A randomized, placebo-controlled, double blind trial to investigate whether vitamin K2 can influence ongoing calcium deposition in patients with type 2 diabetes

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The primary objective is to determine if MK-7 supplementation leads to stabilization or attenuation of ongoing calcium deposition, quantified by 18F- NaF PET/CT imaging in patients with type 2 diabetes.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON45148

Source
ToetsingOnline

Brief title
Vitamin K2 and arterial calcification

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Arterial calcification, cardiovascular disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Hartstichting;Dekkerbeurs

Intervention

Keyword: Arterial calcification, Menaquinone-7, Ongoing calcium deposition, Vitamin K2

Outcome measures

Primary outcome

Ongoing calicum deposition in the femoral artery, quantified by 18F-NaF PET/CT

imaging.

Secondary outcome

- Ongoing calcium deposition in other arteries than the femoral artery, as

quantified by 18F-NaF PET/CT imaging

- Ongoing calcium deposition in the lumbar spine, as quantified by 18F-NaF

PET/CT imaging

- Arterialstiffness, as quantified by pulsecor.

- Dpuc-MGP, as quantified using a sandwich ELISA.

Study description

Background summary

Arterial calcification is an important riskfactor for cardio vascular diseases. Observational studies has shown that vitamin K may reduce or attenuated the proces of ongoing calcium deposition. This could be explained by matrix gla protein (MGP), which is a vitamin K dependent protein. A previous study within our working group has shown that vitamin K supplementation reduce the inactive MGP (dpuc-MGP). Other studies showed that a decrease in inactive MGP reduce the risk of ongoing calcium deposition in the arteries. Therefore this study is conducted to investigate whether vitamin K supplementation reduces or

attenuated ongoing calcium deposition in the arteries.

Study objective

The primary objective is to determine if MK-7 supplementation leads to stabilization or attenuation of ongoing calcium deposition, quantified by 18F-NaF PET/CT imaging in patients with type 2 diabetes.

Study design

Double blind randomized placebo-controlled trial, with a follow up of 6 months.

Intervention

Subjects will be randomized, one group receives daily 360 µg tablets of MK-7 and the other group receives daily placebo tablets during 6 months

Study burden and risks

Each patient will visit the UMC Utrecht 4 times for the 6 months duration of the study. At screening, baseline, after 3 months and after 6 months. At baseline and after 6 months a *whole-body* 18F-NaF PET/CT scan will be made as part of the study, to measure ongoing calcium deposition in the arteries and lumbar spine. One group of participants will receive vitamin K during 6 months. The doses of this supplement is within the physiologic borders and therefore not harmful. Also a 3-day food diary will be acquired at baseline and a weekly compliance questionnaire. Blood samples will be taken at baseline and after 3 and 6 months of follow-up. The burden is relatively high but the risk is low. Previous studies showed no harmfull effect of vitamin K, and the dosages of radioactivity is approximately 11.6 mSv. Due to the radiation of 11.6 mSv from this study, the cancer risk for a 60 year old male increases with 0.04%, given a normal life expectancy. Furthermore, our study participants will probably be older, because the mean age of our study population in the Diabetes Pearl cohort is 68 years. Atom bomb data suggest a delay of several decades between exposure and the occurrence of solid tumours. So, theoretically the PET-CT increases the risk of cancer, but in our cohort with diabetes patients with arterial disease the risk will be very low.

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

- Middle aged men and women, * 40 years.
- Diagnosed with type 2 diabetes.
- Presence of arterial diseases, based on an Ankle Brachial Index (ABI) <0.9 and/or diagnosed with arterial diseases by physician. Arterial disease is defined as:
* Coronary artery disease: angina pectoris, myocardial infarction, coronary revascularization (bypass surgery or angioplasty), or
* Cerebral vascular disease: transient ischemic attack, cerebral infarction, amaurosis fugax, retinal infarction, history of carotid surgery, or
* Peripheral artery disease: symptomatic and documented obstruction of distal arteries of the leg or surgery of the leg (percutaneous transluminal angioplasty, bypass or amputation), or
* Abdominal aortic aneurysm: supra- / infrarenal aneurysm of the aorta (distal aorta anteroposterior diameter * 3 cm, measured with ultrasonography) or a history of AAA surgery, or,
-Written informed consent.

Exclusion criteria

- Subjects participates in another intervention research or study using imaging.

- Contra-indication for undergoing18F-NaF PET/CT scan (claustrophobic patients, pregnancy, breastfeeding).
- Subject underwent amputation of the lower extremities (above the knee).
- Using vitamin K antagonists.
- Known coagulation problems (e.g. history of Venous Trombo Embolism, or polycythemia vera).
- Plasma or blood donor and unwilling to stop during this intervention research.
- Using vitamin supplements that contain vitamin K, or unwilling to stop two weeks before randomisation. If the participants use vitamin D or calcium supplements, it should be constant during the study.
- A mean vitamin K2 intake *120 *g/day measured with a questionnaire.
- Natto or goose liver consumers.
- Known with low kidney function (eGFR <30)
- Incompressible femoral artery, as diagnosed by a physician.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-06-2016
Enrollment:	70
Type:	Actual

Ethics review

Approved WMO

Date:	16-03-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-05-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	26-08-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-11-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	26-01-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-03-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-09-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-09-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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: 25255
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL53572.041.15
OMON	NL-OMON25255