DIETARY NITRATE INTAKE IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON46719

Source
ToetsingOnline

Brief title
Walk-ON

Condition

- Other condition

Synonym
claudication

Health condition

Perifeer Arterieel vaatlijden (vaataandoeningen)

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: dietary nitrate, exercise performance, high nitrate vegetables

Outcome measures

Primary outcome

The primary parameter will be exercise tolerance, measured as peak walking time

Secondary outcome

Exercise tolerance:

* Claudication onset time (COT) and distance (COD)

* VO2

Vascular function:

* Flow mediated dilation (FMD)

* Blood pressure (BP) and heart rate (HR)

* Tissue oxygenation (NIRS)

Nitrate and nitrite:

* Plasma nitrate and nitrite concentrations

* Dietary intake

Study description

Background summary

Recent research has shown that intake of nitrate (NO3) can lead to an increase in plasma nitrite and nitrate levels, and
a reduction in blood pressure at rest and pulmonary oxygen uptake during exercise. These effects are related to the
endogenous production of nitric oxide (NO), which is associated with a rise in plasma nitrite levels. Research in clinical populations is scare.

The consumption of vegetables declared for 60-80% of the daily intake of nitrate. So far, studies using
sodium nitrate (NaNO3) and red beet juice to induce these metabolic effects. A recent study from our group shows that
acute supplementation of nitrate-rich vegetables can provide the same effects as sodium nitrate and red beet juice on
the rise in plasma nitrite and nitrate values and a reduction in blood pressure, in healthy participants.

Based on the gaps in current literature, our main goal will therefore be to gain further insight into the effect the supplementation with concentrated nitrate-rich beet juice, high nitrate vegetables compared with placebo in patients with peripheral arterial disease.

Study objective

The aim of the current study is to compare the acute effect of nitrate supplementation. Therefore, we will assess the impact of concentrated beetroot juice, high nitrate vegetables versus nitrate depleted beetroot juice (placebo) on exercise tolerance (peak walking time (PWT), walking distance (PWD), claudication onset time (COT) and distance (COD), VO2), vascular function (Flow Mediated dilation (FMD), blood pressure (BP), heart rate (HR), tissue oxygenation (NIRS) and plasma nitrate and nitrite.

Study design

randomized cross-over intervention study

Intervention

In a randomized cross-over manner, participants will follow an acute supplementation protocol in which they will a high nitrate meal in de form of vegetables and/or ingest 400 mg (6.5 mmol) nitrate in the form of concentrated red beetroot juice and/or placebo.

Study burden and risks

Participants will be required to report to the laboratory for a total of 4 visits and one screening session for a total of maximally 15 h. Prior to the

first experimental visit, participants will be asked to record their diet for 3 days and refrain from physical exercise for the 24 h preceding the visit. Participants will be asked to avoid caffeine and alcohol for 12 h and 24 h preceding each visit, respectively. Participants will also be asked to arrive fasted, so they are not allowed to eat or drink (except for water) from 22:00 h the evening before.

The burden and risks associated with participation are small. In total, participants will donate twelve blood samples, representing ~7.5 mL over the course of three weeks. Insertion of the needle for blood sampling could result in a small hematoma. In addition, the main time commitment will consist of filling in three food diaries.
The administered dose of nitrate in beetroot juice has been used in multiple clinical and exercise studies and is a commercially available supplement. The most commonly reported side effect is beeturia (red-coloured urine/faeces, 15-20% of the population) and mild gastrointestinal distress (bloating, belching), and occasional reports of mild headache (which may or may not be associated with the nitrate). The vegetables used in the present study are freely available natural products. The only comparison available is from the ingestion of nitrate-rich beverages, which has sometimes been described to lead to mild gastrointestinal distress (bloating, belching) in some cases. The long term effects of nitrate ingestion still need to be fully investigated.
Participants consuming dietary nitrate could potentially benefit from improvement of their cardiovascular (heart and blood vessels) health. There are no notable risks of participating in this study.
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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

- stable intermittent claudication for at least three month;
- ABI (the ratio of BP in the lower legs to the BP in the arms) <0.9 and/or a ABI decreased by more than 0.15 after treadmill testing regardless of their ABI at rest;
- Rutherford classification for chronic limb ischemia 1-4 and/or Fontaine classification stage IIA-IIB or III.

Exclusion criteria

- any condition other than PAD that limits walking;
- patients diagnosed with diagnosed with chronic kidney disease and/or or patients with insulin dependent diabetes;
- previous endovascular or surgical treatment for claudication within the last 12 months
- individuals with critical limb ischemia, who are wheel-chair bound, or who have an above or below-knee amputation;
- using dietary nitrate supplements;

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-06-2018
Enrollment:	21
Type:	Actual

Ethics review

Approved WMO

Date:	24-05-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 26302
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL64448.091.17
OMON	NL-OMON26302