Effects of polyphenol supplementation on inflammation and coronary endothelial function in patients with documented coronary artery disease

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Primary Objective: The primary objective is to assess the effects of the oral administration of a daily dose of 1000 mg polyphenol extract for 3 weeks on biochemical markers of leucocyte recruitment in patients with documented CAD. Secondary…

Ethical review	Approved WMO
Status	Will not start
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON40828

Source
ToetsingOnline

Brief title
PENSION

Condition

- Coronary artery disorders

Synonym
atherosclerosis, coronary artery disease

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: coronary artery disease, endothelial dysfunction, inflammation, polyphenol

Outcome measures

Primary outcome

Primary endpoint:

Assessment of biochemical markers of leucocyte recruitment in patients with CAD

(MCP-1 (CCL2), CCL5, MIF, SDF-1).

Secondary outcome

Secondary endpoints:

- Flow mediated dilatation (FMD): vasoreactivity of the brachial artery

(measured as % change in diameter) at baseline and 3 weeks

- Laser doppler perfusion imaging (LDPI) and iontophoresis: vasoreactivity of

the cutaneous microvasculature at baseline and 3 weeks

- Assessment of coronary endothelial (dys)function by an endothelial-dependent

vasomotion test with acetylcholine (AC). The number of patients with a

paradoxical vasoconstriction to AC is recorded in each study group.

- Blood sampling at baseline and 3 weeks:

Biochemical markers of inflammation (hs-CRP, IL1ß, IL6, IL10, PlGF,

TNF* and VEGFa).

Monocyte chemokine and adhesion molecule profile (CCL2-5, CCR1-2,

CXCR4, LFA1): flowcytometry

Monocyte/macrophage polarization: cell culture, qPCR)

Study description

Background summary

Endothelial dysfunction presents as an early culprit during the initiation and development of atherosclerosis and is manifest in subsequent stages of progressive coronary artery disease (CAD). Polyphenol supplementation has been shown to enhance endothelial function in vitro and reduce the inflammatory status in animal models of atherosclerosis and in patients at high cardiovascular risk. However, the direct effects of polyphenol supplementation on the inflammatory status and the relationship with coronary endothelial function in patients with CAD have not been elucidated.

Study objective

Primary Objective:
The primary objective is to assess the effects of the oral administration of a daily dose of 1000 mg polyphenol extract for 3 weeks on biochemical markers of leucocyte recruitment in patients with documented CAD.

Secondary Objectives:
The secondary objectives are to assess the effects of dietary supplementation with a daily dose for 3 weeks of 1000 mg polyphenol extract on:

- vasoreactivity of the brachial artery (FMD) and the cutaneous microvasculature (laser doppler)

- coronary endothelial function during angiography (vasomotion test)

- biochemical markers of inflammation

- monocyte chemokine and adhesion molecule profile (flowcytometry) and monocyte/macrophage polarization (CAC cell culture, qPCR)

in patients with documented CAD.

Study design

Randomized double-blind placebo-controlled pilot study

Intervention

The intervention group will be treated with a dietary supplement Polyphenols (Vinitrox), while the other group receives a placebo. In addition to the dietary supplement/placebo, all patients undergo at 3 weeks a clinically

indicated coronary angiography, including additional invasive measurements

Study burden and risks

The RWPC is believed to restore dysfunctional endothelial function by several possible mechanisms, e.g. anti-inflammatory action, reducing monocyte recruitment into atheroslerotic lesions, reducing endothelial cell adhesion of inflammatory cells, and induce macrophage polarization towards an anti-inflammatory phenotype. In this way the RWPC will give additional protection to the study subjects. No serious adverse events are expected from the oral administration of the compound in its proposed dose.

All subjects undergo invasive evaluation and/or treatment for coronary artery disease. This investigation generally is not different from the current common practice in cardiology and supported by the guidelines of the ACC/AHA/ESC. The only difference is that patients will undergo vasomotion testing of a non-culprit coronary artery after treatment of the coronary culprit lesion. The risk attributed to the AC test is minimal.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
18 years or older
& scheduled for CAG/PCI for stable angina pectoris
& with documentation of an abnormal peripheral FMD-measurement
& with signed informed consent.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
Patients with unstable angina, vasospastic angina pectoris, recent myocardial infarction, valvular heart disease, clinical evidence of heart failure, left ventricular hypertrophy, uncontrolled hypertension, peripheral vascular disease, LVEF <50%, and/or significant endocrine, hepatic, renal, or inflammatory disease are excluded.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO Date:	06-11-2014
Application type:	First submission
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	NL49183.078.14