2min blocks interval training on a cycle ergometer, alternating between 90% and 50% of their maximal capacity for as long as they could keep up. On the second day, the participants came back in the morning, again after being fasted overnight. They completed the second part of the exercise test consisting of 90 min cycling at 50% of their maximal capacity. Afterwards (=post-exercise condition) the sugar probe solution as well as the casein protein solution was ingested and again blood and urine was sampled at regular intervals for 5 hours. On the third day, the participants came back in the morning, again after being fasted overnight. One single blood sample was drawn.
This complete three-day-protocol was repeated one week later.

Intervention Type
Mixed

Primary outcome measure
Plasma casein and casein-derived peptide levels with and without exercise-induced permeability of the gastrointestinal tract.

Plasma samples are taken at t=0, 15, 30, 60, 90, 120, and 300min after intake of casein directly after the control condition (no exercise) or the 1.5hr cycling test. Levels of casein and casein-derived peptides will be analysed in these plasma samples with ELISA and UPLC-MS/MS.

Secondary outcome measures
1. Intestinal permeability as assessed by multisugar test
Subjects will receive a multisugar solution to assess permeability directly after the control condition (no exercise) or the 1.5hr cycling test. Urine will be collected for 5 hours at hourly intervals after intake. Urinary sugar levels will be analyzed with HPLC
2. Health effects of exercise-induced permeability and plasma casein and casein-derived peptides

Other parameters: serum parameters of inflammation, exercise metabolism, and gastrointestinal function.

Overall study start date
14/06/2013

Completion date
20/12/2013

Eligibility

Key inclusion criteria

1. Male cyclists/triathletes with at least two years of cycling experience
2. Cycling at least two times a week during peak season
3. 18-35 years old
4. Body mass index (BMI) 20-25 kg/m2
5. Meeting criteria of valid max-test
6. Suitable veins for blood sampling

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
35 Years

Sex
Male

Target number of participants
12

Total final enrolment
11

Key exclusion criteria
1. Known symptoms of milk allergy
2. Known symptoms of immune disease, such as diabetes, gastritis, and coeliac disease
3. Known symptoms of intestinal disease, such as Crohn’s Disease, ulcerosis, and irritable bowel syndrome
4. Smoking
5. Use of hard drugs
6. Chronic use of NSAIDs: aspirins, ibuprofen, etc.
7. Using medicines for gastric and/or intestinal function
8. Participation in other scientific studies
9. Blood donation during the last six weeks before the start of the study

Date of first enrolment
23/09/2013

Date of final enrolment
08/11/2013

Locations

Countries of recruitment

Netherlands

Study participating centre
Wageningen University
Wageningen
Netherlands
6708 PB

Sponsor information

Organisation
Wageningen University and Research Centre

Sponsor details
Droevendaalsesteeg 4
Wageningen
Netherlands
6708 PB

Sponsor type
University/education

Website
http://www.wageningenur.nl/nl/Onderzoek-Resultaten/Projecten-EZ/Expertisegebieden/Kennisbasis-onderzoek/Gezond-en-veilig-voedsel-in-ketenperspectief/IPOPcustomized-nutrition-3.htm

ROR
https://ror.org/04qw24q55

Funder(s)

Funder type
University/education

Funder Name
Wageningen University and Research Centre

Alternative Name(s)
Wageningen UR, WUR

Funding Body Type

Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Netherlands

Results and Publications

Publication and dissemination plan
Researchers intend to first publish the results on the effect of exercise on the sugar probe and casein protein test. At this stage it is not known what will happen with other results obtained within this human trial.

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/01/2017	17/12/2020	Yes	No