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Vitamin K therapy to improve vascular health in patients with chronic kidney disease

Submission date
12/02/2015

Recruitment status
No longer recruiting

Registration date
24/02/2015

Overall study status
Completed

Last Edited
24/08/2020

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Chronic kidney disease is a long-term medical condition where the kidneys do work properly. It is a common disease, and particularly so in older people. Kidney problems affect the kidney, and also the health of blood vessels and the heart, leading to an increased risk of heart disease or strokes. Kidney problems lead to blood vessels becoming stiffer than usual, due to a build-up of calcium in the wall of the blood vessel. So finding ways to stop or reverse this stiffening of the blood vessels is really important, and we don't have good treatments for this problem at the moment. Some recent research suggests that vitamin K—a vitamin present in vegetables and dairy foods—might be able to slow down or stop this build-up of calcium in blood vessels. Before we can recommend this as a treatment though, it is important that giving extra vitamin K is tested properly in controlled trials such as this one.

Who can participate?
Patients with chronic kidney disease (stages 3b and 4 - so does not include those on dialysis)

What does the study involve?
Participants are randomly allocated into one of two groups. One group takes 400mcg of vitamin K once a day. The other group takes a placebo once a day. Each participant is asked to go to their study centre first for a screening visit, to see whether they are suitable for the study. They then visit the centre a further three times – at the start of the study, 6 months later and, finally, 12 months later. They undergo a number of tests during these visits including blood pressure measurements when lying down and when stood up, walking speed, strength and balance tests and an x-ray of their abdomen. Investigators also take samples of blood and ask participants to provide a urine sample. A small pencil-like device is also placed over the blood vessel of each participant to measure their pulse to test how stiff their blood vessels are. The electrical activity of their heart is also monitored with a heart tracing. At the end of each visit, participants are asked to take home a diary to record any falls they might have over the next six months. They are also given a blood pressure cuff to wear for the next 24 hours and a supply of the study medication they have been allocated to receive.

What are the possible benefits and risks of participating?
This dose of vitamin K has been used before and is known to be safe but as with all medications

there is a small possibility of side effects. These can include sickness, diarrhoea and dizziness. Having blood taken can cause some bruising. The blood pressure cuff causes mild discomfort to some people. We allow participants to have plenty of rest in between the walking and strength tests so that they are not made overly tired by the tests.

Where is the study run from?
University of Dundee and the University of Glasgow, Scotland (UK)

When is the study starting and how long is it expected to run for?
June 2015 to August 2017

Who is funding the study?
The British Heart Foundation (UK)

Who is the main contact?
Dr Miles Witham
m.witham@dundee.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Miles Witham

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Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
2014CV03

Study information

Scientific Title
Vitamin K therapy to improve vascular health in patients with chronic kidney disease: a randomised controlled trial

Acronym
K4Kidneys

Study objectives
That 1 year of vitamin K2 supplementation (400mcg per day) improves pulse wave velocity compared to placebo in patients with CKD stages 3b and 4

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of Scotland Research Ethics Committee, 16/06/2015, approval number: 15/ES/0085

Study design
Two-centre parallel-group placebo-controlled randomised trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format; please use contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Chronic kidney disease stages 3b and 4

Interventions
400 mcg once daily oral vitamin K2 (MK7 subtype) vs matching placebo

Intervention Type
Supplement

Primary outcome measure
Between-group difference in carotid-femoral pulse wave velocity (PWV) at 12 months using the Sphygmocor system

Secondary outcome measures
All measured at 0,6 and 12 months except for aortic radiography:

1. Vascular health:
1.1. Office and 24 hour blood pressure
1.2. B-type natriuretic peptide
1.3. Central systolic blood pressure and augmentation index derived from applanation tonometry at the radial artery using the Sphygmocor system.
1.4. Pulse wave velocity at 6 months (in addition to the primary outcome measured at 12 months)
2. Insulin and glucose levels to calculate insulin resistance using HOMA-IR
3. Marker of effect of vitamin K: dp-ucMGP levels.
4. Calcium and bone metabolism and turnover:
4.1. Osteocalcin
4.2. Tartrate resistant acid phosphatase-5b
4.3. Parathyroid hormone
4.4. Fetuin
4.5. Fibroblast growth factor-23
4.6. 25-hydroxyvitamin D
4.7. 1,25-hydroxyvitamin D
5. Renal function: We will measure serum creatinine, and urinary protein/creatinine ratio on a spot urine sample at each timepoint
6. Radiological calcification: We will perform lateral abdominal radiography at baseline and 12 months to assess aortic calcification.
7. Physical function:
7.1. Short physical performance battery
7.2 Grip strength at each timepoint
7.3. Monthly falls diary to prospectively record falls

Overall study start date
01/06/2015

Completion date
31/03/2019

Eligibility

Key inclusion criteria
1. Age >18 years
2. CKD stages 3b or 4 (eGFR of >15 ml/min and <45 ml/min by MDRD4 equation)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
166

Total final enrolment
159

Key exclusion criteria
1. Atrial fibrillation
2. Taking warfarin (which antagonises vitamin K) or other coumadin derivatives.
3. Taking vitamin K
4. Unable to give written informed consent
5. Currently enrolled in another trial, or within 30 days of completing another trial
6. Pregnant or (if female and pre-menopausal) not using reliable contraception

Date of first enrolment
01/06/2015

Date of final enrolment
31/05/2016

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Ninewells Hospital and Medical School
Ageing and Health Division of Medicine and Therapeutics
Ninewells Avenue
Dundee
United Kingdom
DD1 9SY

Study participating centre
University of Glasgow
Institute of Cardiovascular and Medical Sciences
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United Kingdom
G12 8TA

Sponsor information

Organisation
Tayside Academic Science Centre (NHS Tayside and University of Dundee)

Sponsor details
TASC, Level 3, Ninewells Hospital
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United Kingdom
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Sponsor type
University/education

Website
http://www.ahspartnership.org.uk/

ROR
https://ror.org/049x86d03

Funder(s)

Funder type
Research organisation

Funder Name
British Heart Foundation

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date
30/09/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request. Anonymised, individual-participant data from the current study will be available to bona-fide researchers upon request from Professor Miles Witham (Miles.Witham@newcastle.ac.uk), subject to submission of a data access request outlining the planned analysis, purpose of the analysis, data required and publication plan, and subject to approval by the Sponsor

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		27/09/2019	27/09/2019	No	No
Results article	results	01/10/2020	24/08/2020	Yes	No
HRA research summary			28/06/2023	No	No