Bicuspid aortic valve stenosis and the effect of vItamin K2 on calciummetabolism on 18F-NaF PET/MRI (BASIK2): a pilot study

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To test the hypothesis that supplementation with vitamin K2 in comparison to placebo (total duration of treatment: 18 months) will slow down aortic valve calcium metabolism (on18F-NaF PET/MRI) after 6 months in subjects with a bicuspid aortic valve...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac valve disorders
Study type	Interventional

Summary

ID

NL-OMON47825

Source
ToetsingOnline

Brief title
BASIK2

Condition

- Cardiac valve disorders
- Cardiac and vascular disorders congenital

Synonym
Aortic valve calcification, aortic valve stenosis

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Aortic valve stenosis, Bicuspid aortic valve, Calciummetabolism, PET/MRI

Outcome measures

Primary outcome

The primary endpoint of the study is the difference in (the mean of) the maximal uptake of 18F-NaF tracer of the aortic valve between the intervention group and the control group after 6 months on 18F-NaF PET/CMR-scan.

Secondary outcome

Secondary endpoints include the difference in mean calcium mass score progression of the aortic valve between the intervention group and the control group after 6 and 18 months on non-contrast CT-scan, whether the primary endpoint predicts or correlates with the results in calcium mass score after 6 and 18 months, whether supplementation with Vitamin K2 reduces progression of aortic valve stenosis, whether it is associated with altered aortic distensibility and flow, whether it is associated with reduced impairment of left ventricular (LV) function, whether serum biomarker values might predict long term diastolic function and whether more AVRs occur in the control group.

Study description

Background summary

A bicuspid aortic valve (BAV, an aortic valve consisting of two leaflets

instead of three) is a common congenital abnormality, occurring in 1-2% of the general population. BAV disease has a very heterogeneous clinical presentation, and occurrence and progression of complications is difficult to predict. Complications most often occurring in BAV are of valvular and vascular nature. Early development of calcified aortic valve disease (CAVD) is one of the most commonly occurring complications. CAVD progression in fact may lead to necessity of valve replacement, since to date, no other therapies have been shown effective in the treatment of CAVD.
Matrix Gla Protein (MGP) is a Vitamin K dependent protein known as an important inhibitory factor in the regulation of calcification. In humans, treatment with vitamin K antagonists results in more valve calcification, indicating the importance of Vitamin K and MGP level. Moreover, supplementation of the food-supplement vitamin K2 (menaquinone) in rats, resulted in regression of arterial calcifications. Although these results support the hypothesis that Vitamin K2 has a inhibitory effect on calcification, no controlled trials exist assessing the effects of the food-supplement Vitamin K2 supplementation on arterial and valvular calcification.

Study objective

To test the hypothesis that supplementation with vitamin K2 in comparison to placebo (total duration of treatment: 18 months) will slow down aortic valve calcium metabolism (on18F-NaF PET/MRI) after 6 months in subjects with a bicuspid aortic valve and mild to moderate calcified aortic valve stenosis..

Study design

A prospective, double-blind randomized controlled trial with one group receiving Vitamin K2 and one group receiving placebo for 18 months.

Intervention

Subjects randomized in the intervention group will receive an oral dose of 360 ug vitamin K2 (menaquinone 7) daily. Subjects randomized in the control group will receive placebo that is identical to the supplement in the intervention group, without MK-7 though. Both subjects and researchers will be blinded to the treatment allocation of subjects.

Study burden and risks

the duration of follow-up is 18 months and patients will visit the outpatient clinic after 6, 12 and 18 months. During these visits, drug-compliance is monitored, an echocardiography will be performed and blood samples will be obtained through standard venipuncture. At baseline and after 6 months, a 18F-NaF PET/CMR-scan will be performed in order to assess calcium metabolism of the aortic valve. Moreover, valvular function and aortic dimensions will be

determined. Also, a calcium score will be determined by non-contrast CT at baseline and after 18 months, in order to assess changes valvular calcification.
No side effects have been reported in subjects using vitamin K2 in a daily dose of 360 ug. Vitamin K2 supplementation does not induce or increase a hypercoagulable state. The average effective radiation dose using this technique of CT-scan is 0.3 mSv and 3.5 mSv for the PET-CMR. The investigation will take 120 minutes including preparation and there has to be venous access for the infusion of the radiolabeled 18F-NaF. Furthermore, patients should not be claustrophobic since the scanner has a relatively narrow bore (60 cm).A total of 24 ml blood will be obtained each study visit. Blood samples will be obtained by venipuncture, which might cause a local hematoma.

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

Known with a bicuspid aortic valve and,
Calcified mild to moderate aortic valve stenosis on prior echocardiography
Age older than 18 years
Informed consent provided.

Exclusion criteria

Absence of calcified aortic valve stenosis on echocardiography, presence of severe aortic valve stenosis, history of aortic valve repair or aortic valve replacement , scheduled for aortic valve replacement or repair , accepted atrial fibrillation, use of oral anticoagulants, claustrophobia, presence of a pacemaker or ICD or ferromagnetic materials in the body, adipositas permagna, history of (non treated) cancer within the previous two years (excep non-melanoma skin cancer, carcinomas or in situ carcinoma of cervix), life expectancy of less than 2 years, wish for near future, or present pregnancy, breast feeding, (active) metabolic or gastrointestinal disease not controlled by current treatment, (history of) soy allergy, use of vitamin K-containing supplements, chronic inflammatory disease, systemic treatment or topical treatment likely to interfere with evaluation of the study parameters, corticoid treatment, participation in a clinical study more recently than one month before the current study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-08-2016

Enrollment:	44
Type:	Actual

Ethics review

Approved WMO Date:	23-12-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-05-2017
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

No registrations found.

In other registers

Register	ID
CCMO	NL54600.068.15

Study results

Date completed:	01-02-2021

Actual enrolment:	44