Vitamin K1 to slow vascular calcification in hemodialysis patients (VitaVasK)

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Ethical review	Not approved
Status	Will not start
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON40146

Source
ToetsingOnline

Brief title
Vitamin K1 and vessel calcification in dialysis

Condition

- Renal disorders (excl nephropathies)
- Embolism and thrombosis

Synonym
vascular calcification

Research involving
Human

Sponsors and support

Primary sponsor: RWTH Aachen
Source(s) of monetary or material Support: ERA EDTA

Intervention

Keyword: Coronary artery and thoracic aortic calcifications, Hemodialysis, Vitamin K1

Outcome measures

Primary outcome

The primary endpoints of this study are

1. Progression of thoracic aortic calcification (absolute change of the volume score at the 18-month (defined as 18 months +/- 4 weeks) MSCT versus the baseline MSCT),

2. Progression of coronary artery calcification (absolute change of the volume score at the 18-month MSCT versus the baseline MSCT).

Secondary outcome

The secondary endpoints of this study are

1. Progression of thoracic aortic calcification (absolute change of the Agatston score at the 18-month MSCT versus the baseline MSCT),

2. Progression of coronary artery calcification (absolute change of the Agatston score at the 18-month MSCT versus the baseline MSCT),

3. Progression of aortic valve calcification (absolute change of the Agatston and volume scores at the 18-month MSCT versus the baseline MSCT),

4. Progression of mitral valve calcification (absolute change of the Agatston and volume scores at the 18-month MSCT versus the baseline MSCT),

5. Mortality from any cause within 18 months after starting the treatment,

6. Major adverse cardiovascular events: myocardial infarction, stroke, acute coronary syndrome, embolism, symptom-driven revascularization, death from

cardiovascular cause within 18 months after starting the treatment

Study description

Background summary

Patients on hemodialysis (HD) exhibit an immensely increased cardiovascular mortality associated with extensive vascular calcification (VC). This offers an * at least partial * explanation for the excessively increased cardiovascular mortality in this population. In the past years, the development of VC was discovered to be actively regulated and influenced by inhibitors of calcification (e.g. matrix Gla protein). Matrix Gla protein (MGP) is a powerful vascular wall-based inhibitor of VC. MGP is produced by vascular smooth muscle cells and requires post-translational modification by vitamin K-dependent gamma carboxylation to be fully active. We are still lacking data supporting the hypothesis that vitamin K supplementation may slow down the progression of VC in HD patients. All HD patients exhibit insufficient carboxylation activity and must be considered vitamin K deficient. Together with the increased VC, they represent an ideal population for interventional trials involving the vitamin K system. In this trial, we also observed that all dialysis patients included had insufficient vitamin K serum levels, indicating that there was no substantial influence of food intake on vitamin K deficiency. In addition, this demonstrates that all patients have vitamin K levels that are too insufficient to allow adequate MGP carboxylation.

Study objective

The aim of the study is to show that a therapy based on a thrice weekly administration (i.e. at each HD session) of vitamin K1 for a period of 18 months attenuates the progression of coronary artery and thoracic aortic calcifications compared to standard treatment. Furthermore, we want to analyse whether the thrice weekly intake (i.e. at each HD session) of vitamin K1 for 18 months leads to an attenuation of the calcification of aortic and mitral valve and reduction of major adverse cardiovascular events (MACE, i.e. sum of myocardial infarction, acute coronary syndrome, symptom-driven revascularization, stroke, embolism, cardiovascular death) all-cause mortality and plasma level of dpucMGP and an increase in the plasma level of dpcMGP.

Study design

The VitaVasK study is a prospective, randomised, multicenter, multinational, controlled clinical trial using a two-arm parallel group design

Intervention

After randomisation, the patient will be treated with Vitamin K1 for 18 months, or the patient won't be treated with Vitamine K1. 3 Visits will take place in these 18 months, where the patient will get a CT scan, physical examination and bloodsamples will be taken. After 36 months and 60 months telephone interviews will take place.

Study burden and risks

The dose of vitamin K1 being administered orally (5 mg) has been previously tested, in some cases in much higher doses, and has it been deemed safe and is well tolerated with hardly any adverse effects. Treatment with vitamin K1 is not known to show undesirable effects or discomfort. Moreover, in the scope of this clinical research, certain risks or undesirable effects that may cause some discomfort may be involved in study-related measures. Relatively minimal risks are to be anticipated, for example, in the blood draws, since merely a small amount of blood is required (each time approximately 18 mL) and the method for blood draw (due to dialysis) would require no additional puncture. Beyond this, the three planned CT examinations carry the risk of exposure to radiation. The radiation exposure from the CTs equals your annual background exposure (ca. 2.1 mSv).

Contacts

Public
RWTH Aachen

Pauwelsstrasse 30
Aachen 52057
DE
Scientific
RWTH Aachen

Pauwelsstrasse 30
Aachen 52057
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Male or female * 18 years of age
Not less than 6 months on hemodialysis
Cardiovascular calcification present (coronary artery volume score > 100)
Written consent to take part in the study
Life expectancy not less than 18 months

Exclusion criteria

Use of vitamin K
Known hypersensitivity against vitamin K1
History of thrombosis
Intake of vitamin K antagonists (e.g. Marcumar®) at baseline or in the 3 months prior to baseline
Inflammatory bowel disease
Short-bowel syndrome
Significant liver dysfunction
Coronary stent
Hemoglobin < 70 g/L
Women who are pregnant or breastfeeding
Women without sufficient contraception
Alcohol or drug abuse
Mental condition rendering the subject unable to understand the nature, scope and possible consequences of the study
Subject unlikely to comply with protocol, e.g. uncooperative attitude, inability to return for follow-up-visits and unlikelihood of completing the study
Participation in a parallel clinical trial or participation in another clinical trial within the previous 3 months
Subjects who are in any state of dependency to the sponsor or the investigators
Employees of the sponsor or the investigators
Subjects who have been committed to an institution by legal or regulatory order

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	80
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Phylloquinone
Generic name:	Vitamine K1
Registration:	Yes - NL outside intended use

Ethics review

Not approved

Date:	10-06-2014
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
EudraCT	EUCTR2010-021264-14-NL
ClinicalTrials.gov	NCT01742273
CCMO	NL45163.068.13