Effects of citrulline on intestinal function during physical exercise

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Specific research objectives:Investigate the effect of orally administered citrulline at:- Circulation of gastrointestinal (GI) system- The occurrence of GI damage, liver and kidneys- The GIpermeability - Production of amino acids- Endothelial...

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

Summary

ID

NL-OMON34293

Source
ToetsingOnline

Brief title
Effects of citrulline during exercise

Condition

- Gastrointestinal vascular conditions

Synonym
decreased splanchnic circulation, splanchnic hypoperfusion

Research involving
Human

Sponsors and support

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

Intervention

Keyword: citrulline, exercise, gut function

Outcome measures

Primary outcome

Key search parameters:

- GI perfusion: tonometry and sublingual sidestream dark field (SDF) imaging of perfusion

- Intestinal damage: Plasma intestinal fatty acid binding protein (I-FABP) and analysis by video capsule

Secondary outcome

- Liver damage: plasma liver FABP (L-FABP), alanine and aspartate aminotransferase (ALT, AST)

- Kidney damage: urinary N-acetyl-beta-(D)-glucosaminidase (NAG)

- GI permeability: sugar in urine and plasma analysis

- Amino acid analysis

- Glycocalyxcomponents in plasma

- Endotoxins and inflammatory markers in plasma

Study description

Background summary

Introduction: The gastrointestinal (GI) system plays an important role in the human body. The wall of the GI system regulates digestion and absorption of nutrients and it also has a very important function as a barrier between the internal and external environment. The penetration of harmful substances and

microbiota of the GI lumen (external environment) into the systemic circulation (internal environment) depends on the barrier.
Previous studies have shown that exercise in healthy subjects leads to splanchnic hypoperfusion, resulting in intestinal damage, increased intestinal permeability and liver damage. The same splanchnic hypoperfusion occurs in patients with compromised circulation, but then with more harmful effects.

Rationale: During episodes of splanchnic hypoperfusion is the de novo synthesis of nitric oxide (nitric oxide, NO) from the amino acid arginine compromised. It is possible that this disturbed NO synthesis plays a role in the development of organ dysfunction function during exercise. By administration of L-citrulline, a precursor of arginine and consequently of NO, NO production may possibly be increased, resulting in less or no organ dysfunction.

Study objective

Specific research objectives:

Investigate the effect of orally administered citrulline at:
- Circulation of gastrointestinal (GI) system
- The occurrence of GI damage, liver and kidneys
- The GIpermeability
- Production of amino acids
- Endothelial function (glycocalyx)
- The release of endotoxins and inflammatory markers

Study design

Crossover dubbelblinded

Intervention

Oral intake of citrulline or placebo alanine

Study burden and risks

Intensive exercise is intense, but for these subjects a weekly if not daily activity.

To take the acid inhibitor, ranitidine, has contraindications. Adverse reactions are: hypersensitivity reactions, however, the overall incidence of adverse reactions is very low (<0.01-0.1%)

Placing a nasogastric (tonometry) catheter is not without risk for the subject. The placement of the catheter may be painful and the subject may vomit. Moreover, 'minor' complications such as nasal bleeding, transient sinusitis and

sore throats, may occur. 'Major' complications have been reported, including stembandparalysis due to incorrect positioning of the catheter, erosion of adjacent mucosa and perforation. Sequelae of a nasogastric catheter are rare and are mainly reported for patients who have abnormalities of the GI system and in whom the catheter tube (five days on average) remains in situ. There are no good studies on the incidence of perforations associated with nasogastric catheters. An estimate could be based on the morbidity and mortality numbers known for diagnostic endoscopy of the upper GI system, in which the overall complication rate for endoscopy (including biopsy) was 0.13% and the associated mortality is 0.004%. In theory, a possible perforation is possible if the video capsule would open and the tiny elements damage the gut wall. Such a complication has not been described in the literature. The nasogastric catheter will be placed by a skilled medical doctor. Nasoduodenal and naso-ileal intubation, have been approved in MEC 08-1-008, 07-1-006 and 09-3-005.

The blood drawing will be performed by a skilled medical doctor. A venous catheter is placed in a dorsal hand vein. The puncture can be painful. Potential risk is the development of a bruise at the site of injection of the needle. This will disappear spontaneously after a few days.

Risks sublingual circulation filming: none.
Risks citrulline intake / alanine: none.

See pages 19 and 20 protocol.

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

male
age 18-35 years
healthy

Exclusion criteria

medical history includes abdominal surgery
use of alcohol, medication or drugs

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-08-2011

Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	07-12-2010
Application type:	First submission
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
ClinicalTrials.gov	NCT01239303
CCMO	NL33697.068.10