Randomized controlled trial to assess the effect of vitamin K supplementation on the rate of elastin degradation in COPD

Published: 17-04-2019
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To evaluate whether supplementation of vitamin K2 decelerates the rate of mature cross-linked elastin degradation inpatients with COPD.

Ethical review	Approved WMO
Status	Pending
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON50316

Source
ToetsingOnline

Brief title
Vitamin K in COPD

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
chronic obstructive pulmonary disease, COPD

Research involving
Human

Sponsors and support

Primary sponsor: CIRO
Source(s) of monetary or material Support: Stichting Astma Bestrijding

Intervention

Keyword: COPD, desmosine, elastin, vitamin K

Outcome measures

Primary outcome

The primary endpoint is the difference in the rate of elastin degradation after 8 weeks of vitamin K supplementation versus placebo (quantified by the plasma desmosine assay).

Secondary outcome

Secondary endpoints are vitamin K-status after 8 weeks of treatment (quantified by dp-ucMGP), proteins induced by vitamin K abcense (PIVKA-II) levels (inversely associated with vitamin K status), vitamin D levels, lung function parameters, questionnaires and exacerbations during the study period. In addition, we want to evaluate if different polymorphisms of the VKORC1 gene are associated with desmosine and dp-ucMGP levels at baseline and after vitamin K2 supplementation.

Study description

Background summary

Elastin is a unique protein providing elasticity and resilience to dynamic organs, such as lungs. Elastin is a basic requirement for both respiration and circulation. The rate of elastin degradation is accelerated in COPD. Desmosine (DES) is an amino acid that is only found in elastin fibers, and consequently, plasma (p)DES levels reflect the rate of elastin degradation. pDES is a strong predictor of mortality in COPD. We regard decelerating elastin degradation as an attractive novel therapeutic target in COPD. Elastin calcification stimulates elastin degradation and vice versa. Elastin calcification is inhibited by Matrix Gla Protein, which needs vitamin K to become activated. Recently, we found significantly lower vitamin K status in COPD patients

compared to controls. Furthermore, we found an inverse association between vitamin K-status and the rate of elastin degradation in both patients with COPD and controls with no lung disease. We hypothesized that improving vitamin K-status by vitamin K2 supplementation would have a favorable decelerating effect on elastin degradation.

Study objective

To evaluate whether supplementation of vitamin K2 decelerates the rate of mature cross-linked elastin degradation in
patients with COPD.

Study design

Double-blind randomized placebo-controlled intervention trial.

Intervention

Randomisation: vitamin K2 or placebo.

Study burden and risks

Participating in the study has negligible risks as adverse side-effects from vitamin K supplementation has never been described in persons who do not use vitamin K antagonists.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Written informed consent
- Diagnosed with COPD based on post-bronchodilator FEV1/GVC <0.70 accordig to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.
-Ability to comply with all study requirements
- Age >40 years

Exclusion criteria

- Pregnant or lactating women, or subjects who intend to become pregnant within the study period
-Subjects using vitamin K1 or K2 as supplements
-Active malignancy or cured malignancy <12 months prior to enrollment
-Use of vitamin K antagonists (acenocoumarol, fenprocoumon) in 12 months prior to inclusion
- expectation of impaired gastro-intestinal uptake of vitamin K such as history of (partial)bowel resection
-Serious mental impairment
-Exacerbation <2 weeks prior to enrolment
-Life expectation of less than 6 months on the basis of concurrent disease

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:	Pending
Start date (anticipated):	01-04-2021
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO Date:	17-04-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-04-2021
Application type:	Amendment
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

ID: 20264
Source: NTR
Title:

In other registers

Register	ID
Other	Nederlands Trial Register: 7694
CCMO	NL63985.068.18
OMON	NL-OMON20264