The effects of discontinuation of vitamin K antagonists on the rate of elastin degradation

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To evaluate whether discontinuation of VKAs results in a higher vitamin K status and deceleration of the rate of mature cross-linked elastin degradation.

Ethical review	Approved WMO
Status	Pending
Health condition type	Coronary artery disorders
Study type	Observational invasive

Summary

ID

NL-OMON45726

Source
ToetsingOnline

Brief title
VKA discontinuation and elastolysis

Condition

- Coronary artery disorders
- Lower respiratory tract disorders (excl obstruction and infection)
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Elastin-degradation, vitamin K deficiency

Research involving
Human

Sponsors and support

Primary sponsor: Canisius Wilhelmina Ziekenhuis
Source(s) of monetary or material Support: R&D rekening Longartsen CWZ

Intervention

Keyword: desmosine, elastin degradation, VKAs

Outcome measures

Primary outcome

The primary endpoint is the change in the rate of elastin degradation

quantified by the plasma desmosine assay.

Secondary outcome

Secondary endpoints are the change in vitamin K status quantified by measuring

plasma levels of dephosphorylated uncarboxylated (dp-uc, i.e. inactive) Matrix

Gla Protein (MGP), the relation between desmosine and dp-ucMGP and differences

of desmosine and dp-ucMGP levels among subjects with different polymorphisms of

the vitamin K 2,3-epoxide reductase complex 1 (VKORC1) gene.

Study description

Background summary

Elastin is a unique protein providing elasticity, resilience and deformability to dynamic tissues, such as lungs and vasculature. Elastin fibers are characterized by their high affinity for calcium. However, calcified elastin is more prone to the degrading effects of proteases and, in turn, partially degraded elastin has an even higher affinity for calcium. A disturbed balance between proteases and anti-proteases is a major underlying mechanism in the development of chronic obstructive pulmonary disease (COPD). Virtually the only protein that can protect elastin from calcification is matrix Gla-protein (MGP), which needs vitamin K for its activation. In COPD patients, a lower vitamin K status is found when compared to control subjects and an inverse association exists between vitamin K status and elastin degradation. In addition, vitamin K status is lower and elastin degradation is accelerated in VKA users.
Vitamin K antagonists (VKAs) are widely used. Nowadays, an increasing number of patients uses direct oral anticoagulants (DOACs), which do not influence vitamin K status. We hypothesize that discontinuation of VKAs results in an

improved vitamin K status and deceleration of elastin degradation. In order to test this hypothesis, we want to conduct an observational study in which the change in elastin degradation* quantified by plasma desmosine concentrations * in patients who discontinue use of VKAs will be used as primary endpoint.

Study objective

To evaluate whether discontinuation of VKAs results in a higher vitamin K status and deceleration of the rate of mature cross-linked elastin degradation.

Study design

Observational study

Study burden and risks

We will draw extra blood collection tubes at two moments. The first time is during one of the last regular INR testing at the anticoagulation clinic, therefore no additional venipuncture has to be performed. At this moment two additional blood collection tubes will be drawn. The second moment is approximately 6 months after discontinuation of VKAs. At this point the patient will undergo an additional venipuncture. Patients are asked to fill in a questionnaire concerning age, gender, length, height, indication for VKA use, duration of VKA use, smoking status and history, presence of COPD and other pulmonary disease, vitamin D supplementation and use of medications. Furthermore, we will record the INR at baseline. Participants may experience some discomfort during blood sampling. Participating in the study has negligible risks.

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

VKA users who will discontinuate VKAs

Exclusion criteria

life expectancy <6 months

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2017
Enrollment:	100
Type:	Anticipated

Ethics review

Approved WMO Date:	29-06-2017
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

No registrations found.

In other registers

Register	ID
CCMO	NL60536.091.17