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

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20264

Source
NTR

Health condition

Chronic Obstructive Pulmonary Disease (COPD)

Sponsors and support

Primary sponsor: CIRO+ (Centre of expertise for chronic organ failure)
Source(s) of monetary or material Support: Stichting Astma Bestrijding

Intervention

Outcome measures

Primary outcome

The primary endpoint is the difference in elastin degradation rate after the intervention between the active and placebo group. Elastin degradation rate is quantified by the change in plasma desmosine levels measured after 8 weeks.

Secondary outcome

Secondary endpoints are the changes in: vitamin K-status (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 concerning psychosocial functioning/functional effects/health status, physical functioning, body composition, arterial stiffness and exacerbations during the study period. In addition, we will 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

Rationale: 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 chronic obstructive pulmonary disease (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 (MGP), a protein which needs vitamin K to become activated. Serum inactive levels of MGP, dephospho-uncarboxylated (dp-uc) MGP, are inversely associated with vitamin K status. 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 subjects with COPD and controls with no lung disease. Vitamin K epoxide reductase (VKOR) is an enzyme that plays a role in vitamin K recycling. Certain polymorphisms in the gene coding for VKOR, the VKOR complex 1 (VKORC1) gene, are associated with reduced vitamin K recycling. Possibly, these polymorphisms are, in part, responsible for inter-individual differences in vitamin K-status. We hypothesize that improving vitamin K-status by vitamin K supplementation could have a favorable decelerating effect on elastin degradation.

Objective: To evaluate whether supplementation of vitamin K2 decelerates the rate of elastin degradation in patients with COPD.

Study design: Double-blind randomized placebo-controlled intervention trial.

Study population: A total of 40 COPD patients who participate in the inpatient rehabilitation program of CIRO.

Intervention: Supplementation of 360 mcg vitamin K2 once daily for eight weeks.

Main study parameters/endpoints: The primary endpoint is the difference in the rate of elastin degradation (quantified by the plasma desmosine assay) after 8 weeks of vitamin K versus placebo supplementation. Secondary endpoints (after 8 weeks of treatment) are:

vitamin K-status (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 concerning psychosocial functioning/functional effects/health status, physical functioning, body composition, arterial stiffness 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.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: This study has two evaluation moments which coincide with the start of rehabilitation and the evaluation assessment of the inpatient rehabilitation program, which implies that there is no additional visit for study participants. The evaluation moments will be scheduled at baseline (t=0, start of rehabilitation) and at the end of the study (t=8, after 8 weeks of rehabilitation). Time between the intake assessment and start of the rehabilitation is 1 to 6 weeks. One tube of blood is drawn at the start of rehabilitation, which implies an additional needle stick for study purposes. After 8 weeks, blood is drawn as part of the standard rehabilitation program and one extra tube of blood will be drawn for this study. The other additional tests for the study (not part of the regular assessments) are arterial stiffness measurements (pulse wave velocity) (at t=0 and t=8). Participating in the study has negligible risks as adverse side-effects from vitamin K2 supplementation have never been described in persons who do not use vitamin K antagonists (VKAs).

Study objective

Vitamin K supplementation will lead to a deceleration of elastin degradation in COPD patients.

Study design

Baseline and 8 weeks (i.e. after pulmonary rehabilitation)

Intervention

Patients participating in a 8-week inpatient rehabilitation program at CIRO+ will be randomized to receive either 360 mcg vitamin K2 or placebo orally once a day during 8 weeks.

Contacts

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Eligibility criteria

Inclusion criteria

- Written informed consent

- Diagnosed with COPD based on post-bronchodilator FEV1/FVC <0.70 according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria

- Participating in the inpatient rehabilitation program of rehabilitation center CIRO (Horn, The Netherlands)

- 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 K as supplements or multivitamin supplements containing vitamin K

- 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 gasto-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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2019
Enrollment:	40
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 50316
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL7452
NTR-old	NTR7694
CCMO	NL63985.068.18
OMON	NL-OMON50316

Study results