The effects of nutritional supplements on postprandial nitric oxide bioactivity in abdominally obese men

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lipid metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON46749

Source
ToetsingOnline

Brief title
Nutritional supplements and nitric oxide bioactivity

Condition

- Lipid metabolism disorders

Synonym
Insulin Resistance Syndrome, Metabolic Syndrome, Syndrome X

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Nutricia,Stichting Life Sciences Health - TKI (trade name Health Holland)

Intervention

Keyword: Bioactivity, Nitric oxide, Nutritional supplements

Outcome measures

Primary outcome

Measurements will be performed before and two hours after consumption of the high fat milkshake and the five interventional products. The primary endpoint is the difference in postprandial change in FMD between the five interventional products.

Secondary outcome

Secondary outcomes are the postprandial effects of the interventional products on retinal microvascular function, plasma cGMP (as indicator of nitric oxide bioactivity), plasma markers for low-grade systemic inflammation and endothelial dysfunction, blood pressure, and serum lipid and plasma glucose metabolism.

Study description

Background summary

Obese people have a disturbed postprandial metabolism and thereby a decreased postprandial vascular function. Nitric oxide plays an important role in the postprandial vascular function. Multiple studies already focused on various nutritional compounds to improve the postprandial vascular function by increasing the nitric oxide bioactivity. However, the vast majority of the trials has been performed with relatively high doses of the individual components, which are problematic to convert into daily food measures, thereby preventing translation of these findings. Well-designed trails studying the effect of feasible amounts of nutritional supplements on the bioactivity of nitric oxide and vascular function are missing.

Study objective

The primary objective of the proposed study is to evaluate the effect of the high dose or L-arginine (3.0 gram) and a lower dose of L-arginine (1.5 gram) compared with a placebo supplement on postprandial vascular function, assessed by brachial artery flow-mediated vasodilation (FMD), in abdominally obese male volunteers. Secondary objectives are to examine postprandial effects on retinal vascular function, plasma cGMP (as indicator of nitric oxide bioactivity), plasma markers for low-grade systemic inflammation and endothelial dysfunction, blood pressure, and serum lipid and plasma glucose metabolism.

Study design

The proposed study will have a randomized, double-blind cross-over design. The total study duration will be at least 8 weeks, including one baseline test day and five experimental test days, each separated by a washout period of at least 1 week.

Intervention

At the start of the study, the participants will have a baseline test day. On this test day, the subjects will only receive a high fat milkshake and the 3 hours after ingestion of the milkshake will be studied. After completion of the baseline test day the subjects will take a daily supplement with co-factors (i.e. vitamins and minerals) for the entire study period. After 4 weeks, the participants will start with the five experimental test days, each separated with at least one week. On the five experimental test days, the subjects will receive in random order one of the five interventional products and a high fat milkshake. The postprandial response of the ingestion of the interventional product and the high fat milkshake will be studied for 4 hours. The five interventional products are: (1) co-factors*, (2) co-factors, 0.2 g nitrate and 1.2 mg nitrite, (3) co-factors, 0.2 g nitrate, 1.2 mg nitrite and 0.8 g L-arginine, (4) co-factors, 0.2 g nitrate, 1.2 mg nitrite and 1.5 g L-arginine, (5) co-factors and 3.0 g L-arginine.

* Co-factors: a supplement containing vitamins and minerals in a dose lower than the Recommended Daily Intake. This subjects will take this supplement with co-factors during the complete study period (after the baseline test day till the final experimental test day).

Study burden and risks

Subjects will be screened to determine eligibility during one visit of 15 minutes. During these screening visits, anthropometric measurements will be performed and blood pressure will be determined. In addition, a venous blood sample (5.5 mL) will be drawn. Subjects will take a daily supplement with vitamins and minerals during the complete study period. During the study there will be five experimental test days in which subjects receive in random order

one of the five interventional products ((1) co-factors, (2) co-factors, 0.2 g nitrate and 1.2 mg nitrite, (3) co-factors, 0.2 g nitrate, 1.2 mg nitrite and 0.8 g L-arginine, (4) co-factors, 0.2 g nitrate, 1.2 mg nitrite and 1.5 g L-arginine, (5) co-factors and 3.0 g L-arginine). At the start of the study there will be a baseline test day in which the subjects only receive a high fat milkshake. No direct health benefit for the study participants is expected. Investigational products are safe and all ingredients to prepare the high fat milkshake are commercially available and approved for human consumption. There are no side effects for the investigation products or the high fat milkshake. On the baseline test day and the five experimental test days a postprandial test will take place and blood will be sampled (6 x 76.0 mL with an interval of at least one week inter-between). During the 3-hour postprandial period, participants are allowed to drink one glass of water and are free to walk-around. Some study subjects may report pain during venipuncture. Insertion of the cannula can cause some discomfort and possible a hematoma or bruise. Some men may also report pain during the insertion of the cannula. Vascular measurements will be performed before and two hours after meal intake. These measurements are routine and are not expected to lead to physical side effects. Time investment for the participants is approximately 24 hours, excluding travel time.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

Universiteitsingel 50
Maastricht 6229 ER
NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

Universiteitsingel 50
Maastricht 6229 ER
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Men
- Aged between 40-70 years
- Waist circumference >= 102
- Fasting plasma glucose < 7.0 mmol/L
- Fasting serum total cholesterol < 8.0 mmol/L
- Stable body weight (weight gain or loss < 3 kg in the past three months)
- Willingness to give up being a blood donor from 8 weeks before the start of the study, during the study and for 4 weeks after completion of the study
- No difficult venipuncture as evidenced during the screening visit
- No current smoker
- No diabetic patients
- No familial hypercholesterolemia
- No abuse of drugs
- No more than 3 alcoholic consumptions per day
- No use of medication known to treat blood pressure, lipid or glucose metabolism
- No use of an investigational product within another biomedical intervention trial within the previous 1-month
- No intolerance or allergy to the ingredients of the intervention products (e.g. lactose or gluten)
- No severe medical conditions that might interfere with the study, such as epilepsy, asthma, kidney failure or renal insufficiency, chronic obstructive pulmonary disease, inflammatory bowel diseases, auto inflammatory diseases and rheumatoid arthritis
- No active cardiovascular disease like congestive heart failure or cardiovascular event, such as an acute myocardial infarction or cerebrovascular accident
- Willingness to give up the use of antibacterial mouth wash or antibacterial toothpaste, chewing-gum and tongue-scraping on the morning of each experimental test day

Exclusion criteria

- Women
- Fasting plasma glucose >= 7.0 mmol/L
- Fasting serum total cholesterol >= 8.0 mmol/L
- Current smoker, or smoking cessation <12 months
- Diabetic patients
- Familial hypercholesterolemia

- Abuse of drugs
- More than 3 alcoholic consumptions per day
- Unstable body weight (weight gain or loss > 3 kg in the past three months)
- Use medication known to treat blood pressure, lipid or glucose metabolism
- Use of an investigational product within another biomedical intervention trial within the previous 1-month
- Intolerance or allergy to the intervention products (e.g. lactose or gluten)
- Severe medical conditions that might interfere with the study, such as epilepsy, asthma, kidney failure or renal insufficiency, chronic obstructive pulmonary disease, inflammatory bowel diseases, auto inflammatory diseases and rheumatoid arthritis
- Active cardiovascular disease like congestive heart failure or cardiovascular event, such as an acute myocardial infarction or cerebrovascular accident
- Not willing to give up being a blood donor from 8 weeks before the start of the study, during the study or for 4 weeks after completion of the study
- Not or difficult to venipuncture as evidenced during the screening visit

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-11-2018
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	01-08-2018

Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-03-2019
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	NL64503.068.18